FLAVIN DERIVATIVES

RELATED APPLICATIONS

This application claims priority from U.S. Provisional Application Number 61/188,619, filed August 11, 2008, and U.S. Provisional Application Number 61/211,314, filed March 25, 2009, the contents of each of which are incorporated by reference in their entirety.

TECHNICAL FIELD

[0001] The present invention relates to flavin derivatives and their use and compositions for use as riboswitch ligands and/or anti-infectives. The invention also provides methods of making novel flavin derivatives.

BACKGROUND OF THE INVENTION

[0002] The fast growing rate of antibiotic resistance over the past decades has raised serious concerns that the antibiotic treatment options currently available will soon be ineffective. With the widespread usage of antibiotics in combination with the rapid growing rate of bacterial resistance in stark contrast with the decade-old chemical scaffolds available for their treatment, it is imperative that new drugs are developed in the battle against bacterial pathogens.

[0003] In many bacteria and fungi, RNA structures termed riboswitches regulate the expression of various genes crucial for survival or virulence. Typically located within the 5'-untranslated region (5'-UTR) of certain mRNAs, members of each known class of riboswitch can fold into a distinct, three-dimensionally structured receptor that recognizes a specific organic metabolite. When the cognate metabolite is present at sufficiently high concentrations during transcription of the mRNA, the riboswitch receptor binds to the metabolite and induces a structural change in the nascent mRNA that prevents expression of the open reading frame (ORF), thereby altering gene expression. In the absence of the cognate metabolite, the riboswitch folds into a structure that does not interfere with the expression of the ORF.

[0004] Sixteen different classes of riboswitches have been reported. Members of each class of riboswitch bind to the same metabolite and share a highly conserved sequence and secondary structure. Riboswitch motifs have been identified that bind to thiamine

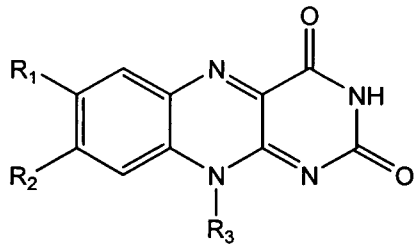
pyrophosphate (TPP), flavin mononucleotide (FMN), glycine, guanine, 3'-5'-cyclic eiguanylic acid (c-di-GMP), molybdenum cofactor, glucosamine-6-phosphate (GlcN6P), lysine, adenine, and adocobalamin (AdoCbl) riboswitches. Additionally, four dinstinct riboswitch motifs have been identified that recognize S-adenosylmethionine (SAM) I, II and III, IV and two distinct motifs that recognize pre-queosine-1 (PreQ1). Several antimetabolite ligands have also been identified that bind to known riboswitch classes, including pyrithiamine pyrophosphate (PTPP) which binds TPP riboswitches, *L*-aminoethylcysteine (AEC) and DL-4-oxalysine which bind to lysine riboswitches and roseoflavin and FMN which bind to FMN riboswitches.The riboswitch-receptors bind to their respective ligands in an interface that approaches the level of complexity and selectivity of proteins. This highly specific interaction allows riboswitches to discriminate against most intimately related analogs of ligands. For instance, the receptor of a guanine-binding riboswitch from *Bacillus subtilis* forms a three-dimensional structure such that the ligand is almost completely enveloped. The guanine is positioned between two aromatic bases and each polar functional group of the guanine hydrogen bonds with four additional riboswitch nucleotides surrounding it. This level of specificity allows the riboswitch to discriminate against most closely related purine analogs. Similarly, studies of the SAM-binding riboswitches reveal that nearly every functional group of SAM is critical in binding the ligands, allowing it to discriminate highly similar compounds such as S-adenosylhomocysteine (SAH) and S-adenosylmethionine (SAM), which only differ by a single methyl group. Likewise, TPP riboswitches comprise one subdomain that recognizes every polar functional group of the 4-amino-5-hydroxymethyl-2-methylpyrimidine (HMP) moiety, albeit not the thiazole moiety, and another subdomain that coordinates two metal ions and several water molecules to bind the negatively charged pyrophosphate moiety of the ligand. Similar to TPP, guanine and SAM riboswitches, FMN riboswitches form receptor structures that are highly specific for the natural metabolite FMN. It is by this highly specific interaction that allows for the design of small molecules for the regulation of specific genes.

[0005] FMN riboswitches are of particular interest of this invention because it is believed that the riboswitch binds to flavin mono-nucleotide (FMN) and represses the expression of enzymes responsible for riboflavin and FMN biosynthesis. Riboflavin is a water-soluble vitamin that is converted by flavokinases and FAD synthases to co-factors FMN and FAD, which are indispensable cofactors involved in energy metabolism and

metabolism of fats, ketones, carbohydrates and proteins crucial for all living organisms. Although vertebrates rely on uptake of vitamin from their gut for riboflavin sources, most prokaryotes, fungi and plants synthesize the necessary riboflavin for survival. It is therefore suggested that compounds that are selective for FMN riboswitch may be useful targets against bacterial pathogens in shutting down biosynthesis of riboflavin crucial for survival or virulence. In addition, no examples of the FMN, TPP, nor any other riboswitch class have presently been identified in humans. Therefore, riboswitches appear to offer the potential for the discovery of selective antipathogenic drugs. It is therefore the objective of this invention to provide novel flavin derivatives for targeting FMN riboswitches and methods of treating infections comprising administering flavin derivatives.

SUMMARY OF THE INVENTION

[0006] The current invention relates to a compound of formula I:



Formula I

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl) or C_{3-7} cycloalkyl;

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -N(R_4)(R_5), C_{3-7}cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl);

(iii) R_3 is H or C_{1-8} alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -OP(O)(OR_9)(OR_{17}), -OP(O)(OR_9)($NR_{13}R_{14}$), -OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$), -

$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -CN, $-C(O)OR_9$, $-C(O)N(H)(R_8)$, $-OR_{10}$, $-C(O)N(R_6)(R_7)$, and $-N(R_6)(R_7)$; or

(iv) R_1 and R_2 are connected so as to form a cyclic ring structure optionally containing one or more heteroatoms selected from N, O and S (e.g., $-OCH_2CH_2O-$);

(v) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{4-7}heterocycle (e.g., piperazinyl), and C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is optionally substituted with one or more groups selected from $-OR_{11}$, $-C(O)OR_9$, $-N(R_6)(R_7)$ (e.g., amino or dimethylamino), C_{1-8}alkoxyl (e.g., methoxy), C_{6-10}aryl (e.g., phenyl), C_{5-10} heteroaryl (e.g., pyridinyl) wherein said aryl or heteroaryl are optionally substituted with halo (e.g.,4-fluorophenyl), and C_{4-7}heterocycle wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl);

(vi) R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl or ethyl), $-C_{1-8}$alkyl-OR_{11}, $-C(O)OR_9$, $-C_{1-8}$alkyl-$C(O)OR_9$, $-C_{1-8}$alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$C(O)N(H)R_8$, $-C_{1-8}$alkyl-$P(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$ $-C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl and aryl wherein said aryl is optionally substituted with $-COOR_9$;

(vii) R_8 is H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), $-OR_{11}$ or –OBn;

(viii) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

(ix) R_{10} is H, C_{1-8}alkyl (e.g., methyl or ethyl), $-C_{1-8}$alkyl-OR_{11}, $-C_{1-8}$alkyl-$C(O)OR_9$, $-C_{1-8}$alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$C(O)N(H)R_8$, $-C_{1-8}$alkyl-$P(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-

$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-N(H)-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl, or aryl wherein said aryl is optionally substituted with $-COOR_9$, or $-C_{1-4}$alkyl-$OC(O)R_{12}$;

(x) R_{11} is H, or $-C_{1-4}$alkyl-$OC(O)R_{12}$ (e.g., $-CH_2$-$OC(O)R_{12}$);

(xi) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy);

(xii) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-COOH, -CH(isopropyl)-COOH, -CH(isobutyl)-COOH, -CH(sec-butyl)-COOH), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or $-CH(CH_2CH_2COOH)$-COOH); and

(xiii) R_{18} is H or C_{1-8}alkyl;

in free, salt or prodrug form.

[0007] The invention further relates to a compound of Formula I as follows:

1.1 a Compound of Formula I, wherein R_1 is H, C_{1-8}alkyl (e.g., methyl) or C_{3-7}cycloalkyl;

1.2 a Compound of Formula I or 1.1, wherein R_1 is H;

1.3 a Compound of Formula I or 1.1, wherein R_1 is C_{3-7}cycloalkyl;

1.4 a Compound of Formula I or 1.1, wherein R_1 is C_{1-8}alkyl;

1.5 a Compound of Formula I or 1.1 or 1.4, wherein R_1 is methyl;

1.6 a Compound of Formula I or any of 1.1-1.5, R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -$N(R_4)(R_5)$, C_{3-7}cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., hydroxyethylpiperazin-1-yl);

1.7 a Compound of Formula I or any of 1.1-1.6, wherein R_2 is C_{1-8}alkyl (e.g., methyl or ethyl);

1.8 a Compound of Formula I or any of 1.1-1.7, wherein R_2 is methyl;

1.9 a Compound of Formula I or any of 1.1-1.7, wherein R_2 is ethyl;

1.10 a Compound of Formula I or any of 1.1-1.6, wherein R_2 is C_{1-8}alkoxy;

1.11 a Compound of Formula I or any of 1.1-1.6 or 1.10, wherein R_2 is methoxy;

1.12 a Compound of Formula I or any of 1.1-1.6 or 1.10, wherein R_2 is ethoxy;

1.13 a Compound of Formula I or any of 1.1-1.6, wherein R_2 is C_{3-7} cycloalkyl;

1.14 a Compound of Formula I or any of 1.1-1.6, wherein R_2 is $-N(R_4)(R_5)$ and R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{4-7} heterocycle (e.g., piperazinyl), and C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is optionally substituted with one or more groups selected from $-OR_{11}$, $-C(O)OR_9$, $-N(R_6)(R_7)$ (e.g., amino or dimethylamino), C_{1-8}alkoxyl (e.g., methoxy), C_{6-10}aryl (e.g., phenyl), C_{5-10}heteroaryl (e.g., pyridinyl) wherein said aryl or heteroaryl are optionally substituted with halo (e.g.,4-fluorophenyl), and C_{4-7}heterocycle wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl);

1.15 Formula 1.14, wherein either R_4 or R_5 is H;

1.16 Formula 1.14, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl);

1.17 Formula 1.14 or 1.16, wherein either R_4 or R_5 is methyl;

1.18 Formula 1.14 or 1.16, wherein either R_4 or R_5 is ethyl;

1.19 Formula 1.14, wherein either R_4 or R_5 is C_{3-7}cycloalkyl (e.g., cyclopropyl or cyclopentyl);

1.20 Formula 1.14 or 1.19, wherein either R_4 or R_5 is cyclopropyl or cyclopentyl;

1.21 Formula 1.14, wherein either R_4 or R_5 is C_{4-7} heterocycle (e.g., piperazinyl);

1.22 Formula 1.14 or 1.21, wherein either R_4 or R_5 is piperazinyl;

1.23 Formula 1.14, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with C_{4-7}heterocycle, which heterocycle is optionally substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl);

1.24 Formula 1.14 or 1.23, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with C_{4-7} heterocycle;

1.25 Formula 1.14, 1.23 or 1.24, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with morpholinyl;

1.26 Formula 1.14, 1.23, 1.24 or 1.25, wherein either R_4 or R_5 is $-CH_2CH_2$-morpholine;

1.27 Formula 1.14 or 1.23, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with C_{4-7}heterocycle, which C_{4-7}heterocycle is substituted with C_{1-8}alkyl (e.g., 4-methylpiperazin-1-yl);

1.28 Formula 1.14, 1.23 or 1.27, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with 4-methylpiperazin-1-yl;

1.29 Formula 1.14, 1.23, 1.27 or 1.28, wherein either R_4 or R_5 is $-CH_2CH_2$-(4-methylpiperazin-1-yl);

1.30 Formula 1.14, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with $-C(O)OR_9$;

1.31 Formula 1.14 or 1.30, wherein either R_4 or R_5 is $-CH_2CH_2C(O)OR_9$ and R_9 is H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl), and R_{12} is as hereinbefore described in Formula I;

1.32 Formula 1.31, wherein either R_4 or R_5 is $-CH_2CH_2C(O)OH$;

1.33 Formula 1.31, wherein either R_4 or R_5 is $-CH_2CH_2C(O)O$-(*tert*-butyl);

1.34 Formula 1.31, wherein either R_4 or R_5 is - C_{1-8} alkyl-$C(O)O-C_{1-4}$alkyl-$OC(O)R_{12}$ (e.g., $-CH_2CH_2C(O)OCH_2OC(O)R_{12}$ $-CH_2CH_2C(O)OCH_2$-$OC(O)R_{12}$);

1.35 Formula 1.14, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with C_{6-10}aryl (e.g., phenyl) or C_{5-10} heteroaryl (e.g., pyridinyl) which aryl and heteroaryl is optionally substituted with halo;

1.36 Formula 1.14 or 1.35, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with phenyl which phenyl is optionally substituted with halo (e.g., fluoro);

1.37 Formula 1.14, 1.35 or 1.36, wherein either R_4 or R_5 is $-CH_2CH_2$-(4-fluorophenyl);

1.38 Formula 1.14 or 1.35, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with C_{5-10} heteroaryl (e.g., pyridinyl);

1.39 Formula 1.14 or 1.35, wherein either R_4 or R_5 is $-CH_2CH_2$-(pyridin-2-yl);

1.40 Formula 1.14, wherein either R_4 or R_5 is C_{1-8}alkyl wherein said alkyl is substituted with $-OR_{11}$ wherein R_{11} is H or $-C_{1-4}$alkyl-$OC(O)R_{12}$;

1.41 Formula 1.14 or 1.40, wherein either R_4 or R_5 is hydroxyethyl;

1.42 Formula 1.14 or 1.40, wherein either R_4 or R_5 is –ethyl-O-C_{1-4}alkyl-$OC(O)R_{12}$;

1.43 Formula 1.14, wherein either R_4 or R_5 is C_{1-8}alkyl wherein said alkyl is substituted with C_{1-6}alkoxyl (e.g., methoxy);

1.44 Formula 1.14 or 1.43, wherein either R_4 or R_5 is methoxyethyl;

1.45 Formula 1.14, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with $-N(R_6)(R_7)$ and wherein R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl or ethyl), -C_{1-8}alkyl-OR_{11}, -$C(O)OR_9$, $-C_{1-8}$alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$ -C_{1-8}alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl and aryl wherein said aryl is optionally substituted with $-COOR_9$;

1.46 Formula 1.14, wherein either R_4 or R_5 is C_{1-8}alkyl (e.g., methyl or ethyl) wherein said alkyl is substituted with $-N(R_6)(R_7)$ and R_6 and R_7 are independently selected from H, C_{1-8}alkyl, and $C(O)OR_9$;

1.47 Formula 1.45 or 1.46 or 1.47, wherein either R_6 or R_7 is H;

1.48 Formula 1.45 or 1.46, wherein either R_6 or R_7 is C_{1-8}alkyl (e.g., methyl);

1.49 Formula 1.45 or 1.46 or 1.48, wherein either R_6 or R_7 is methyl;

1.50 Formula 1.45 or 1.46, wherein either R_6 or R_7 is -C_{1-8}alkyl-OR_{11};

1.51 Formula 1.45 or 1.50, wherein either R_6 or R_7 is - CH_2CH_2OH;

1.52 Formula 1.45, wherein either R_6 or R_7 is - C_{1-8} alkyl-C(O)O-C_{1-4}alkyl-$OC(O)R_{12}$;

1.53 Formula 1.45 or 1.46, wherein either R_6 or R_7 is –C_{1-8}alkyl-C(O)OH,

1.54 Formula 1.45, 1.46 or 1.53, wherein either R_6 or R_7 is – $CH_2CH_2C(O)OH$;

1.55 Formula 1.45 or 1.46, wherein either R_6 or R_7 is –C_{1-8}alkyl-C(O)OR_9 and R_9 is H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

1.56 Formula 1.45, 1.46 or 1.55, wherein either R_6 or R_7 is –C_{1-8}alkyl-C(O)OC_{1-4}alkyl-$OC(O)R_{12}$;

1.57 Formula 1.45, 1.46 or 1.55, wherein either R_6 or R_7 is – $CH_2CH_2CH_2$-C(O)O-C_{1-4}alkyl-$OC(O)R_{12}$;

1.58 Formula 1.45, 1.46 or 1.55, wherein either R_6 or R_7 is – $CH_2CH_2C(O)O$-tert-butyl;

1.59 Formula 1.45 or 1.46, wherein either R_6 or R_7 is -$CH_2CH_2CH_2C(O)O$-tert-butyl;

1.60 Formula 1.45, wherein either R_6 or R_7 is –C_{1-8} alkyl-C(O)N(H)R_8;

1.61 Formula 1.45 or 1.60, wherein either R_6 or R_7 is –$(CH_2)_3$-C(O)N(H)R_8;

1.62 Formula 1.61, wherein R_8 is –OBn;

1.63 Formula 1.61, wherein R_8 is –OR_{11};

1.64 Formula 1.45, wherein either R_6 or R_7 is C_{1-8} alkyl-P(O)(OR_9)(OR_{17}) and R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or

more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl;

1.65 Formula 1.45 or 1.64 wherein either R_6 or R_7 is $-CH_2CH_2-P(O)(OH)_2$;

1.66 Formula 1.45 or 1.64 wherein either R_6 or R_7 is $-CH_2CH_2-P(O)(O-C_{1-8}alkyl)_2$;

1.67 Formula 1.45 or 1.64 wherein either R_6 or R_7 is $-CH_2CH_2-P(O)(OH)(O-C_{1-8}alkyl)$;

1.68 Formula 1.45, wherein either R_6 or R_7 is $-C_{1-8}alkyl-P(O)(OR_9)(NR_{13}R_{14})$ and R_9, R_{13}, R_{14}, are as hereinbefore described in Formula I;

1.69 Formula 1.45 or 1.64 wherein either R_6 or R_7 is $-CH_2CH_2-P(O)(O-phenyl)(N(H)CH(CH_3)COOH)$;

1.70 Formula 1.45 or 1.64 wherein either R_6 or R_7 is $-CH_2CH_2-P(O)(OH)(N(H)CH(CH_3)COOH)$;

1.71 Formula 1.45 or 1.64 wherein either R_6 or R_7 is $-C_{1-8}alkyl-P(O)(NR_{13}R_{14})(NR_{15}R_{16})$;

1.72 Formula 1.45 or 1.64 wherein either R_6 or R_7 is $-CH_2CH_2-P(O)(N(H)CH(CH_3)COOH)_2$;

1.73 Formula 1.45, wherein either R_6 or R_7 is $-C_{1-8}alkyl-OP(O)(OR_9)(OR_{17})$ and R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), $-C_{1-4}alkyl-OC(O)R_{12}$, phenyl and Bn wherein phenyl and Bn are optionally substituted with halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

1.74 Formula 1.45 or 1.73 wherein either R_6 or R_7 is $-CH_2CH_2-OP(O)(OH)_2$;

1.75 Formula 1.45 or 1.73 wherein either R_6 or R_7 is $-CH_2CH_2-OP(O)(O-C_{1-8}alkyl)_2$;

1.76 Formula 1.45 or 1.73 wherein either R_6 or R_7 is $-CH_2CH_2-OP(O)(OH)(O-C_{1-8}alkyl)$;

1.77 Formula 1.45, wherein either R_6 or R_7 is $-C_{1-8}alkyl-OP(O)(OR_9)(NR_{13}R_{14})$ and R_9, R_{13}, R_{14}, are as hereinbefore described in Formula I;

1.78 Formula 1.45 or 1.77 wherein either R_6 or R_7 is $-CH_2CH_2$-OP(O)(O-phenyl)(N(H)CH(CH_3)COOH);

1.79 Formula 1.45 or 1.77 wherein either R_6 or R_7 is $-CH_2CH_2$-OP(O)(OH)(N(H)CH(CH_3)COOH);

1.80 Formula 1.45 wherein either R_6 or R_7 is -C_{1-8}alkyl-OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$);

1.81 Formula 1.45 or 1.80 wherein either R_6 or R_7 is $-CH_2CH_2$-OP(O)(N(H)CH(CH_3)COOH)$_2$;

1.82 Formula 1.45, wherein either R_6 or R_7 is -C_{1-8}alkyl-N(H)-S(O)$_2$(CF_3);

1.83 Formula 1.45 or 1.82, wherein either R_6 or R_7 is $-(CH_2)_3$-N(H)-S(O)$_2$(CF_3);

1.84 Formula 1.45, wherein either R_6 or R_7 is 7,8-dimethyl-isoalloxazin-10-yl-ethyl;

1.85 Formula I, or any of 1.1-1.6 or 1.14, wherein R_2 is $-NH_2$;

1.86 Formula I, or any of 1.1-1.6 or 1.14, wherein R_2 is methylamino;

1.87 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is dimethylamino;

1.88 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is diethylamino;

1.89 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is –N(H)-CH_2CH_2-(morpholin-4-yl);

1.90 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is –N(H)-CH_2CH_2-(4-methyl-piperazin-1-yl);

1.91 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is –N(H)-CH_2CH_2OH;

1.92 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is –N(H)-$CH_2CH_2OCH_3$;

1.93 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is –N(H)CH_2CH_2-N(H)-C(O)O-*tert*-butyl;

1.94 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is –N(H)-cyclopropyl;

1.95 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is 4-methylpiperazin-1-yl;

1.96 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is –N(H)CH_2CH_2-(4-fluorophenyl);

1.97 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is –N(H)CH_2CH_2-(pyridine-2-yl);

1.98 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is $-N(H)CH_2CH_2NH_2$;

1.99 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is $-N(H)CH_2CH_2CH_2NH_2$;

1.100 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is $-N(H)CH_2CH_2N(CH_3)_2$;

1.101 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is $-N(H)-CH_2CH_2COOH$;

1.102 Formula I or any of 1.1-1.6 or 1.14, wherein R_2 is $-N(H)-CH_2CH_2COO$-*tert*-butyl;

1.103 Formula I or any of 1.1-1.6, wherein R_2 is halo;

1.104 Formula I or any of 1.1-1.6, wherein R_2 is chloro;

1.105 Formula I or any of 1.1-1.6, wherein R_2 is C_{4-7} heterocycle (e.g., piperazinyl or pyrolidinyl) optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., hydroxyethyl);

1.106 Formula I or any of 1.1-1.6, wherein R_2 is 4-(hydroxyethyl)piperazin-1-yl;

1.107 Formula I or any of 1.1-1.6, wherein R_2 is pyrrolidin-1-yl;

1.108 Formula I or any of 1.1-1.6, wherein R_1 and R_2 are connected so as to form a cyclic ring structure optionally containing one or more heteroatoms selected from N, O and S (e.g., $-OCH_2CH_2O-$);

1.109 Any of the foregoing formulae, wherein R_3 is H or C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -$OP(O)(OR_9)(OR_{17})$, -$OP(O)(OR_9)(NR_{13}R_{14})$, -$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$P(O)(OR_9)(OR_{17})$, -$P(O)(OR_9)(NR_{13}R_{14})$, -$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -CN, -$C(O)OR_9$, -$C(O)N(H)(R_8)$, -$OR_{10}$, -$C(O)N(R_6)(R_7)$, and -$N(R_6)(R_7)$; wherein:

R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl or ethyl), -C_{1-8}alkyl-OR_{11}, -$C(O)OR_9$, $-C_{1-8}$alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$ -

C_{1-8}alkyl-OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -C_{1-8}alkyl-N(H)-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl and aryl wherein said aryl is optionally substituted with –$COOR_9$;

R_8 is H, C_{1-8} alkyl (e.g., methyl or t-butyl), -OR_{11} or –OBn;

R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

R_{10} is H, C_{1-8}alkyl (e.g., methyl or ethyl), -C_{1-8}alkyl-OR_{11}, –C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), –C_{1-8}alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-N(H)-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl, or aryl wherein said aryl is optionally substituted with –$COOR_9$, or –C_{1-4}alkyl-$OC(O)R_{12}$;

R_{11} is H or –C_{1-4}alkyl-$OC(O)R_{12}$ (e.g., –CH_2-$OC(O)R_{12}$);

R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy);

R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-COOH, -CH(isopropyl)-COOH, -CH(isobutyl)-COOH, -CH(sec-butyl)-COOH), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –$CH(CH_2CH_2COOH)$-COOH);

R_{18} is H or C_{1-8}alkyl;

1.110 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl);

1.111 Any of 1.1-1.109, wherein R_3 is n-butyl;

1.112 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more $-OR_{10}$ and R_{10} is H, C_{1-8}alkyl (e.g., methyl or ethyl), -C_{1-8}alkyl-OR_{11}, $-C_{1-8}$alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl, or aryl wherein said aryl is optionally substituted with $-COOR_9$, or $-C_{1-4}$alkyl-$OC(O)R_{12}$ and R_8, R_9, R_{11}-R_{18} are as hereinbefore described in Formula I;

1.113 Formula 1.112, wherein R_{10} is H;

1.114 Formula 1.112, wherein R_{10} is C_{1-8}alkyl (e.g., methyl, ethyl or propyl);

1.115 Formula 1.112, wherein R_{10} is -C_{1-8}alkyl-OR_{11};

1.116 Formula 1.112, wherein R_{10} is $-C_{1-8}$alkyl-$C(O)OR_9$;

1.117 Formula 1.112, wherein R_{10} is -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$);

1.118 Formula 1.112, wherein R_{10} is $-C_{1-8}$alkyl-$C(O)N(H)R_8$;

1.119 Formula 1.112, wherein R_{10} is -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$;

1.120 Formula 1.112, wherein R_{10} is -C_{1-8}alkyl-$P(O)$ $(OR_9)(NR_{13}R_{14})$;

1.121 Formula 1.112, wherein R_{10} is -C_{1-8}alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$;

1.122 Formula 1.112, wherein R_{10} is -C_{1-8}alkyl-$OP(O)(OR_9)(OR_{17})$;

1.123 Formula 1.112, wherein R_{10} is -C_{1-8}alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$;

1.124 Formula 1.112, wherein R_{10} is -C_{1-8}alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$;

1.125 Formula 1.112, wherein R_{10} is -C_{1-8}alkyl-$N(H)$-$S(O)_2(CF_3)$;

1.126 Formula 1.112, wherein R_{10} is 7,8-dimethyl-isoalloxazin-10-yl-ethyl;

1.127 Formula 1.112, wherein R_{10} is aryl optionally substituted with $-COOR_9$;

1.128 Formula 1.112, wherein R_{10} is $-C_{1-4}$alkyl-$OC(O)R_{12}$;

1.129 Any of formulae 1.112-1.128, wherein R_3 is C_{1-8}alkyl further substituted with at least one $-OR_{10}$ group, wherein R_{10} is H (e.g., polyhydroxylated);

1.130 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with -$N(R_6)(R_7)$, wherein R_6 and R_7 are described in any one of Formulae 1.47-1.84;

1.131 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with –$C(O)N(R_6)(R_7)$, wherein R_6 and R_7 are described in any one of Formulae 1.47-1.84;

1.132 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with -$OP(O)(OR_9)(OR_{17})$;

1.133 Formula 1.132 wherein R_3 is– C_{1-8}alkyl-$OP(O)(OH)_2$;

1.134 Formula 1.132 wherein R_3 is – C_{1-8}alkyl-$OP(O)(O\text{-}C_{1-8}alkyl)_2$;

1.135 Formula 1.132 wherein R_3 is –CH_2CH_2-$OP(O)(OH)(O\text{-}C_{1-8}$alkyl);

1.136 Formula 1.132, wherein R_3 is –$(CH_2)_4$-$OP(O)(OR_9)(OR_{17})$, –$(CH_2)_5$-$OP(O)(OR_9)(OR_{17})$, –$(CH_2)_6$-$OP(O)(OR_9)(OR_{17})$ or –$(CH_2)_7$-$OP(O)(OR_9)(OR_{17})$;

1.137 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with -$OP(O)(OR_9)(NR_{13}R_{14})$;

1.138 Formula 1.137 wherein R_3 is –C_{1-8}alkyl-OP(O)(O-phenyl)(N(H)$CH(CH_3)$COOH);

1.139 Formula 1.137 wherein R_3 is – C_{1-8}alkyl-OP(O)(OH)(N(H)$CH(CH_3)$COOH);

1.140 Formula 1.137 wherein R_3 is – C_{1-8}alkyl-$OP(O)(O\text{-}C_{1-8}$alkyl)(N(H)$CH(CH_3)$COOH);

1.141 Formula 1.137, wherein R_3 is –$(CH_2)_4$-$OP(O)(OR_9)(NR_{13}R_{14})$, –$(CH_2)_5$-$OP(O)(OR_9)(NR_{13}R_{14})$, –$(CH_2)_6$-$OP(O)(OR_9)(NR_{13}R_{14})$ or –$(CH_2)_7$-$OP(O)(OR_9)(NR_{13}R_{14})$;

1.142 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with $OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$;

1.143 Formula 1.142, wherein R_3 is $-C_{1-8}$alkyl-$OP(O)(N(H)CH(CH_3)COOH)_2$;

1.144 Formula 1.142, wherein R_3 is $-(CH_2)_4$-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-(CH_2)_5$-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-(CH_2)_6$-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$ or $-(CH_2)_7$-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$;

1.145 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with $-P(O)(OR_9)(OR_{17})$;

1.146 Formula 1.145 wherein R_3 is $—C_{1-8}$alkyl-$P(O)(OH)_2$;

1.147 Formula 1.145 wherein R_3 is $—C_{1-8}$alkyl-$P(O)(O\text{-}C_{1-8}alkyl)_2$;

1.148 Formula 1.145 wherein R_3 is $—C_{1-8}$alkyl-$P(O)(OH)(O\text{-}C_{1-8}alkyl)$;

1.149 Formula 1.145, wherein R_3 is $-(CH_2)_4$-$P(O)(OR_9)(OR_{17})$, $-(CH_2)_5$-$P(O)(OR_9)(OR_{17})$, $-(CH_2)_6$-$P(O)(OR_9)(OR_{17})$ or $-(CH_2)_7$-$P(O)(OR_9)(OR_{17})$;

1.150 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with $-P(O)(OR_9)(NR_{13}R_{14})$;

1.151 Formula 1.150 wherein R_3 is $-C_{1-8}$alkyl-$P(O)$(O-phenyl)$(N(H)CH(CH_3)COOH)$;

1.152 Formula 1.150 wherein R_3 is $-C_{1-8}$alkyl-$P(O)(OH)(N(H)CH(CH_3)COOH)$;

1.153 Formula 1.150, wherein R_3 is $-(CH_2)_4$-$P(O)(OR_9)(NR_{13}R_{14})$, $-(CH_2)_5$-$P(O)(OR_9)(NR_{13}R_{14})$, $-(CH_2)_6$-$P(O)(OR_9)(NR_{13}R_{14})$ or $-(CH_2)_7$-$P(O)(OR_9)(NR_{13}R_{14})$;

1.154 Any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with $-P(O)(NR_{13}R_{14})(NR_{15}R_{16})$;

1.155 Formula 1.154 wherein R_3 is $—C_{1-8}$alkyl-$P(O)(N(H)CH(CH_3)COOH)_2$;

1.156 Formula 1.154, wherein R_3 is $-(CH_2)_4$-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-(CH_2)_5$-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-(CH_2)_6$-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$ or $-(CH_2)_7$-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$;

1.157 Formula I or any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl optionally substituted -C(O)OR_9;

1.158 Formula I or any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl substituted with one or more –OR_{10};

1.159 Any of the preceding formulae, wherein R_8 is H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), -OR_{11} or –OBn;

1.160 Any of the preceding formulae, wherein R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), –C_{1-4}alkyl-OC(O)R_{12}, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

1.161 Any of the preceding formulae, wherein R_9 and R_{17} are independently C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl);

1.162 Any of the preceding formulae, wherein R_9 and R_{17} are independently H;

1.163 Any of formulae 1.1-1.160, wherein R_9 and R_{17} are independently –C_{1-4}alkyl-OC(O)R_{12};

1.164 Any of formulae 1.1-1.160, wherein R_9 and R_{17} are independently phenyl or Bn wherein phenyl and Bn are optionally substituted with halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

1.165 Any of formulae 1.1-1.160, wherein R_9 and R_{17} are independently phenyl;

1.166 Any of the preceding formulae wherein R_{11} is H or –C_{1-4}alkyl-OC(O)R_{12};

1.167 Any of the preceding formulae wherein R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxyl);

1.168 Any of the preceding formulae wherein R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-COOH, -CH(isopropyl)-COOH, -CH(isobutyl)-COOH, -CH(sec-butyl)-COOH), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with hydroxyC_{1-8}alkyl (e.g., -

CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –CH(CH_2CH_2COOH)-COOH);

1.169 Any of formulae 1.1-1.168 wherein R_{13}, R_{14}, R_{15} and R_{16} are independently H or -CH(CH_3)COOH;

1.170 Any of the preceding formulae wherein R_3 is further substituted with –OR_{10};

1.171 Any of formulae 1.1-1.169 wherein R_{18} is H;

1.172 Any of formulae 1.1-1.169 wherein R_{18} is C_{1-8}alkyl;

1.173 Formula I or any of 1.1-1.109 wherein R_3 is H;

1.174 Formula I or any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl);

1.175 Formula I or any of 1.1-1.109, wherein R_3 is n-butyl;

1.176 Formula I or any of 1.1-1.109, wherein R_3 is –$(CH_2)_5OH$;

1.177 Formula I or any of 1.1-1.109, wherein R_3 is –$(CH_2)_4OH$;

1.178 Formula I or any of 1.1-1.109, wherein R_3 is –$(CH_2)_3OH$;

1.179 Formula I or any of 1.1-1.109, wherein R_3 is (2S,3S,4R)-2,3,4,5-tetrahydroxypentyl;

1.180 Formula I or any of 1.1-1.109, wherein R_3 is–$(CH_2)_5OP(O)(OH)_2$;

1.181 Formula I or any of 1.1-1.109, wherein R_3 is 5-dihydrogenphosphate-(2S,3S,4R)-2,3,4-trihydroxypentyl;

1.182 Formula I or any of 1.1-1.109, wherein R_3 is 5-phosphonate-(2S,3S,4R)-2,3,4-trihydroxypentyl;

1.183 Formula I or any of 1.1-1.109, wherein R_3 is –$(CH_2)_4C(O)OH$;

1.184 Formula I or any of 1.1-1.109, wherein R_3 is –$(CH_2)_5C(O)OH$;

1.185 Formula I or any of 1.1-1.109, wherein R_3 is –$(CH_2)_6C(O)OH$;

1.186 Formula I or any of 1.1-1.109, wherein R_3 is –$(CH_2)_7C(O)OH$;

1.187 Formula I or any of 1.1-1.109, wherein R_3 is –$(CH_2)_6C(O)OCH_3$;

1.188 Formula I or any of 1.1-1.109, wherein R_3 is is –$(CH_2)_6C(O)N(H)OH$;

1.189 Formula I or any of 1.1-1.109, wherein R_3 is $CH_2CH_2N(H)CH_2CH_2CH_2$-C(O)OH;

1.190 Formula I or any of 1.1-1.109, wherein R_3 is $CH_2CH_2N(H)CH_2CH_2CH_2$-C(O)O-*tert*-butyl;

1.191 Formula I or any of 1.1-1.109, wherein R_3 is $-CH_2CH_2N(H)$-(3-carboxyphenyl);

1.192 Formula I or any of 1.1-1.109, wherein R_3 is $-CH_2CH_2N(H)-CH_2CH_2CH(NH_2)COOH$;

1.193 Formula I or any of 1.1-1.109, wherein R_3 is $-CH_2CH_2N(H)CH_2CH_2-P(O)(OH)_2$;

1.194 Formula I or any of 1.1-1.109, wherein R_3 is $-(CH_2)_6P(O)(OH)_2$;

1.195 Formula I or any of 1.1-1.109, wherein R_3 is $-(CH_2)_6P(O)(O-phenyl)(N(H)CH(CH_3)COOH)$;

1.196 Formula I or any of 1.1-1.109, wherein R_3 is $-(CH_2)_6P(O)(O-phenyl)(N(H)CH(CH_3)COO-C_{1-8}alkyl)$;

1.197 Formula I or any of 1.1-1.109, wherein R_3 is $-CH_2CH_2N(H)-CH_2CH_2CH_2C(O)N(H)$-OBn;

1.198 Formula I or any of 1.1-1.109, wherein R_3 is $-CH_2CH_2N(H)-CH_2CH_2CH_2-C(O)N(H)(OR_9)$ (e.g., $-CH_2CH_2N(H)-CH_2CH_2CH_2-C(O)N(H)(OH)$, $-CH_2CH_2N(H)-CH_2CH_2CH_2-C(O)N(H)(O-CH_2-O-C(O)-^t$Butyl or $-CH_2CH_2N(H)-CH_2CH_2CH_2-C(O)N(H)(O-CH_2-O-C(O)-O-^t$Butyl);

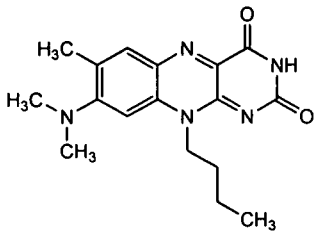
1.199 Formula I or any of 1.1-1.109, wherein R_3 is $-(CH_2)_6-C(O)N(H)(OH)$;

1.200 Formula I or any of 1.1-1.109, wherein R_3 is $-CH_2CH_2N(H)CH_2CH_2CH_2-N(H)-S(O)_2CF_3$;

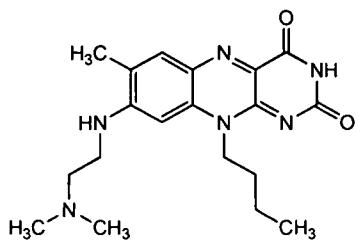
1.201 Formula I or any of 1.1-1.109, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more -CN;

1.202 Formula I or any of 1.1-1.109, wherein R_3 is $-(CH_2)_4$-CN;

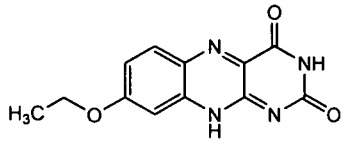
1.203 any of the preceding formulae wherein the Compound of Formula I is selected from any of the following:



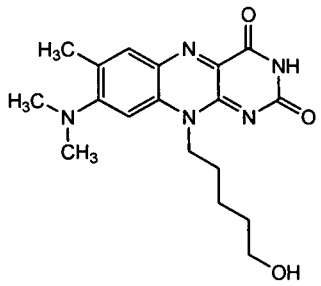
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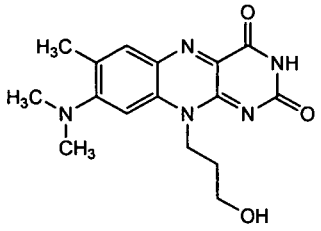
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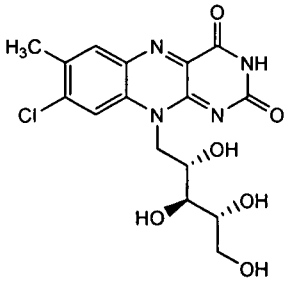
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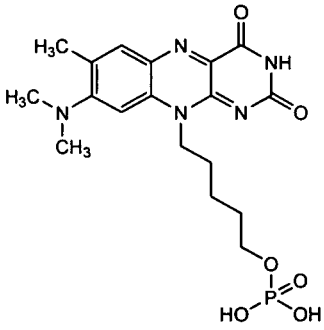
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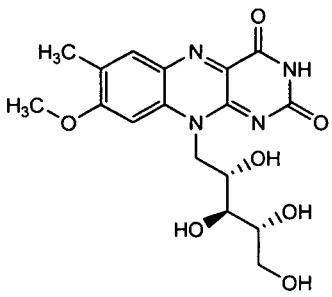
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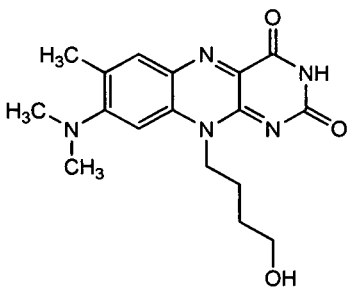
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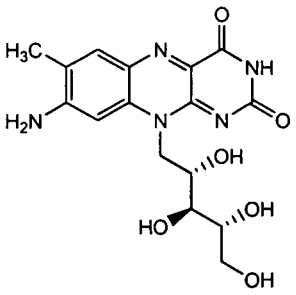
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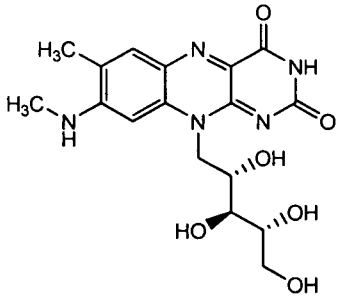
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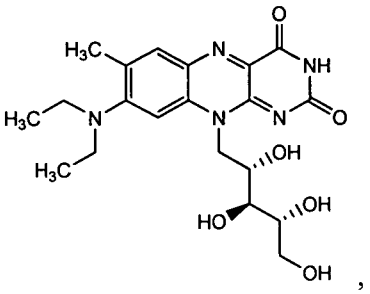
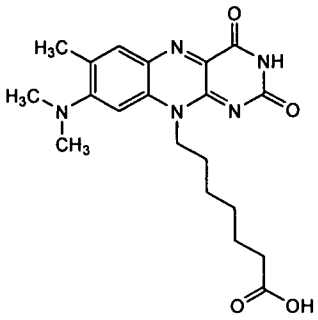
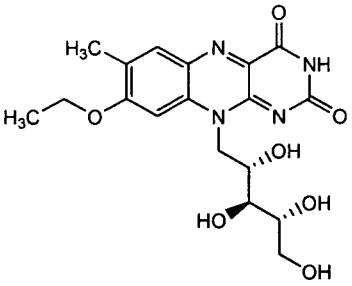
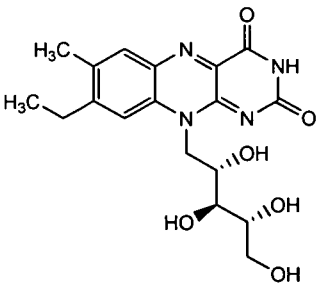
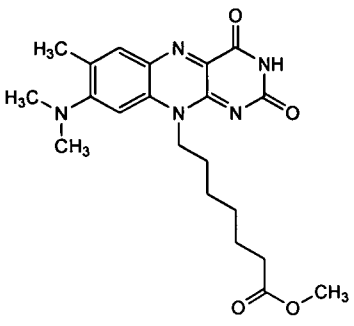
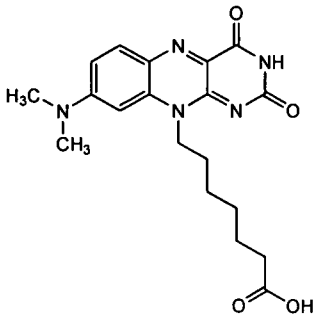
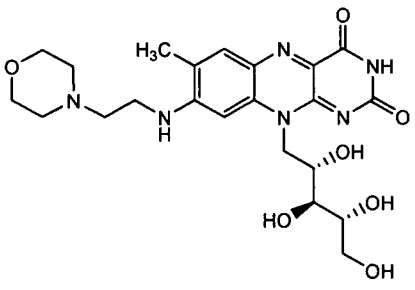
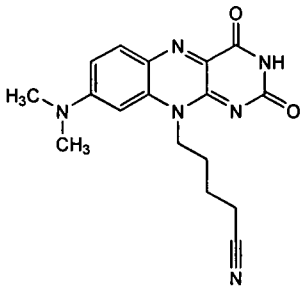


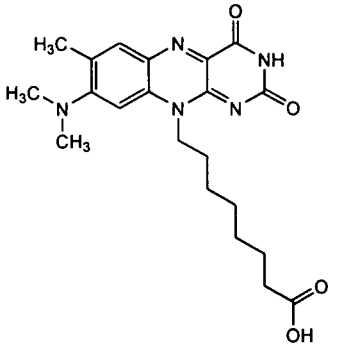
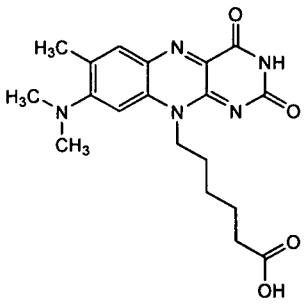
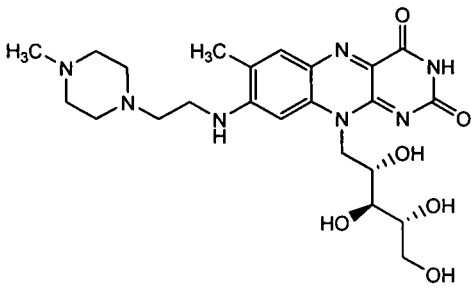
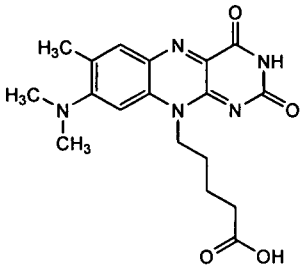
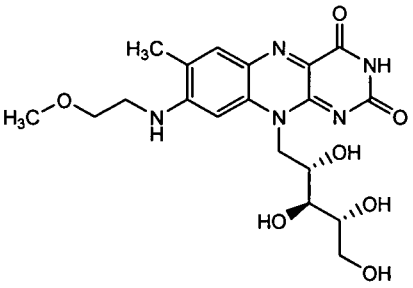
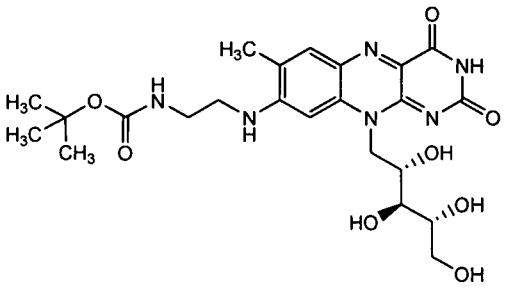
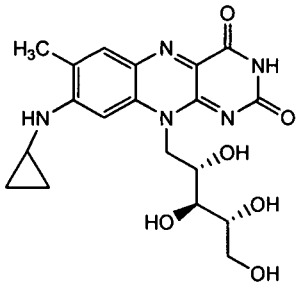
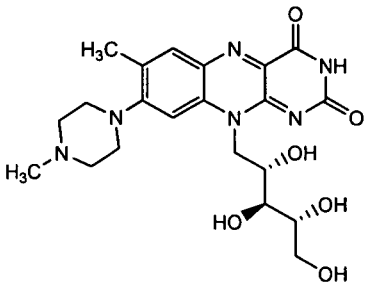
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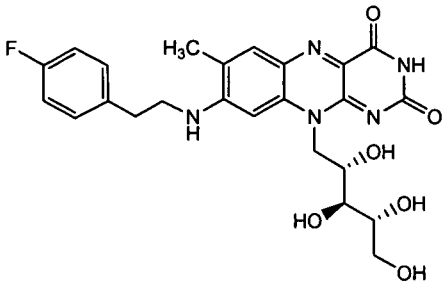
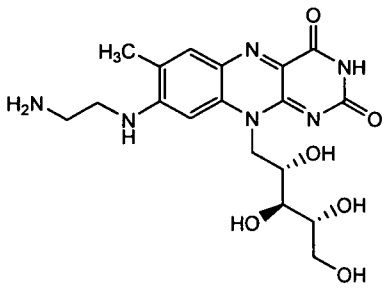
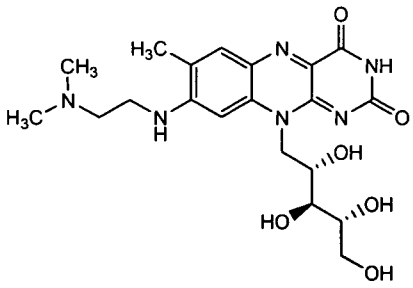
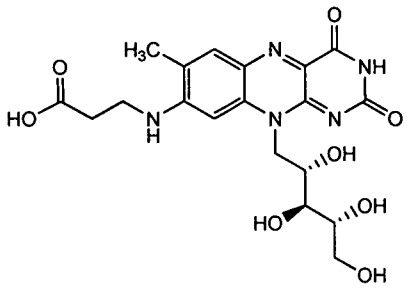
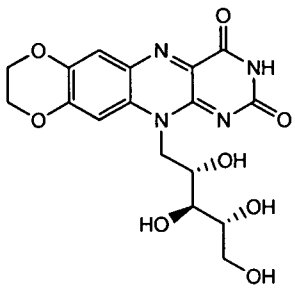
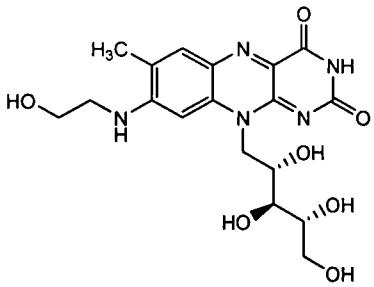
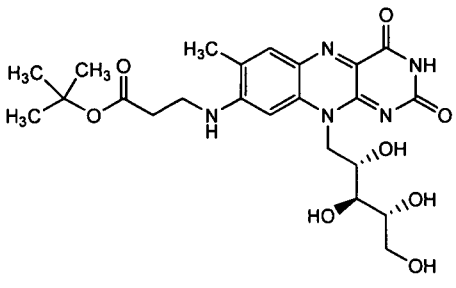


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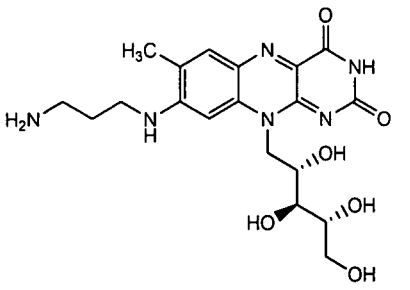
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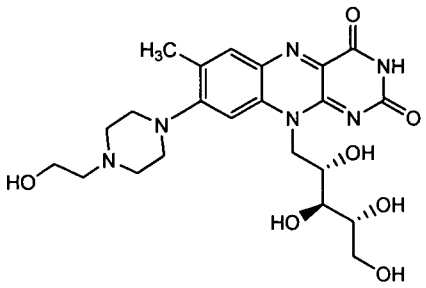

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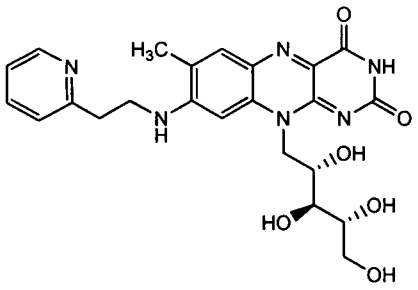
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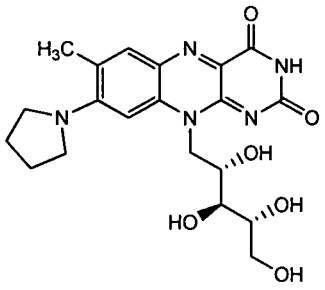
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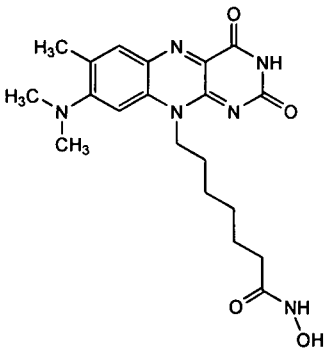
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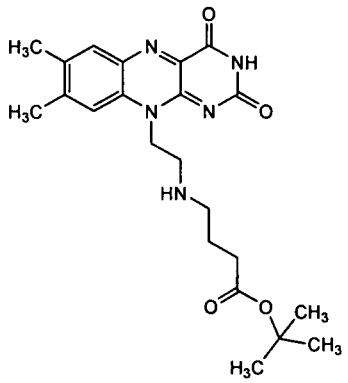
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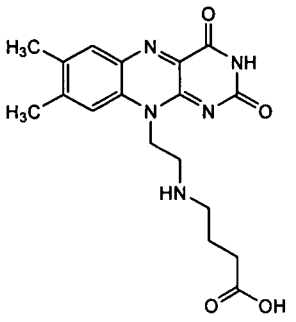
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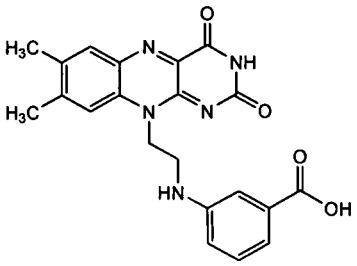
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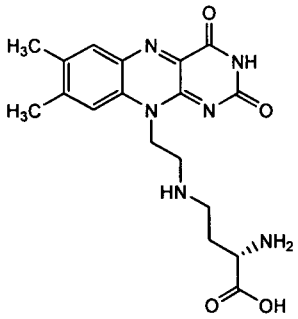
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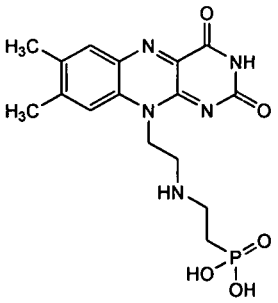
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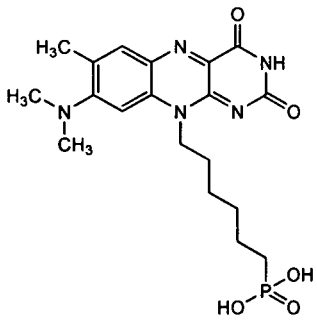
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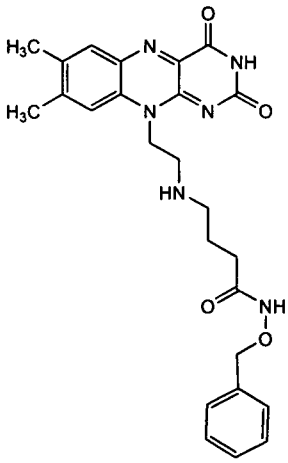
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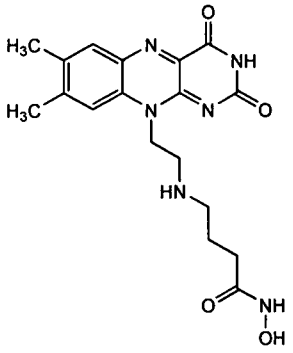
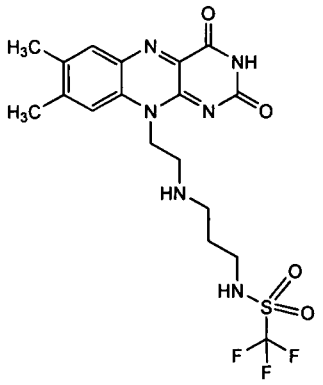
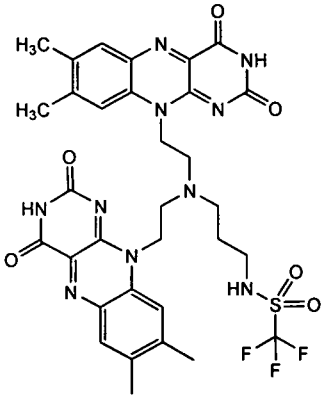
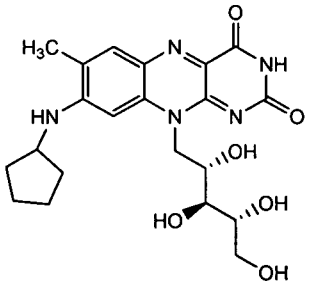
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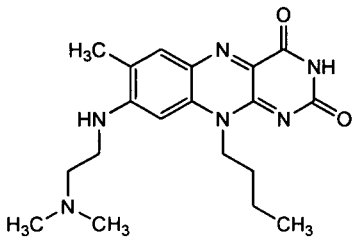
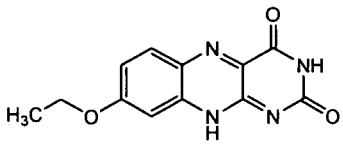
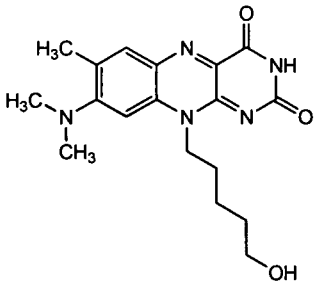
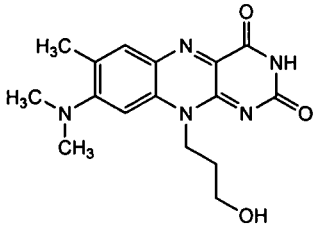


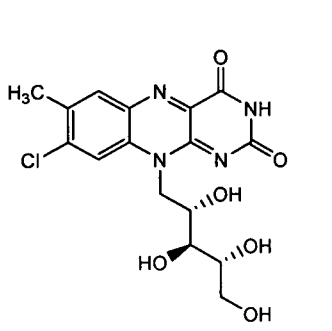
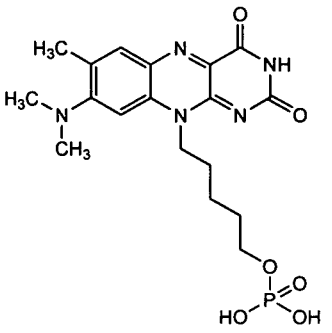
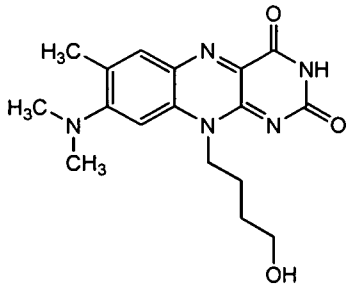
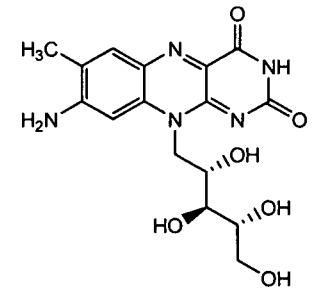
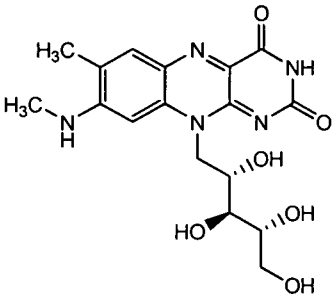
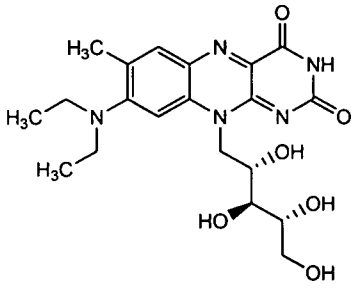
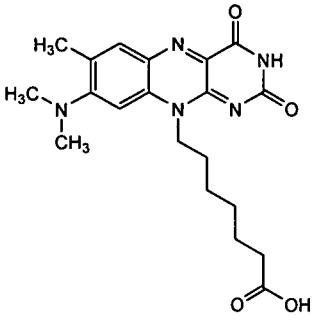
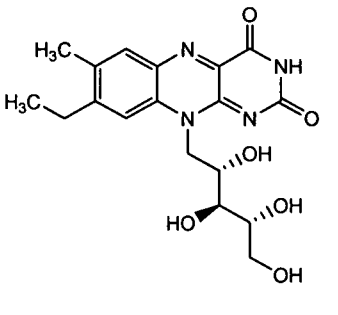
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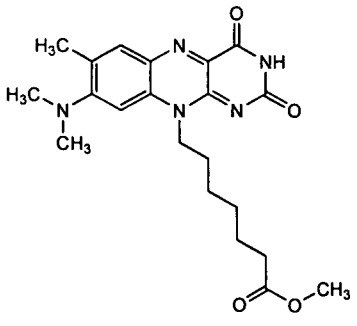





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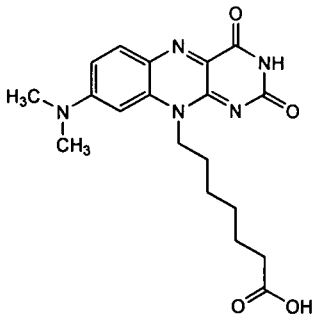
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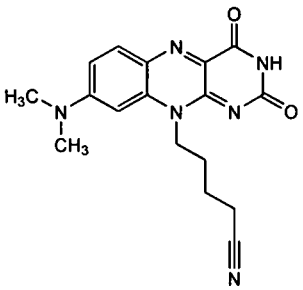

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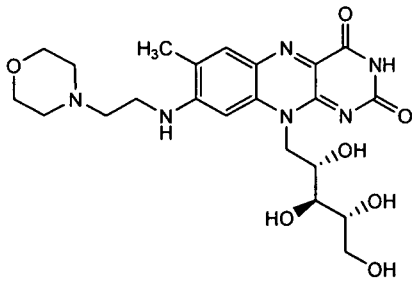


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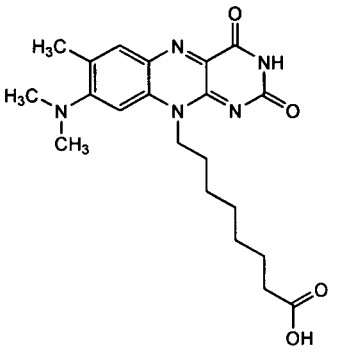
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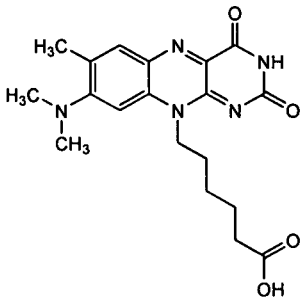


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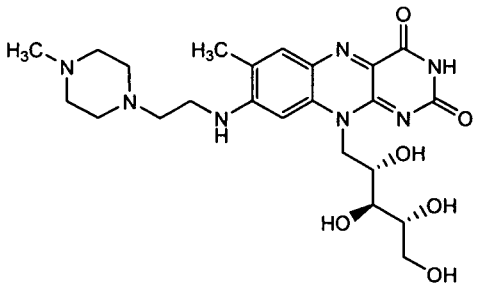
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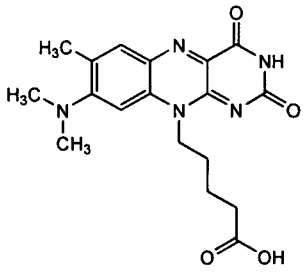
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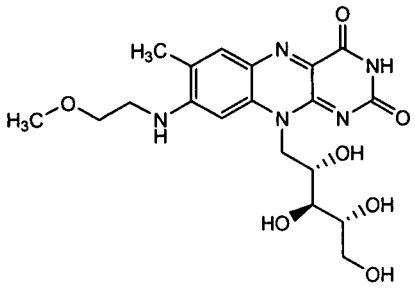
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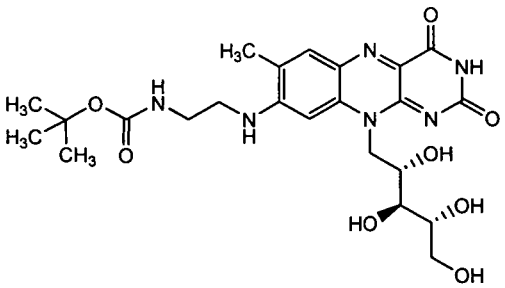


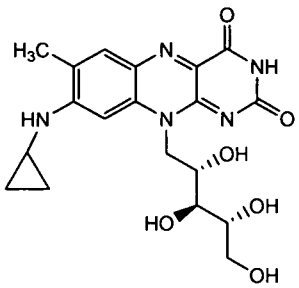
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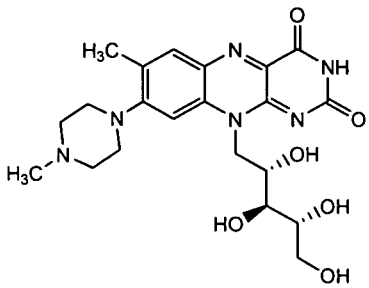


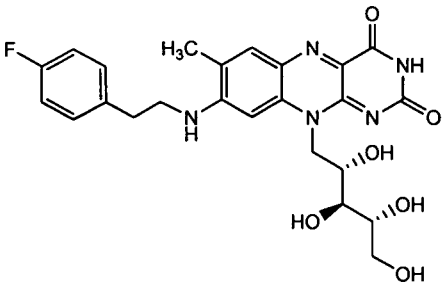
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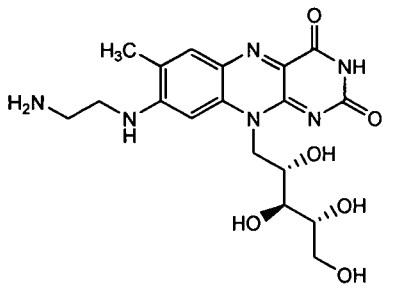

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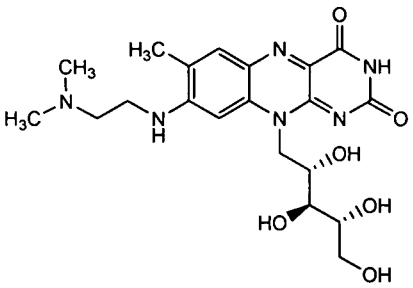

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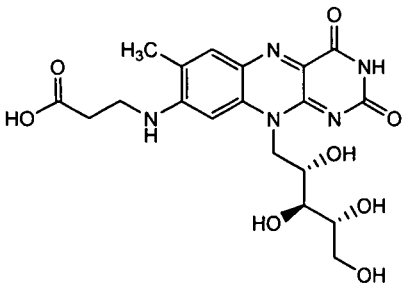
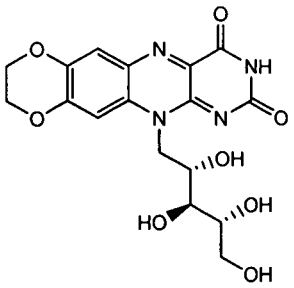
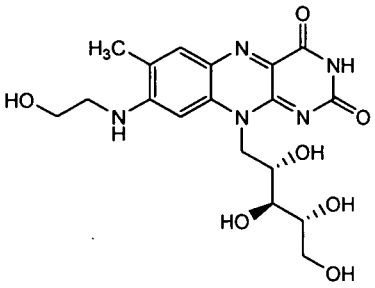
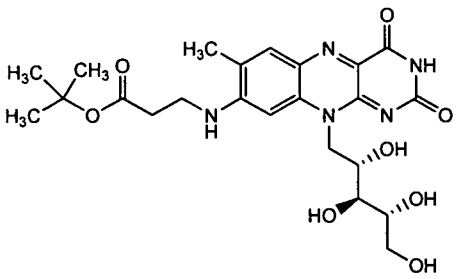
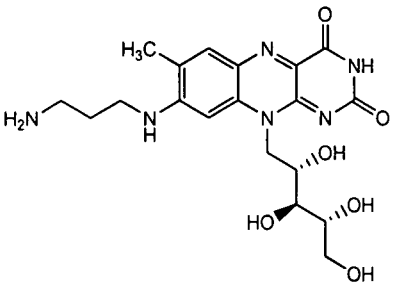
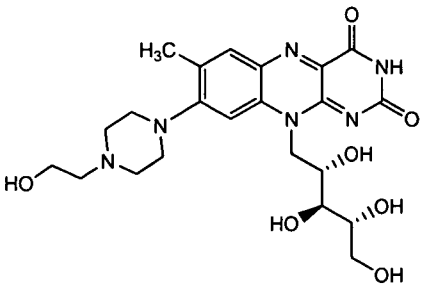

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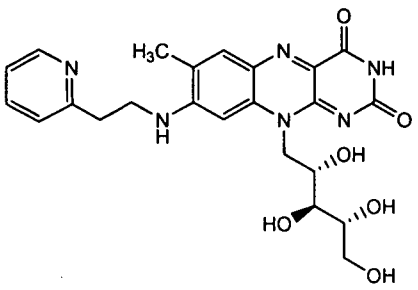
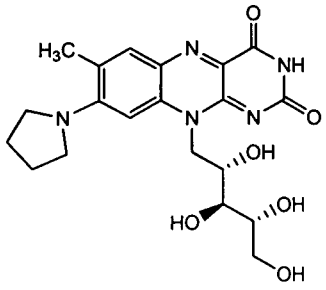
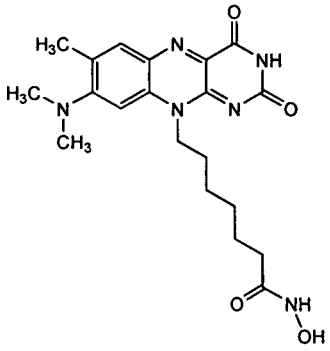
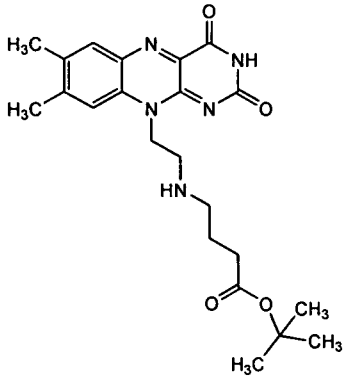
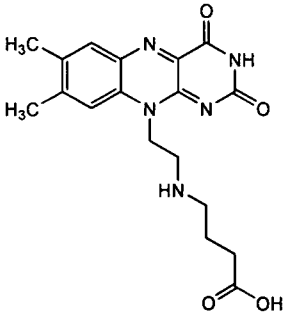
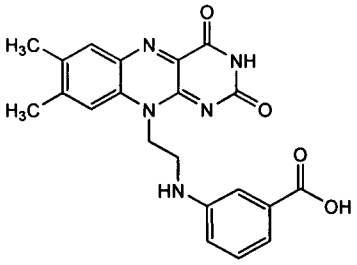
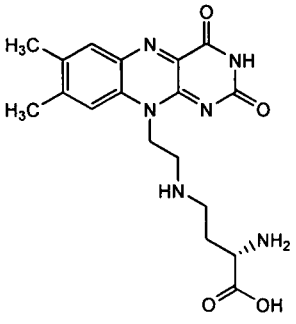
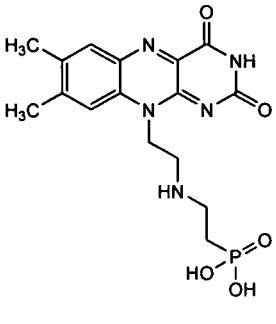

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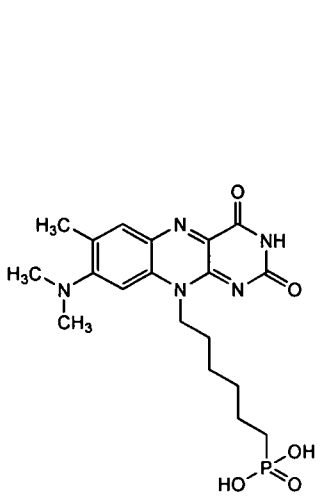
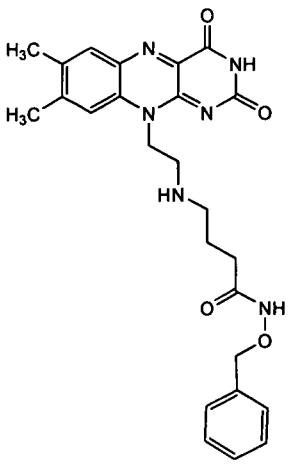
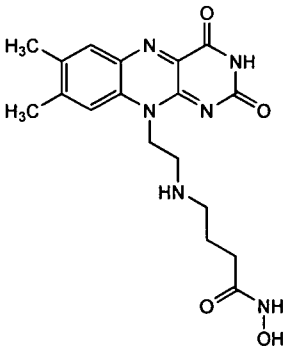
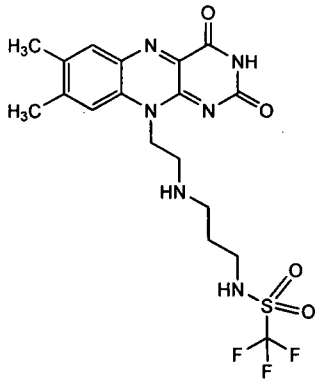
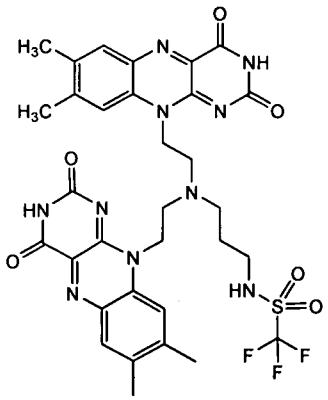
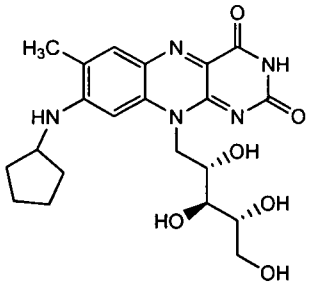

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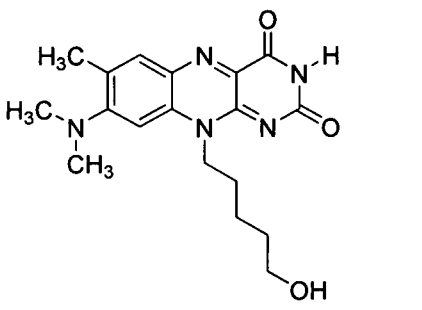
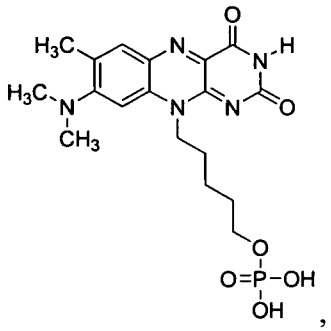
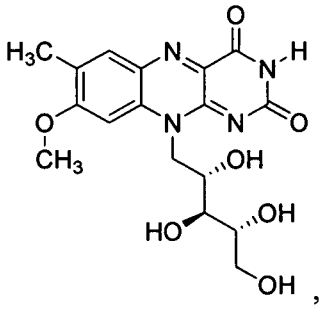
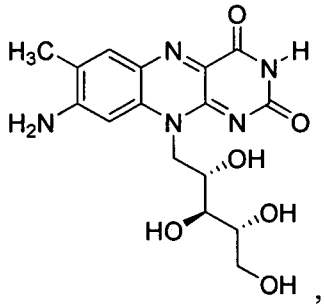
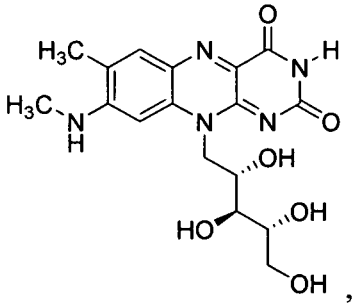
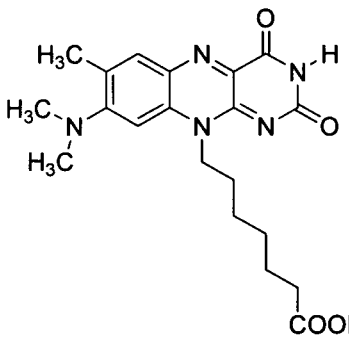
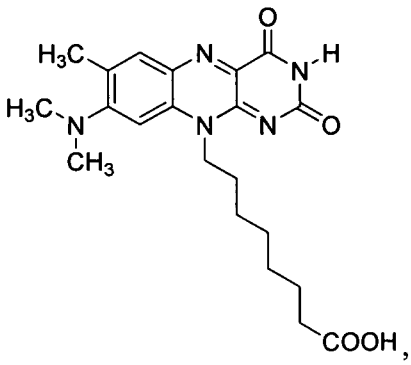
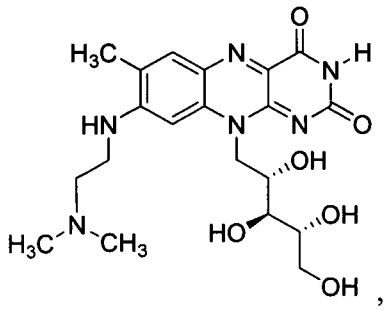
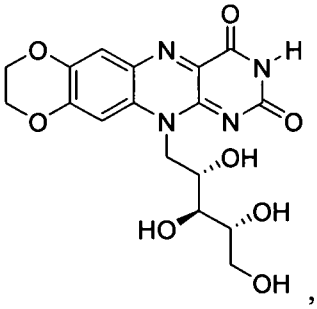
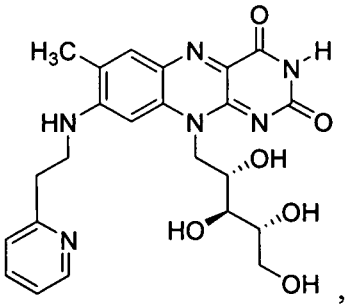

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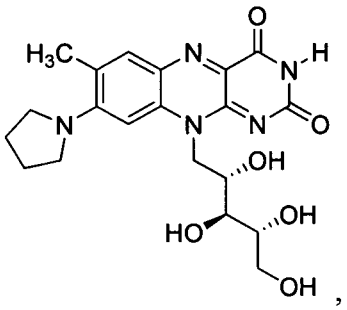
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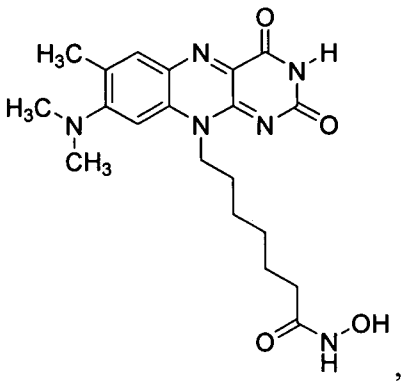

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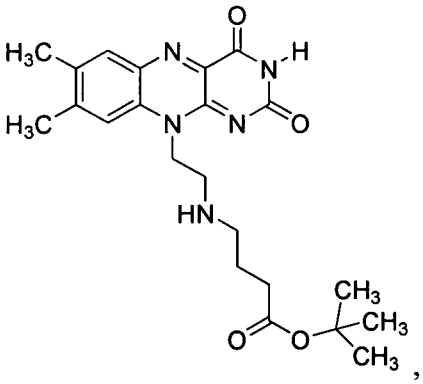

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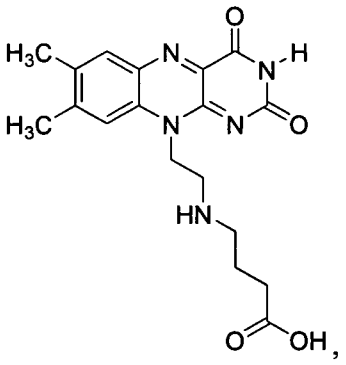
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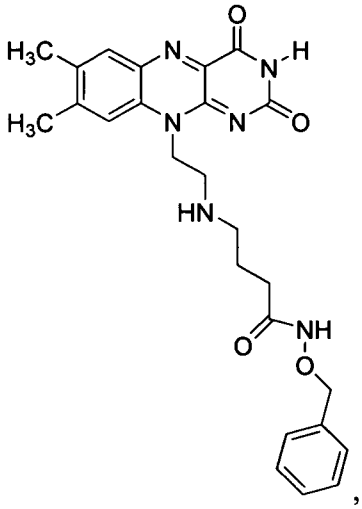

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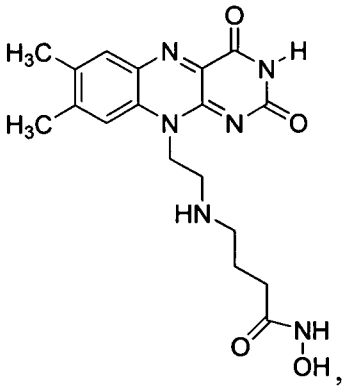


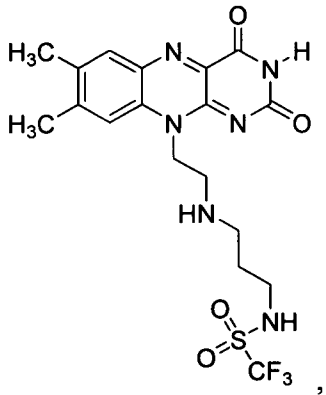


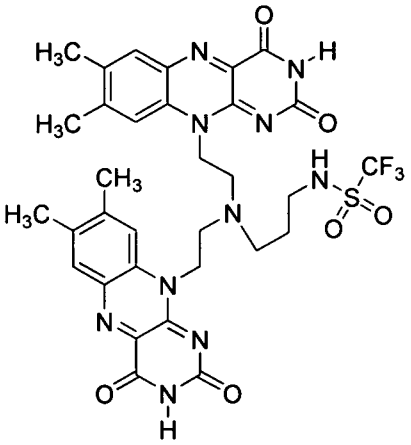




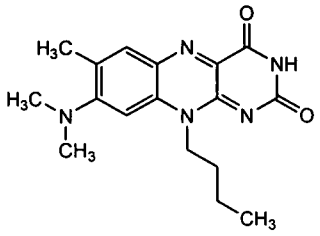

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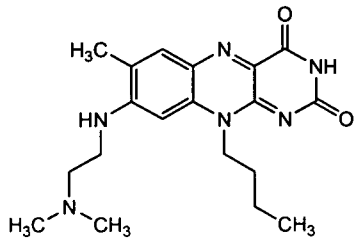

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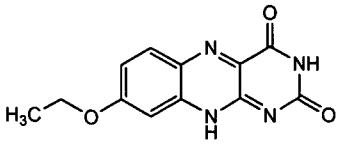

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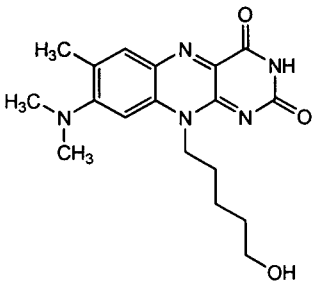
1.206 any of Formula I or 1.1-1.202 wherein a Compound of Formula I is selected from any of the following:


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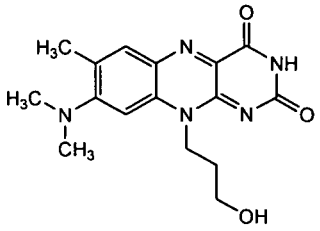

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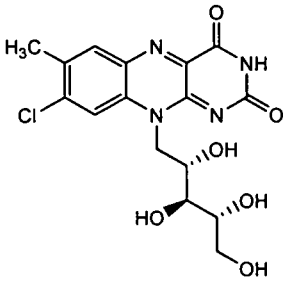
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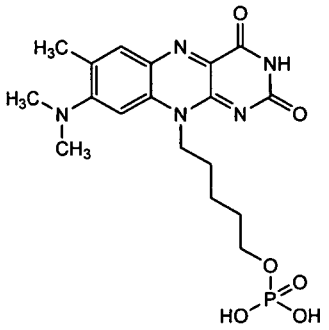
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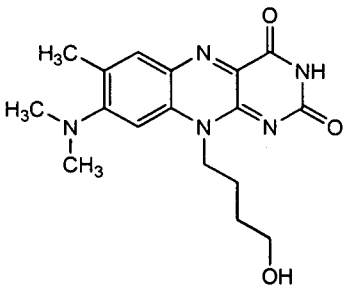
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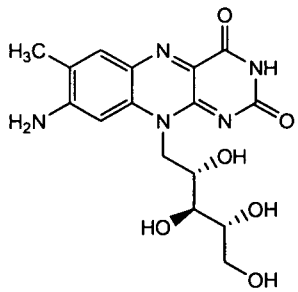
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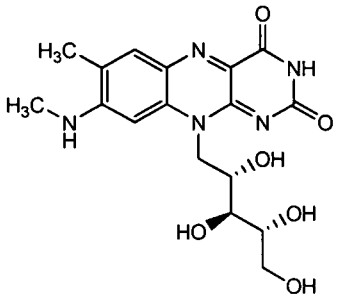
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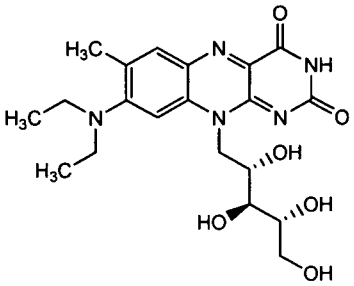
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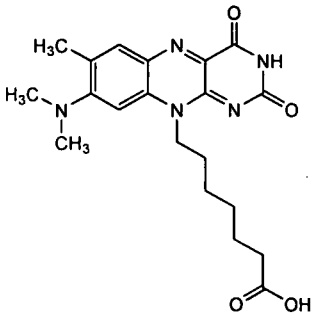
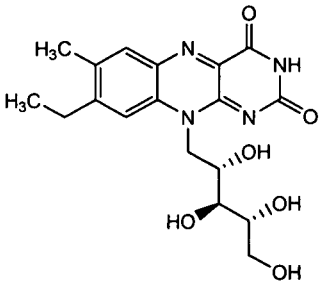
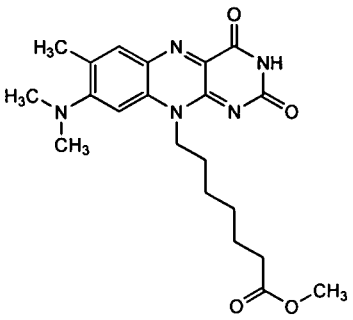
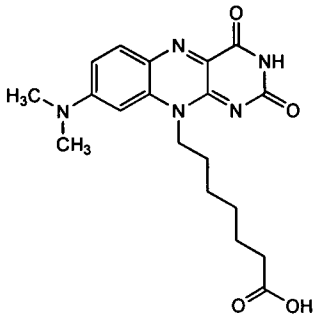
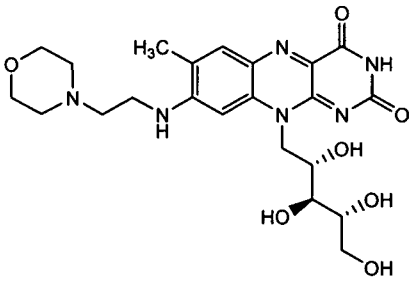
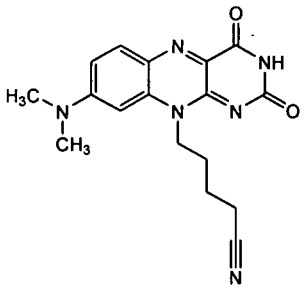
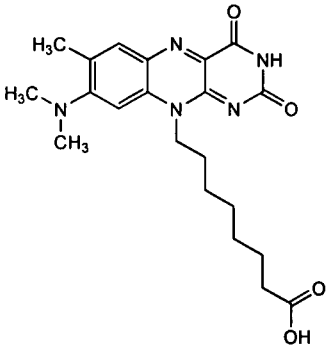
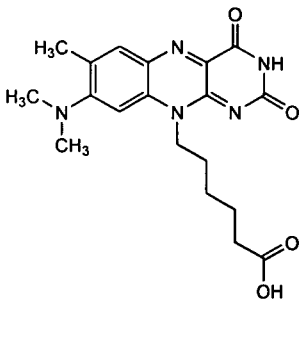


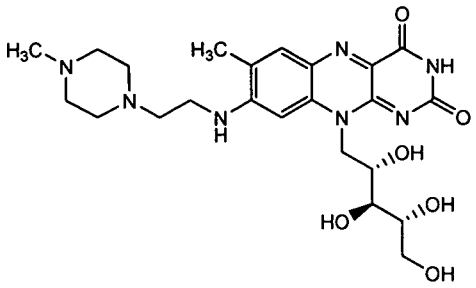
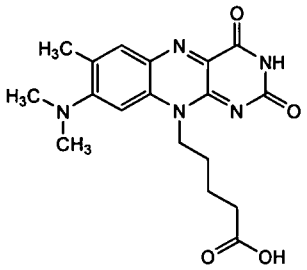
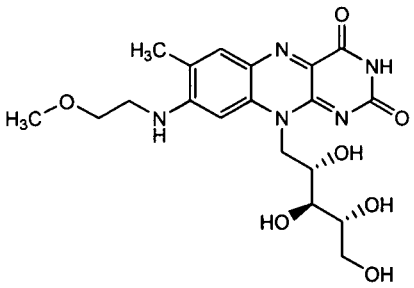
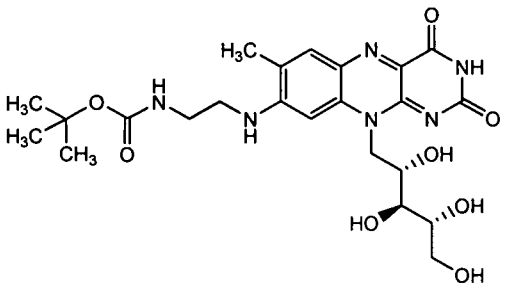
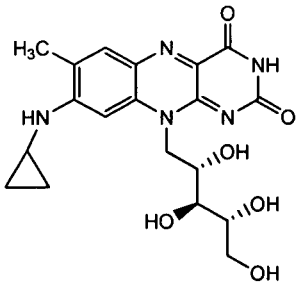
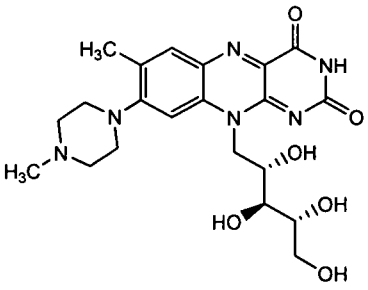
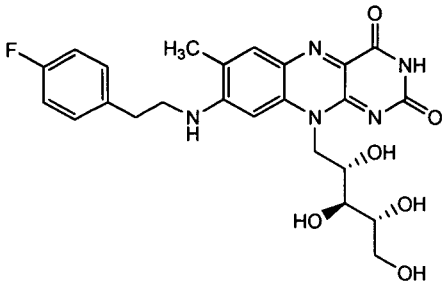
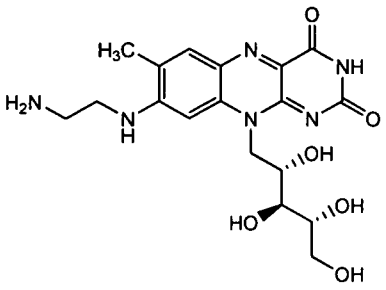
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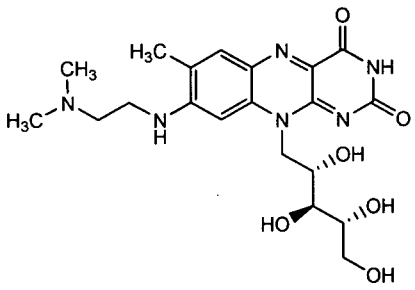


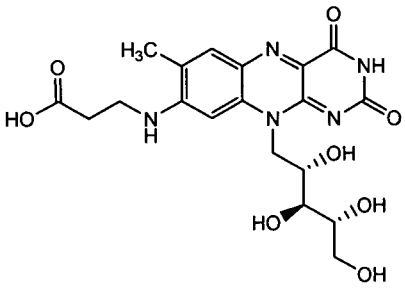
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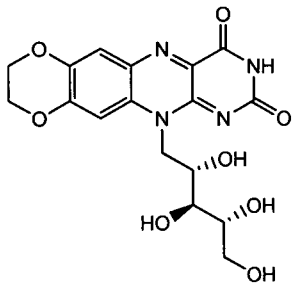
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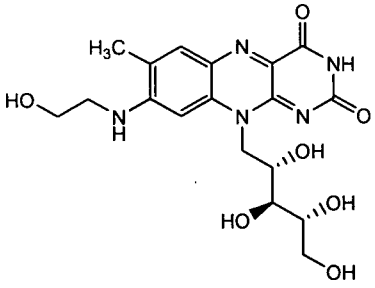

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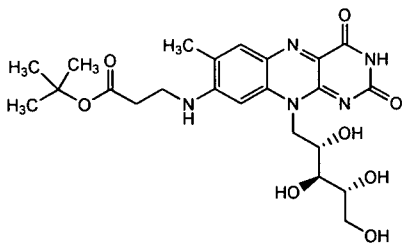

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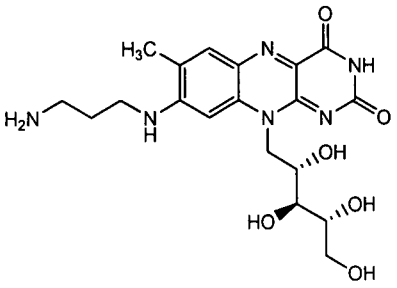

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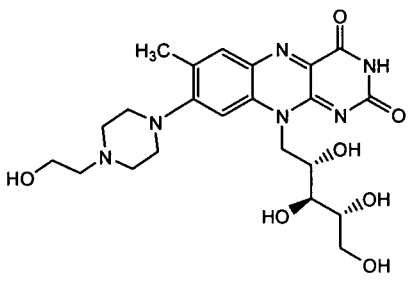

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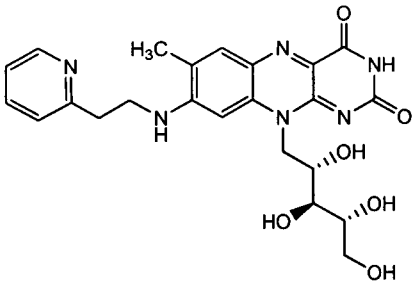

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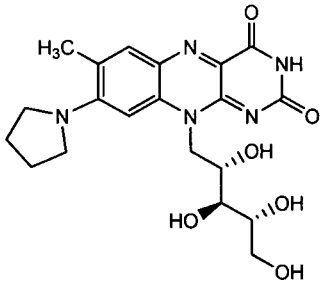

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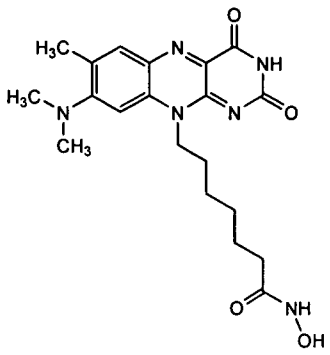
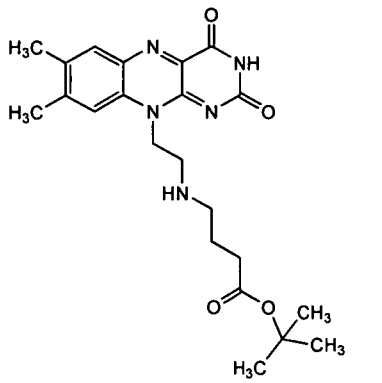
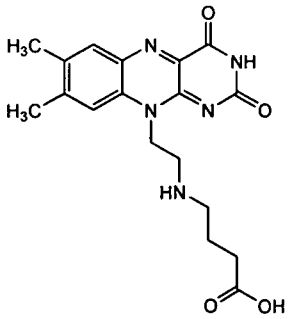
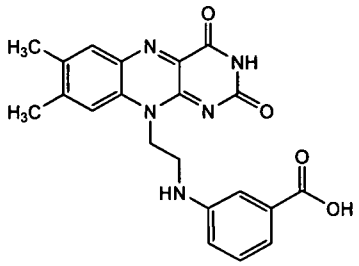
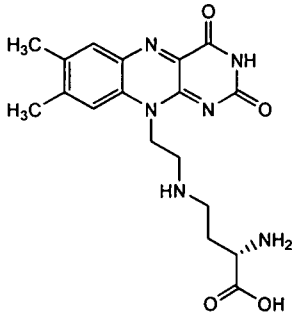
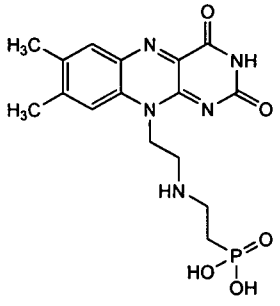
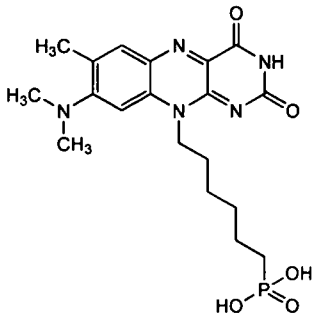
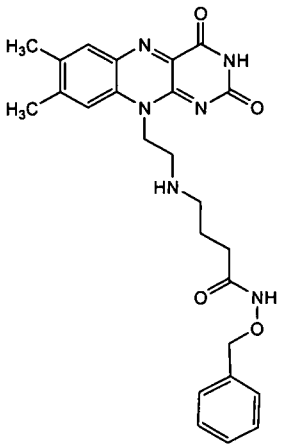

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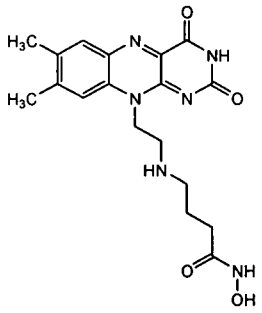
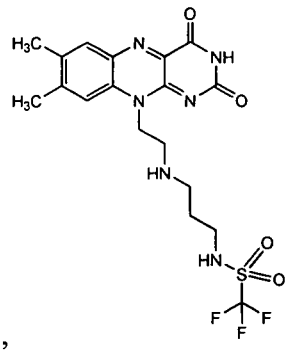
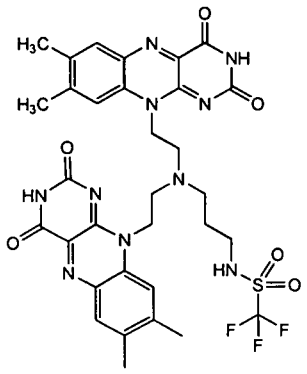
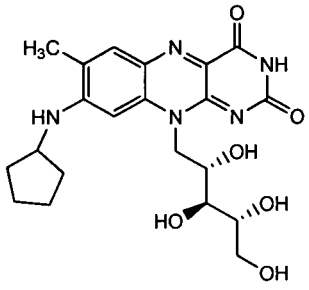

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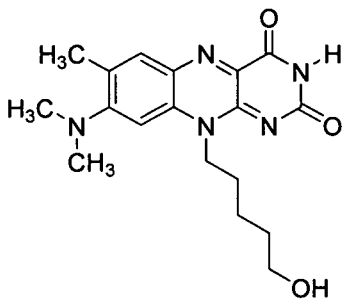
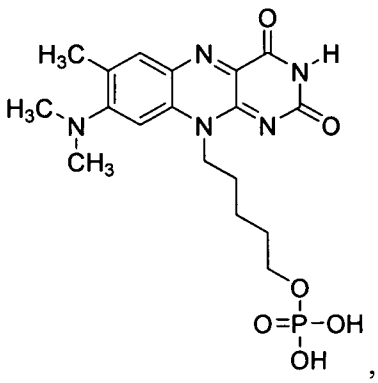
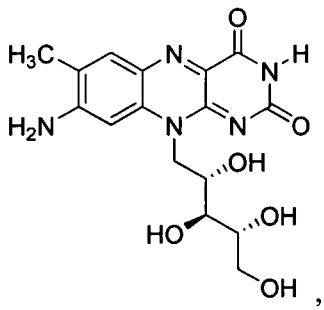
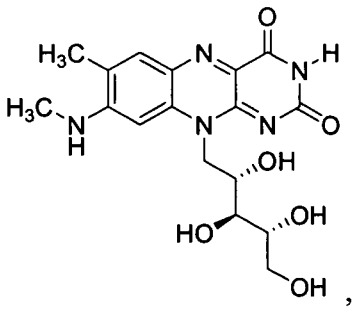
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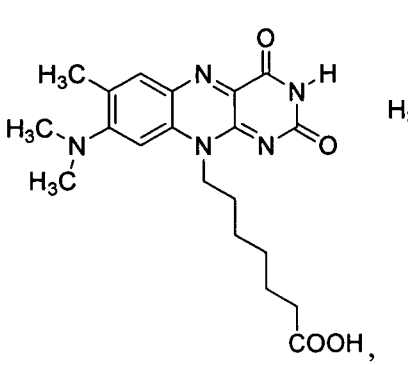
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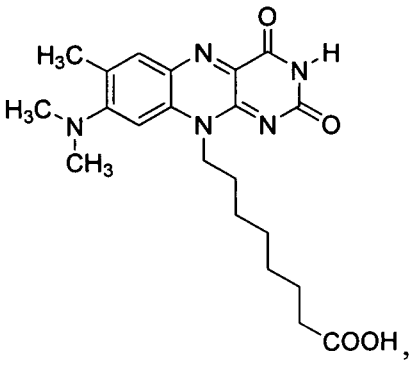

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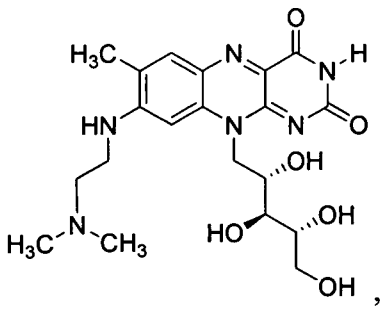

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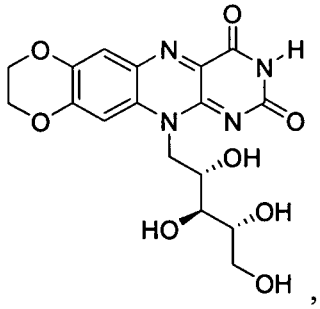
1.207 any of Formula I or 1.1-1.203 wherein a Compound of Formula I is selected from any of the following:

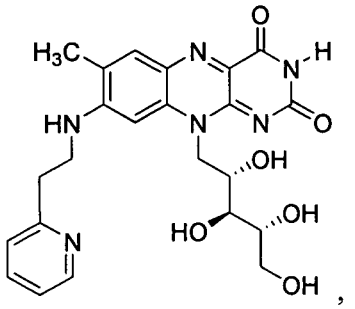

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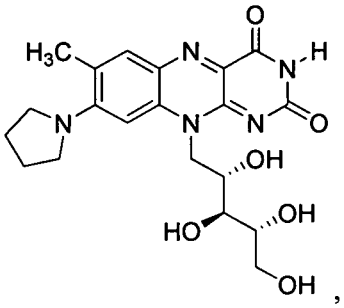


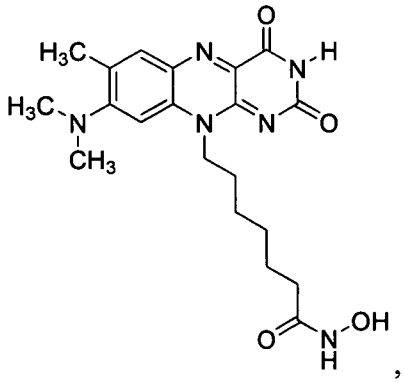


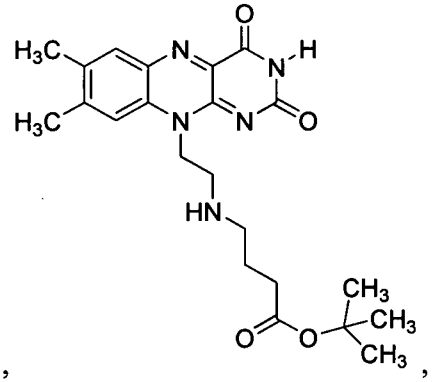


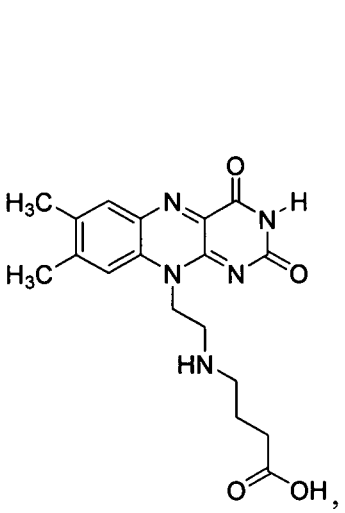


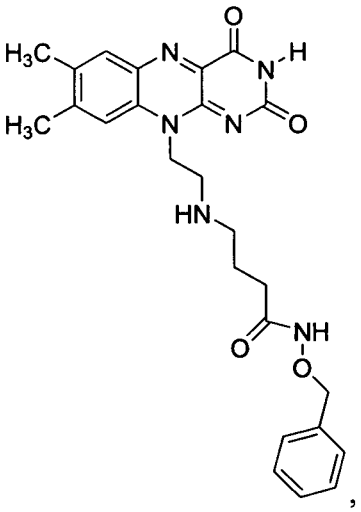


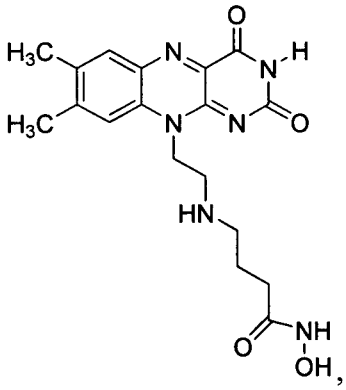


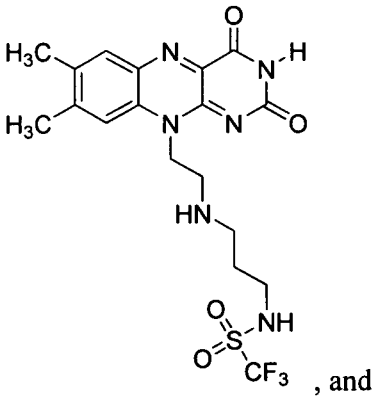




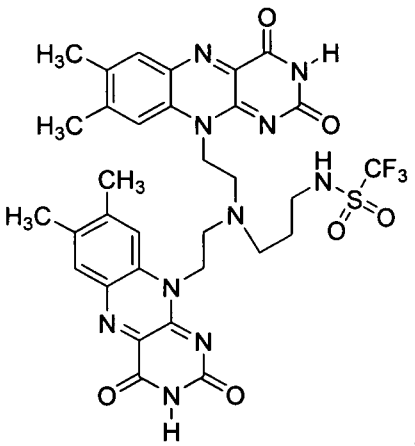






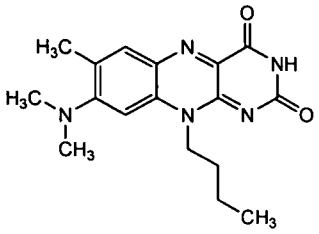
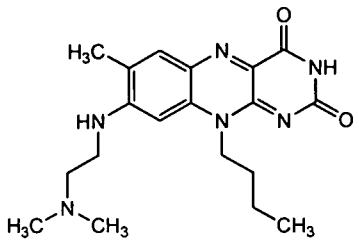
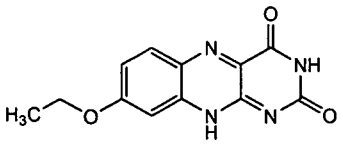
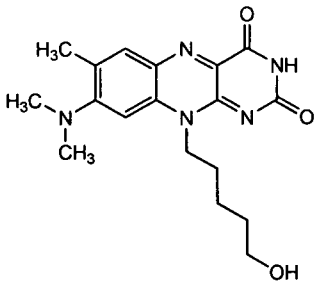
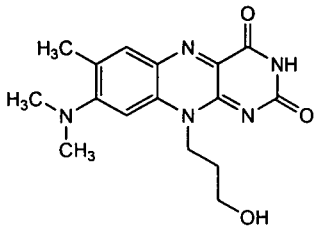
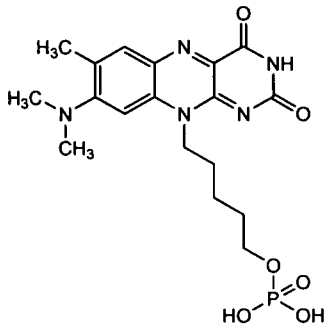
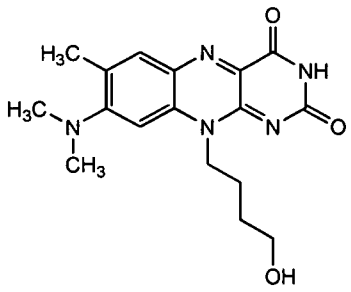
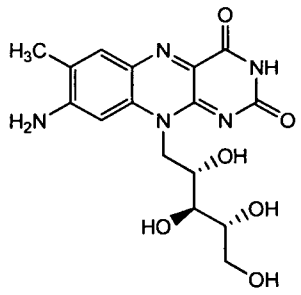
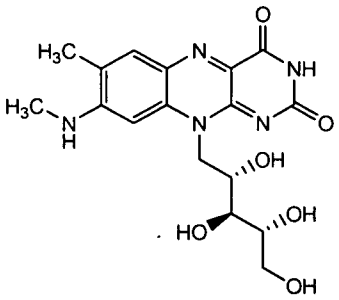
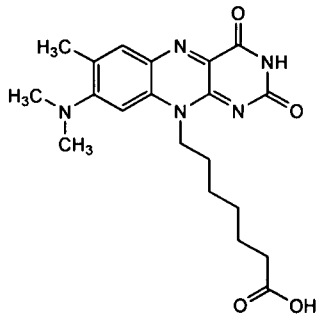


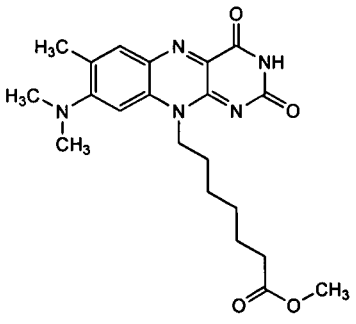
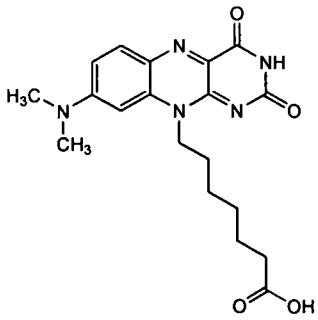
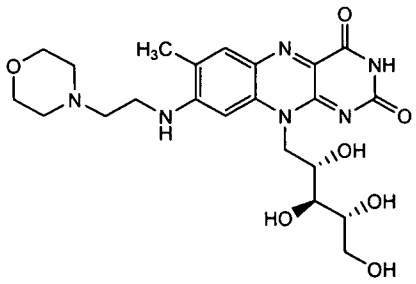
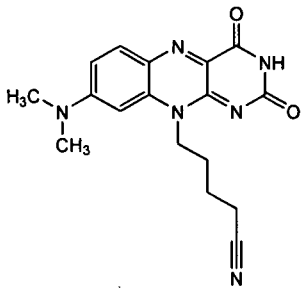
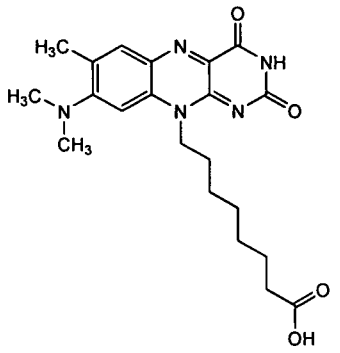
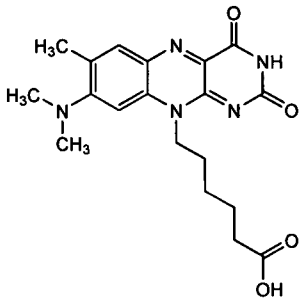
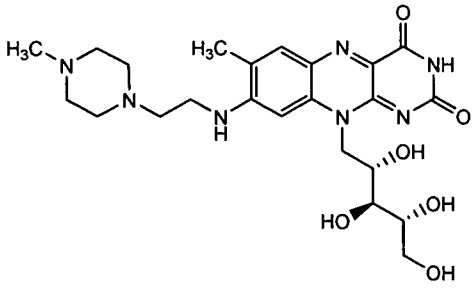
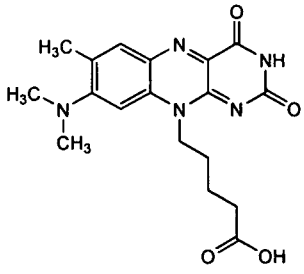
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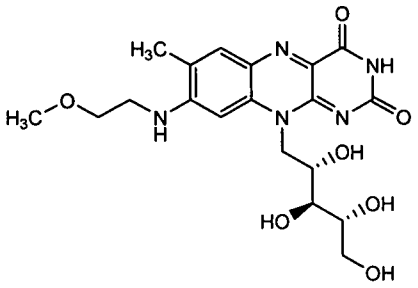


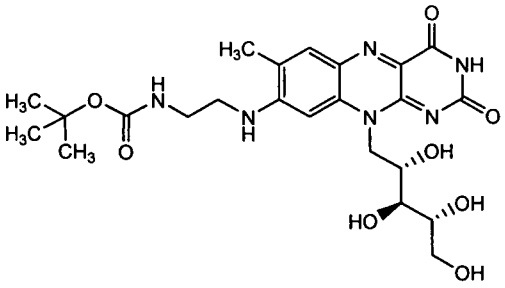
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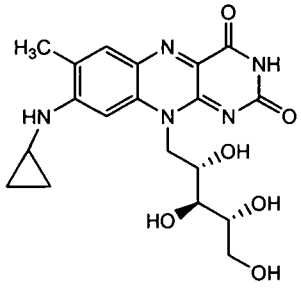
1.208 any of Formula I or 1.1-1.202 wherein a Compound of Formula I is selected from any of the following:

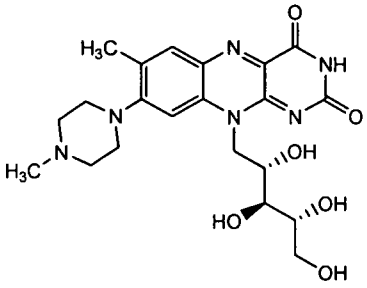

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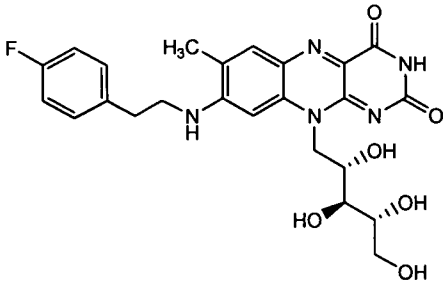

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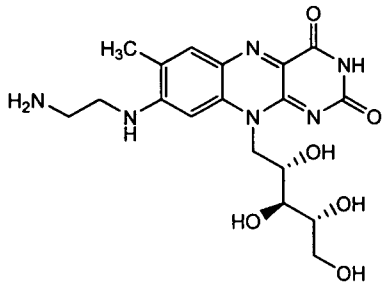

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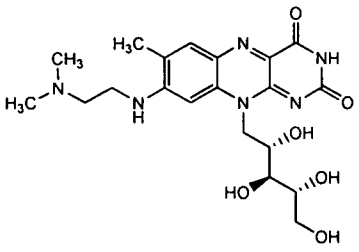

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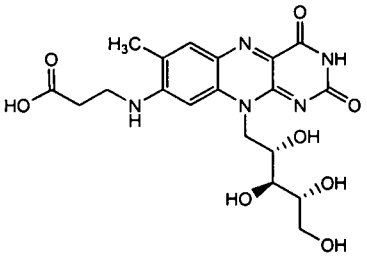

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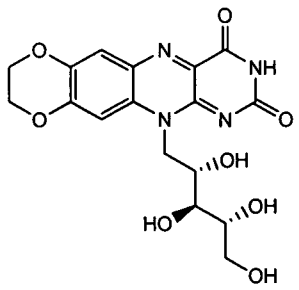
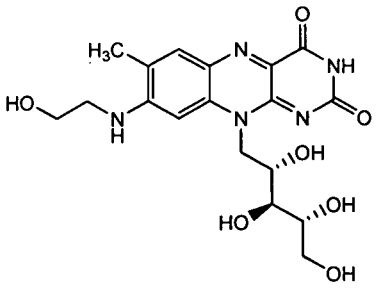
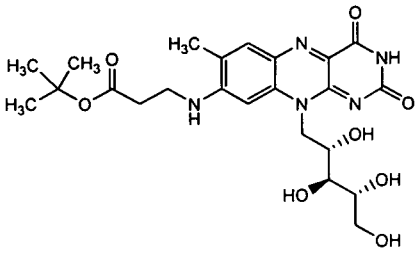
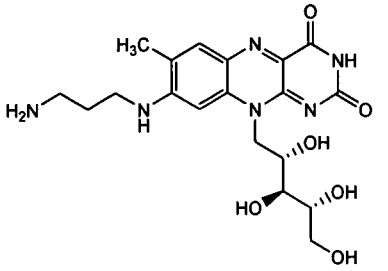
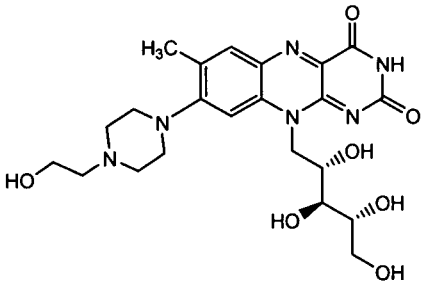
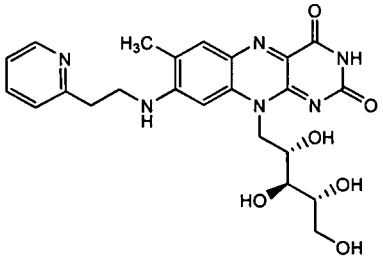
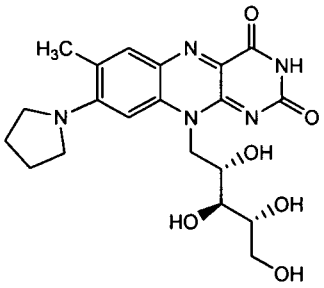
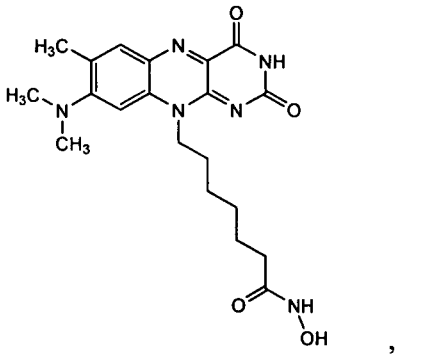

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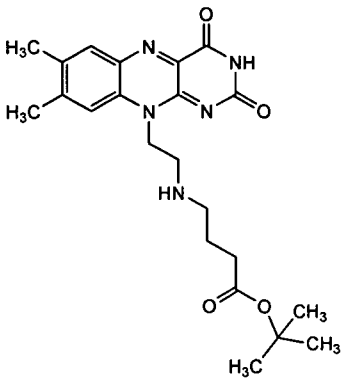
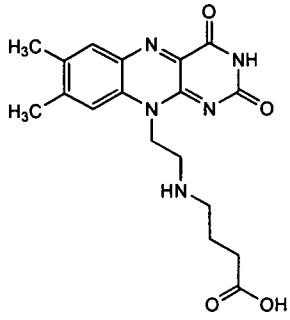
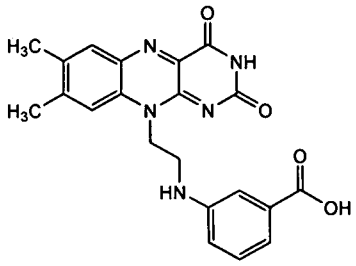
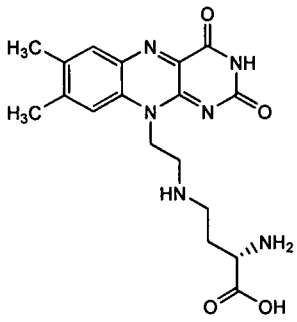
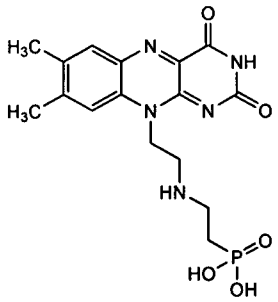
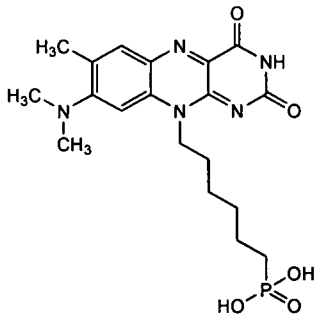
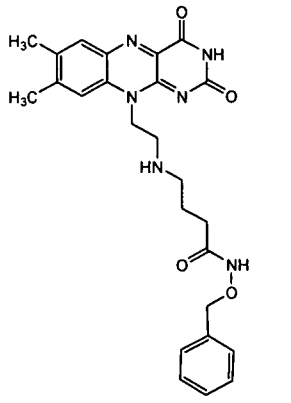
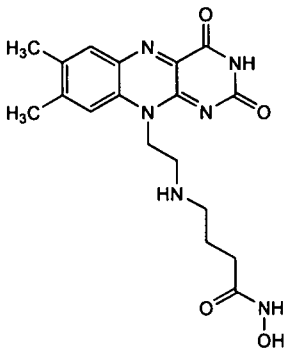

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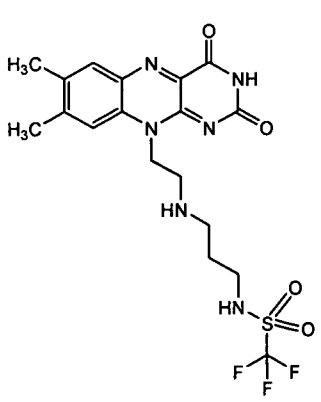
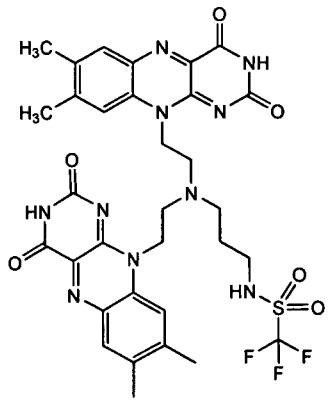

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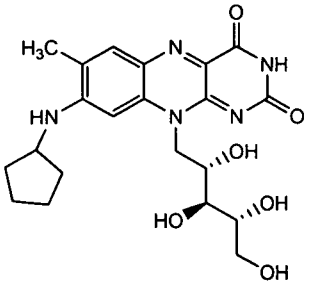

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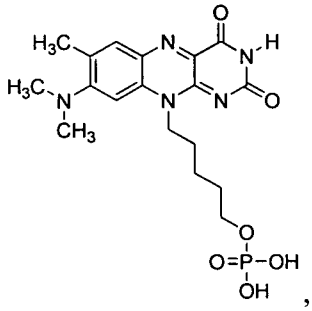
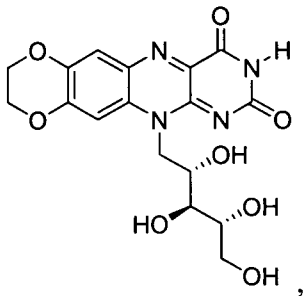

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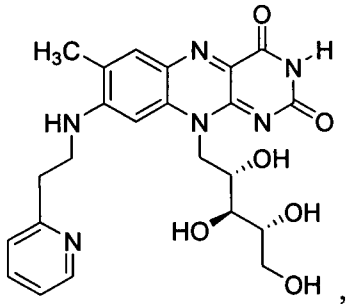
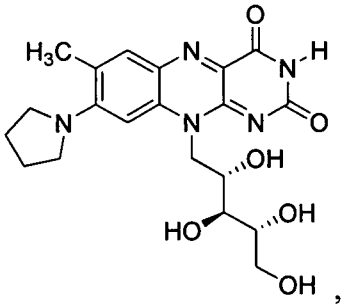

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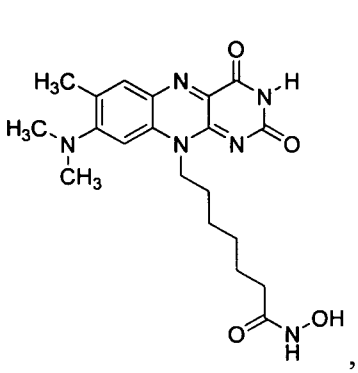
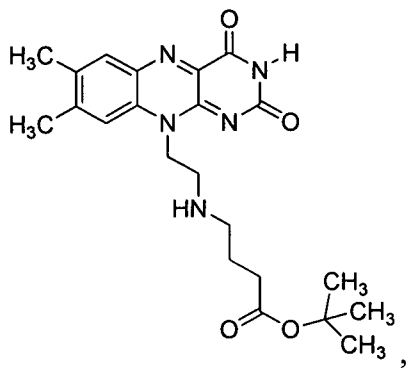
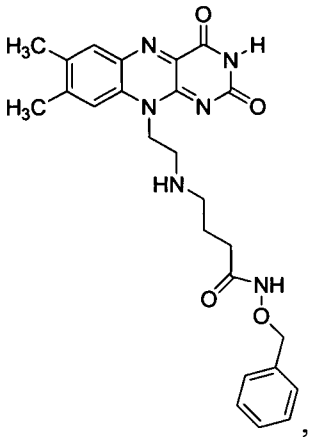
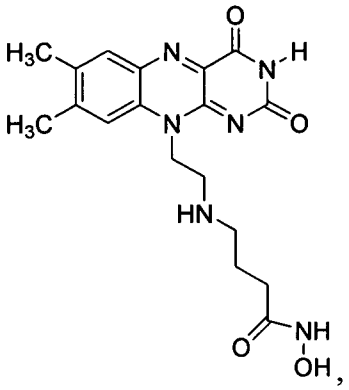
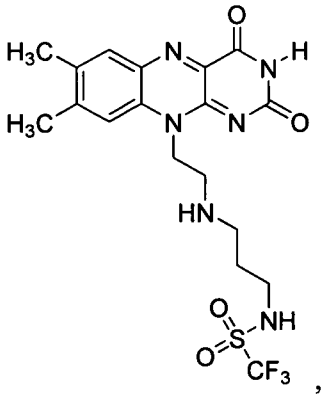
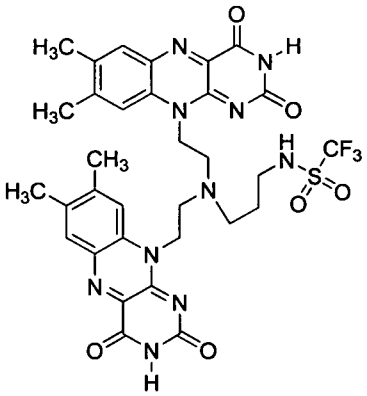
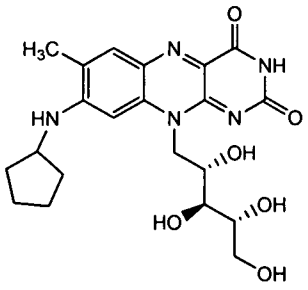

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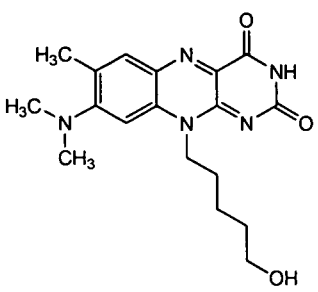
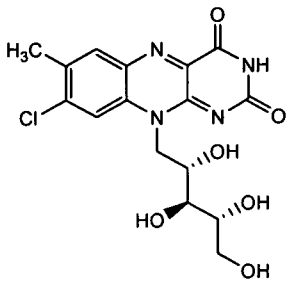
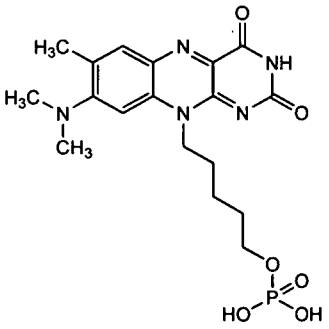
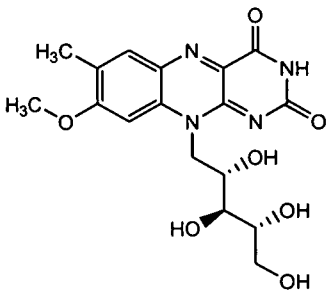
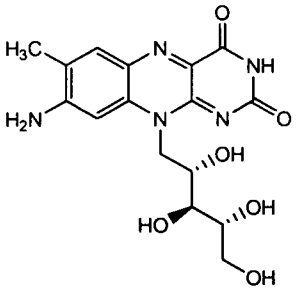
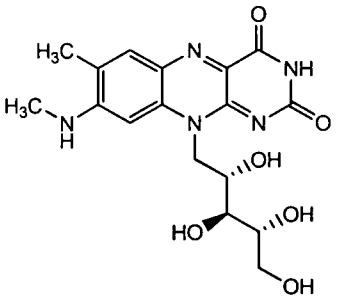
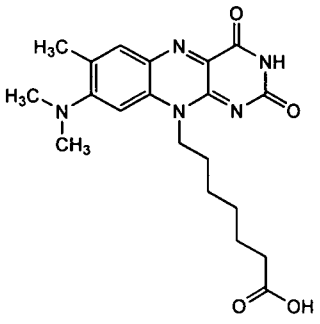
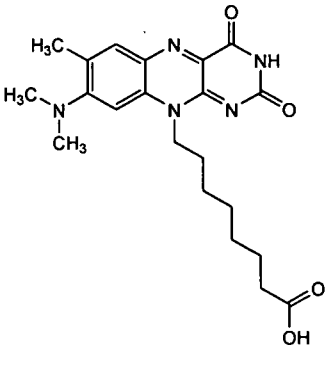
1.209 any of Formula I or 1.1-1.202 wherein a Compound of Formula I is selected from any of the following:

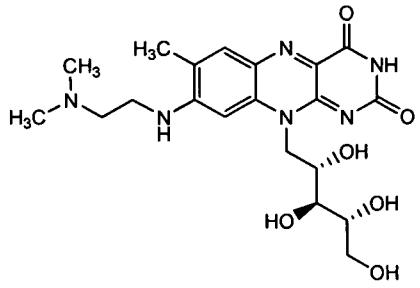

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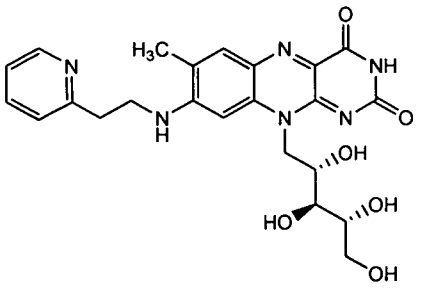

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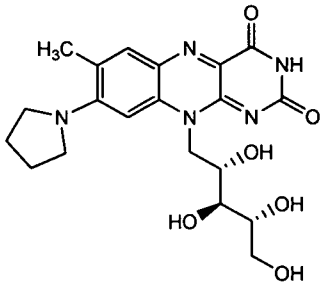
1.210 any of Formula I or 1.1-1.202 wherein the Compound of Formula I is selected from any of the following:


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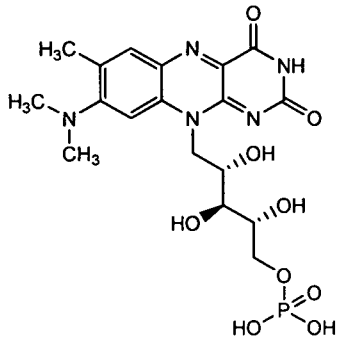
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, and ,

1.211 any of 1.1-1.202, wherein the Compound of Formula I is:

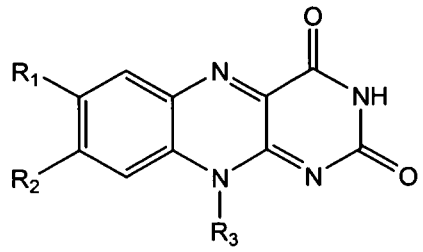


;

1.212 any of the preceding formulae wherein the Compound of Formula I binds to FMN riboswitch, e.g., with an IC_{50} of less than or equal to 10μM, preferably less than 1μM, more preferably less than 100 nM, most preferably less than 10nM in a binding assay, for example, as described in Example 1 and/or has a minimum inhibitory concentration (MIC) of less than 128μg/mL, preferably less than 32 μg/mL, in an assay, for example, as described in Example 1A;

in free, salt or prodrug form.

[0008] In another embodiment, the invention relates to a compound of Formula I(i):



Formula I(i)

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl) or C_{3-7} cycloalkyl;

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -N(R_4)(R_5), C_{3-7}cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl); or

(iii) R_1 and R_2 are connected so as to form a cyclic ring structure optionally containing one or more heteroatoms selected from N, O and S (e.g., –OCH_2CH_2O-);

(iv) R_3 is H or C_{1-8} alkyl (e.g., methyl, ethyl, n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -OP(O)(OR_9)(OR_{17}), -OP(O)(OR_9)($NR_{13}R_{14}$), -OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$), -P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -CN, -C(O)OR_9, -C(O)N(H)(R_8), -OR_{10}, -C(O)N(R_6)(R_7), and -N(R_6)(R_7);

(v) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{4-7}heterocycle (e.g., piperazinyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from –OR_{11}, –C(O)OR_9, -N(R_6)(R_7) (e.g., amino or dimethylamino), C_{1-8}alkoxyl (e.g., methoxy), C_{6-10}aryl (e.g., phenyl), C_{5-10} heteroaryl (e.g., pyridinyl) wherein said aryl or heteroaryl are optionally substituted with halo (e.g.,4-fluorophenyl), and C_{4-7}heterocycle wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl);

(vi) R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-propyl, n-butyl), -C_{1-8}alkyl-OR_{11}, -$C(O)OR_9$, –C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), –C_{1-8}alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$ -C_{1-8}alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl and aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

(vii) R_8 is H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), -OR_{11} or –OBn;

(viii) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

(ix) R_{10} is H, C_{1-8}alkyl (e.g., methyl or ethyl), -C_{1-8}alkyl-OR_{11}, –C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), –C_{1-8}alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)$ $(OR_9)(NR_{13}R_{14})$, -C_{1-8}alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl, or aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$, or –C_{1-4}alkyl-$OC(O)R_{12}$;

(x) R_{11} is H, or –C_{1-4}alkyl-$OC(O)R_{12}$ (e.g., –CH_2-$OC(O)R_{12}$);

(xi) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy);

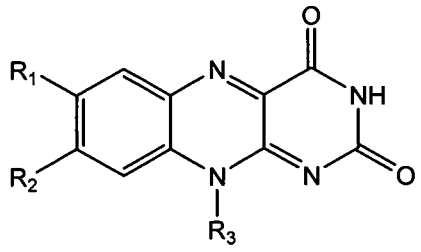
(xii) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$, -CH(isopropyl)-$COOR_{18}$, -CH(isobutyl)-$COOR_{18}$, -CH(sec-butyl)-$COOR_{18}$), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with

hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –CH(CH_2CH_2COOH)-COOH);

(xiii) R_{18} is H or C_{1-8}alkyl (e.g., ethyl);

in free, salt or prodrug form.

[0009] In still another embodiment, the invention relates to a compound of Formula I(ii):



Formula I(ii)

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -N(R_4)(R_5);

(iii) R_3 is C_{1-8} alkyl (e.g., methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -OP(O)(OR_9)(OR_{17}), -OP(O)(OR_9)($NR_{13}R_{14}$), -OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$), -P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -CN, -C(O)OR_9, -C(O)N(H)(R_8), -OR_{10}, -C(O)N(R_6)(R_7), and -N(R_6)(R_7);

(iv) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from –OR_{11};

(v) R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-propyl, n-butyl),–C_{1-8}alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 (e.g., -CH_2CH_2CH(NH_2)COOH), –C_{1-8}alkyl-C(O)N(H)R_8, -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -C_{1-8}alkyl-OP(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-OP(O)(OR_9)($NR_{13}R_{14}$) -C_{1-8}alkyl-OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), 7,8-

dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl and aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

(vi) R_8 is H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl);

(vii) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

(viii) R_{10} is –C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$, or –C_{1-4}alkyl-$OC(O)R_{12}$;

(ix) R_{11} is H, or –C_{1-4}alkyl-$OC(O)R_{12}$ (e.g., –CH_2-$OC(O)R_{12}$);

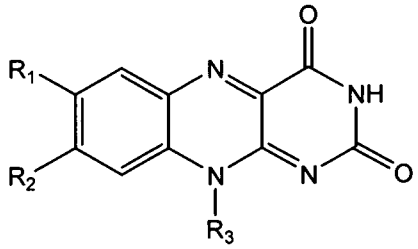
(x) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy);

(xi) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$, -CH(isopropyl)-$COOR_{18}$, -CH(isobutyl)-$COOR_{18}$, -CH(sec-butyl)-$COOR_{18}$), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –$CH(CH_2CH_2COOH)$-COOH); and

(xii) R_{18} is H or C_{1-8}alkyl (e.g., ethyl);

in free, salt or prodrug form.

[0010] The invention further relates to a compound of Formula I(iii) as follows:



Formula I(iii)

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy), -N(R_4)(R_5);

(iii) R_3 is C_{1-8} alkyl (e.g., methyl, ethyl, n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$), -P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -C(O)OR_9, -OR_{10}, -C(O)N(R_6)(R_7), and -N(R_6)(R_7);

(iv) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from –OH;

(v) R_6 and R_7 are independently selected from H, –C_{1-8}alkyl (e.g., methyl), –C_{1-8}alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl, wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

(vi) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), –C_{1-4}alkyl-OC(O)R_{12};

(vii) R_{10} is H, –C_{1-8}alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$);

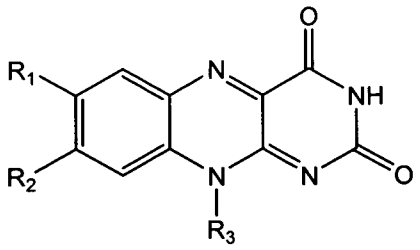
(viii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl);

(ix) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$, -CH(isopropyl)-$COOR_{18}$, -CH(isobutyl)-$COOR_{18}$, -CH(sec-butyl)-$COOR_{18}$);

(x) R_{18} is H or C_{1-8}alkyl (e.g., ethyl);

in free, salt or prodrug form.

[0011] In still another embodiment, the invention relates to a compound of Formula I(iv):



Formula I(iv)

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -$N(R_4)(R_5)$;

(iii) R_3 is C_{1-8}alkyl-$N(R_6)(R_7)$, C_{1-8}alkyl-$C(O)N(R_6)(R_7)$, C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, C_{1-8}alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, C_{1-8}alkyl-$C(O)OR_9$, C_{1-8}alkyl-OR_{10};

(iv) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from $-OR_{11}$;

(v) R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-propyl, n-butyl),–C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl and aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

(vi) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$;

(vii) R_{10} is H, $-C_{1-8}$alkyl-$C(O)OR_9$, $-C_{1-8}$alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$P(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl wherein said aryl and alkyl are optionally substituted with $-COOR_9$;

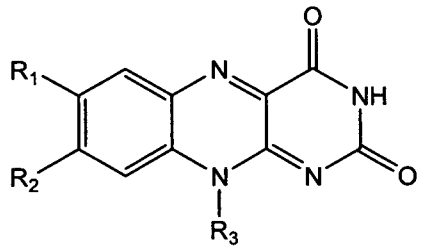
(viii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl);

(ix) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$);

(x) R_{18} is H or C_{1-8}alkyl (e.g., ethyl or t-butyl);

in free, salt or prodrug form.

[0012] In still another embodiment, the invention relates to a compound of Formula I(v):



Formula I(v)

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), $-N(R_4)(R_5)$;

(iii) R_3 is C_2alkyl-$N(R_6)(R_7)$, C_{1-2}alkyl-$C(O)N(R_6)(R_7)$, C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, C_{1-8}alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, C_{1-8}alkyl-$C(O)OR_9$, C_{1-8}alkyl-OR_{10};

(iv) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from $-OR_{11}$;

(v) R_6 and R_7 are independently selected from –C_{1-8}alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl and aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

(vi) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), –C_{1-4}alkyl-OC(O)R_{12};

(vii) R_{10} is H, –C_{1-8}alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

(viii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl);

(ix) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$);

(x) R_{18} is H or C_{1-8}alkyl (e.g., ethyl or t-butyl);

in free, salt or prodrug form.

[0013] In yet another embodiment, the invention provides a compound of Formula I, wherein R_3 is C_{1-8} alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl) substituted with one or more groups selected from -OP(O)(OR_9)(OR_{17}), -OP(O)(OR_9)($NR_{13}R_{14}$), -OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$), -P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -CN, -C(O)OR_9, -C(O)N(H)(R_8), -OR_{10}, -C(O)N(R_6)(R_7), and -N(R_6)(R_7) and the other substituents are defined in Formula I or any of 1.1-1.212, in free, salt or prodrug form.

[0014] In another embodiment, the invention provides a compound of formula I or I(i)-I(v) as follows:

1.213. Formula I, or any of 1.1-1.212, e.g., any of 1.1-1.109, 1.112, 1.130, 1.131, 1.132, 1.137, 1.142, 1.145, 1.150, 1.154, 1.157, 1.158, 1.212, or Formula I(i), I(ii), wherein R_3 is C_{1-8} alkyl (e.g., methyl, ethyl, n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -OP(O)(OR_9)(OR_{17}), -OP(O)(OR_9)($NR_{13}R_{14}$), -OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -P(O)(OR_9)(OR_{17}), -

$P(O)(OR_9)(NR_{13}R_{14})$, $-P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -CN, $-C(O)OR_9$, $-C(O)N(H)(R_8)$, $-OR_{10}$, $-C(O)N(R_6)(R_7)$, and $-N(R_6)(R_7)$;

1.214. Formula I, or any of 1.1-1.212, e.g., any of 1.1-1.109, 1.112, 1.130, 1.131, 1.132, 1.137, 1.142, 1.145, 1.150, 1.154, 1.157, 1.158, 1.212, or any of Formulae I(i)-I(iii), 2.10, wherein R_3 is C_{1-8} alkyl (e.g., methyl, ethyl, n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from $-P(O)(OR_9)(OR_{17})$, $-P(O)(OR_9)(NR_{13}R_{14})$, $-P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C(O)OR_9$, $-OR_{10}$, $-C(O)N(R_6)(R_7)$, and $-N(R_6)(R_7)$;

1.215. Formula I, or any of 1.1-1.212, e.g., any of 1.1-1.109, 1.112, 1.130, 1.131, 1.132, 1.137, 1.142, 1.145, 1.150, 1.154, 1.157, 1.158, 1.212, or any of Formulae I(i)-I(iv) or 2.10-1.214, wherein R_3 is C_{1-8}alkyl-$N(R_6)(R_7)$, C_{1-8}alkyl-$C(O)N(R_6)(R_7)$, C_{1-8}alkyl- $P(O)(OR_9)(OR_{17})$, C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, C_{1-8}alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, C_{1-8}alkyl-$C(O)OR_9$, C_{1-8}alkyl-OR_{10};

1.216. Formula I, or any of 1.1-1.212, e.g., any of 1.1-1.109, 1.112, 1.130, 1.131, 1.132, 1.137, 1.142, 1.145, 1.150, 1.154, 1.157, 1.158, 1.212, or any of Formulae I(i)-I(v) or 2.10-1.215, wherein R_3 is R_3 is C_2alkyl-$N(R_6)(R_7)$, C_{1-2}alkyl-$C(O)N(R_6)(R_7)$, C_{1-8}alkyl- $P(O)(OR_9)(OR_{17})$, C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, C_{1-8}alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, C_{1-8}alkyl-$C(O)OR_9$, C_{1-8}alkyl-OR_{10};

1.217. any of Formulae 2.10-1.216, wherein R_3 is C_{1-8}alkyl (e.g., ethyl) substituted with $-N(R_6)(R_7)$;

1.218. any of formulae 2.10-1.216, wherein R_3 is C_{1-8}alkyl (e.g., methyl) substituted with $-C(O)N(R_6)(R_7)$;

1.219. any of formulae 2.12-1.218, wherein R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-propyl, n-butyl), $-C_{1-8}$alkyl-OR_{11}, $-C(O)OR_9$, $-C_{1-8}$alkyl-$C(O)OR_9$, $-C_{1-8}$alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$C(O)N(H)R_8$, $-C_{1-8}$alkyl-$P(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$ $-C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-

N(H)-S(O)$_2$(CF$_3$), 7,8-dimethyl-isoalloxazin-10-yl-C$_{1-8}$alkyl and aryl wherein said aryl and alkyl are optionally substituted with –COOR$_9$;

1.220. any of formulae 2.12-1.218, wherein R$_6$ and R$_7$ are independently selected from R$_6$ and R$_7$ are independently selected from –C$_{1-8}$alkyl-C(O)OR$_9$, -C$_{1-8}$alkyl(amine)-C(O)OR$_9$ (e.g., -CH$_2$CH$_2$CH(NH$_2$)COOH), –C$_{1-8}$alkyl-C(O)N(H)R$_8$, -C$_{1-8}$alkyl-P(O)(OR$_9$)(OR$_{17}$), -C$_{1-8}$alkyl-P(O)(OR$_9$)(NR$_{13}$R$_{14}$), -C$_{1-8}$alkyl-P(O)(NR$_{13}$R$_{14}$)(NR$_{15}$R$_{16}$), -C$_{1-8}$alkyl-OP(O)(OR$_9$)(OR$_{17}$), -C$_{1-8}$alkyl-OP(O)(OR$_9$)(NR$_{13}$R$_{14}$) -C$_{1-8}$alkyl-OP(O)(NR$_{13}$R$_{14}$)(NR$_{15}$R$_{16}$), 7,8-dimethyl-isoalloxazin-10-yl-C$_{1-8}$alkyl and aryl wherein said aryl and alkyl are optionally substituted with –COOR$_9$;

1.221. any of formulae 2.12-1.218, wherein R$_6$ and R$_7$ are independently selected from –C$_{1-8}$alkyl-COOR$_9$ (e.g., -methyl-COOR$_9$, -ethyl-COOR$_9$, -propyl-COOR$_9$, hexyl-COOR$_9$), wherein said alkyl is optionally substituted with –COOR$_9$ (e.g., -C(H)(COOR$_9$)-CH$_2$CH$_2$-COOR$_9$ or -C(H)(COOR$_9$)- CH$_2$-COOR$_9$);

1.222. any of formulae 2.12-1.218, wherein R$_6$ and R$_7$ are independently selected from R$_6$ and R$_7$ are independently selected from –C$_{1-8}$alkyl-C(O)OR$_9$, -C$_{1-8}$alkyl(amine)-C(O)OR$_9$ (e.g., -CH$_2$CH$_2$CH(NH$_2$)COOH), -C$_{1-8}$alkyl-P(O)(OR$_9$)(OR$_{17}$), -C$_{1-8}$alkyl-P(O)(OR$_9$)(NR$_{13}$R$_{14}$), -C$_{1-8}$alkyl-P(O)(NR$_{13}$R$_{14}$)(NR$_{15}$R$_{16}$), 7,8-dimethyl-isoalloxazin-10-yl-C$_{1-8}$alkyl, or aryl, wherein said aryl and alkyl are optionally substituted with –COOR$_9$;

1.223. any of formulae 2.12-1.218, wherein R$_6$ and R$_7$ are independently –C$_{1-8}$alkyl-C(O)OR$_9$ wherein said alkyl is optionally substituted with –COOR$_9$;

1.224. any of formulae 2.12-1.218, wherein R$_6$ and R$_7$ are independently -C$_{1-8}$alkyl(amine)-C(O)OR$_9$ (e.g., -CH$_2$CH$_2$CH(NH$_2$)COOH);

1.225. any of formulae 2.12-1.218, wherein R$_6$ and R$_7$ are independently -C$_{1-8}$alkyl-P(O)(NR$_{13}$R$_{14}$)(NR$_{15}$R$_{16}$);

1.226. any of formulae 2.12-1.218, wherein R$_6$ and R$_7$ are independently -C$_{1-8}$alkyl-P(O)(OR$_9$)(OR$_{17}$);

1.227. any of formulae 2.12-1.218, wherein R$_6$ and R$_7$ are independently 7,8-dimethyl-isoalloxazin-10-yl-C$_{1-8}$alkyl;

1.228. any of formulae 2.12-1.218, wherein R_6 and R_7 are independently aryl wherein said aryl is optionally substituted with –$COOR_9$;

1.229. any of formulae 2.12-1.228, wherein R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$, -CH(isopropyl)-$COOR_{18}$, -CH(isobutyl)-$COOR_{18}$, -CH(sec-butyl)-$COOR_{18}$), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –CH(CH_2CH_2COOH)-COOH);

1.230. any of formulae 2.12-1.228, wherein R_{13}, R_{14}, R_{15} and R_{16} are independently H, C_{1-8}alkyl;

1.231. any of formulae 2.12-1.228, wherein R_{13}, R_{14}, R_{15} and R_{16} are independently -$CH(CH_3)COOR_{18}$;

1.232. Formula I, or any of 1.1-1.212, e.g., any of 1.1-1.109, 1.157, 1.212, or any of Formulae I(i)-I(iv), 1.213-1.222, wherein R_3 is –C_{1-8}alkyl-$C(O)OR_9$;

1.233. Formula I, or any of 1.1-1.212, e.g., any of 1.1-1.109, 1.112, 1.158, 1.212, or any of Formulae I(i)-I(v) or 2.10-1.222, wherein R_3 is –C_{1-8}alkyl-OR_{10};

1.234. formula 1.233, wherein R_{10} is selected from H, C_{1-8}alkyl (e.g., methyl or ethyl), -C_{1-8}alkyl-OR_{11}, –C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)$COOH), –C_{1-8}alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$N(H)\text{-}S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl, or aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$, or –C_{1-4}alkyl-$OC(O)R_{12}$;

1.235. formula 1.233, wherein R_{10} is selected from–C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)$COOH), -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

1.236. formula 1.233, wherein R_{10} is –C_{1-8}alkyl-$C(O)OR_9$;

1.237. formula 1.233, wherein R_{10} is -propyl-$COOR_9$

1.238. any of Formulae I(i)-I(iv), 2.10-1.236, wherein R_9 is ethyl;

1.239. any of Formulae I(i)-I(iv), 2.10-1.236, wherein R_9 is t-butyl;

1.240. any of Formulae I(i)-I(iv), 2.10-1.236, wherein R_9 is isopropyl;

1.241. any of Formulae I(i)-I(iv), 2.10-1.236, wherein R_9 is n-butyl;

1.242. any of Formulae I(i)-I(iv), 2.10-1.241, wherein R_{18} is ethyl;

1.243. any of Formulae I(i)-I(iv), 2.10-1.241, wherein R_9 and R_{17} are independently H or $-CH_2-OC(O)R_{12}$;

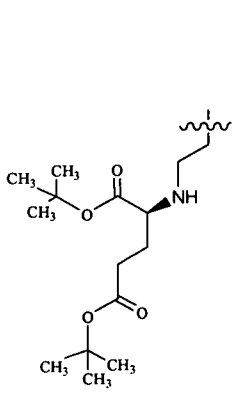
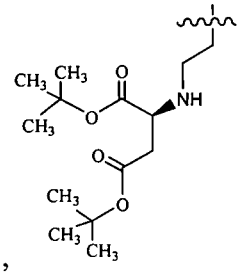
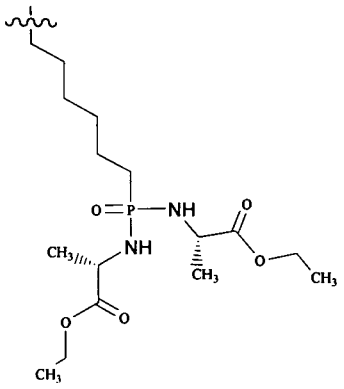
1.244. any of Formulae I(i)-I(iv), 2.10-1.237, wherein R_9 and R_{17} are independently H;

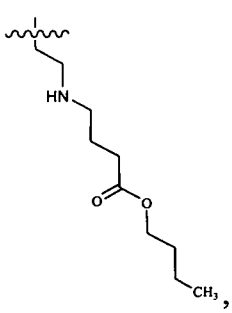
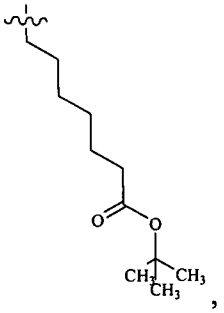
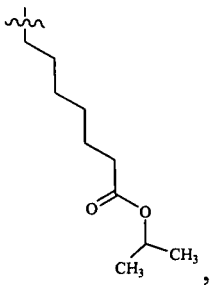
1.245. any of Formulae I(i)-I(iv), 2.10-1.237, wherein R_9 and R_{17} are independently $-CH_2-OC(O)R_{12}$;

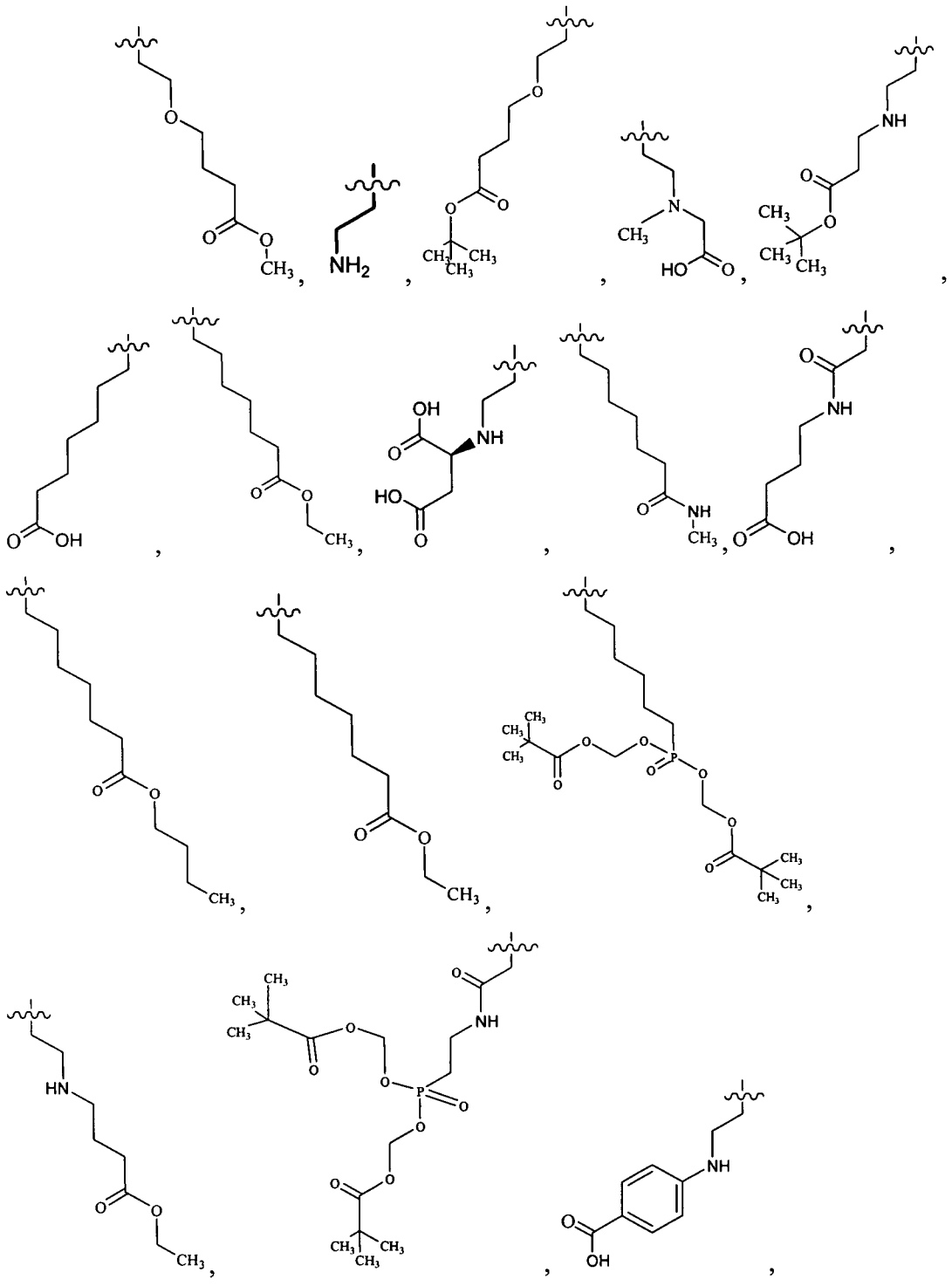
1.246. any of Formulae I(i)-I(iv), 2.10-1.237, wherein R_9 and R_{17} are independently C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl);

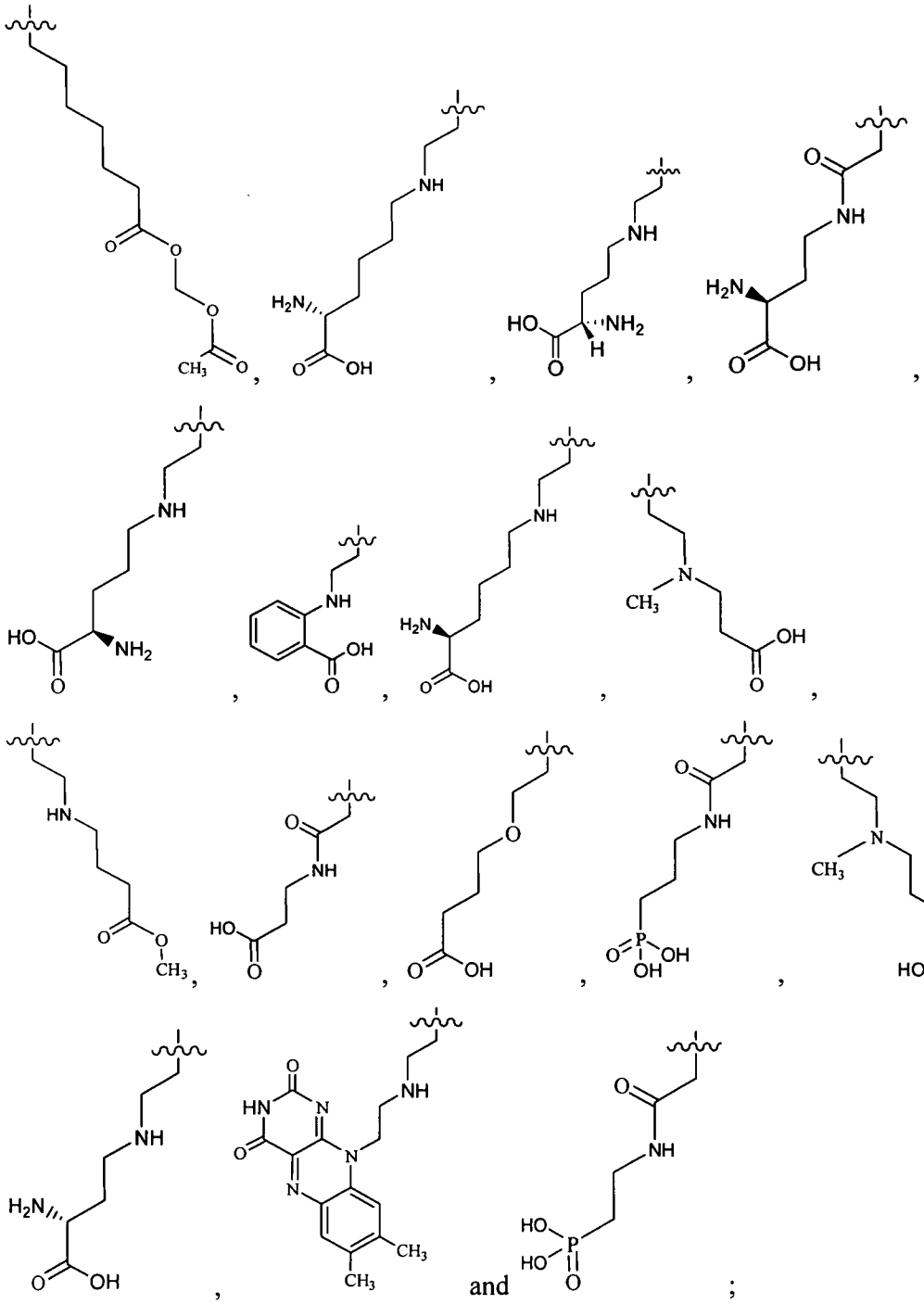
1.247. any of Formulae I(i)-I(iv), 2.10-1.237, wherein R_9 and R_{17} are independently phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

1.248. any of the preceding formulae, wherein R_3 is selected from any of the following:


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and ;

1.249. formulae 1.248, wherein R_6 and R_7 are independently selected from –C_{1-8}alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl, wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

1.250. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.249,,wherein R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -N(R_4)(R_5), C_{3-7}cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl);

1.251. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.250,wherein R_2 is dimethylamino;

1.252. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.250,, wherein R_2 is cyclopropylamino;

1.253. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.250,, wherein R_2 is chloro;

1.254. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.250,, wherein R_2 is H;

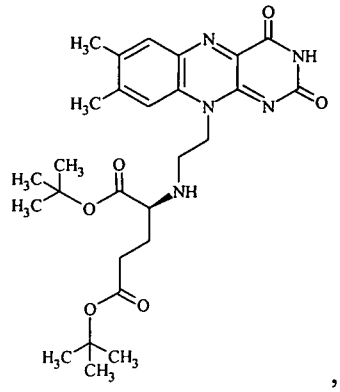
1.255. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.250,, wherein R_2 is 2,2-dimethylpropyl;

1.256. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.250,, wherein R_2 is hydroxyl-C_{1-8}alkylamino (e.g., hydroxyethylamino);

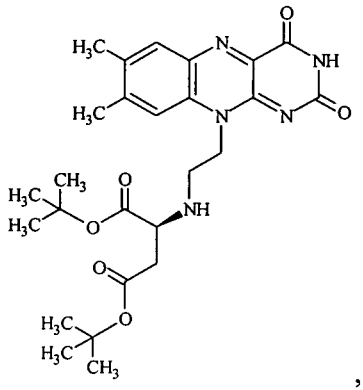
1.257. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.256, wherein R_1 is H, C_{1-8} alkyl (e.g., methyl) or C_{3-7} cycloalkyl;

1.258. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.256, wherein R_1 is H, C_{1-8} alkyl (e.g., methyl);

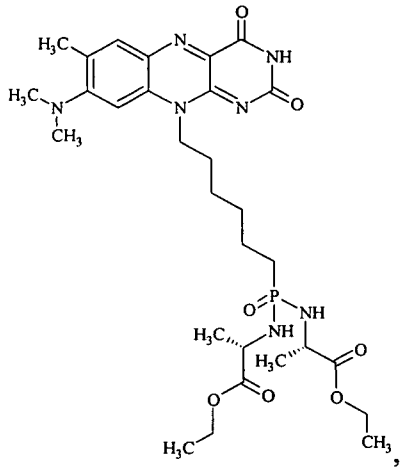
1.259. Formula I, or any of 1.1-1.212, or any of formulae I(i)-I(iv), e.g., any of 1.213-1.258, selected from any of the following:

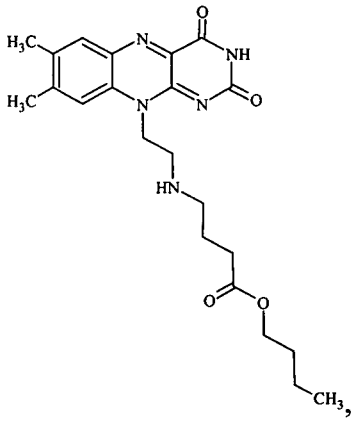


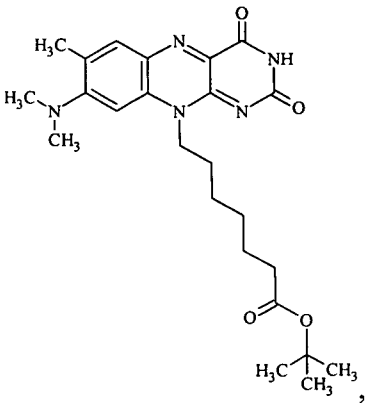
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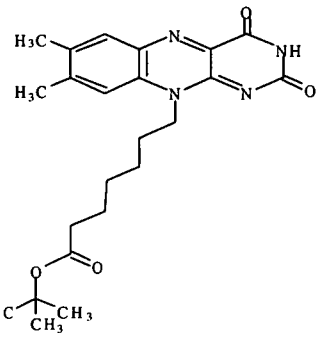


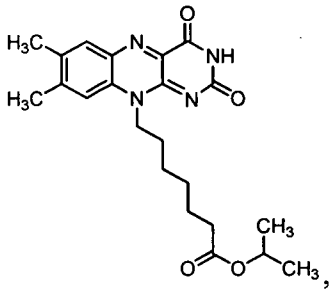
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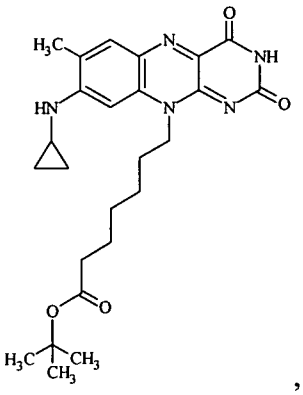


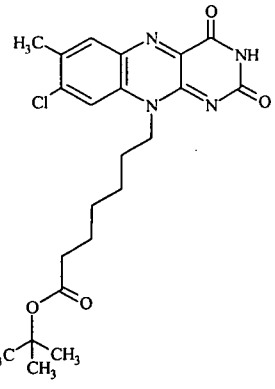


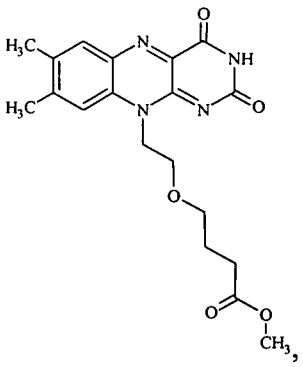


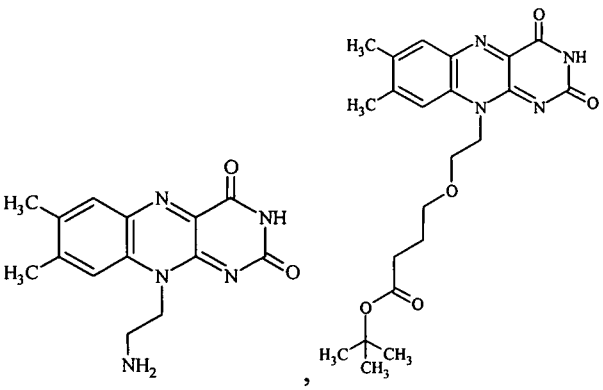


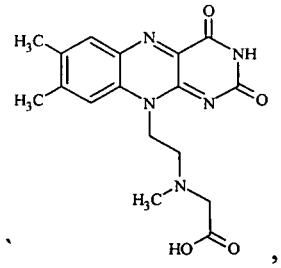
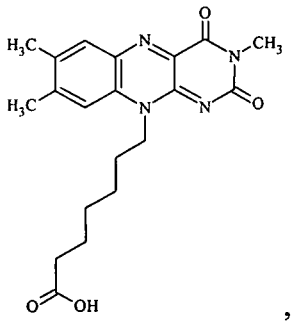
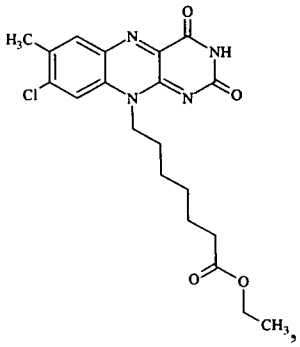
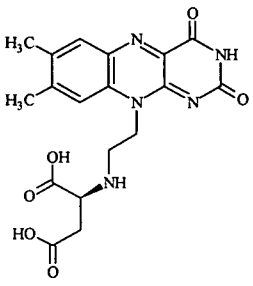
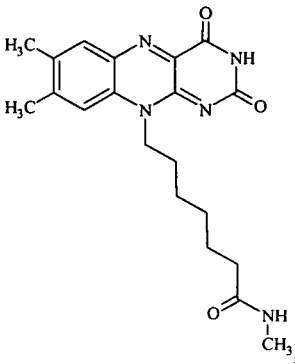
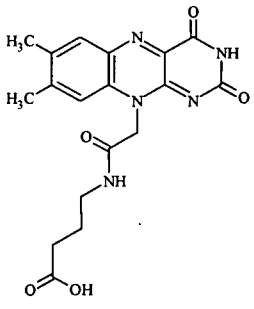
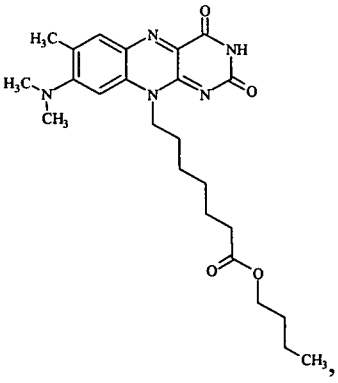
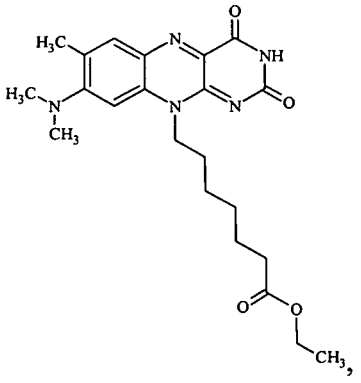


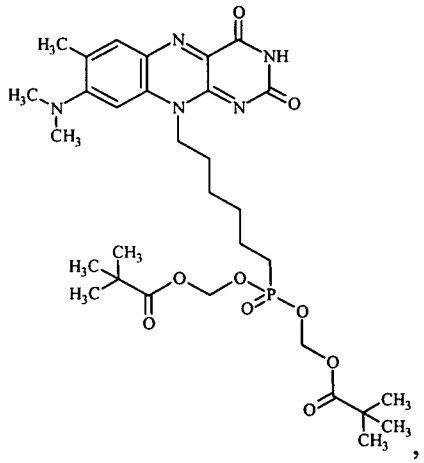
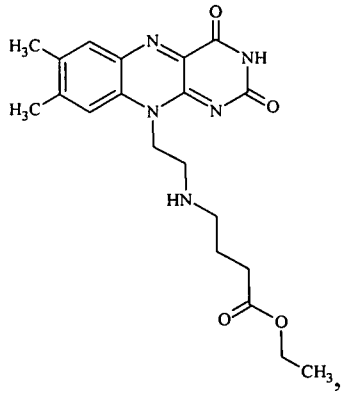
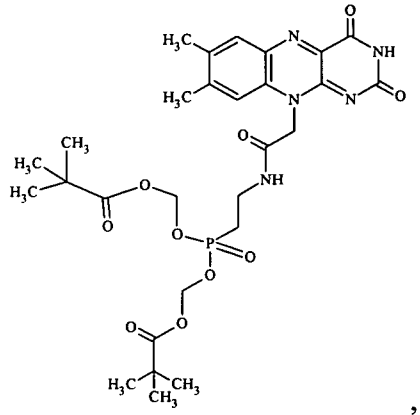
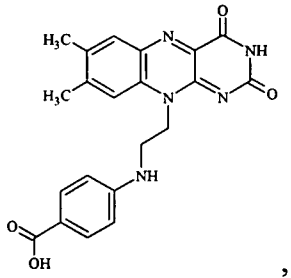
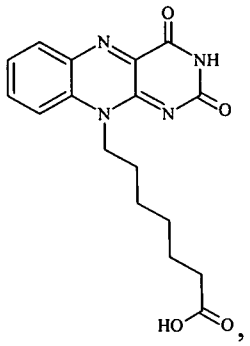
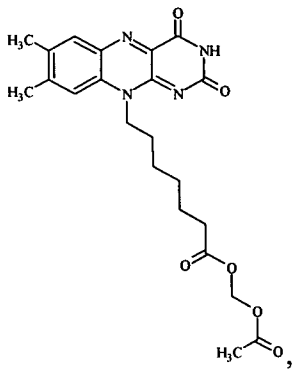
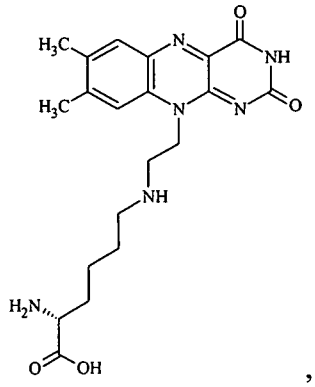
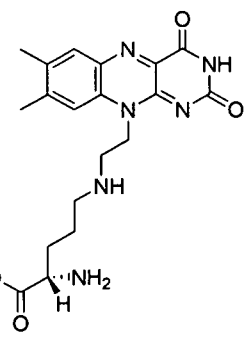
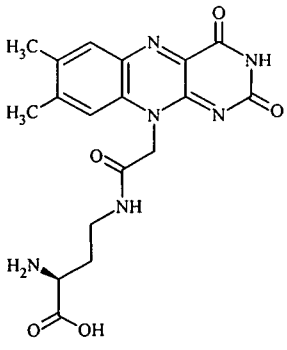
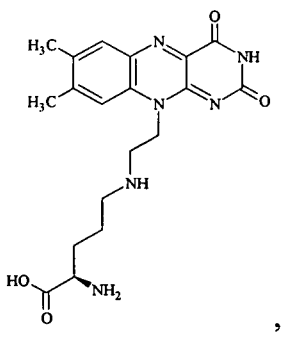


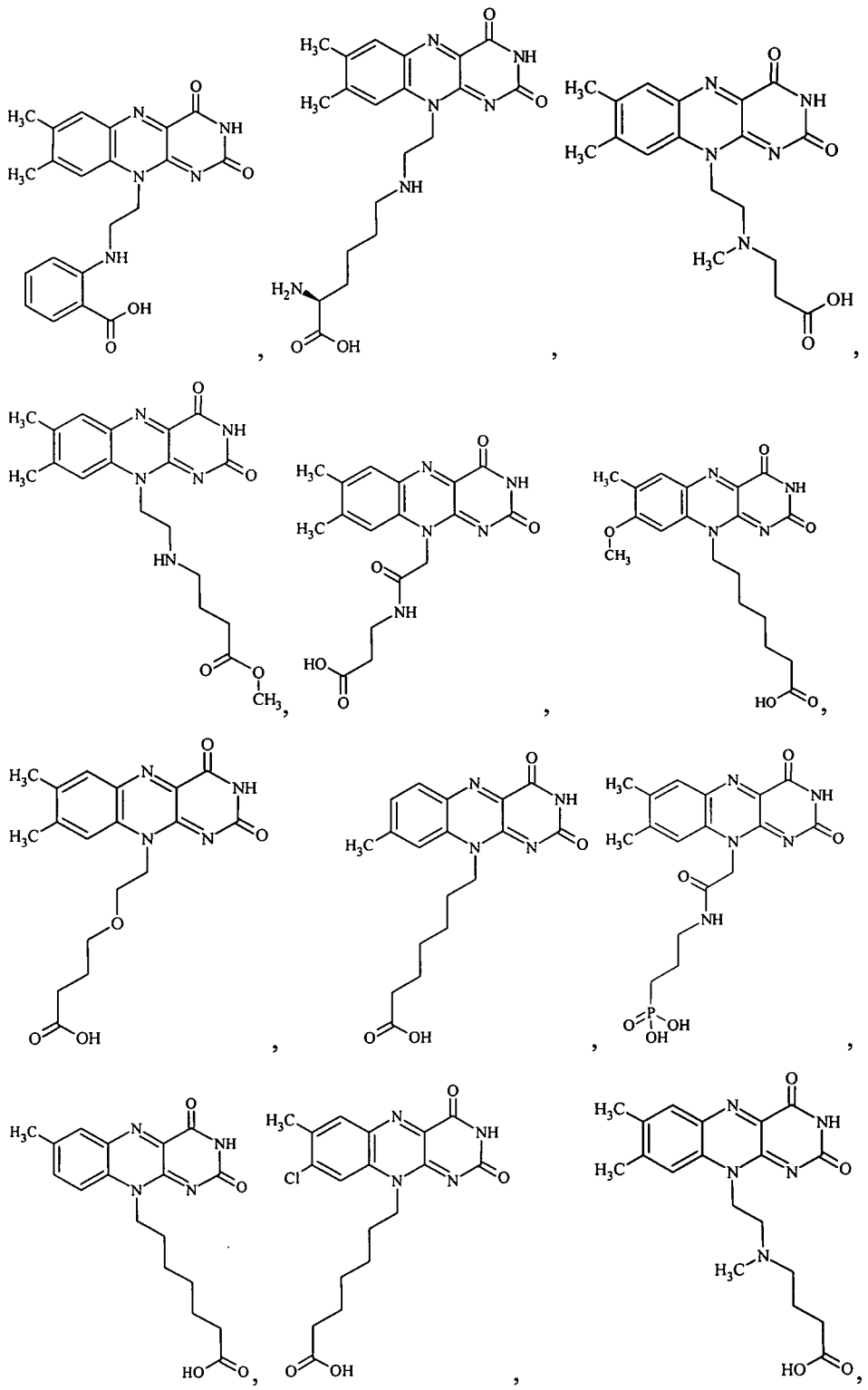


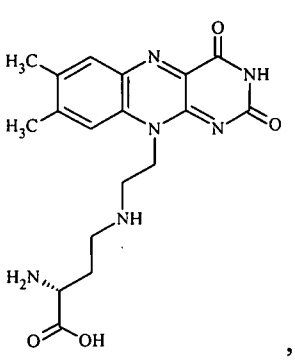
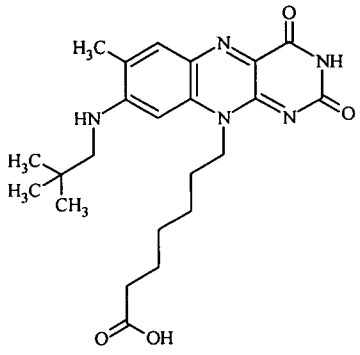
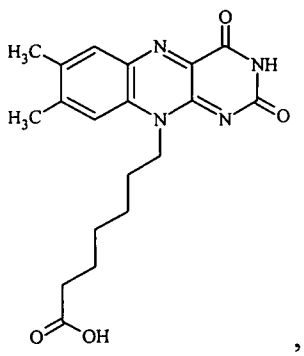
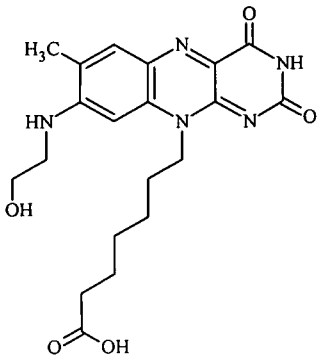
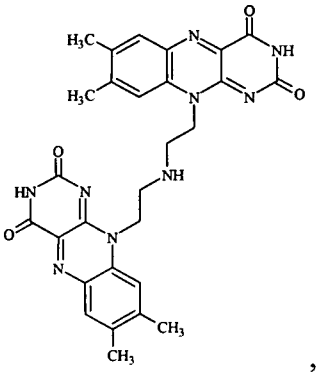
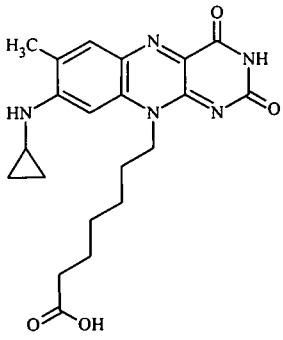
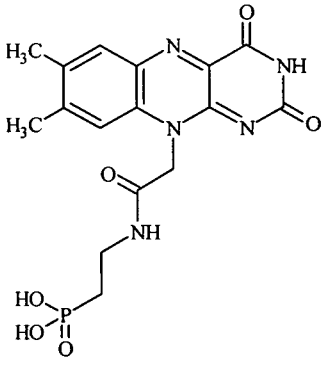



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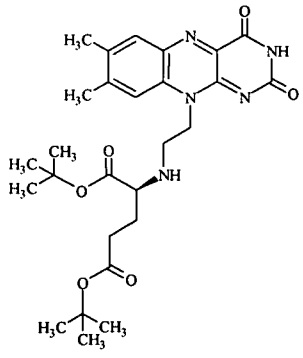
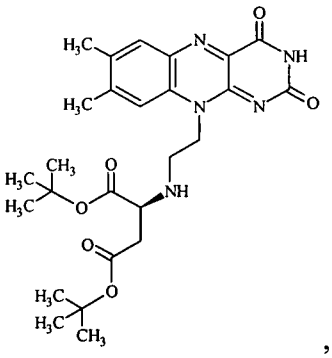
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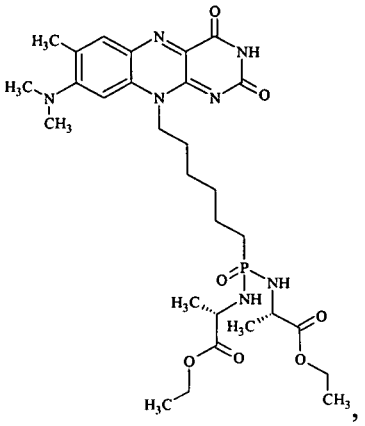

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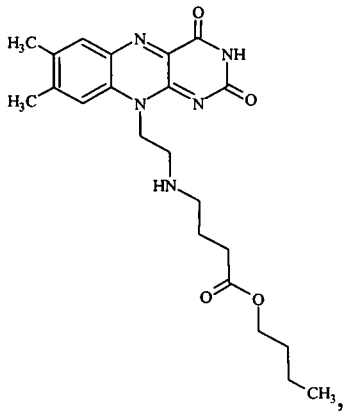

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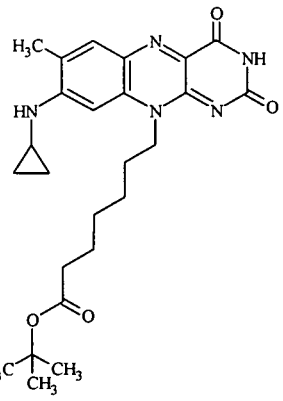

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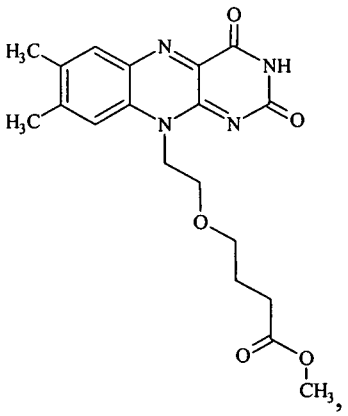
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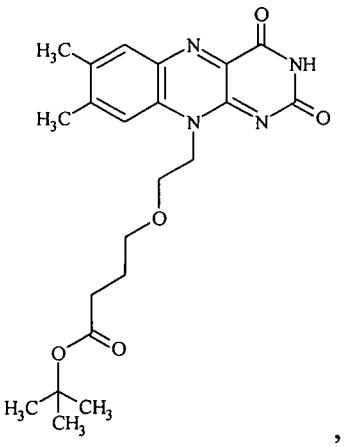
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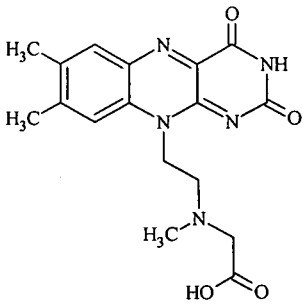
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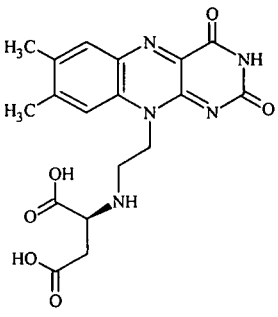
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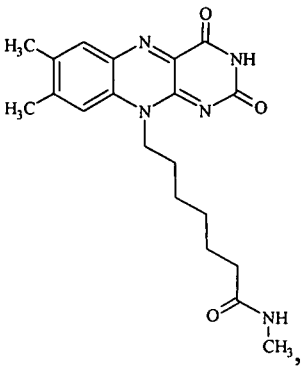
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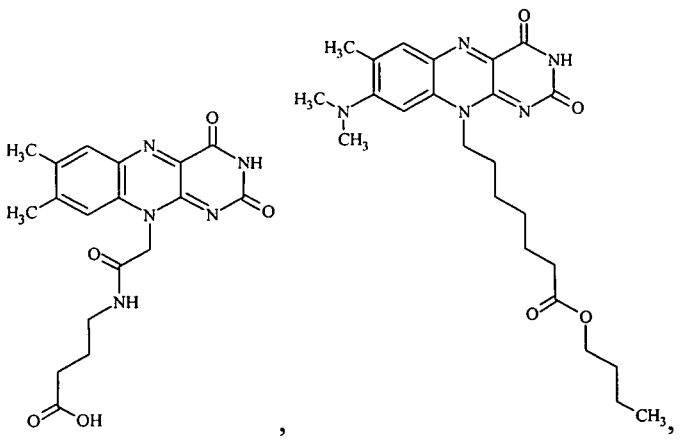
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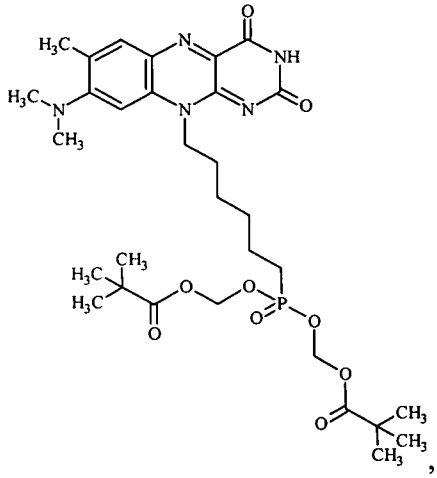
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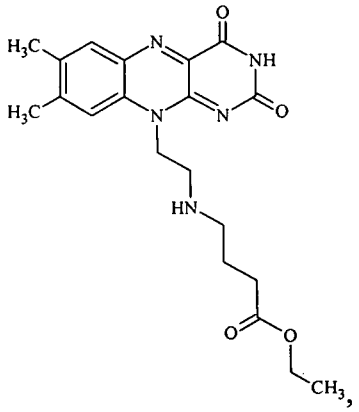
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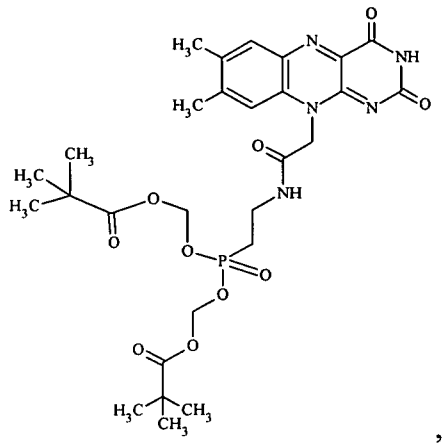
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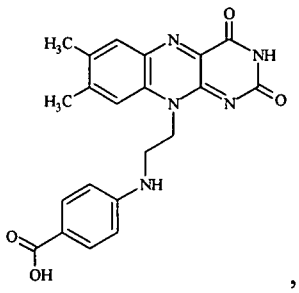
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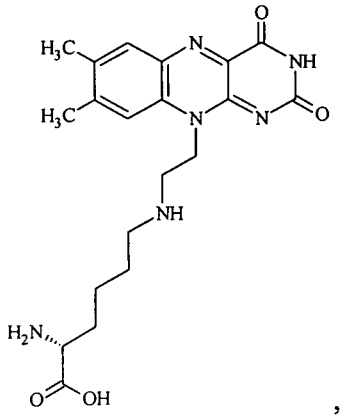
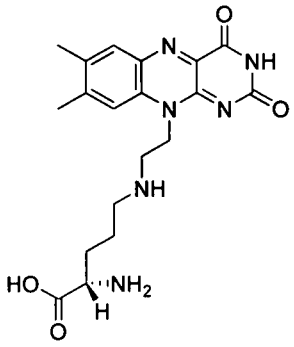
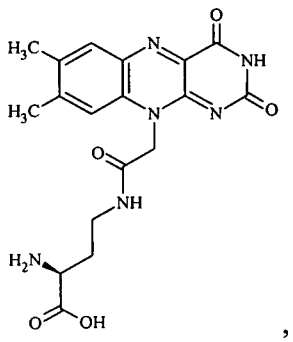
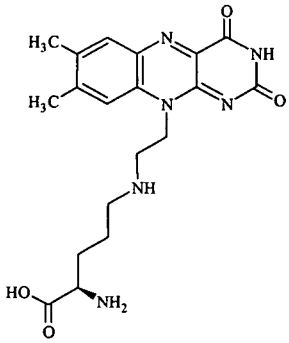
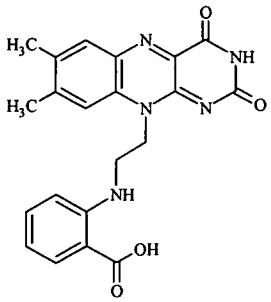
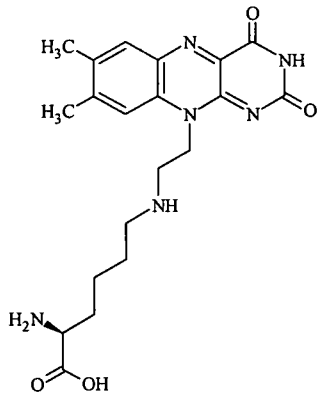
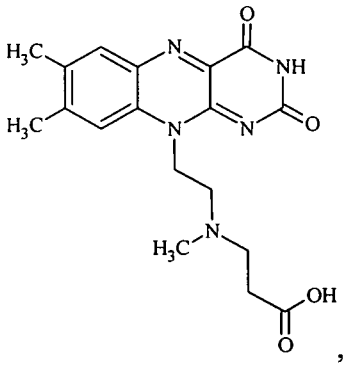
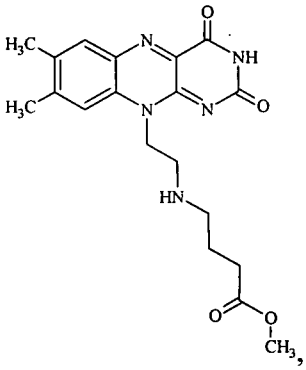
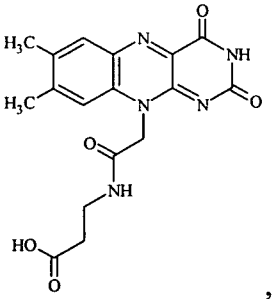
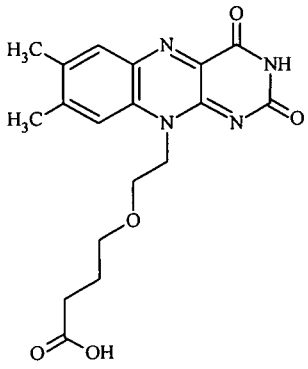
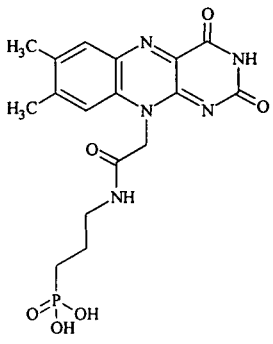
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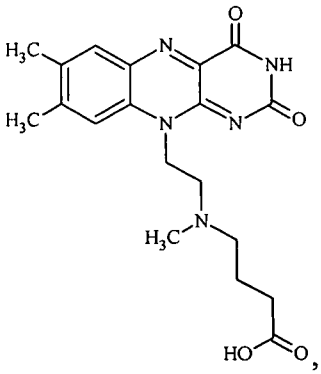
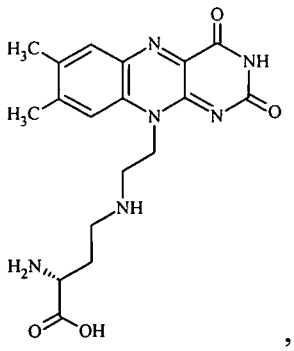
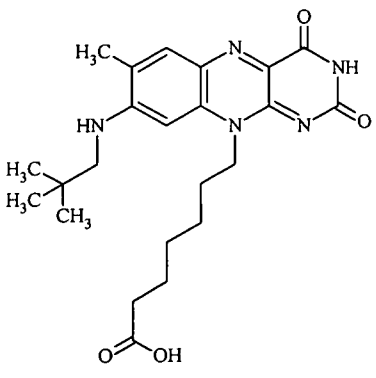
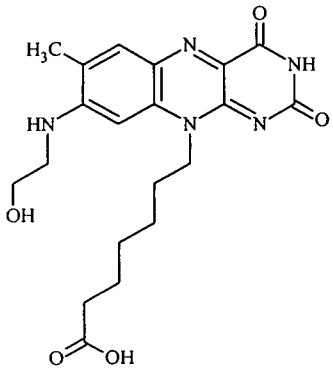
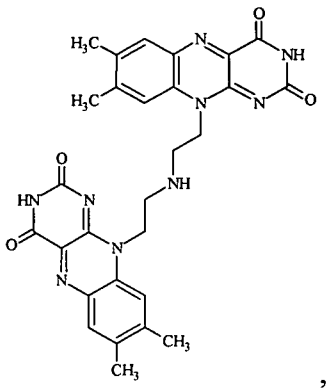
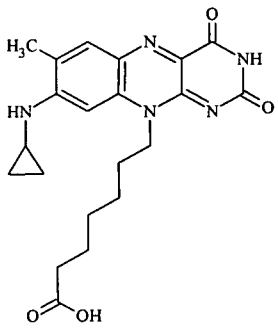
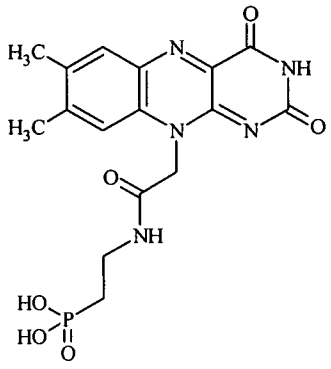


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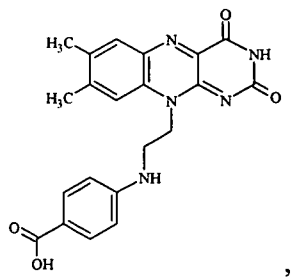
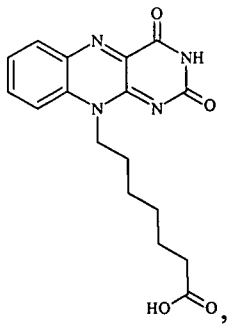
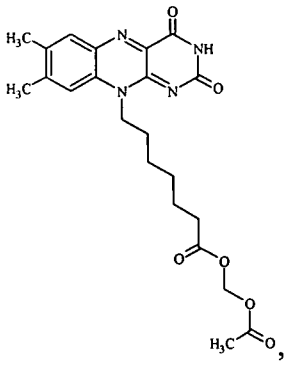


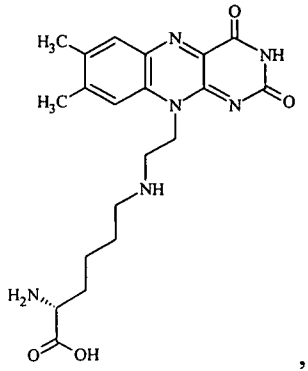
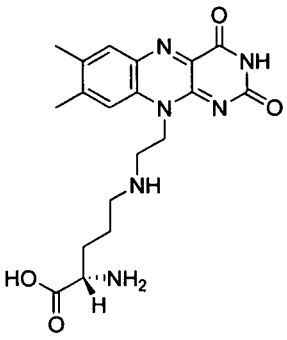
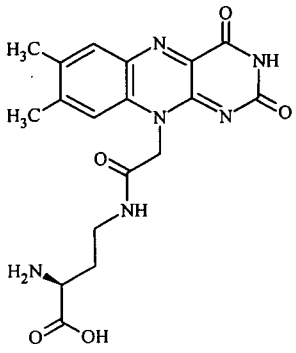
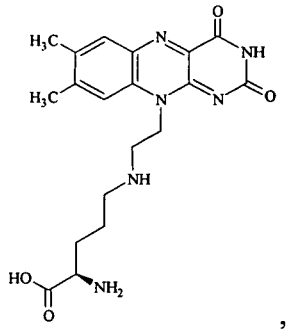
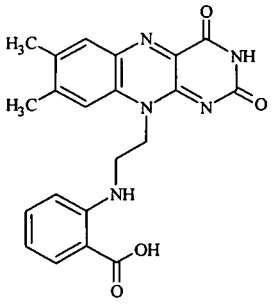
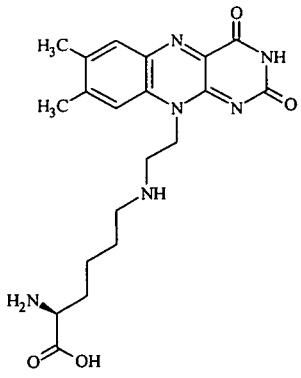
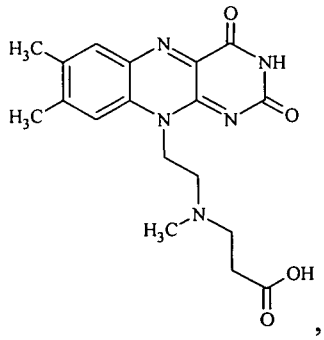
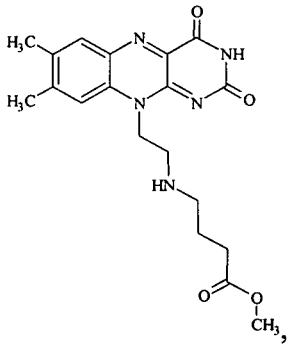
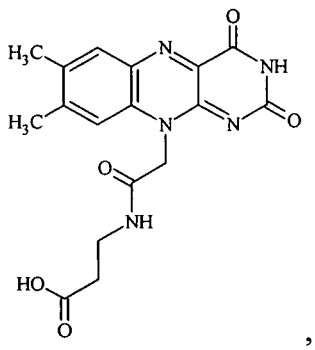
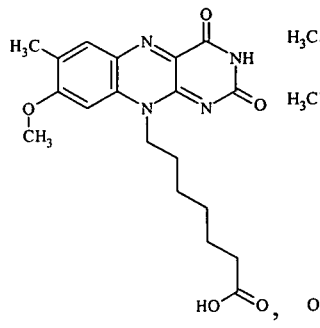
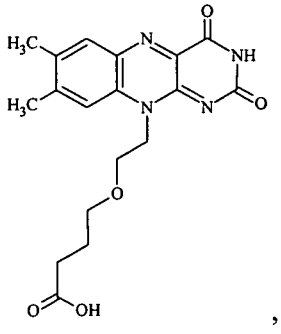
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1.261. Formula I, or any of 1.1-1.259, selected from any of the following:

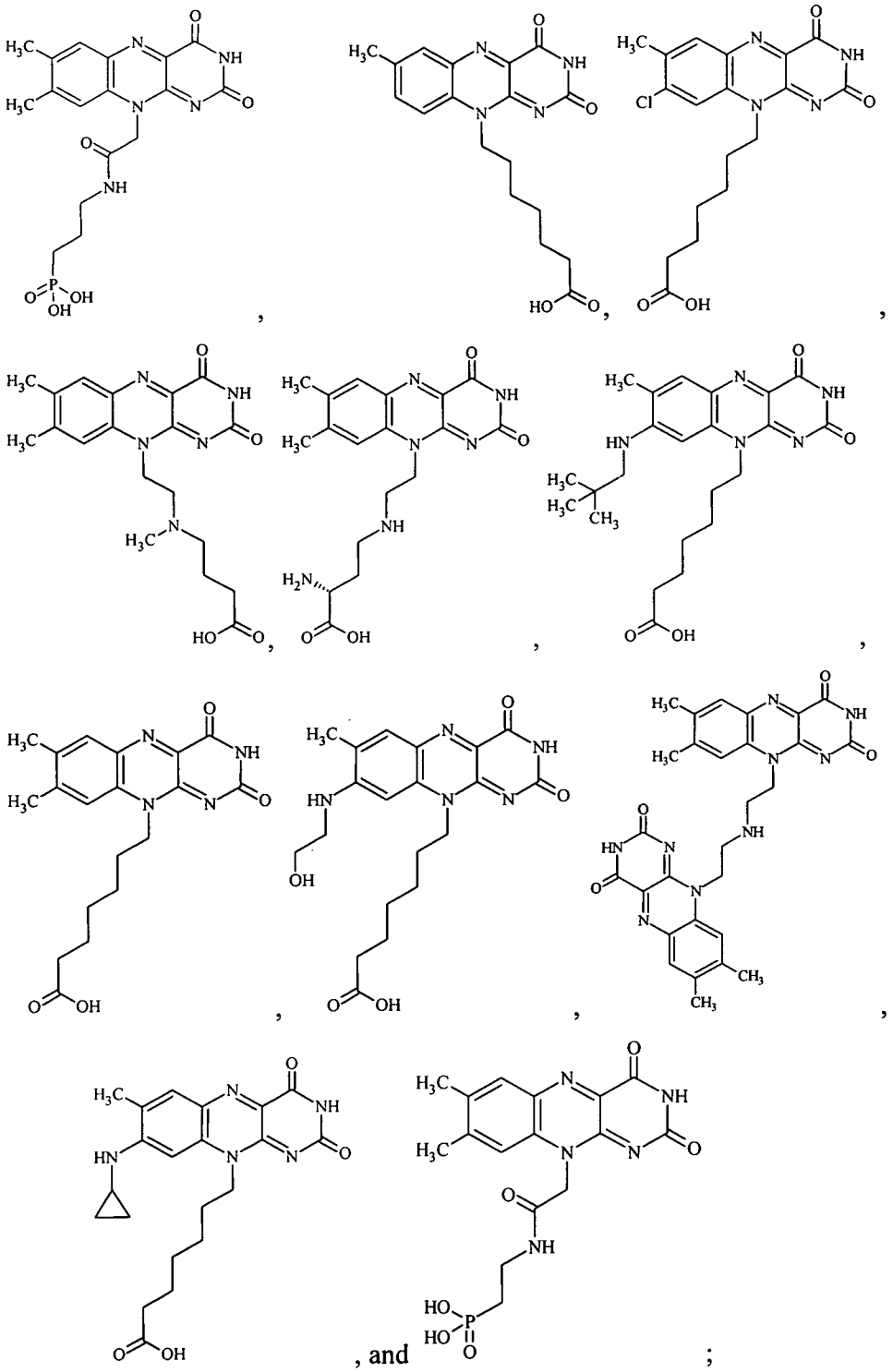

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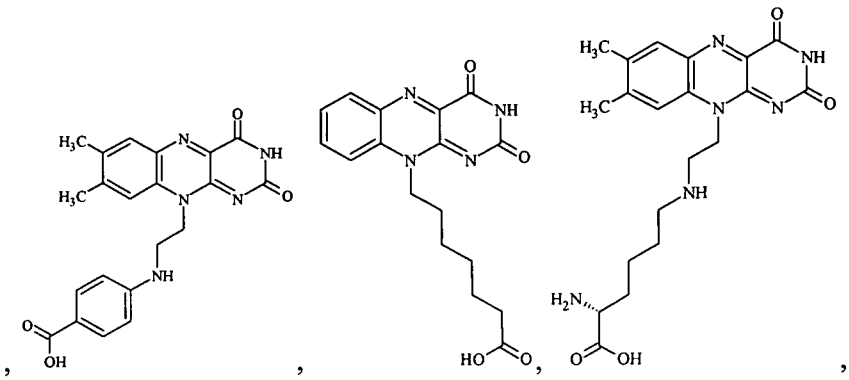
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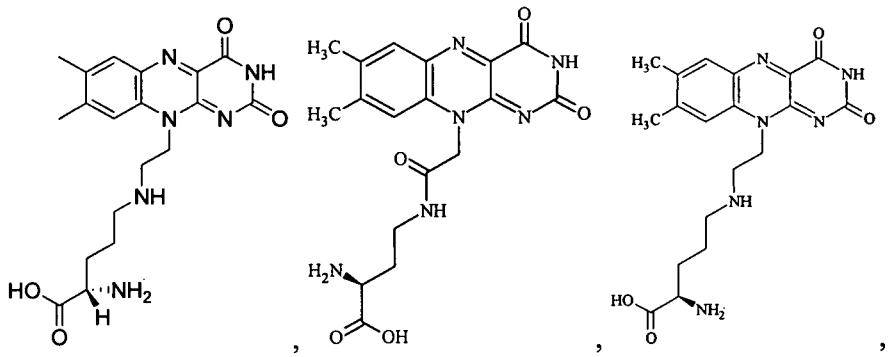
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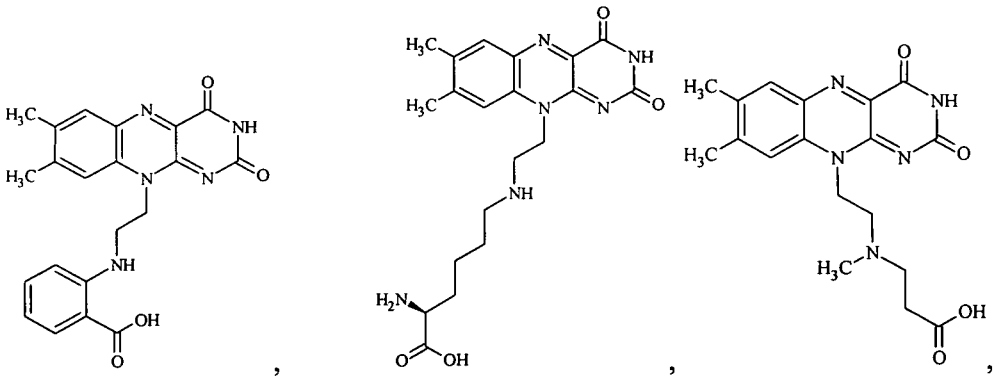
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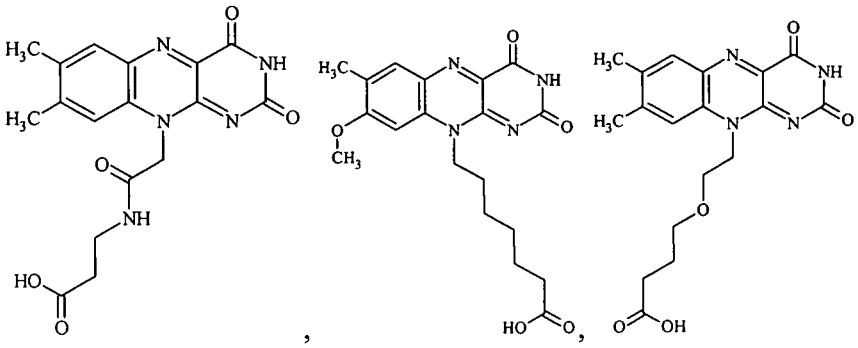


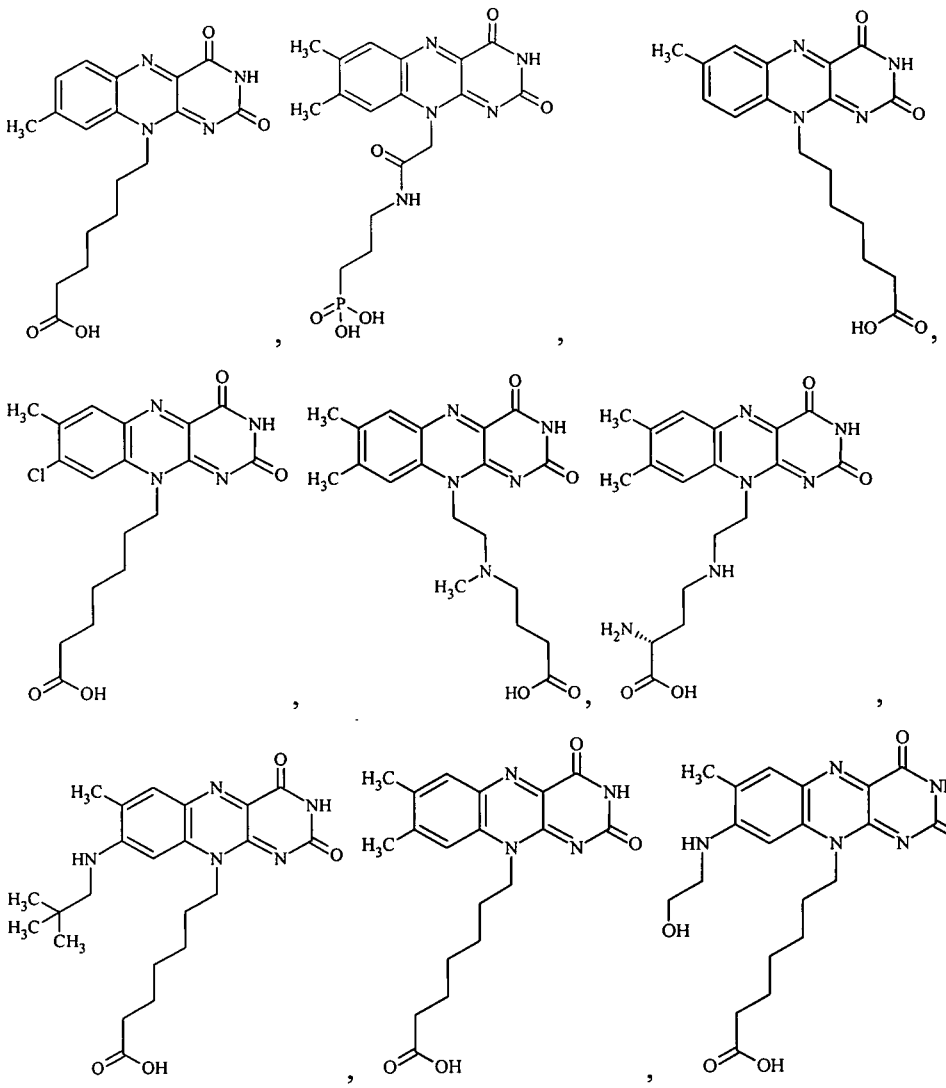
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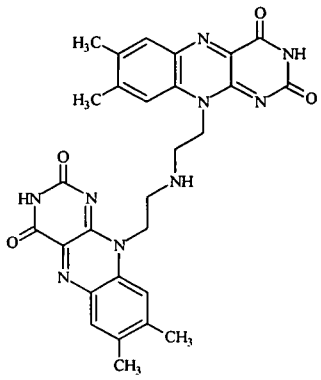
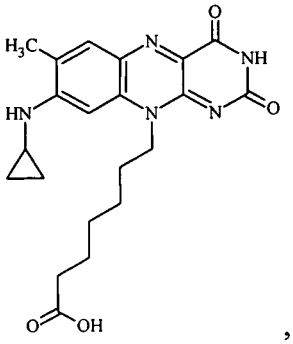
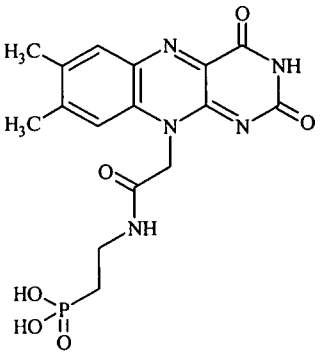




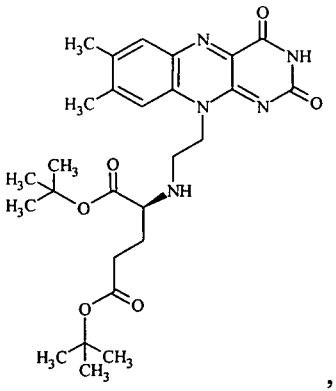
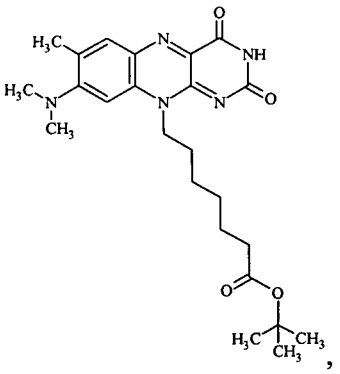
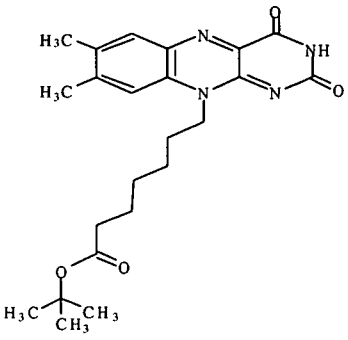
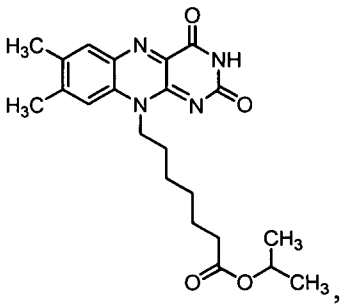


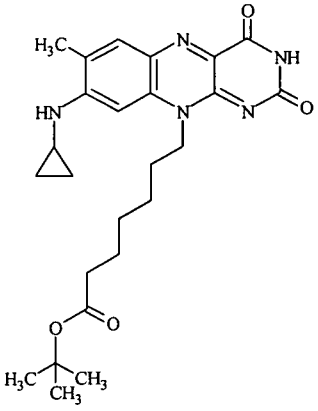
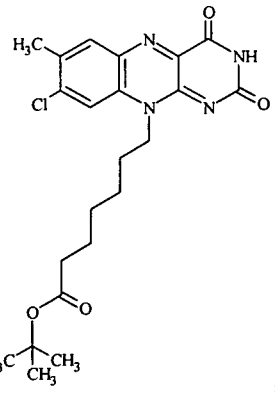
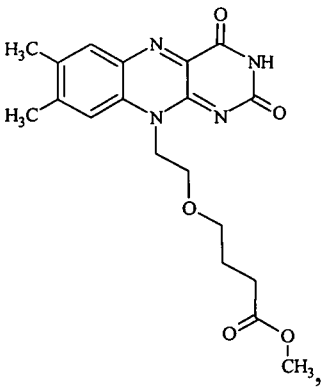
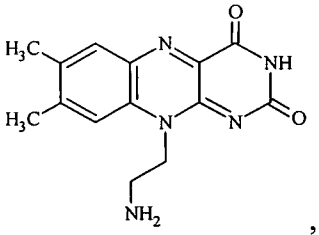
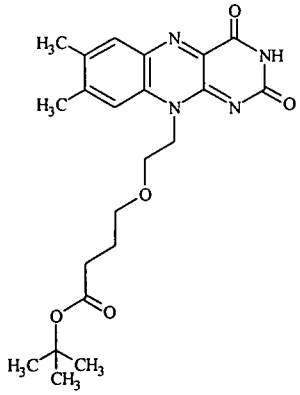
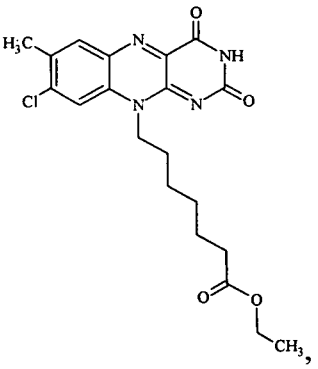
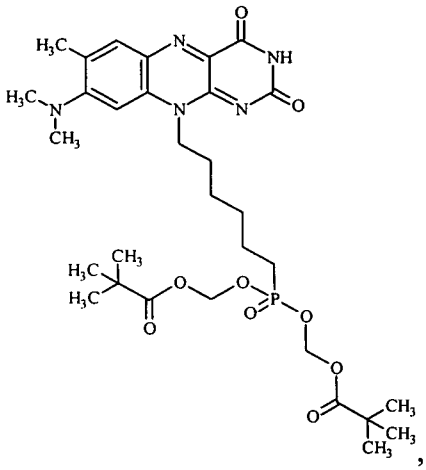
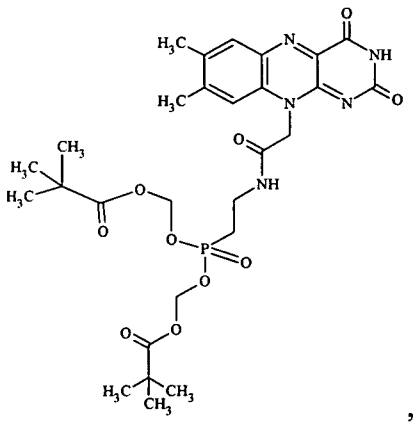
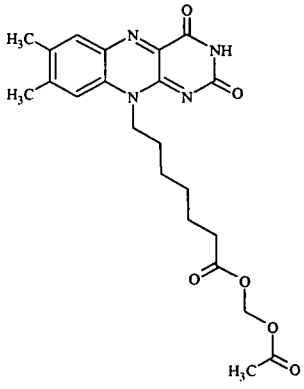
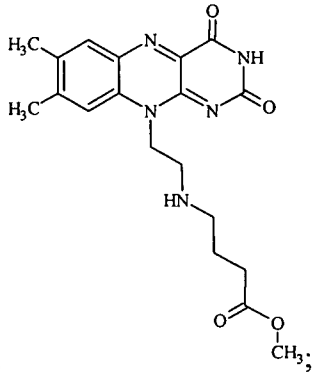




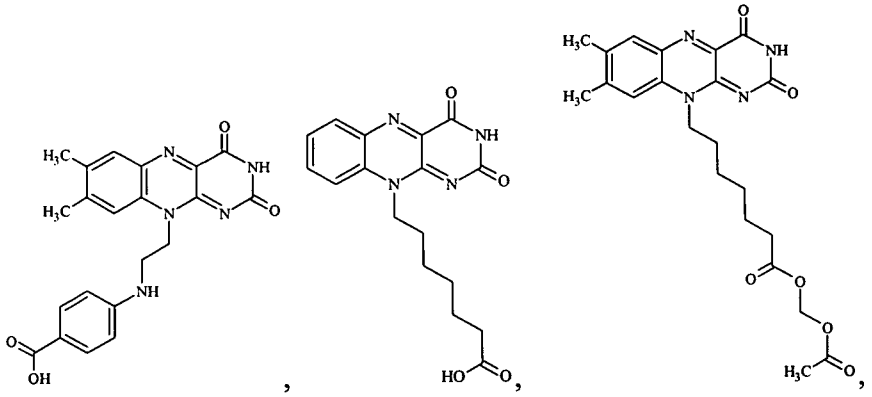

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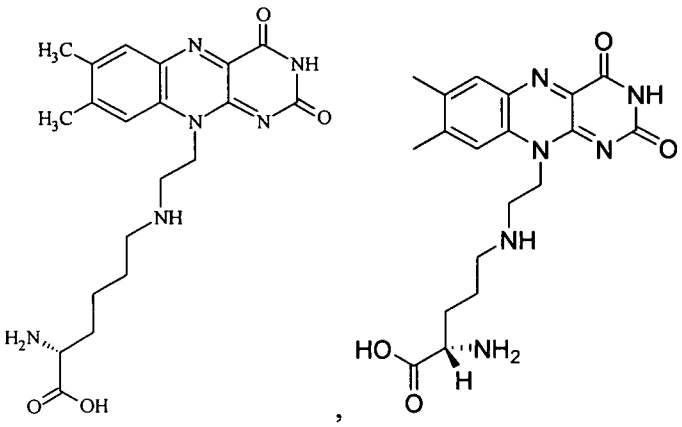
1.263. Formula I, or any of 1.1-1.259, selected from any of the following:

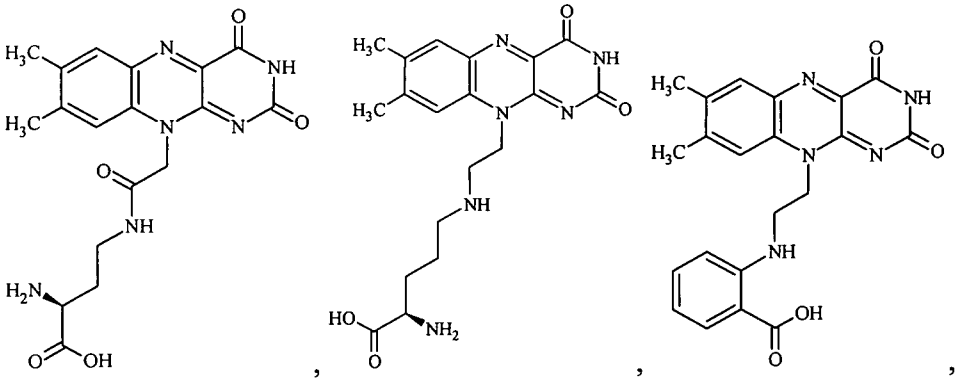

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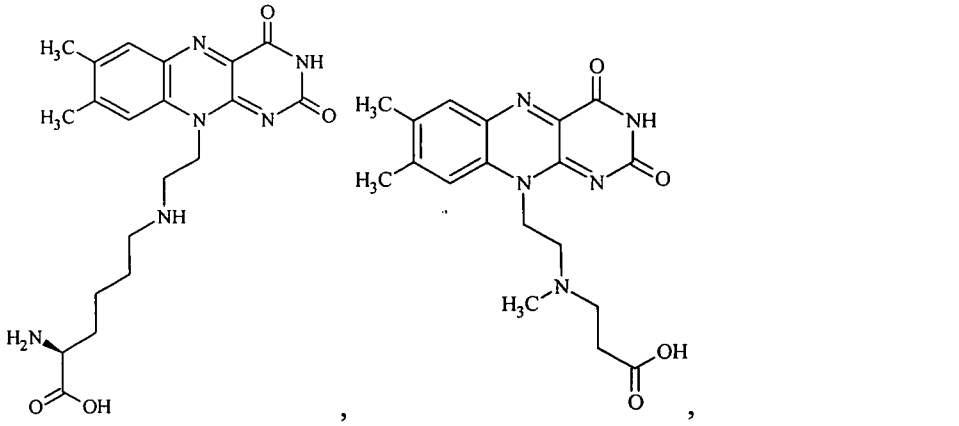

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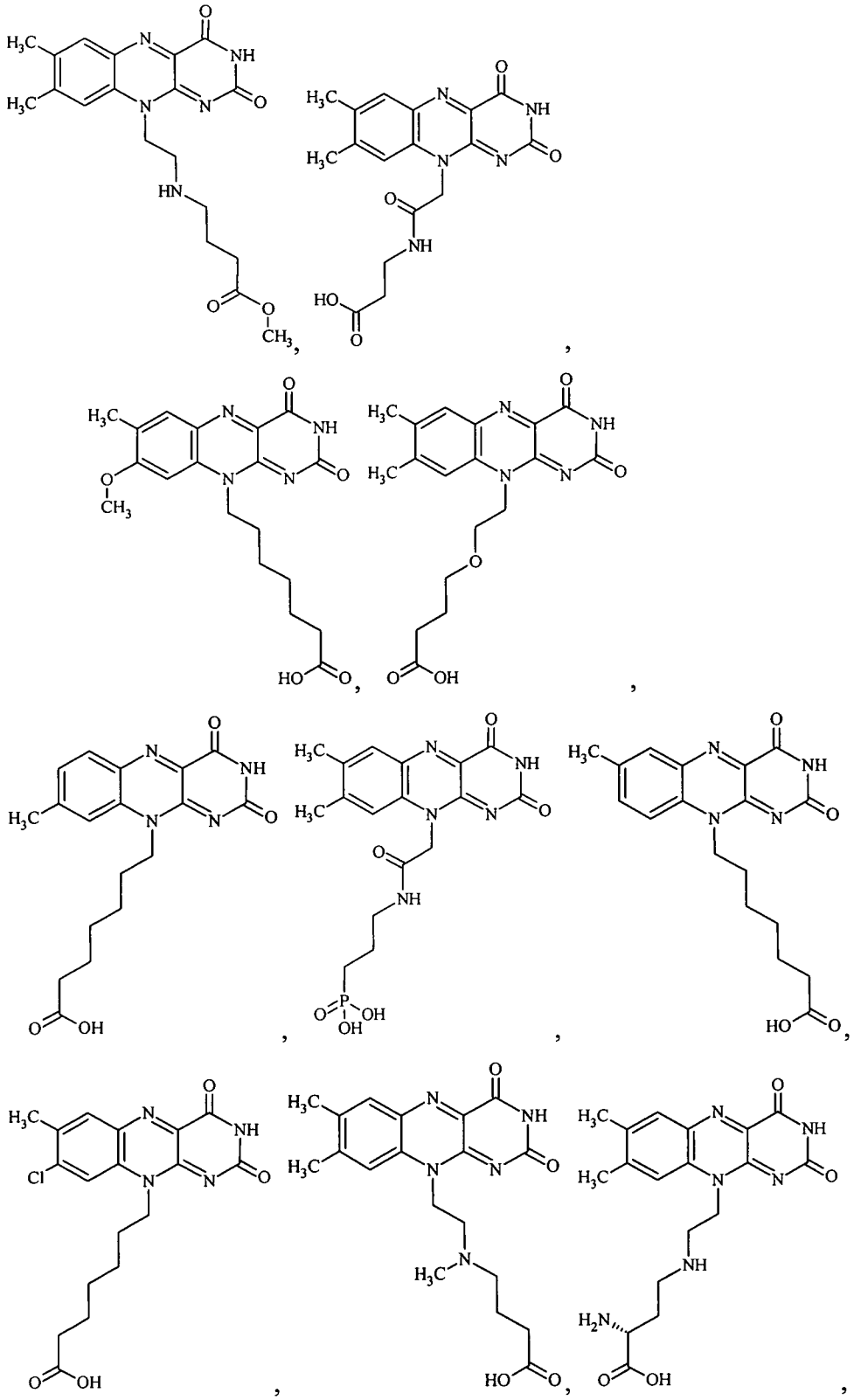
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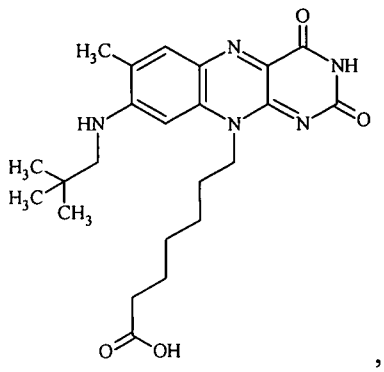
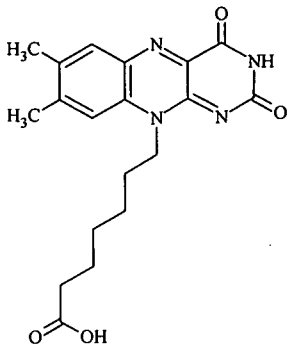
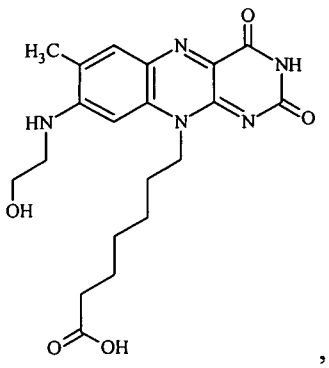
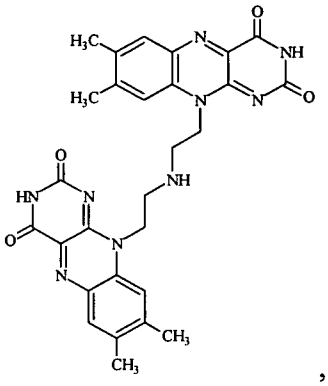
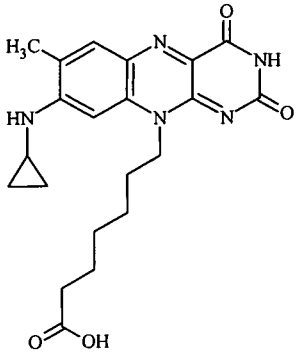
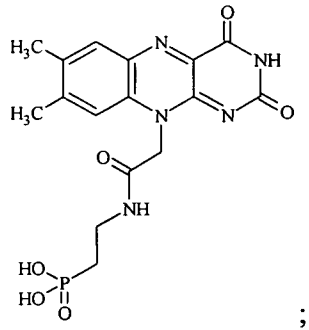

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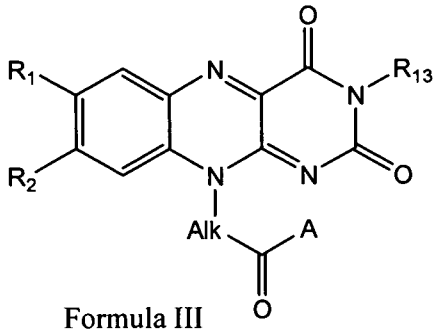



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1.265. Formula I, or any of 1.1-1.264, wherein the Compound of Formula I binds to FMN riboswitch, e.g., with an IC_{50} of less than or equal to 10μM, preferably less than 1μM, more preferably less than 100 nM, most preferably less than 10nM in a binding assay, for example, as described in Example 1 and/or has a minimum inhibitory concentration of less than 128μg/mL, preferably less than 32μg/mL in an assay, for example, as described in Example 1A,

in free, salt or prodrug form.

[0015] In a particular aspect, the invention relates to a Compound of formula III,



Formula III

wherein:

(i) Alk is C_{1-8} alkyl (e.g., n-butyl, n-pentyl, n-hexyl, 6,6-dimethylhexyl, n-heptyl);

(ii) A is $-OR_9$ or $-N(R_{14})(R_{15})$;

(iii) R_9 is H, $-C_{1-8}$alkyl (e.g., methyl, ethyl, n-propyl, isopropyl, 1-methylpropyl, t-butyl, n-butyl, 1,1-dimethylpropyl, 2,2-dimethylpropyl, hex-5-ynyl), -haloC_{1-8}alkyl (e.g., 2,2,2-trifluoroethyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, $-C_{1-4}$alkyl-O-C_{1-4}alkyl (e.g., $-C(CH_3)(CH_3)OCH_3$ or $-C(CH_3)(CH_3)CH_2OCH_3$), $-C_{1-4}$alkyl-C(O)-(morphylin-4-yl), $-C_{3-7}$cycloalkyl (e.g., cyclopentyl, cyclohexyl), C_{3-7}cycloalkyl-C_{1-4}alkyl (e.g., norbornan-2-yl-methyl) wherein the cycloalkyl is optionally substituted with hydroxy group; aryl (e.g., phenyl) or aryl-C_{1-4}alkyl (e.g, Benzyl, 1-methyl-2-phenylethyl), wherein said aryl is optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl, 2-methoxyphenyl, 2-(3,4-dihydroxyphenyl)ethyl);

(iv) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(v) R_2 is H, halo (e.g., chloro), -O-C_{3-7}cycloalkyl (e.g., -O-cyclopentyl), -O-C_{0-7} alkylC_{3-7}cycloalkyl (e.g., -O-cyclopentyl, -O-CH_2-cyclopentyl), -$N(R_4)(R_5)$, -(CH_2)-$N(R_4)(R_5)$, -C_{0-4}alkyl-C_{3-7}cycloalkyl (e.g., cyclopropyl, cyclopentylmethyl), heteroC_{3-7}cycloalkyl (e.g., pyrrolidin-1-yl), 1-cyclopropyl-6-fluoro-7-[4-piperazin-1-yl]-4-oxo-quinoline-3-carboxylic acid), C_{1-8}alkyl (e.g., methyl or ethyl) or $-O-C_{1-8}$alkyl (e.g., methoxy), wherein the alkyl group is optionally substituted with one or more halo (e.g., fluoro) or hydroxy groups (e.g., trifluoromethyl, -O-CH_2CH_2OH);

(vi) R_4 and R_5 are independently

a. H,

b. $-C_{0-4}$alkyl-C_{3-7}cycloalkyl (e.g., cyclopropyl, cyclopentyl, cyclohexyl or cyclopentyl-methyl),

c. heteroC_{3-7}cycloalkyl (e.g., pyrrolidinyl, e.g., pyrrolidin3-yl),

d. aryl (e.g., phenyl or 2,2-dimethylpropyl),

e. aryl-C_{1-8}alkyl wherein the aryl is optionally substituted with halo (e.g., 4-fluorophenylethyl),

f. $-(CH_2)_3-N(H)-(CH_2)_4-N(H)-(CH_2)_3-N(H)_2$,

g. -C_{1-8}alkyl (e.g., methyl) wherein said alkyl is optionally substituted with one or more hydroxy groups (e.g., 2,3-dihydroxypropyl, 2,3,4,5,6-pentahydroxyhexyl, hydroxyethyl);

(vii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy); and

(viii) R_{13} is H or C_{1-4}alkyl (e.g., methyl);

(ix) R_{14} and R_{15} are independently H, -OH, $-S(O)_2CH_3$, -OBn or -C_{1-4}alkyl (e.g., methyl),

in free, salt or prodrug form.

[0016] In another embodiment, the invention relates to the following formulae:

3.1 a compound of Formula III, wherein Alk is C_{1-8} alkyl (e.g., n-butyl, n-pentyl, n-hexyl, 6,6-dimethylhexyl, n-heptyl);

3.2 a compound of Formula III or 3.1, wherein Alk is C_{4-8} alkyl alkyl (e.g., n-butyl, n-pentyl, n-hexyl, 6,6-dimethylhexyl, n-heptyl

3.3 a compound of Formula III or 3.1, wherein Alk is n-hexyl or 6,6-dimethylhexyl;

3.4 a compound of Formula III, or any of 3.1-3.3, wherein A is $-OR_9$ or $-N(R_{14})(R_{15})$;

3.5 a compound of Formula III, or any of 3.1-3.3, wherein A is $-OR_9$;

3.6 a compound of Formula III, or any of 3.1-3.5, wherein R_9 is H, $-C_{1-8}$alkyl (e.g., methyl, ethyl, n-propyl, isopropyl, 1-methylpropyl, t-butyl, n-butyl, 1,1-dimethylpropyl, 2,2-dimethylpropyl, hex-5-ynyl), -haloC_{1-8}alkyl (e.g., 2,2,2-trifluoroethyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, $-C_{1-4}$alkyl-O-C_{1-4}alkyl (e.g., $-C(CH_3)(CH_3)OCH_3$ or $-C(CH_3)(CH_3)CH_2OCH_3$), $-C_{1-4}$alkyl-C(O)-(morphylin-4-yl), $-C_{3-7}$cycloalkyl (e.g., cyclopentyl, cyclohexyl), C_{3-7}cycloalkyl-C_{1-4}alkyl (e.g.,

norbornan-2-yl-methyl) wherein the cycloalkyl is optionally substituted with hydroxy group; aryl (e.g., phenyl) or aryl-C_{1-4}alkyl (e.g, Benzyl, 1-methyl-2-phenylethyl), wherein said aryl is optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl, 2-methoxyphenyl, 2-(3,4-dihydroxyphenyl)ethyl);

3.7 a compound of Formula III, or any of 3.1-3.5, wherein R_9 is $-C_{1-8}$alkyl (e.g., methyl, ethyl, n-propyl, isopropyl, 1-methylpropyl, t-butyl, n-butyl, 1,1-dimethylpropyl, 2,2-dimethylpropyl, hex-5-ynyl);

3.8 a compound of Formula III, or any of 3.1-3.5, wherein R_9 is H;

3.9 a compound of Formula III, or any of 3.1-3.5, wherein R_9 is haloC_{1-8}alkyl (e.g., 2,2,2-trifluoroethyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, $-C_{1-4}$alkyl-O-C_{1-4}alkyl (e.g., -$C(CH_3)(CH_3)OCH_3$ or -$C(CH_3)(CH_3)CH_2OCH_3$), $-C_{1-4}$alkyl-C(O)-(morphylin-4-yl), $-C_{3-7}$cycloalkyl (e.g., cyclopentyl, cyclohexyl), C_{3-7}cycloalkyl-C_{1-4}alkyl (e.g., norbornan-2-yl-methyl) wherein the cycloalkyl is optionally substituted with hydroxy group; aryl (e.g., phenyl) or aryl-C_{1-4}alkyl (e.g, Benzyl, 1-methyl-2-phenylethyl), wherein said aryl is optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl, 2-methoxyphenyl, 2-(3,4-dihydroxyphenyl)ethyl);

3.10 a compound of Formula III, or any of 3.1-3.3, wherein A is $-N(R_{14})(R_{15})$;

3.11 a compound of Formula 3.10, wherein R_{14} and R_{15} are independently H, -OH, -$S(O)_2CH_3$, -OBn or -C_{1-4}alkyl (e.g., methyl);

3.12 a compound of Formula III or any of 3.1-3.11, wherein R_1 is H, C_{1-8} alkyl (e.g., methyl);

3.13 a compound of Formula III or any of 3.1-3.12, wherein R_2 is H, halo (e.g., chloro), -O-C_{3-7}cycloalkyl (e.g., -O-cyclopentyl), -O-C_{0-7} alkylC_{3-7}cycloalkyl (e.g., -O-cyclopentyl, -O-CH_2-cyclopentyl), $-N(R_4)(R_5)$, $-(CH_2)-N(R_4)(R_5)$, -C_{0-4}alkyl-C_{3-7}cycloalkyl (e.g., cyclopropyl, cyclopentylmethyl), heteroC_{3-7}cycloalkyl (e.g., pyrrolidin-1-yl), 1-cyclopropyl-6-fluoro-7-[4-piperazin-1-yl]-4-oxo-quinoline-3-carboxylic acid), C_{1-8}alkyl (e.g., methyl or ethyl) or $-O-C_{1-8}$alkyl (e.g., methoxy), wherein the alkyl group is optionally substituted with one or more halo (e.g., fluoro) or hydroxy groups (e.g., trifluoromethyl, -O-CH_2CH_2OH);

3.14 a compound of Formula III or any of 3.1-3.12, wherein R_2 is $-N(R_4)(R_5)$;

3.15 a compound of Formula 3.14, wherein R_4 and R_5 are independently H, $-C_{0-4}$alkyl-C_{3-7}cycloalkyl (e.g., cyclopropyl, cyclopentyl, cyclohexyl or cyclopentyl-methyl), heteroC_{3-7}cycloalkyl (e.g., pyrrolidinyl, e.g., pyrrolidin3-yl), aryl (e.g., phenyl or 2,2-dimethylpropyl), aryl-C_{1-8}alkyl wherein the aryl is optionally substituted with halo (e.g., 4-fluorophenylethyl), $-(CH_2)_3-N(H)-(CH_2)_4-N(H)-(CH_2)_3-N(H)_2$, -$C_{1-8}$alkyl (e.g., methyl) wherein said alkyl is optionally substituted with one or more hydroxy groups (e.g., 2,3-dihydroxypropyl, 2,3,4,5,6-pentahydroxyhexyl, hydroxyethyl);

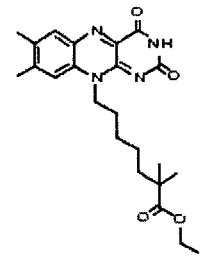
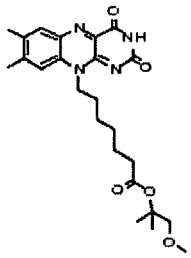
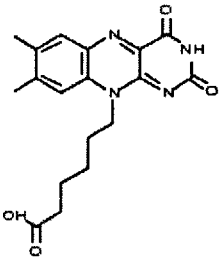
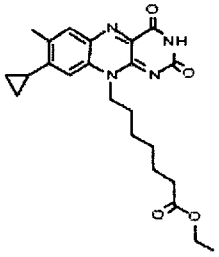
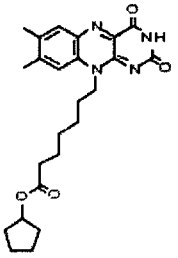
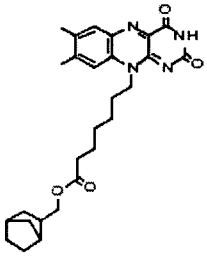
3.16 a compound of Formula 3.14, wherein R_4 is H and R_5 is aryl (e.g., phenyl);

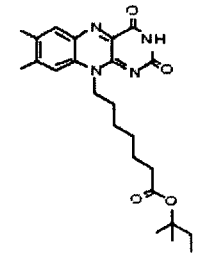
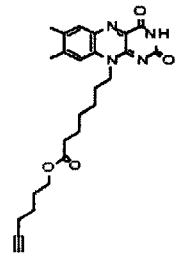
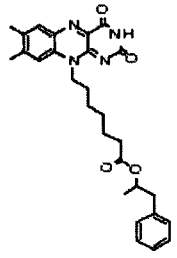
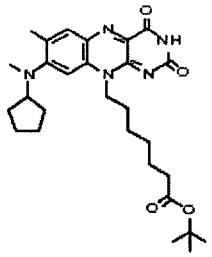
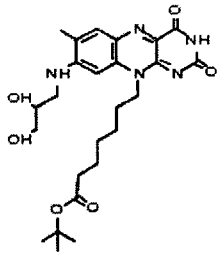
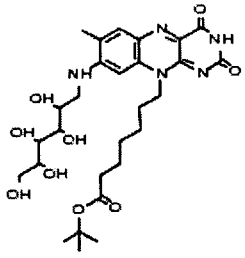
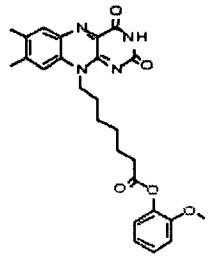
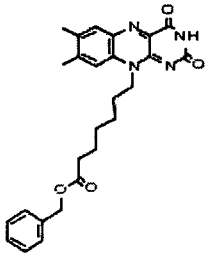
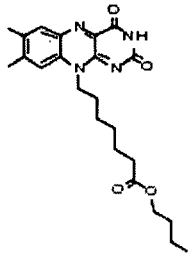
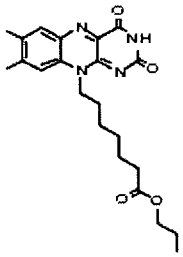
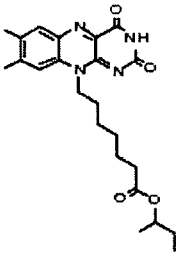
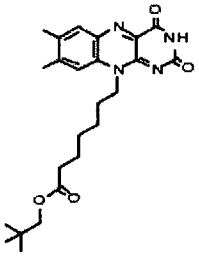
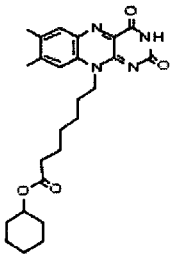
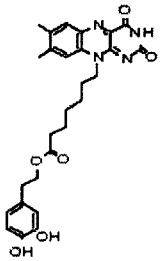
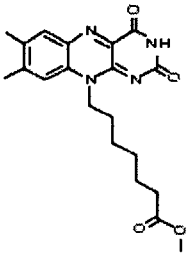
3.17 a compound of Formula 3.14, wherein R_4 and R_5 are -C_{1-8}alkyl (e.g., methyl);

3.18 a compound of Formula III or any of 3.1-3.17, wherein R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy);

3.19 a compound of Formula III or any of 3.1-3.18, wherein R_{13} is H or C_{1-4}alkyl (e.g., methyl)

3.20 a compound of Formula III or any of 3.1-3.19 wherein said compound is selected from the following:

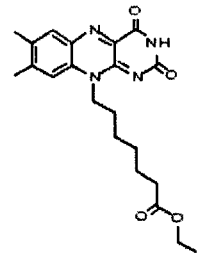
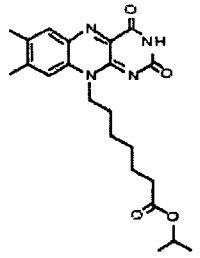
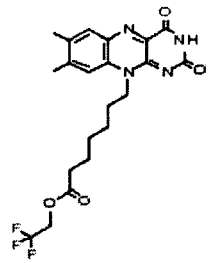
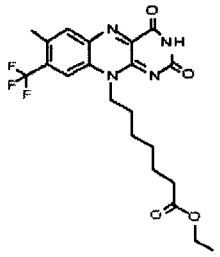
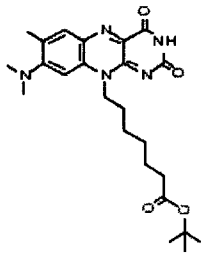
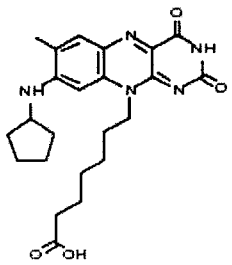
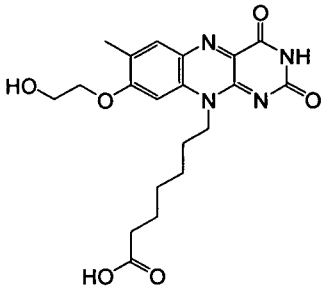
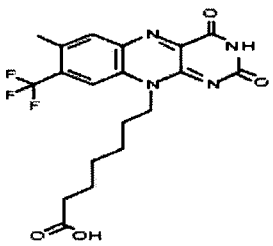
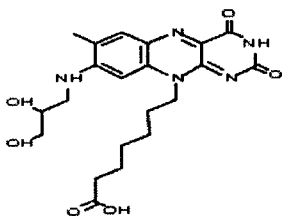
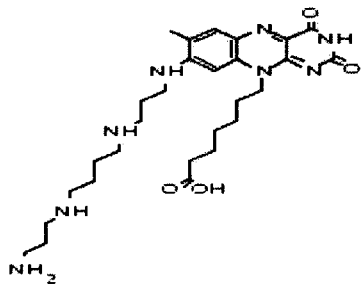
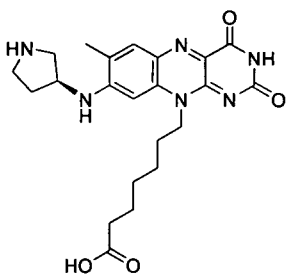
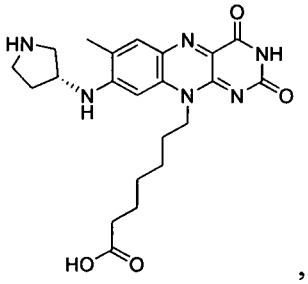
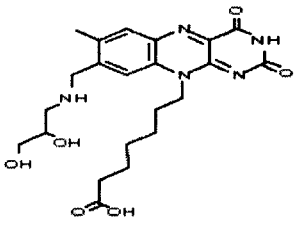
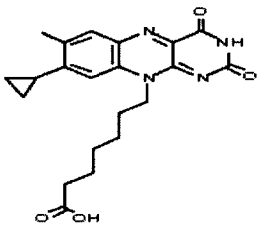
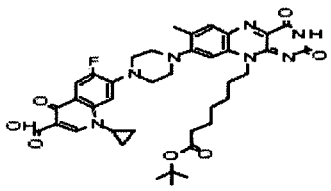

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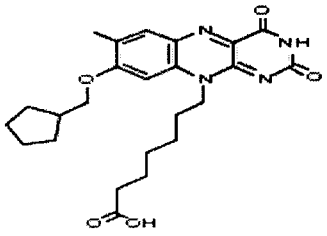
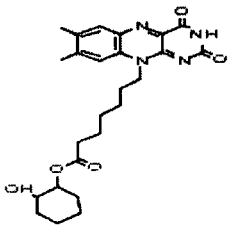
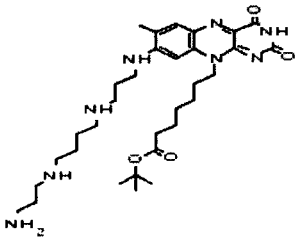
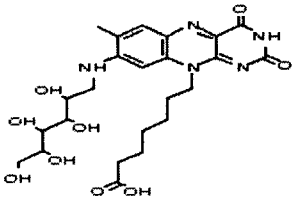
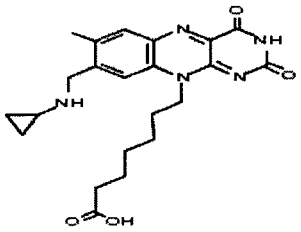
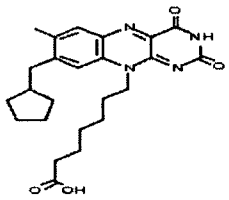
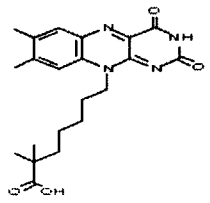
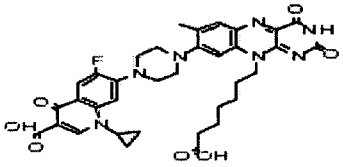
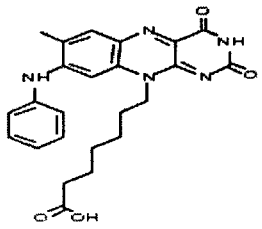
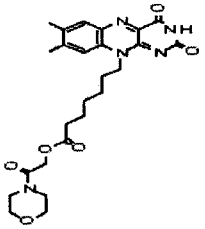
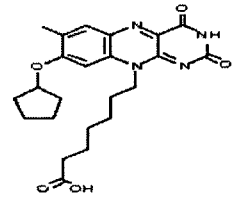
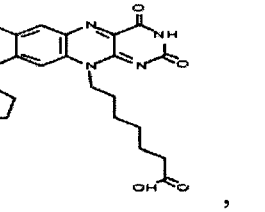
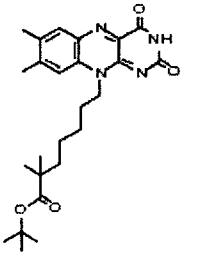
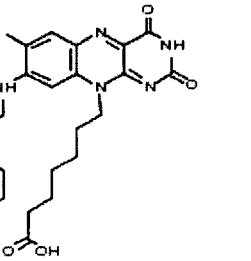
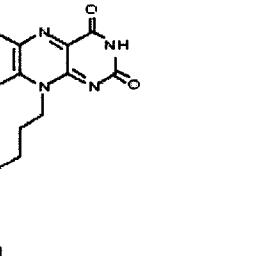

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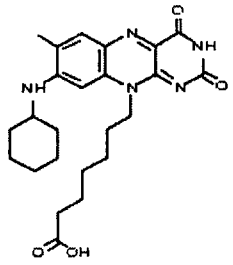
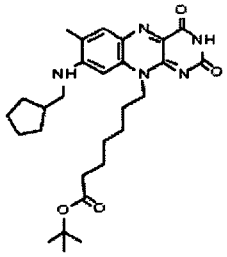
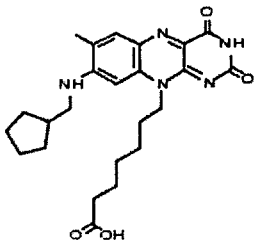
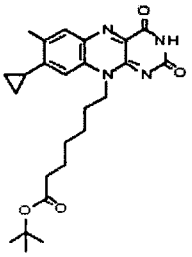

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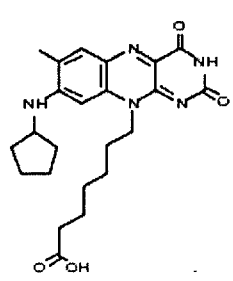
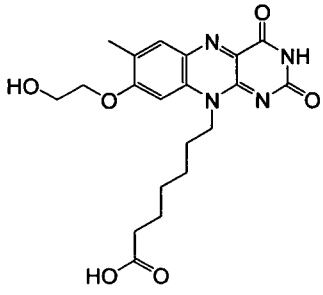
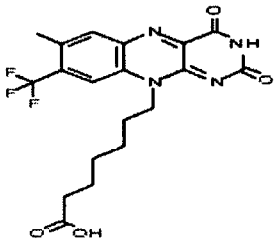
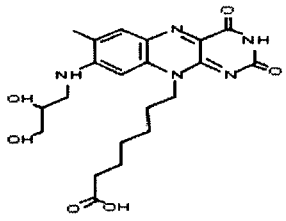
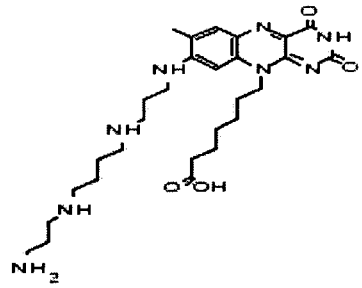
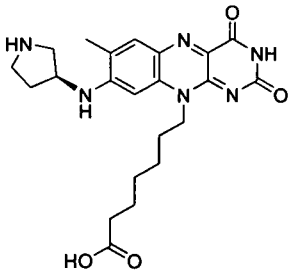
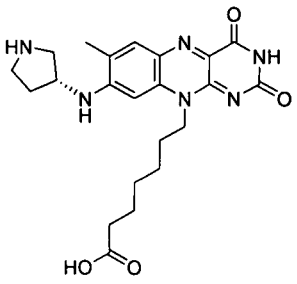
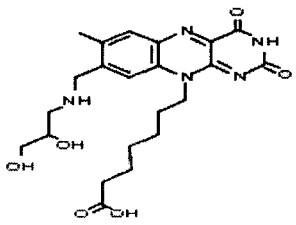
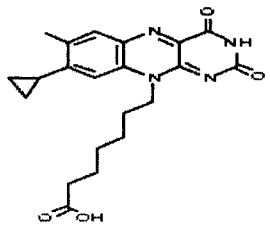
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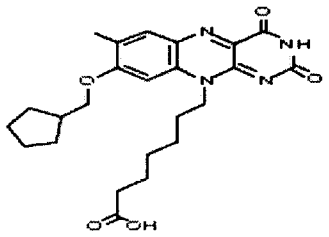
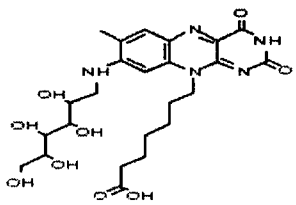
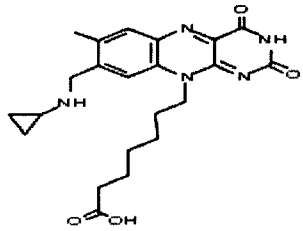
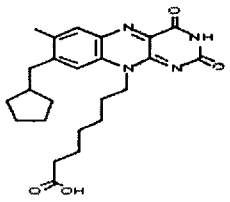
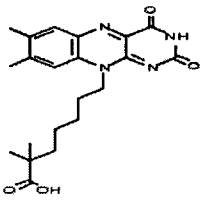
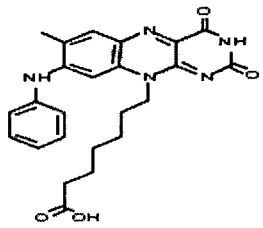
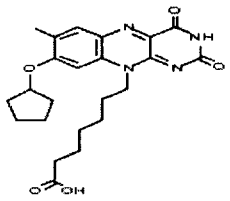
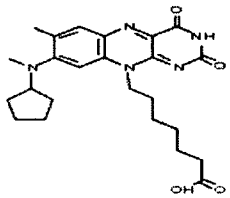
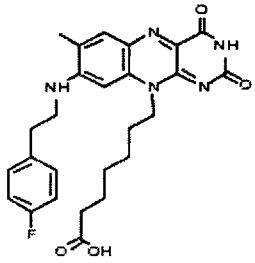
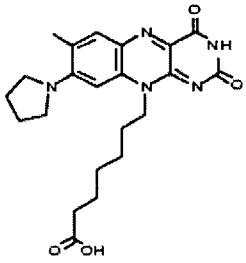
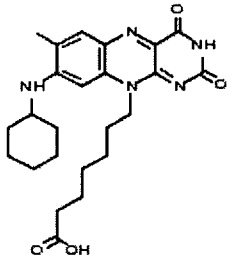
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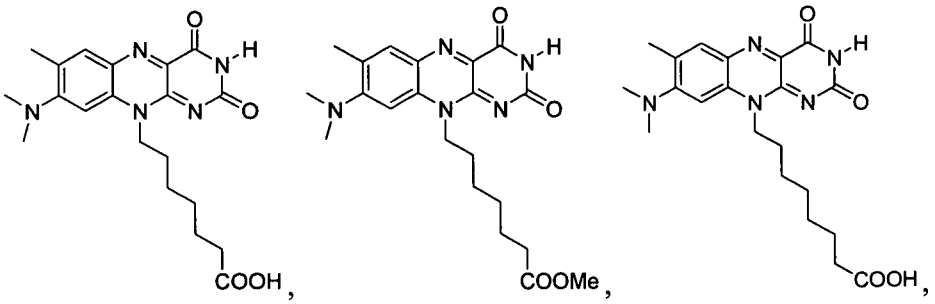

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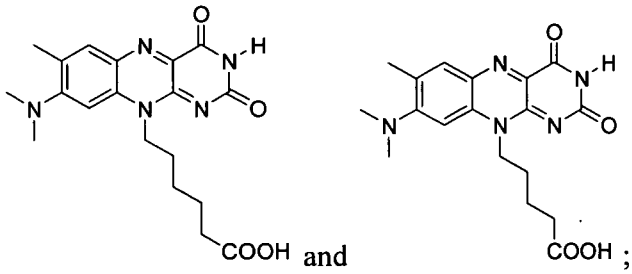
3.21 a compound of Formula III or any of 3.1-3.19 wherein said compound is selected from any one of the following:


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3.22 a compound of Formula III or any of 3.1-3.19 wherein said compound is selected from anyone of the following:

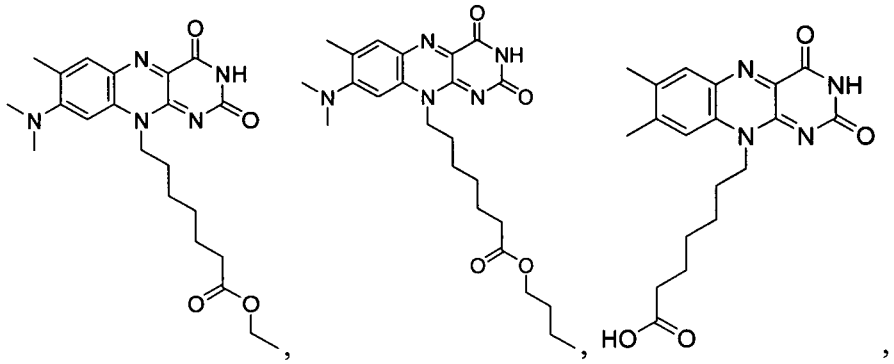


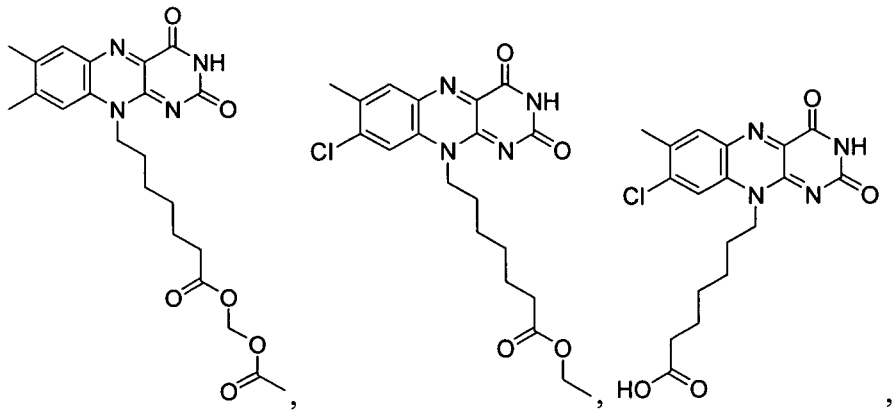


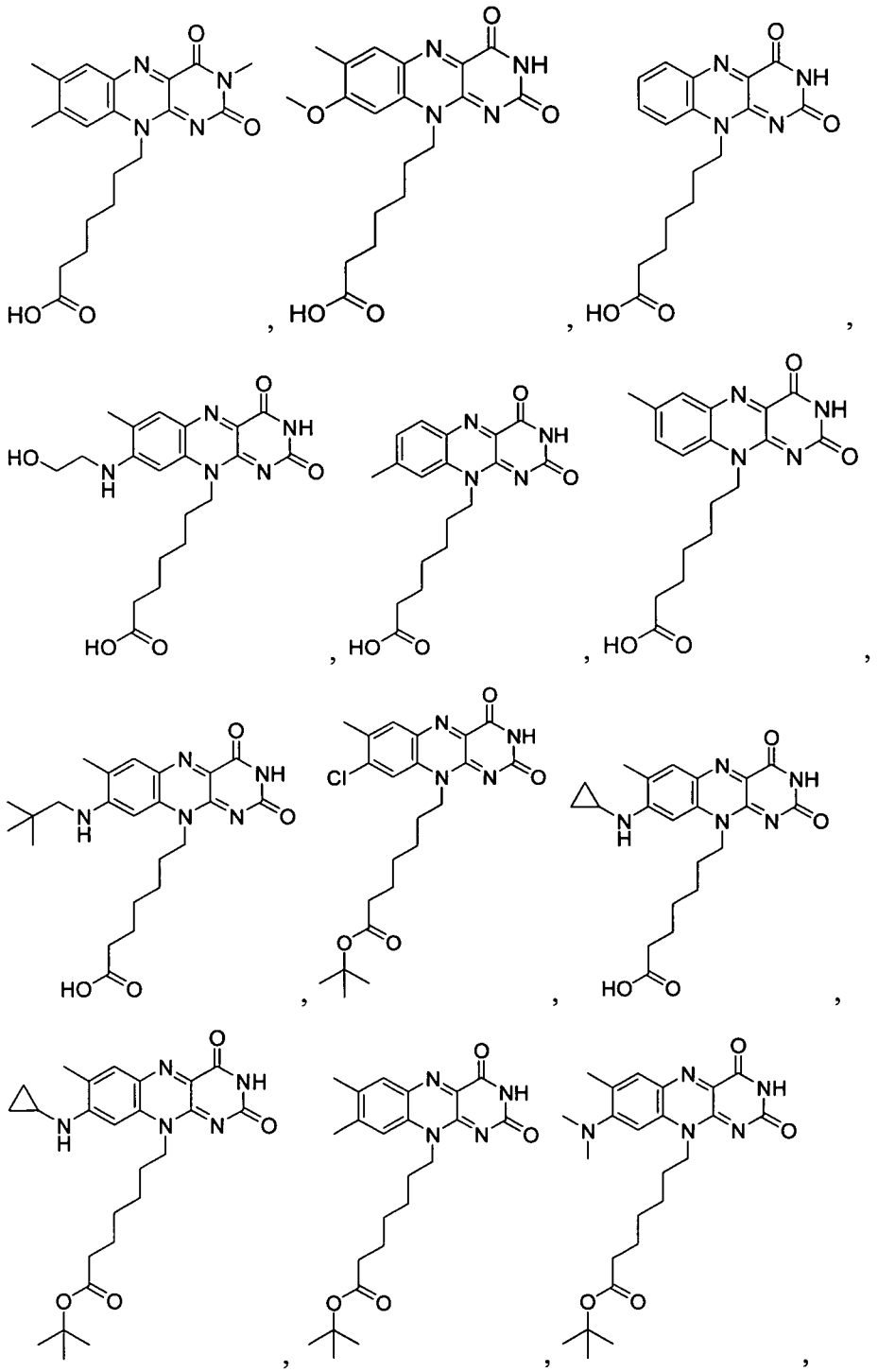
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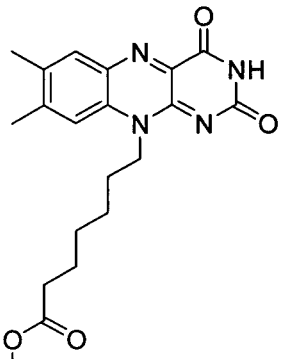
;

3.23 a compound of Formula III or any of 3.1-3.19 wherein said compound is selected from the following:



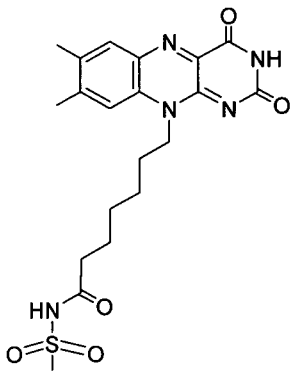
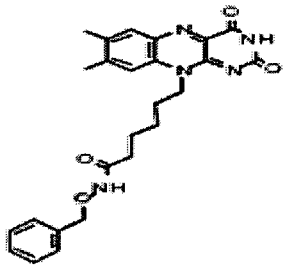
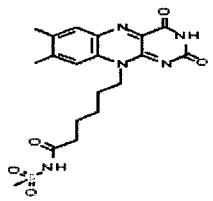




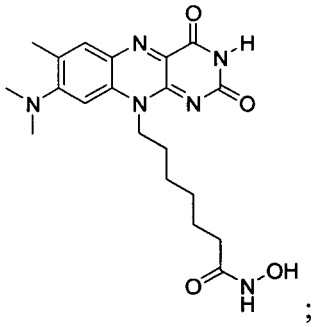


and  ;

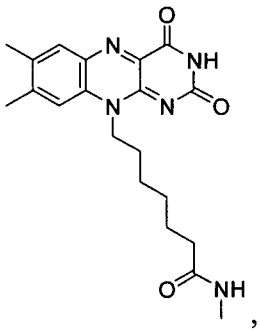
3.24 a compound of Formula III or any of 3.1-3.19 wherein said compound is selected from the following:

 ,  and  ;

3.25 a compound of Formula III or any of 3.1-3.19 wherein said compound is:

 ;

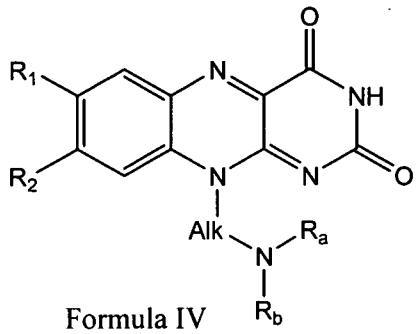
3.26 a compound of Formula III or any of 3.1-3.19 wherein said compound is:

 ,

3.27 any of the preceding formulae wherein the Compound (a) binds to FMN riboswitch, e.g., with an IC_{50} of less than or equal to 10μM, preferably less than 1μM, more preferably less than 100 nM, most preferably less than 10nM in a binding assay, for example, as described in Example 1 and/or (b) has a minimum inhibitory concentration (MIC) of less than 128μg/mL, preferably less than 32μg/mL, in an assay, for example, as described in Example 1A;

in free, salt or prodrug form.

[0017] In a particular aspect, the invention relates to a Compound of formula IV,



Formula IV

wherein:

(i) Alk is C_{1-8} alkyl (e.g., ethyl or n-butyl);

(ii) R_a and R_b are independently H, -C_{1-4}alkyl (e.g., methyl), -$(CH_2)_3C(NH_2)(COOH)CHF_2$, -$(CH_2)_3N(H)C(=NH)NH_2$, -$(CH_2)_5NH_2$, -$(CH_2)_2C(H)(OH)COOH$, -$C(O)(CH_2)_2COOH$, -$C_{1-4}$alkyl-$C(O)OR_9$ (e.g., -$CH_2CH_2CH_2CH_2C(O)OR_9$, -$CH_2CH_2CH_2C(O)OR_9$,-$CH_2CH_2C(O)OR_9$ or -$CH_2C(O)OR_9$, -$C(CH_3)(CH_3)C(O)OR_9$), -$C(O)CH_3$, aryl (e.g., phenyl), -C(O)-aryl, aryl-C_{1-4}alkyl (e.g., benzyl, naphtha-1-ylmethyl, naphth-2-ylmethyl, phenylethyl, phenylpropyl, naphtha-1-ylethyl), heteroaryl, heteroaryl-C_{1-4}alkyl (e.g., pyrid-2-ylmethyl, pyrid-3-ylmethyl or quinoxalinyl), wherein said aryl and heteroaryl groups are optionally substituted with one or more groups selected from –$C(O)OR_9$, -NH_2, -$S(O)_2NH_2$, -CH_2NH_2, halo (e.g., chloro), C_{1-4}alkoxy (e.g., methoxy), C_{1-4}alkyl (e.g., methyl);

(iii) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(iv) R_2 is H, halo (e.g., chloro), -O-C_{3-7}cycloalkyl (e.g., -O-cyclopentyl), -$N(R_4)(R_5)$, C_{3-7}cycloalkyl (e.g., cyclopropyl), C_{1-8}alkyl (e.g., methyl or

ethyl) or –O-C_{1-8}alkyl wherein the alkyl group is optionally substituted with one or more halo or hydroxyl groups (e.g., trifluoromethyl, -O-CH_2CH_2OH);

(v) R_4 and R_5 are independently H, C_{3-7}cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{1-8}alkyl (e.g., methyl) wherein said alkyl is optionally substituted with one or more hydroxy groups (e.g., 2,3-dihydroxypropyl, 2,3,4,5,6-pentahydroxyhexyl);

(vi) R_9 is H or C_{1-4}alkyl (e.g., t-butyl, isopropyl, methyl);

(vii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy),

in free, salt or prodrug form.

[0018] In another embodiment, the invention relates to the following formulae:

4.1 a compound of Formula IV, wherein Alk is C_{1-8} alkyl (e.g., ethyl or n-butyl);

4.2 a compound of Formula IV, wherein Alk is ethyl;

4.3 a compound of Formula IV, wherein Alk is n-butyl;

4.4 a compound of Formula IV, 4.1, 4.2 or 4.3 is wherein R_a and R_b are independently H, -C_{1-4}alkyl (e.g., methyl), -$(CH_2)_3C(NH_2)(COOH)CHF_2$, -$(CH_2)_3N(H)C(=NH)NH_2$, -$(CH_2)_5NH_2$, -$(CH_2)_2C(H)(OH)COOH$, -$C(O)(CH_2)_2COOH$, -$C_{1-4}$alkyl-$C(O)OR_9$ (e.g., - $CH_2CH_2CH_2CH_2C(O)OR_9$, - $CH_2CH_2CH_2C(O)OR_9$, -$CH_2CH_2C(O)OR_9$, -$CH_2C(O)OR_9$ or - $C(CH_3)(CH_3)C(O)OR_9$), -$C(O)CH_3$, aryl (e.g., phenyl), -C(O)-aryl, aryl-C_{1-4}alkyl (e.g., benzyl, naphtha-1-ylmethyl, naphth-2-ylmethyl, phenylethyl, phenylpropyl, naphtha-1-ylethyl), heteroaryl, heteroaryl-C_{1-4}alkyl (e.g., pyrid-2-ylmethyl, pyrid-3-ylmethyl or quinoxalinyl), wherein said aryl and heteroaryl groups are optionally substituted with one or more groups selected from –$C(O)OR_9$, -NH_2, -$S(O)_2NH_2$, -CH_2NH_2, halo (e.g., chloro), C_{1-4}alkoxy (e.g., methoxy), C_{1-4}alkyl (e.g., methyl);

4.5 a compound of Formula IV, 4.1, 4.2 or 4.3, wherein R_a is H and R_b is aryl (e.g., phenyl), aryl-C_{1-4}alkyl (e.g., benzyl, naphtha-1-ylmethyl, naphth-2-ylmethyl, phenylethyl, phenylpropyl, naphtha-1-ylethyl), heteroaryl, heteroaryl-C_{1-4}alkyl (e.g., pyrid-2-ylmethyl, pyrid-3-ylmethyl or quinoxalinyl), wherein said aryl and heteroaryl groups are optionally substituted with one or more groups selected

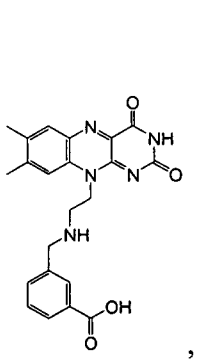
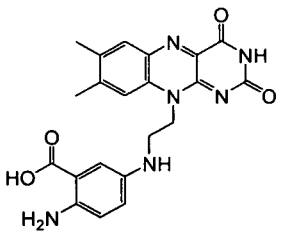
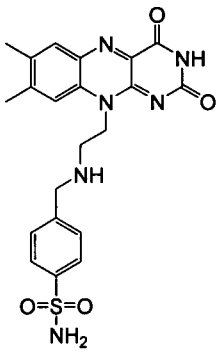
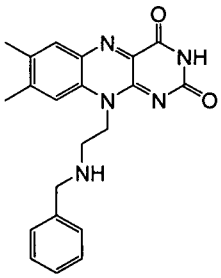
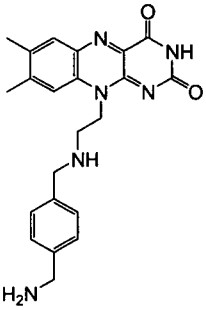
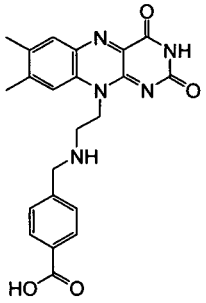
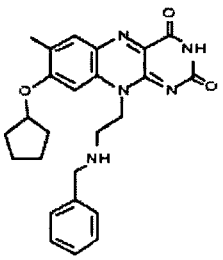
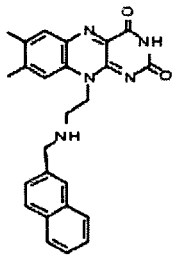
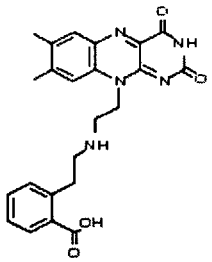
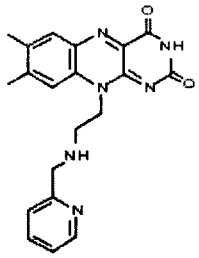
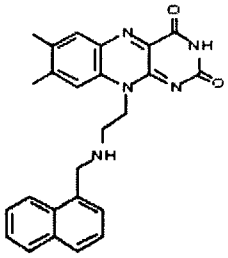
from –C(O)OR_9, -NH_2, -$S(O)_2NH_2$, -CH_2NH_2, halo (e.g., chloro), C_{1-4}alkoxy (e.g., methoxy), C_{1-4}alkyl (e.g., methyl);

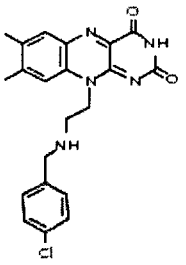
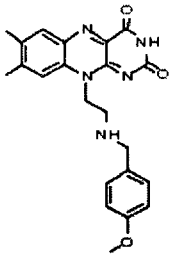
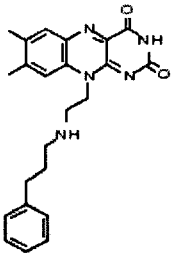
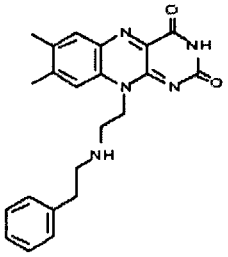
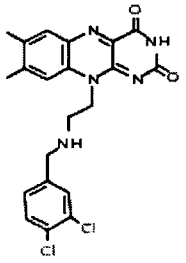
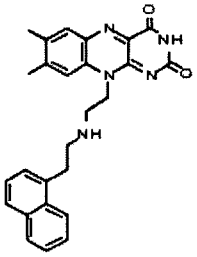
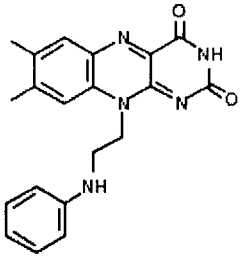
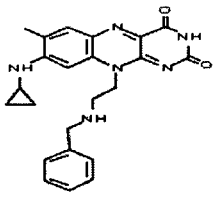
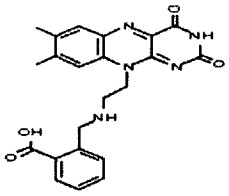
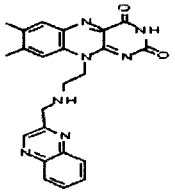
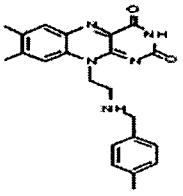
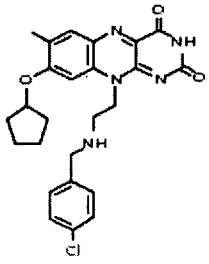
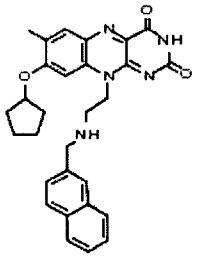
4.6 a compound of Formula IV, or any of 4.1-4.5, wherein R_9 is H or C_{1-4}alkyl (e.g., t-butyl, isopropyl, methyl);

4.7 a compound of Formula IV, or any of 4.1-4.5, wherein R_9 is H;

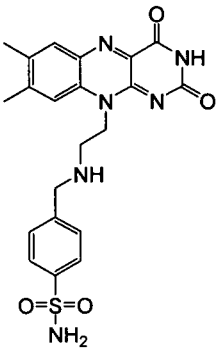
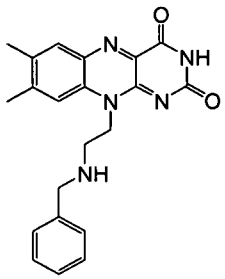
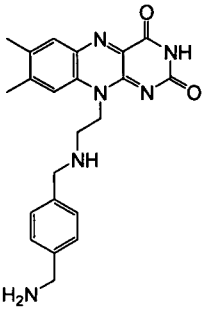
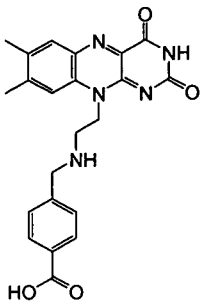
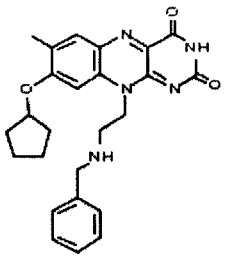
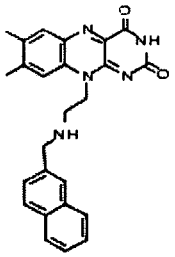
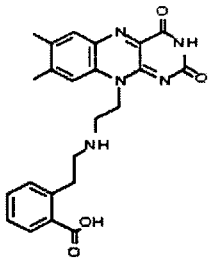
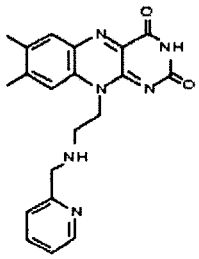
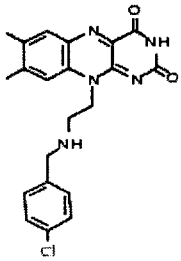
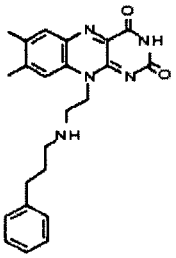
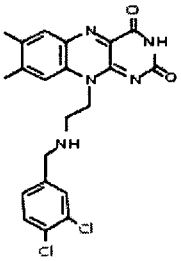
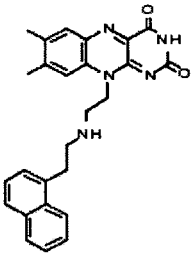
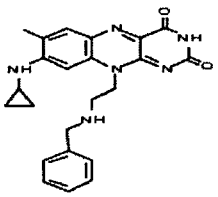
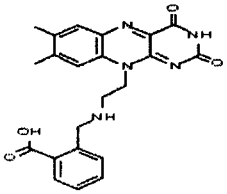
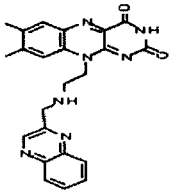
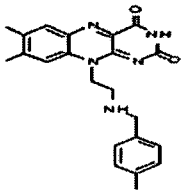
4.8 a compound of Formula IV, or any of 4.1-4.5, wherein R_9 is C_{1-4}alkyl (e.g., t-butyl, isopropyl, methyl);

4.9 a compound of Formula IV or any of 4.1-4.8 wherein said compound is selected from any one of the following:

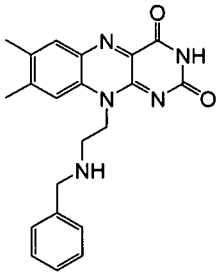
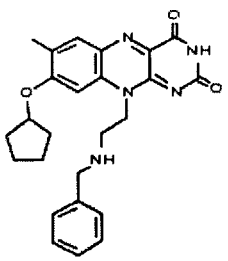
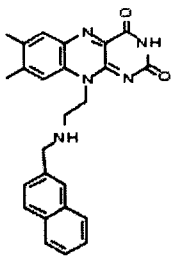
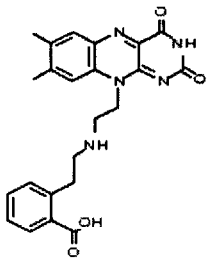
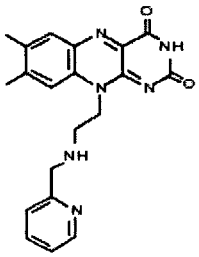
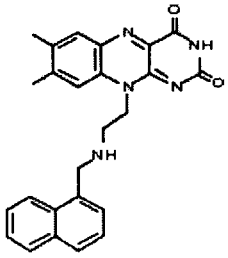
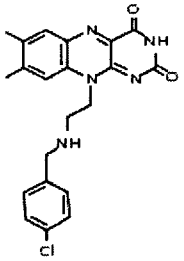
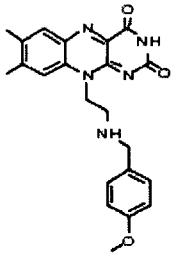
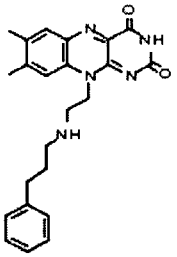
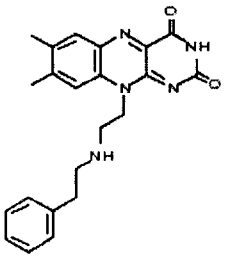
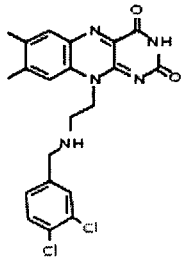
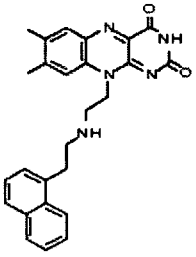
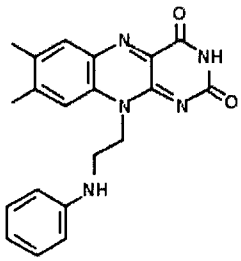
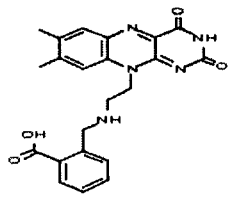
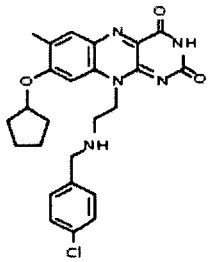

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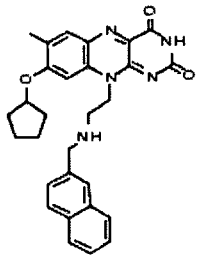

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4.10 a compound of Formula IV or any of 4.1-4.6 wherein said compound is selected from any one of the following:


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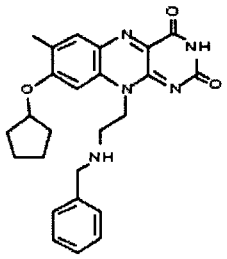
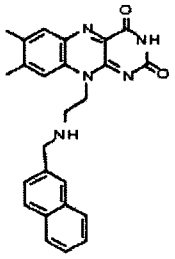
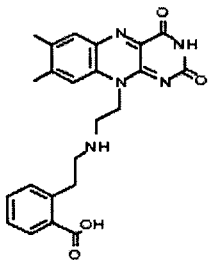
4.11 a compound of Formula IV or any of 4.1-4.6 wherein said compound is selected from any one of the following:

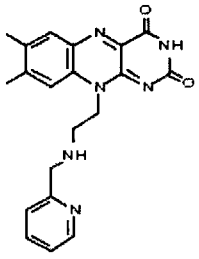
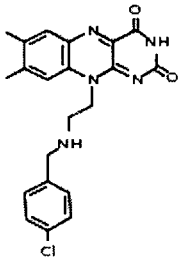
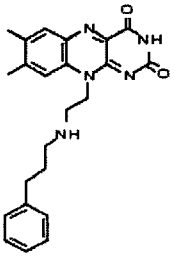

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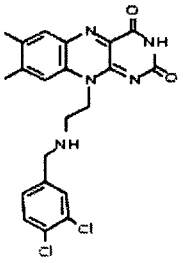
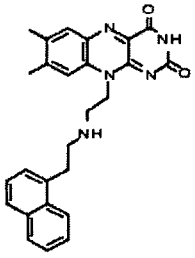


and ;

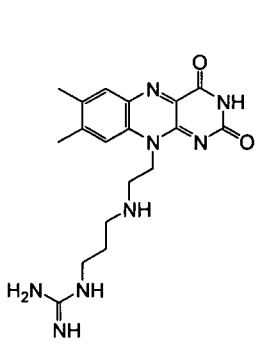
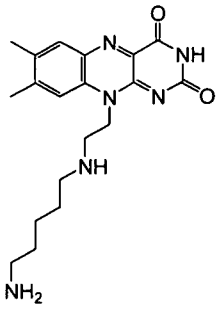
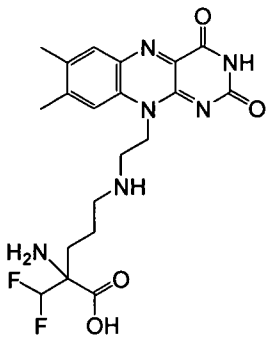
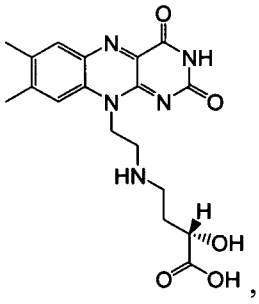
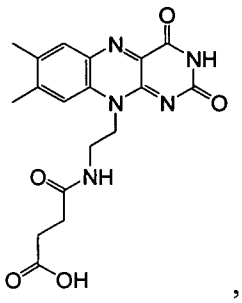
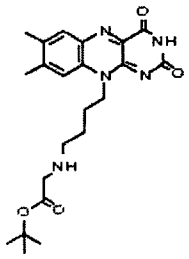
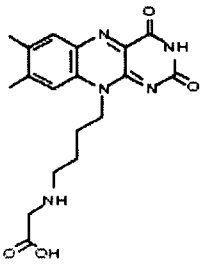
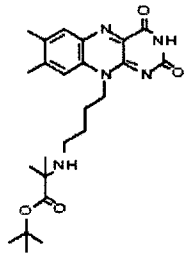
4.12 a compound of Formula IV or any of 4.1-4.6 wherein said compound is selected from any one of the following:


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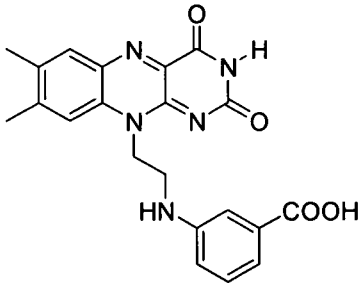

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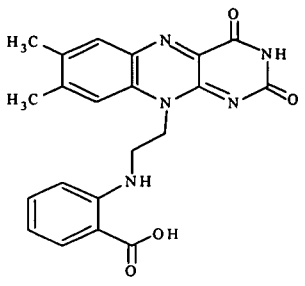
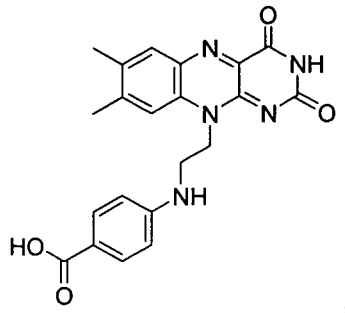
4.13 a compound of Formula IV or any of 4.1-4.6 wherein said compound is selected from any one of the following:








and

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4.14 a compound of Formula IV or any of 4.1-4.6 wherein said compound is:


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4.15 a compound of Formula IV or any of 4.1-4.6 wherein said compound is selected from:

and ;

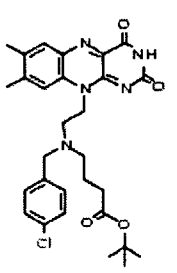
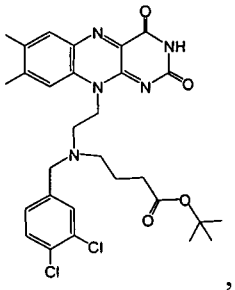
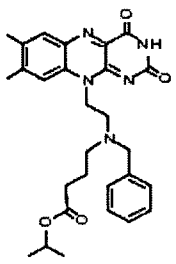
4.16 a compound of Formula IV, 4.1, 4.2 or 4.3, wherein R_a is -C_{1-4}alkyl (e.g., methyl) or -C_{1-4}alkyl-C(O)OR_9 (e.g., -$CH_2CH_2CH_2C(O)OR_9$) and R_b is aryl (e.g., phenyl), aryl-C_{1-4}alkyl (e.g., benzyl, naphtha-1-ylmethyl, naphth-2-ylmethyl, phenylethyl, phenylpropyl, naphtha-1-ylethyl), heteroaryl, heteroaryl-C_{1-4}alkyl (e.g., pyrid-2-ylmethyl), wherein said aryl and heteroaryl groups are optionally substituted with one or more groups selected from –C(O)OR_9, -NH_2, -$S(O)_2NH_2$, -CH_2NH_2, halo (e.g., chloro), C_{1-4}alkoxy (e.g., methoxy), C_{1-4}alkyl (e.g., methyl);

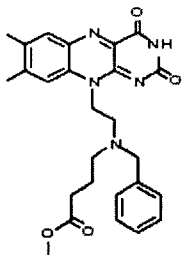
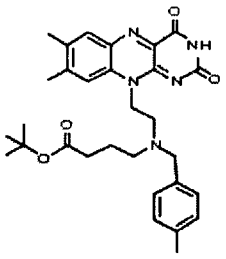
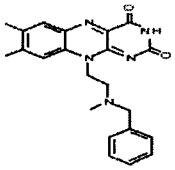
4.17 a compound of Formula IV or any of 4.1, 4.2, 4.3, 4.12-4.16, wherein R_9 is H or C_{1-4}alkyl (e.g., t-butyl, isopropyl, methyl);

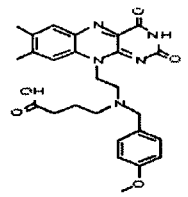
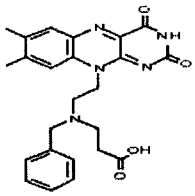
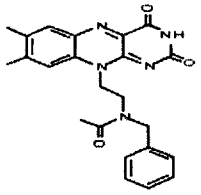
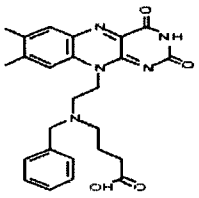
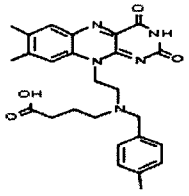
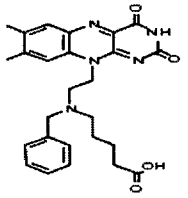
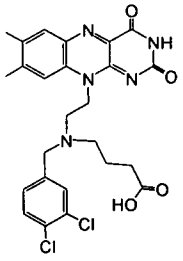
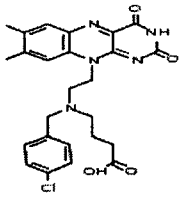
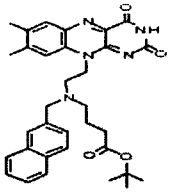
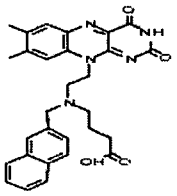
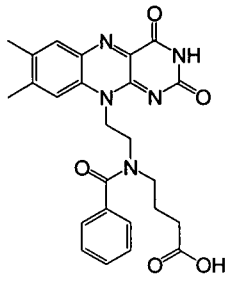
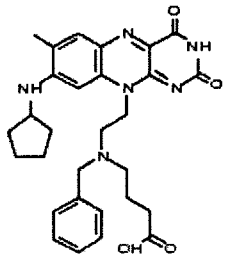
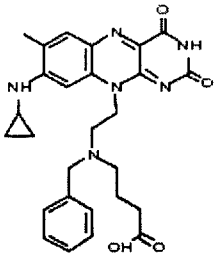
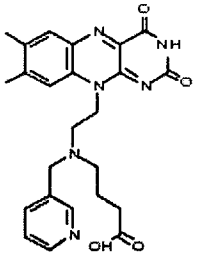
4.18 compound of Formula IV or any of 4.1, 4.2, 4.3, 4.12-4.16, wherein R_9 is H;

4.19 compound of Formula IV or any of 4.1, 4.2, 4.3, 4.12-4.16, wherein R_9 is C_{1-4}alkyl (e.g., t-butyl, isopropyl, methyl);

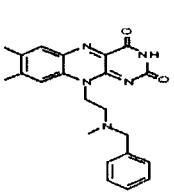
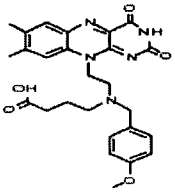
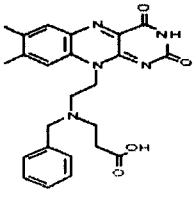
4.20 a compound of Formula IV or any of 4.1, 4.2, 4.3, 4.12-4.19, wherein said compound is selected from any one of the following:

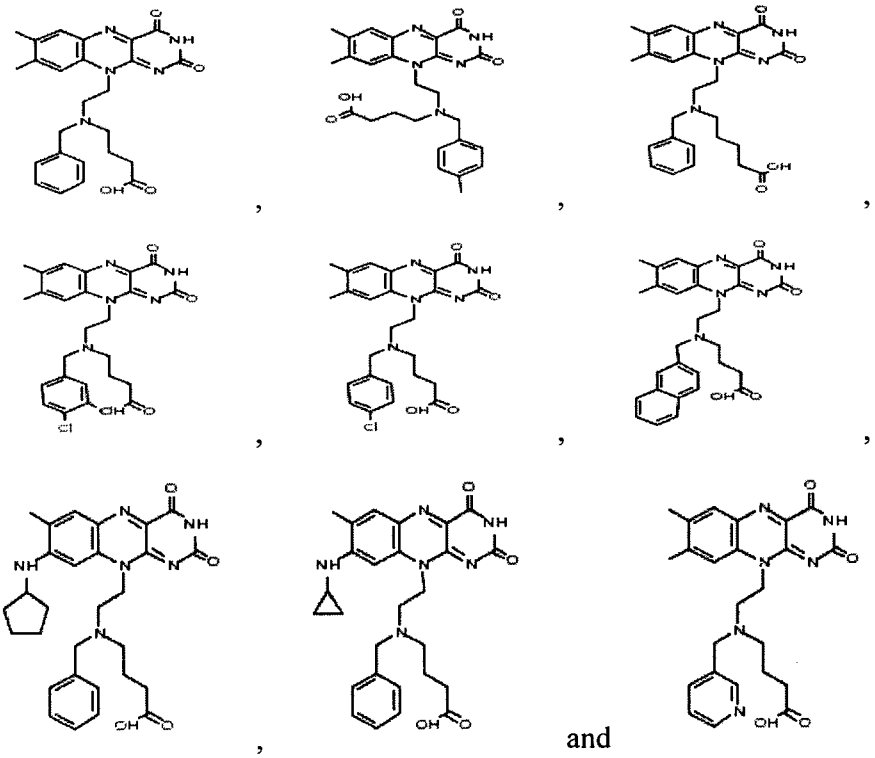

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and ;

4.21 a compound of Formula IV or any of 4.1, 4.2, 4.3, 4.12-4.19, wherein said compound is selected from any one of the following:


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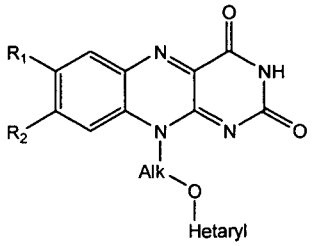


and ;

4.22 any of the preceding formulae wherein the Compound of Formula III (a) binds to FMN riboswitch, e.g., with an IC_{50} of less than or equal to 10μM, preferably less than 1μM, more preferably less than 100 nM, most preferably less than 10nM in a binding assay, for example, as described in Example 1 and/or (b) has a minimum inhibitory concentration (MIC) of less than 128μg/mL, preferably less than 32μg/mL, in an assay, for example, as described in Example 1A;

in free, salt or prodrug form.

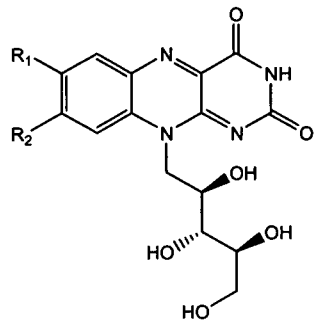
[0019] In still another embodiment, the invention relates to a compound of Formula V:



Formula V

wherein Alk is C_{1-6}alkyl and hetaryl is heteroaryl (e.g., pyrimidin-2-yl) and R_1 and R_2 are independently H, C_{1-4}alkyl (e.g., methyl), in free or salt form.

[0020] In yet another embodiment, the invention relates to a compound of Formula VI:



Formula VI

wherein R_1 is H or C_{1-4}alkyl (e.g., methyl) and R_2 is cyano, in free, salt or prodrug form.

[0021] In the first aspect, the invention provides a method for the treatment or prophylaxis of a bacterial infection (Method I) comprising administering to a subject in need thereof an effective amount of a compound of formula I, e.g., any of Methods 1.1-1.212, or a compound of any of Formulae I(i)-I(v), e.g., any of 1.213-1.265, in free, pharmaceutically acceptable salt or prodrug form, as herein before described, with the proviso that: (a) when R_1 is methyl and R_2 is chloro, then R_3 is not methyl; (b) when R_1 is H and R_2 is dimethylamine, then R_3 is not H; (c) when R_3 is (2R,3S,4S)-2,3,4,5-tetrahydroxypentyl or 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl, and R_1 is methyl, then R_2 is not methyl; (d) when R_3 is (2R,3S,4S)-2,3,4,5-tetrahydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino; (e) when R_1 is methyl and R_2 is alkoxy, then R_3 is not 2,3,4,5-tetrahydroxypentyl; and (f) when the bacterial infection is an infection by chlamydophila psittacci, then R_3 is not -$(CH_2)_{2-6}$-phosphate, when R_1 and R_2 are independently selected from a group consisting of C_{1-5} alkyl, C_{1-5} alkoxy, amino, hydrogen and halogen group. In a further embodiment of this aspect, Method I further provides the proviso that when R_3 is 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino.

[0022] In a preferred embodiment, Method I comprises administering to a subject in need thereof an effective amount of a compound of formula I, wherein R_3 is C_{1-8} alkyl substituted with –$COOR_9$, -$P(O)(OR_9)(OR_{17})$, -$P(O)(OR_9)(NR_{13}R_{14})$, -$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$OP(O)(OR_9)(OR_{17})$, -$OP(O)(OR_9)(NR_{13}R_{14})$, -$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, in free, pharmaceutically acceptable salt or prodrug form. In another preferred embodiment, Method I comprises administering to a subject in need thereof an effective amount of a compound of formula I, wherein R_3 is C_{1-8} alkyl

substituted with –$COOR_9$, -$P(O)(OR_9)(OR_{17})$, -$P(O)(OR_9)(NR_{13}R_{14})$, -$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$OP(O)(OR_9)(OR_{17})$, -$OP(O)(OR_9)(NR_{13}R_{14})$, -$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, and at least one of R_9 and R_{17} is C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$, phenyl or Bn wherein phenyl and Bn are optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl), or at least one of R_{13}, R_{14}, R_{15} and R_{16} is -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-COOH, -CH(isopropyl)-COOH, -CH(isobutyl)-COOH, -CH(sec-butyl)-COOH), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –CH(CH_2CH_2COOH)-COOH), in free, pharmaceutically acceptable salt or prodrug form. In still another preferred embodiment, Method I comprises administering to a subject in need thereof an effective amount of a compound of formula I, wherein R_3 is C_{1-8} alkyl substituted with -$P(O)(OR_9)(NR_{13}R_{14})$, -$OP(O)(OR_9)(NR_{13}R_{14})$, and at least one of R_9 and R_{17} is C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$, phenyl or Bn wherein phenyl and Bn are optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl), and at least one of R_{13}, R_{14}, R_{15} and R_{16} is -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-COOH, -CH(isopropyl)-COOH, -CH(isobutyl)-COOH, -CH(sec-butyl)-COOH), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with C_{1-8}alkyl hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –CH(CH_2CH_2COOH)-COOH), in free, pharmaceutically acceptable salt or prodrug form. In a particular embodiment, Method I comprises administering to a subject in need thereof an effective amount of a compound of formula 1.204, in free, pharmaceutically acceptable salt or prodrug form. In another embodiment, Method I comprises administering to a subject in need thereof an effective amount of a compound of formula 1.210, in free, pharmaceutically acceptable salt or prodrug form. In still another embodiment, Method I comprises administering to a subject in need thereof an effective amount of a compound of any of Formulae I(i)-I(v), e.g., any of 1.213-1.265, in free, pharmaceutically acceptable salt or prodrug form.

[0023] In still another embodiment of the first aspect, the invention provides a method for the treatment or prophylaxis of a bacterial infection (Method I(a)) comprising administering to a subject in need thereof an effective amount of a compound of formula

III, e.g., any of formulae 3.1-3.27, in free, pharmaceutically acceptable salt or prodrug form. In a preferred embodiment, the invention provides Method I(a), wherein the compound of Formula III is a compound selected from any one of those described in formulae 3.20-3.26, in free, pharmaceutically acceptable salt or prodrug form.

[0024] In still another embodiment of the first aspect, the invention provides a method for the treatment or prophylaxis of a bacterial infection (Method I(b)) comprising administering to a subject in need thereof an effective amount of a compound of formula IV, e.g., any of formulae 4.1-4.22, in free, pharmaceutically acceptable salt or prodrug form. In a preferred embodiment, the invention provides Method I(a), wherein the compound of Formula III is a compound selected from any one of those described in formula 4.9-4.15 or 4.20-4.21, in free, pharmaceutically acceptable salt or prodrug form.

[0025] In another embodiment of the first aspect, the invention provides a method for the treatment or prophylaxis of a bacterial infection (Method I(c)) comprising administering to a subject in need thereof an effective amount of a compound of formula V, or VI, in free, pharmaceutically acceptable salt or prodrug form.

[0026] In a further embodiment, Method I, I(i) to I(v), I(a)-I(c) as hereinbefore described, are useful for the treatment or prophylaxis of a Gram-positive or Gram-negative bacterial infection (which methods shall be Method I-A, I(i)-A to I(v)-A, I(a)-A, I(b)-A and I(c)-A). In another specific embodiment, Method I, I(i)-I(v), I(a), I(b) and I(c) are useful for treating a bacterial infection including, but not limited to an infection by one or more of the following bacteria: *Moraxella catarrhalis, Klebsiella pneumoniae, Staphylococcus epidermidis, Streptococcus viridans, Enterococcus faecium, Staphylococcus aureus, Bacillus anthracis, Francisella tularensis, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Brucella melitensis, Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Salmonella enterica, Vibrio cholerae, Enterococcus faecalis* and *Yersinia pestis* (which methods shall be Method I-B, I(i)-B to I(v)-B, I(a)-B, I(b)-B). In addition to these bacteria, Method I, I(a), I(b) and I(c) are also useful for treating an infection by *Bacillus subtilis, Streptococcus pyogenes, Borrelia burgdorferi* and/or *Borrelia burgdorferi* bacteria. In a preferred embodiment, Method I, I(i)-I(v), I(a), I(b) and I(c) are useful for treating an infection by one or more of the following bacteria: *Staphylococcus aureus, Staphylococcus epidermidis, Bacillus subtilis, Enterococcus faecalis, Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Pseudomonas aeruginosa, Klebsiella*

pneumoniae, Haemophilus influenzae, Acinetobacter baumannii. In another preferred embodiment, Method I, I(i)-I(v), I(a), I(b) and I(c) are useful for treating an infection by the *Staphylococcus aureus* and/or *Staphylococcus epidermidis* bacteria. In a particular embodiment, Method I, I(i)-I(v), I(a), I(b) and I(c) are useful for treating a *Staphylococcus aureus* infection (Method I-C, I(i)-C to I(v)-C, I(a)-C, I(b)-C, I(c)-C).

[0027] In a further embodiment, Method I as hereinbefore described is useful for the treatment or prophylaxis of a disease, infection or condition selected from a group consisting of anthrax, staphylococcal scalded skin syndrome (staph infections), pneumonia, impetigo, boils, cellulitis folliculitis, furuncles, carbuncles, scalded skin syndrome, abscesses, meningitis, osteomyelitis endocarditis, Toxic Shock Syndrome (TSS), septicemia, acute sinusitis, otitis media, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, brain abscess, tularemia, urinary tract infection, empyema, food poisoning, diarrhea and conjunctivitis, comprising administering to a subject in need thereof an effective amount of a Compound of Formula I, e.g., any of 1.1-1.212, or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, preferably formula 1.259-1.264, in free, pharmaceutically acceptable salt or prodrug form (Method I-D).

[0028] In still another embodiment, Method I(a) as hereinbefore described is useful for the treatment or prophylaxis of a disease, infection or condition selected from a group consisting of anthrax, staphylococcal scalded skin syndrome (staph infections), pneumonia, impetigo, boils, cellulitis folliculitis, furuncles, carbuncles, scalded skin syndrome, abscesses, meningitis, osteomyelitis endocarditis, Toxic Shock Syndrome (TSS), septicemia, acute sinusitis, otitis media, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, brain abscess, tularemia, urinary tract infection, empyema, food poisoning, diarrhea and conjunctivitis, comprising administering to a subject in need thereof an effective amount of a Compound of Formula III, e.g., any of 3.1-3.27, in free, pharmaceutically acceptable salt or prodrug form. (Method I(a)-D).

[0029] In yet another embodiment, Method I(b) as hereinbefore described is useful for the treatment or prophylaxis of a disease, infection or condition selected from a group consisting of anthrax, staphylococcal scalded skin syndrome (staph infections), pneumonia, impetigo, boils, cellulitis folliculitis, furuncles, carbuncles, scalded skin syndrome, abscesses, meningitis, osteomyelitis endocarditis, Toxic Shock Syndrome (TSS), septicemia, acute sinusitis, otitis media, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, brain abscess, tularemia, urinary tract infection, empyema, food

poisoning, diarrhea and conjunctivitis, comprising administering to a subject in need thereof an effective amount of a Compound of Formula IV, e.g., any of 4.1-4.22, preferably any of 4.9-4.15 or 4.20-4.21, in free, pharmaceutically acceptable salt or prodrug form. (Method I(b)-D).

[0030] In still another embodiment, Method I(c) as hereinbefore described is useful for the treatment or prophylaxis of a disease, infection or condition selected from a group consisting of anthrax, staphylococcal scalded skin syndrome (staph infections), pneumonia, impetigo, boils, cellulitis folliculitis, furuncles, carbuncles, scalded skin syndrome, abscesses, meningitis, osteomyelitis endocarditis, Toxic Shock Syndrome (TSS), septicemia, acute sinusitis, otitis media, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, brain abscess, tularemia, urinary tract infection, empyema, food poisoning, diarrhea and conjunctivitis, comprising administering to a subject in need thereof an effective amount of a Compound of Formula V or VI, in free, pharmaceutically acceptable salt or prodrug form. (Method I(c)-D).

[0031] Without being bound to any particular theory, it is believed that various compounds of the current invention are useful in methods of treating a bacterial infection via a novel mechanism, e.g., by utilizing riboswitch-ligand binding to alter gene expression, thereby affecting downstream riboflavin biosynthesis. As such, various Compounds of the Invention, e.g., various Compounds of Formula I, e.g., various compounds of formulae 1.1-1.212, e.g., any of 1.204; various compounds of formulae I(i)-I(v), e.g., various compounds of Formulae 1.213-1.265, e.g., any of formulae 1.261 or 1.262; various compounds of formula III, e.g., various compounds of formulae 3.1-3.27, e.g., any of 3.21 or 3.22, various compounds of formula 3.23; or various compounds of formula IV, e.g., various compounds of formulae 4.1-4.22, e.g., any of formula 4.10, 4.12 or 4.21, in free, pharmaceutically acceptable salt or prodrug form, are effective in treating an infection wherein traditional antibiotics are rendered ineffective due to drug resistance. Therefore, in a particular embodiment, the invention provides Method I or any of Methods I-A to I-D as hereinbefore described wherein the infection is by an infectious agent which is resistant to a drug that is not a riboswitch ligand (Method I-E). In a further embodiment, the infection is resistant to one or more drugs selected from a group consisting of a penicillin, vancomycin, cephlorsporin and methicillin. In a particular embodiment, the infection is a methicillin-resistant *Staphylococcus aureus* infection. In another embodiment, the invention provides Method I(a) as hereinbefore described

wherein the infection is by an infectious agent which is resistant to a drug that is not a riboswitch ligand, e.g., an infectious agent resistant to one or more drugs selected from a group consisting of a penicillin, vancomycin, cephlorsporin and methicillin, e.g., a methicillin-resistant *Staphylococcus aureus* infection (Method I(a)-E). In still another embodiment, the invention provides Method I(b) as hereinbefore described wherein the infection is by an infectious agent which is resistant to a drug that is not a riboswitch ligand, e.g., an infectious agent resistant to one or more drugs selected from a group consisting of a penicillin, vancomycin, cephlorsporin and methicillin, e.g., a methicillin-resistant *Staphylococcus aureus* infection (Method I(b)-E). In yet another embodiment, the invention provides Method I(c) as hereinbefore described wherein the infection is by an infectious agent which is resistant to a drug that is not a riboswitch ligand, e.g., an infectious agent resistant to one or more drugs selected from a group consisting of a penicillin, vancomycin, cephlorsporin and methicillin, e.g., a methicillin-resistant *Staphylococcus aureus* infection (Method I(c)-E).

[0032] In another embodiment, Methods I-A through I-E encompass a compound of Formula I as described in Method I, with the further proviso that when R_3 is 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino.

[0033] In a second aspect, the invention provides a method for the treatment or prophylaxis of a fungal infection (Method II) comprising administering to a subject in need thereof an effective amount of a compound of formula I, e.g., any of formulae 1.1-1.212, or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, as hereinbefore described, in free, pharmaceutically acceptable salt or prodrug form, with the proviso that: (a) when R_1 is methyl and R_2 is chloro, then R_3 is not methyl; (b) when R_1 is H and R_2 is dimethylamine, then R_3 is not H; and (c) when R_1 is H or C_{1-6} alkyl, and R_2 is hydrogen, halo, C_{1-6}alkyl, C_{1-6}alkoxy, dialkylamino or $-NHCH_2CH(OH)CH(OH)CH(OH)CH_2OH$, then R_3 is not H, $CH_2CH_2CH(OH)CH(OH)CH_2OH$, $-CH_2CH_2OH$, $CH_2CH(OH)CH(OH)CH(OH)-CH_2OH$, $CH_2CH(OH)CH(OH)CH(OH)CH(OH)CH_3$ or $CH_2CH(OH)CH(OH)CH(OH)-CH_2OPO_3$.

[0034] In a preferred embodiment, Method II comprises administering to a subject in need thereof an effective amount of a compound of formula I, wherein R_3 is C_{1-8} alkyl substituted with $-COOR_9$, $-P(O)(OR_9)(OR_{17})$, $-P(O)(OR_9)(NR_{13}R_{14})$, $-P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-OP(O)(OR_9)(OR_{17})$, $-OP(O)(OR_9)(NR_{13}R_{14})$, -

$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, and at least one of R_9 and R_{17} is C_{1-8} alkyl (e.g., methyl, ethyl or t-butyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, phenyl or Bn wherein phenyl and Bn are optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl), or at least one of R_{13}, R_{14}, R_{15} and R_{16} is -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-COOH, -CH(isopropyl)-COOH, -CH(isobutyl)-COOH, -CH(sec-butyl)-COOH), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –CH(CH_2CH_2COOH)-COOH), in free, pharmaceutically acceptable salt or prodrug form. In still another preferred embodiment, Method II comprises administering to a subject in need thereof an effective amount of a compound of formula I, wherein R_3 is C_{1-8}alkyl substituted with -$P(O)(OR_9)(NR_{13}R_{14})$, -$OP(O)(OR_9)(NR_{13}R_{14})$, and at least one of R_9 and R_{17} is C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, phenyl or Bn wherein phenyl and Bn are optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl), and at least one of R_{13}, R_{14}, R_{15} and R_{16} is -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-COOH, -CH(isopropyl)-COOH, -CH(isobutyl)-COOH, -CH(sec-butyl)-COOH), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with C_{1-8}alkyl hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –CH(CH_2CH_2COOH)-COOH), in free, pharmaceutically acceptable salt or prodrug form. In yet another preferred embodiment, Method II comprises administering to a subject in need thereof an effective amount of a compound of formula 1.204 in free, pharmaceutically acceptable salt or prodrug form. In anotherpreferred embodiment, Method I comprises administering to a subject in need thereof an effective amount of a compound of formula 1.210, in free, pharmaceutically acceptable salt or prodrug form. In still another embodiment, Method II comprises administering to a subject in need thereof an effective amount of a compound of formula 1.259 -1.261, in free, pharmaceutically acceptable salt or prodrug form.

[0035] In another embodiment of the second aspect, the invention provides a method for the treatment or prophylaxis of a fungal infection (Method II(a)) comprising administering to a subject in need thereof an effective amount of a compound of formula III, e.g., any of 3.1-3.27, in free, pharmaceutically acceptable salt or prodrug form. In a preferred embodiment, Method II(a) comprises administering to a subject in need thereof

an effective amount of a compound selected from any of those set forth in formula 3.21, in free, pharmaceutically acceptable salt or prodrug form.

[0036] In still another embodiment of the second aspect, the invention provides a method for the treatment or prophylaxis of a fungal infection (Method II(b)) comprising administering to a subject in need thereof an effective amount of a compound of formula IV, e.g., any of 4.1-4.22, in free, pharmaceutically acceptable salt or prodrug form. In a preferred embodiment, Method II(b) comprises administering to a subject in need thereof an effective amount of a compound selected from any of those set forth in any of formulae 4.9-4.15 or 4.20-4.21, in free, pharmaceutically acceptable salt or prodrug form.

[0037] In yet another embodiment of the second aspect, the invention provides a method for the treatment or prophylaxis of a fungal infection (Method II(c)) comprising administering to a subject in need thereof an effective amount of a compound of formula V or VI, in free, pharmaceutically acceptable salt or prodrug form.

[0038] In a third aspect, the invention provides use of a Compound of Formula I, e.g., any of 1.1-1.212, or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, as hereinbefore described in Method I, in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a bacterial infection. In a further aspect, the invention provides use of a Compound of Formula I, with the further proviso that when when R_3 is 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino as hereinbefore described in Method I in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a bacterial infection. In another embodiment of the third aspect, the invention provides use of a Compound of Formula III, e.g., any of 3.1-3.27, preferably a compound selected from any of those set forth in formula 3.21, in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a bacterial infection. In still another embodiment of the third aspect, the invention provides use of a Compound of Formula IV, e.g., any of 4.1-4.22, preferably a compound selected from any of those set forth in any of formulae 4.9-4.15 or 4.20-4.21, in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a bacterial infection. In yet another embodiment of the third aspect, the invention provides use of a Compound of Formula V or VI, in free, pharmaceutically acceptable salt or prodrug form, in the

manufacture of a medicament for the treatment or prophylaxis of a bacterial infection. In another specific embodiment, the infection is a Gram-positive or Gram-negative infection. In still another specific embodiment, the infection is an infection of one or more bacteria selected from a group consisting of *Moraxella catarrhalis, Klebsiella pneumoniae, Staphylococcus epidermidis, Streptococcus viridans, Enterococcus faecium, Staphylococcus aureus, Bacillus anthracis, Francisella tularensis, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Brucella melitensis, Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Salmonella enterica, Vibrio cholerae, Enterococcus faecalis* and *Yersinia pestis*. In addition to these bacteria, use of the compounds of the invention as hereinbefore described may also be for the treatment of an infection by the *Bacillus subtilis, Streptococcus pyogenes* and/or *Borrelia burgdorferi* bacteria. In a preferred embodiment, the bacteria is selected from any one of the following: *Staphylococcus aureus, Staphylococcus epidermidis, Bacillus subtilis, Enterococcus faecalis, Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Haemophilus influenzae, Acinetobacter baumannii*. In another preferred embodiment, the infection is by the *Staphylococcus aureus* and/or *Staphylococcus epidermidis* bacteria. In a further embodiment, the invention provides use as herein described in the manufacture of a medicament for the treatment or prophylaxis of a condition, disease or infection selected from anthrax, staphylococcal scalded skin syndrome (staph infections), pneumonia, impetigo, boils, cellulitis folliculitis, furuncles, carbuncles, scalded skin syndrome, abscesses, meningitis, osteomyelitis endocarditis, Toxic Shock Syndrome (TSS), septicemia, acute sinusitis, otitis media, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, brain abscess, tularemia, urinary tract infection, empyema, food poisoning, diarrhea and conjunctivitis.

[0039] In yet another embodiment, the invention provides use of various Compounds of Formula I, e.g., various compounds of formulae 1.1-1.212, e.g., any of 1.204, or various compounds of formulae I(i)-I(v), e.g., various compounds of formulae 1.213-1.265, e.g., any of formula 1.261 or 1.262, as hereinbefore described in Methods I (i.e., use as hereinbefore described), wherein said infection is resistant to a drug that is not a riboswitch ligand. In a further embodiment, the invention provides use of a Compound of Formula I, with the further proviso that when when R_3 is 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino as

hereinbefore described in Method I , in free, pharmaceutically acceptable salt or prodrug form, wherein said infection is resistant to a drug that is not a riboswitch ligand. In another further embodiment, the infection is resistant to one or more drugs selected from a group consisting of penicillin, vancomycin, cephlorsporin and methicillin. In a particular embodiment, the infection is a methicillin-resistant *Staphylococcus aureus* infection.

[0040] In still another embodiment, the invention provides use of a Compound of Formula III, e.g., various compounds of formulae 3.1-3.27, e.g., any of 3.21, in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a bacterial infection as hereinbefore described, wherein the infection is by an infectious agent which is resistant to a drug that is not a riboswitch ligand, e.g., an infectious agent resistant to one or more drugs selected from a group consisting of a penicillin, vancomycin, cephlorsporin and methicillin, e.g., a methicillin-resistant *Staphylococcus aureus* infection. In yet another embodiment, the invention provides use of various Compound of Formula IV, e.g., various compounds of formulae 4.1-4.22, e.g., any of formula 4.10, 4.12 or 4.21, in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a bacterial infection as hereinbefore described, wherein the infection is by an infectious agent which is resistant to a drug that is not a riboswitch ligand, e.g., an infectious agent resistant to one or more drugs selected from a group consisting of a penicillin, vancomycin, cephlorsporin and methicillin, e.g., a methicillin-resistant *Staphylococcus aureus* infection. In still another embodiment, the invention provides use of a Compound of Formula V or VI, wherein the infection is by an infectious agent which is resistant to a drug that is not a riboswitch ligand, e.g., an infectious agent resistant to one or more drugs selected from a group consisting of a penicillin, vancomycin, cephlorsporin and methicillin, e.g., a methicillin-resistant *Staphylococcus aureus* infection

[0041] In a fourth aspect, the invention provides use of a Compound of Formula I, e.g., any of 1.1-1.212 or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, preferably formula 1.260 or 1.261, as hereinbefore described in Method II, in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a fungal infection. In another embodiment of the fourth aspect, the invention provides use of a Compound of Formula III, e.g., any of 3.1-3.27, in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a fungal infection. In another embodiment of the fourth

aspect, the invention provides use of a Compound of Formula IV, e.g., any of 4.1-4.22, in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a fungal infection. In still another embodiment of the fourth aspect, the invention provides use of a Compound of Formula V or VI, e.g., in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment or prophylaxis of a fungal infection

[0042] In a fifth aspect, the invention provides a pharmaceutical composition comprising a Compound of Formula I, e.g., any of 1.1-1.212, preferably 1.203-1.211, or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, preferably formula 1.259-1.264 as hereinbefore described in any of Method I or II, in free, pharmaceutically acceptable salt form, in admixture with a pharmaceutically acceptable diluent or carrier.

[0043] In an sixth aspect, the invention provides a method for the treatment of an infection in a plant comprising administering to such plant an effective amount of a Compound of Formula I, e.g., any of 1.1-1.212, as hereinbefore described, preferably, 1.203-1.211, or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, preferably formula 1.259-1.264, in free, salt or prodrug form. In another embodiment of the sixth aspect, the invention provides a method for the treatmentof an infection in a plant comprising administering to such plant an effective amount of a Compound of Formula III, e.g., any of 3.1-3.27, as hereinbefore described, preferably 3.21-3.26, in free salt or prodrug form. In still another embodiment of the sixth aspect, the invention provides a method for the treatmentof an infection in a plant comprising administering to such plant an effective amount of a Compound o Formula IV, e.g. any of 4.1-4.22, as hereinbefore described, preferably 4.10-4.15 or 4.20-4.21, in free, salt or prodrug form. In yet another embodiment of the sixth aspect, the invention provides a method for the treatmentof an infection in a plant comprising administering to such plant an effective amount of a Compound of Formula V or VI in free, pharmaceutically acceptable salt form, as hereinbefore described. In another embodiment, the infection is a bacterial or fungal infection.

[0044] In a seventh aspect, the invention provides novel compound of Formula II, which comprises Compounds of Formula I, e.g., any of 1.1-1.212, as hereinbefore described in Method I or II, in free or salt form, which compound further comprises the following proviso:

(a) when R_1 is methyl and R_2 is chloro, then R_3 is not methyl;

(b) when R_1 is H and R_2 is dimethylamine, then R_3 is not H;

(c) when R_3 is (2R,3S,4S)-2,3,4,5-tetrahydroxypentyl or 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl, and R_1 is methyl, then R_2 is not methyl;

(d) when R_3 is (2R,3S,4S)-2,3,4,5-tetrahydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino;

(e) when R_1 is methyl and R_2 is alkoxy, then R_3 is not 2,3,4,5-tetrahydroxypentyl;

(f) when R_1 and R_2 are independently selected from a group consisting of C_{1-5} alkyl, C_{1-5} alkoxy, amino, hydrogen and halogen group, R_3 is not -$(CH_2)_{2-6}$-phosphate.

(g) when R_3 is 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino;

(h) when R_3 is -$(CH_2)_{2-6}$-phosphate or -$(CH_2)_{2-6}$-(sodium phosphate), then R_1 and R_2 are not C_{1-5}alkyl, C_{1-5}alkoxy, amino, hydrogen or halogen group;

(i) when R_1 is H or C_{1-6}alkyl, and R_2 is hydrogen, halo, C_{1-6}alkyl, C_{1-6}alkoxy, dialkylamino or –$NHCH_2CH(OH)CH(OH)CH(OH)CH_2OH$, then R_3 is not H, $CH_2CH_2CH(OH)CH(OH)CH_2OH$, -$CH_2CH_2OH$, $CH_2CH(OH)CH(OH)CH(OH)$-CH_2OH, $CH_2CH(OH)CH(OH)CH(OH)CH(OH)CH_3$ or $CH_2CH(OH)CH(OH)$-$CH(OH)CH_2OPO_3$;

(j) when R_1 and R_2 are both H, R_3 is not –$(CH_2)_{0-2}CH_2$-$N(R')_2$ or –$(CH_2)_{0-2}CH_2$-$N^+(R')_3$-X^- wherein R' is H or alkyl and X is Cl^-, F^-, oxalate, methosulfate, Br^-;

(k) when R_1 is H and R_2 is chloro, then R_3 is not –alkyl-$N(R^a)(R^b)$ wherein R^a is alkyl and R^b is hydroxyalkyl;

(l) when R_1 and R_2 and are selected from H, amine, polyamine, halogen, saccharide or C_{1-7} alkyl wherein the C atoms of the alkyl group may be replaced with N or O, wherein said alkyl group may be substituted with halogen, OH, NH_2, COOH, OR^d, NR^dR^e, $CONR^dR^e$, wherein R^d and R^e are independently alkyl, and aryl group, then R_3 is not H, amine, polyamine, halogen, saccharide or C_{1-7} alkyl wherein the C atoms of the alkyl group may be replaced with N or O, wherein said alkyl group may be substituted with halogen, OH, NH_2, COOH, OR^d, NR^dR^e, $CONR^dR^e$, wherein R^d and R^e are independently alkyl, or aryl group;

(m) when R_1 is methyl and R_2 is –$N(H)CH_3$, then R_3 is not –CH_2-$(CHOH)_3$-CH_2OH;

(n) when R_1 and R_2 are both ethyl, then R_3 is not –CH_2-$(CHOH)_3$-CH_2OH;

(o) when R_1 and R_2 are methyl, then R_3 is not H, alkyl, polysaccharide or an alkyl etherified or acylated glycoside of polysaccharide;

(p) when R_3 is H, C_{1-7}alkyl, C_{1-7}haloalkyl, C_{1-7}hydroxyalkyl, C_{1-7}aminoalkyl, C_{1-7} carboxyalkyl, or C_{5-20}arylC_{1-7}alkyl, then R_1 and R_2 are not H, halo, or C_{1-7}alkyl optionally substituted with –OH, halo, -COOH, -N(R_f)(R_g), or -C(O)N(R_f)(R_g), wherein R_f and R_g are independently H, C_{1-7}alkyl, C_{3-20}heterocycle, C_{5-20}aryl;

(q) when R_1 and R_2 are H or lower alkyl, the R_3 is not lower alkyl; and

(r) the Compound of Formula II is not riboflavin 5'-(hydrogensulfate), 7,8-dimethyl-10-(D-allityl) isoalloxazine.

[0045] In a particular embodiment, the compound of Formula II is as follows:

2.1 Formula II, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), substituted with at least one -CN, -C(O)N(H)(R_8), -OR_{10}, –C_{1-4}alkyl-OC(O)R_{12} or -OP(O)(OR_9)(OR_{17}), wherein R_9 and R_{17} of -OP(O)(OR_9)(OR_{17}) are independently selected from C_{1-8} alkyl (e.g., methyl, ethyl or t-butyl), phenyl or Bn optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

R_{10} is -C_{1-8}alkyl-OR_{11} wherein R_{11} is –C_{1-4}alkyl-OC(O)R_{12}, –C_{1-8}alkyl-C(O)N(H)R_8, -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -C_{1-8}alkyl-OP(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-OP(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -C_{1-8}alkyl-N(H)-S(O)$_2$(CF_3), 7,8-dimethyl-isoalloxazin-10-yl-ethyl or aryl substituted with –$COOR_9$;

all the other substituents are hereinbefore described in Formula I;

2.2 Formula II, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), optionally substituted with at least one -C(O)OH, -OR_{10}, -C(O)N(R_6)(R_7), or -N(R_6)(R_7);

R_2 is C_{4-7} heterocycle (e.g., piperazinyl or pyrrolidinyl) optionally substituted or C_{3-7}cycloalkyl substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl);

all the other substituents are hereinbefore described in Formula I;

2.3 Formula II, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), substituted with at least one -C(O)N(R_6)(R_7), or -N(R_6)(R_7);

R_6 and R_7 are independently:

(i) -C(O)OR_9, –C_{1-8}alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 wherein R_9

is C_{1-8}alkyl;

(ii) –C_{1-8}alkyl-C(O)N(H)R_8; or

(iii) -C_{1-8}alkyl-P(O)$(OR_9)_2$, C_{1-8}alkyl-OP(O)$(OR_9)_2$, -C_{1-8}alkyl-N(H)-S(O)$_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl or aryl optionally substituted with –$COOR_9$;

all the other substituents are hereinbefore described in Formula I;

2.4 Formula II, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl) substituted with -OP(O)$(OR_9)(OR_{17})$,;

R_9 and R_{17} of -OP(O)$(OR_9)(OR_{17})$ are H;

R_2 is C_{6-8}alkyl, C_{6-8}alkoxy, -N$(R_4)(R_5)$, C_{3-7}cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl); or R_1 and R_2 are connected so as to form a cyclic ring structure containing –OCH_2CH_2O-;

R_4 and R_5 are independently C_{3-7}cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{4-7}heterocycle (e.g., piperazinyl), C_{3-8}alkyl or C_{1-8}alkyl substituted with –OH, –C(O)OR_9, -N$(R_6)(R_7)$ (e.g., amino, dimethylaminoethyl), C_{1-8}alkoxyl (e.g., methoxy), C_{6-10}aryl (e.g., phenyl), C_{5-10}heteroaryl (e.g., pyridinyl) optionally substituted with halo (e.g.,4-fluorophenyl), or C_{4-7}heterocycle optionally substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl); and

all the other substituents are hereinbefore described in Formula I;

2.5 Formula 2.4, wherein R_4 and R_5 are independently C_{3-7}cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{4-7}heterocycle (e.g., piperazinyl), C_{6-8}alkyl or C_{1-8}alkyl substituted with –OH, –C(O)OR_9, -N$(R_6)(R_7)$ (e.g., amino, dimethylamino), C_{1-8}alkoxyl (e.g., methoxy), C_{6-10}aryl (e.g., phenyl), C_{5-10}heteroaryl (e.g., pyridinyl) optionally substituted with halo (e.g.,4-fluorophenyl), or C_{4-7}heterocycle optionally substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl);

2.6 Formula 2.4, wherein R_4 and R_5 are independently selected from C_{3-7}cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{4-7}heterocycle (e.g., piperazinyl), and C_{1-8}alkyl substituted with one or more groups selected from –OR_{11}, –C(O)OR_9, -N$(R_6)(R_7)$ (e.g., amino, dimethylamino), C_{1-8}alkoxyl (e.g.,

methoxy), C_{6-10}aryl (e.g., phenyl), C_{5-10}heteroaryl (e.g., pyridinyl) optionally substituted with halo (e.g.,4-fluorophenyl), and C_{4-7}heterocycle optionally substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl);

2.7 Formula II, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), substituted with one or more groups selected from-$OP(O)(OR_9)(OR_{17})$, -CN, $-C(O)OR_9$, $-C(O)N(H)(R_8)$, $-OR_{10}$, $-C(O)N(R_6)(R_7)$, or $-N(R_6)(R_7)$;

R_9 and R_{17} of $OP(O)(OR_9)(OR_{17})$ and $-C(O)OR_9$ are independently C_{1-8} alkyl (e.g., methyl, ethyl or t-butyl), phenyl or Bn optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl), or $-C_{1-4}$alkyl-$OC(O)R_{12}$;

all the other substituents are hereinbefore described in Formula I;

2.8 Formula II, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), substituted with at least one $-OR_{10}$, group wherein R_{10} is H;

R_2 is $-N(R_4)(R_5)$, C_{3-7}cycloalkyl substituted with or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl);

R_4 and R_5 are independently H, C_{4-7}heterocycle (e.g., piperazinyl) substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl), or C_{1-8}alkyl (e.g., methyl or ethyl) substituted with $-C(O)OR_9$ wherein R_9 of $-C(O)OR_9$ is C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl),$-C_{1-4}$alkyl-$OC(O)R_{12}$, phenyl or Bn wherein said phenyl or Bn are optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl), $-N(R_6)(R_7)$, C_{6-10}aryl (e.g., phenyl) or C_{5-10}heteroaryl (e.g., pyridinyl) wherein said aryl or heteroaryl is substituted with halo (e.g.,4-fluorophenyl), provided that R_4 and R_5 are not both H;

R_6 and R_7 are independently selected from:

(i) $-C(O)OR_9$, $-C_{1-8}$alkyl-$C(O)OR_9$, $-C_{1-4}$alkyl-$OC(O)R_{12}$ or $-C_{1-8}$alkyl(amine)-$C(O)OR_9$ wherein R_9 of $-C(O)OR_9$, $-C_{1-8}$alkyl-$C(O)OR_9$ or $-C_{1-8}$alkyl(amine)-$C(O)OR_9$ is C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), phenyl or Bn optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl,

3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl), ;

(ii) $-C_{1-8}$alkyl-C(O)N(H)R_8; or

(iii) -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -C_{1-8}alkyl-OP(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-OP(O)(OR_9)($NR_{13}R_{14}$) -C_{1-8}alkyl-OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -C_{1-8}alkyl-N(H)-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl or aryl optionally substituted with $-COOR_9$;

all the other substituents are hereinbefore described in Formula I;

2.9 Formula 2.8, wherein R_3 is further substituted with -OP(O)(OR_9)(OR_{17});

2.10 Formula 2.8 or 2.9, wherein R_3 is 5-phosphate-(2S,3S,4R)-2,3,4-trihydroxypentyl;

2.11 Formula II, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), substituted with a -N(R_6)(R_7);

R_2 is C_{1-8} alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -N(R_4)(R_5), C_{3-7} cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl);

all the other substituents are hereinbefore described in Formula I;

2.12 Formula II, wherein R_3 is C_{1-8}alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), optionally substituted with $-C(O)OR_9$ wherein R_9 of $-C(O)OR_9$ is C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, phenyl or Bn wherein said phenyl and Bn are optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -N(R_4)(R_5), C_{3-7}cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl);

all the other substituents are hereinbefore described in Formula I;

2.13 Formula II, wherein R_3 is C_{1-8}alkyl substituted with at least one $-COOR_9$, or -OP(O)(OR_9)(OR_{17})

R_2 is -N(R_4)(R_5), C_{3-7}cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl)

R_4 and R_5 are independently selected from H, C_{3-7}cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{4-7}heterocycle (e.g., piperazinyl), and C_{3-8}alkyl wherein said alkyl is optionally substituted with one or more –OR_{11}, –C(O)OR_9, -N(R_6)(R_7) (e.g., amino, dimethylamino), C_{1-8}alkoxyl (e.g., methoxy), C_{6-10}aryl (e.g., phenyl) or C_{5-10}heteroaryl (e.g., pyridinyl) optionally substituted with halo (e.g.,4-fluorophenyl), or C_{4-7}heterocycle optionally substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl);

all the other substituents are hereinbefore described in Formula I;

2.14 Formula II, wherein R_3 is -C_{1-8}alkyl–C(O)OR_9 or -C_{1-8}alkyl–OP(O)(OR_9)(OR_{17}) group wherein the alkyl group is optionally substituted with -OH;

R_9 and R_{17} of -C_{1-8}alkyl–C(O)OR_9 and -C_{1-8}alkyl–OP(O)(OR_9)(OR_{17}) are independently C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl),–C_{1-4}alkyl-OC(O)R_{12}, phenyl or Bn where in said phenyl and Bn are optionally substituted with halo or C_{1-4}alkoxy (3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl), ;

all the other substituents are hereinbefore described in Formula I;

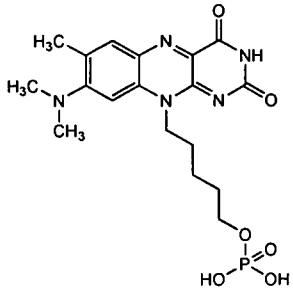
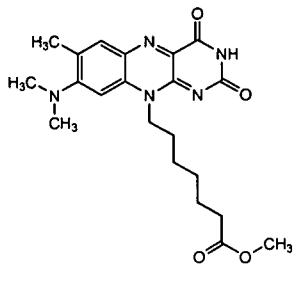
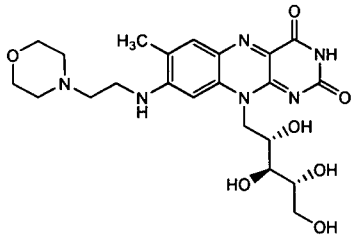
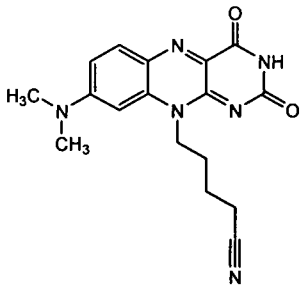
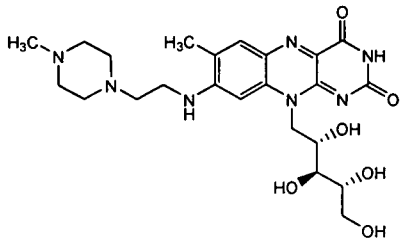
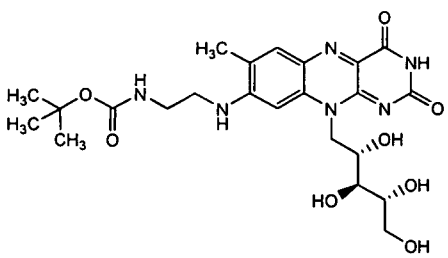
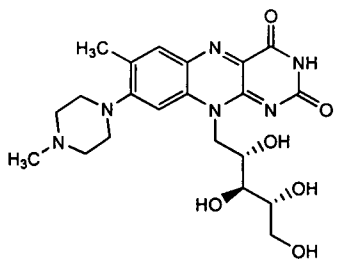
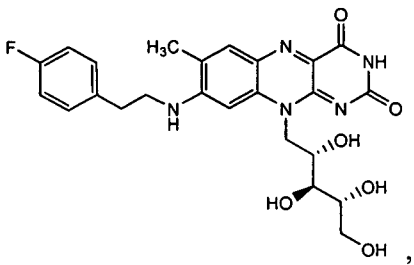
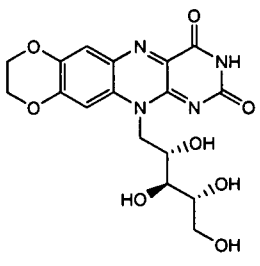
2.15 Formula II, wherein R_3 is -C_{1-8}alkyl substituted with one or more groups selected from OP(O)(OR_9)($NR_{13}R_{14}$), -OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$), or -P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$),

all the other substituents are hereinbefore described in Formula I;

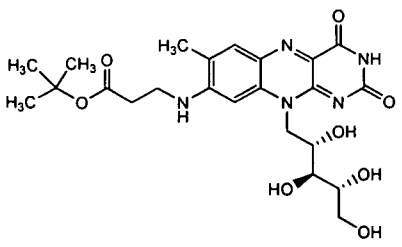
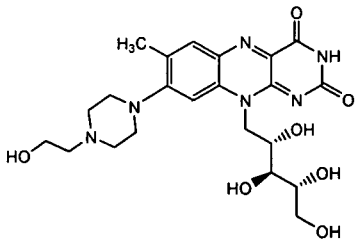
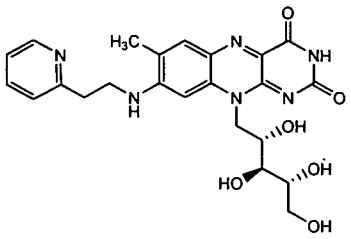
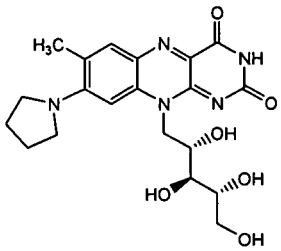
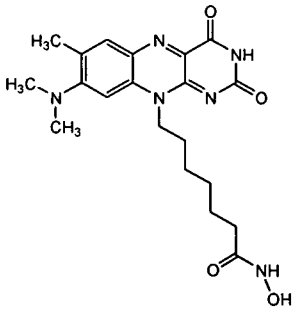
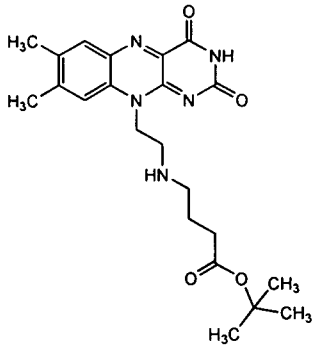
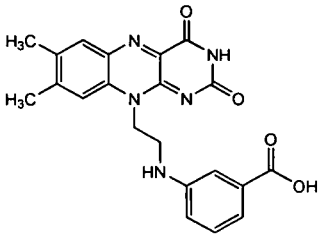
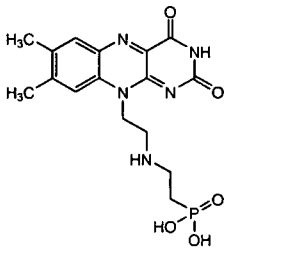
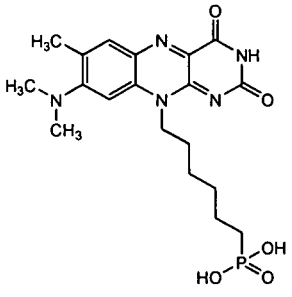
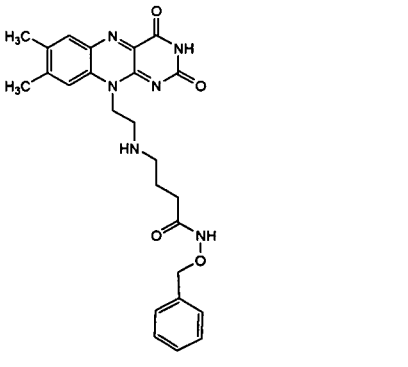
2.16 Formula 2.15, wherein R_3 is further substituted with one or more –OR_{10} wherein R_{10} is H;

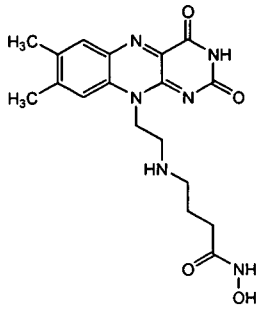
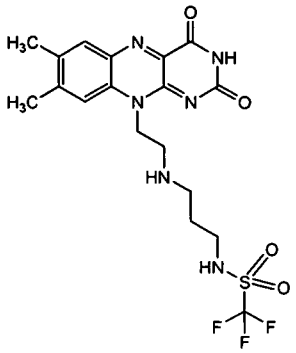
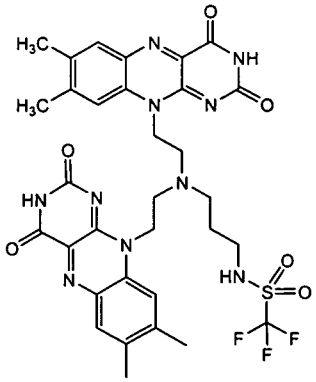
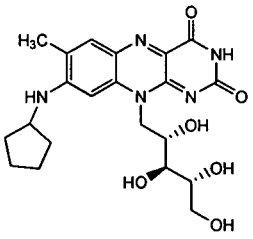
all the other substituents are hereinbefore described in Formula I;

2.17 A compound of Formula II, selected from:


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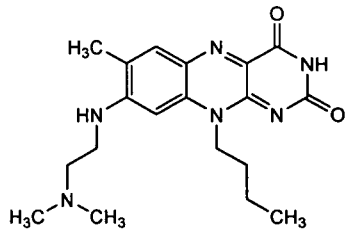
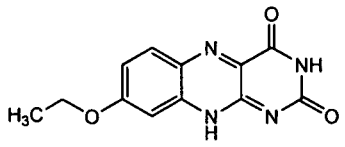
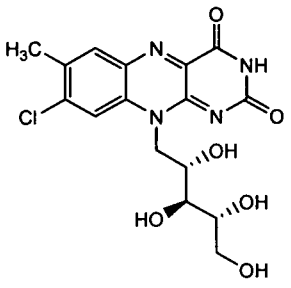
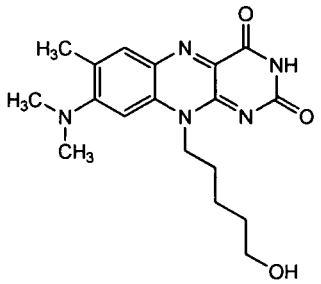
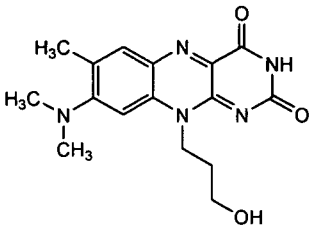
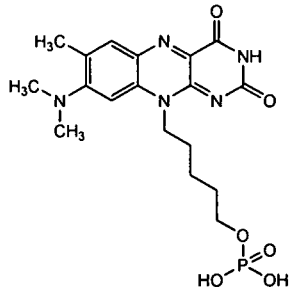
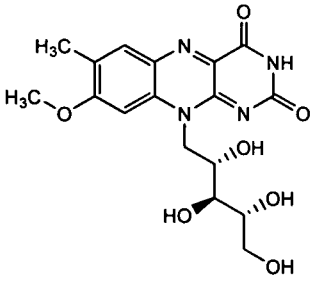
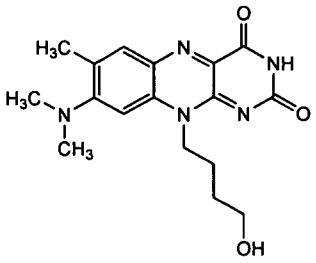
in free, salt or prodrug form.

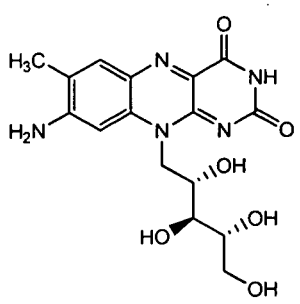
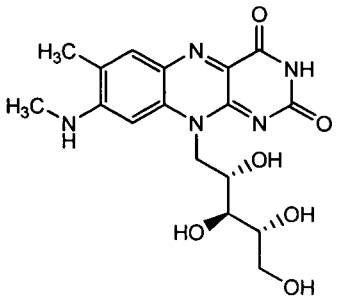
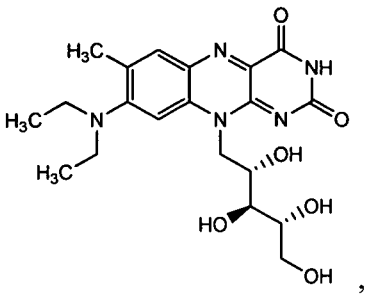
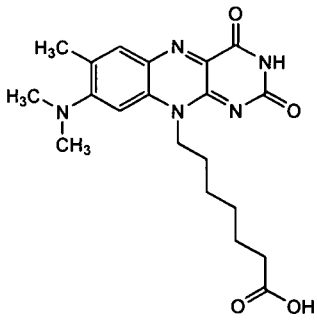
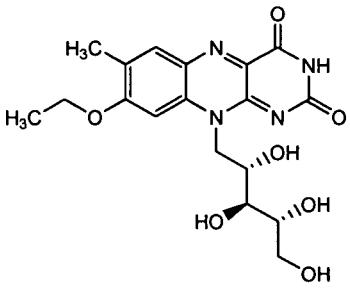
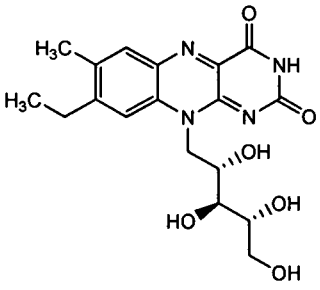
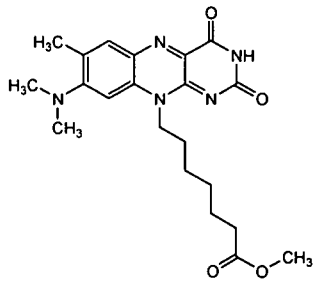
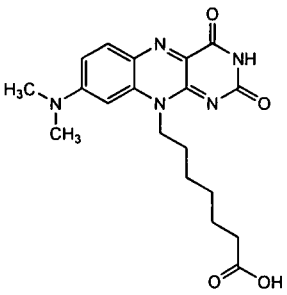
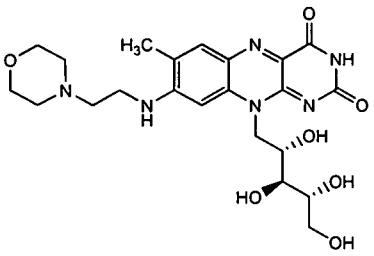
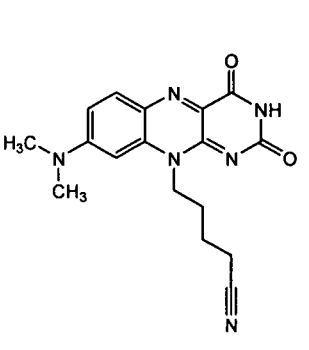
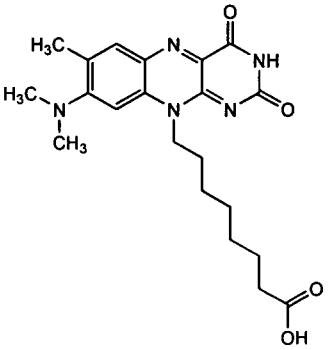
[0046] In another embodiment, novel compound of Formula II or any of 1.1-1.202, 1.209 or any of 2.1-2.17 bind to FMN riboswitch, e.g., with an IC_{50} of less than or equal to 10μM, preferably less than 1μM, more preferably less than 100 nM, most preferably less than 10nM in a binding assay, for example, as described in Example 1. In an eighth aspect, the invention provides a novel compound wherein said compound is or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, preferably formula 1.259, 1.260 or 1.261, in free, salt or prodrug form. In a further embodiment, the invention provides novel compound selected from any compounds disclosed in Table 1, in free, salt or prodrug form.

[0047] In still another embodiment of the eighth aspect, the invention provides novel compound of Formula III, e.g., any of 3.1-3.27, preferably a compound selected from any of those set forth in formula 3.20 or 3.21, in free, salt or prodrug form. In yet another embodiment of the eighth aspect, the invention provides novel compound of Formula IV, e.g., any of 4.1-4.22, preferably a compound selected from any of those set forth in formula 4.9 or 4.20, in free, salt or prodrug form. In another embodiment of the eighth aspect, the invention provides novel compound of Formula V or VI, free, salt or prodrug form.

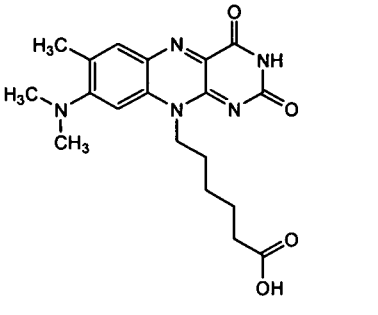
[0048] In a nineth aspect, the invention provides a Compound of Formula II, e.g., any of 2.1-2.17 as novel FMN riboswitch ligand. The invention also provides a compound of or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, preferably formula 1.261 or 1.262, in free, salt or prodrug form as novel FMN riboswitch ligand.

[0049] In another aspect, the invention provides a riboswitch ligand which comprises a compound of Formula I, e.g., any of 1.1- 1.212 or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, or Formula II, or any of 2.1-2.17, in free or salt form. In another embodiment, the riboswitch ligand of the invention bind to FMN riboswitch, e.g., with an IC_{50} of less than or equal to 10μM, preferably less than 1μM, more preferably less than 100 nM, most preferably less than 10nM in a binding assay, for example, as described in Example 1. In a further embodiment, the invention provides a riboswitch ligand selected from:


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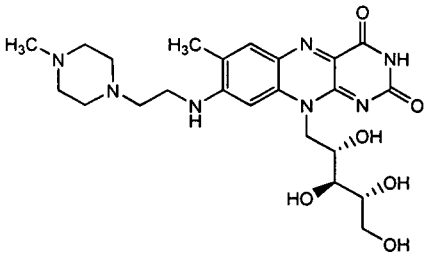
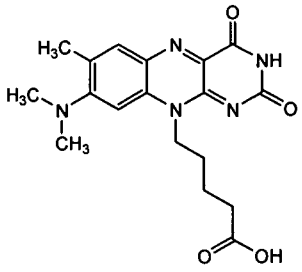
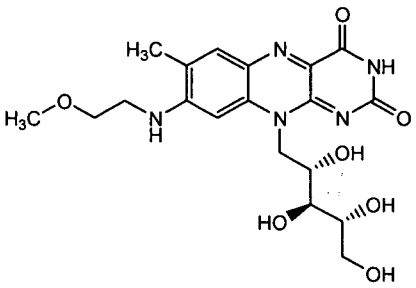
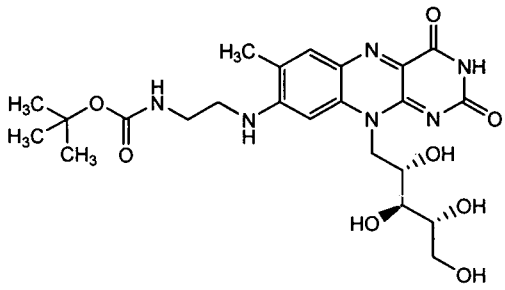
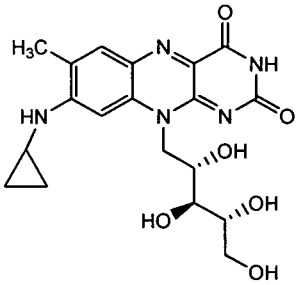
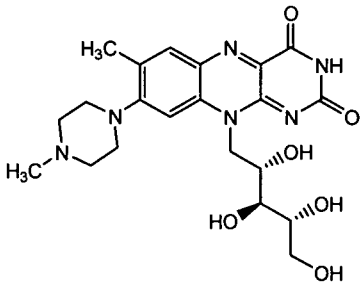
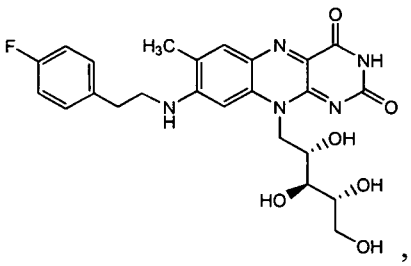
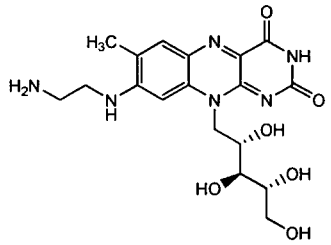
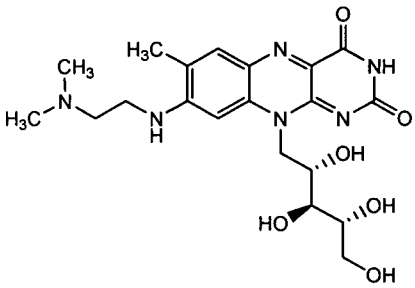
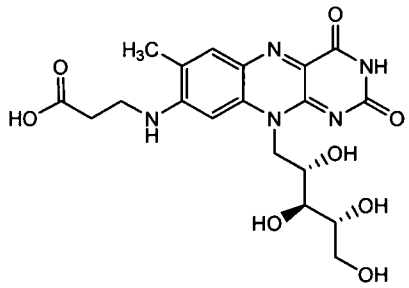
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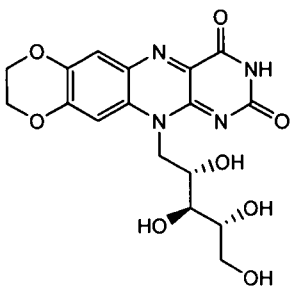
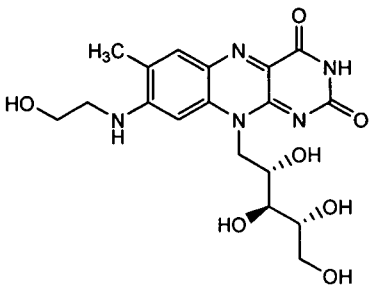
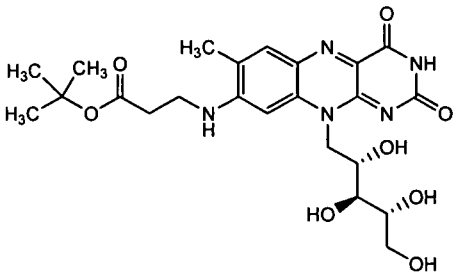
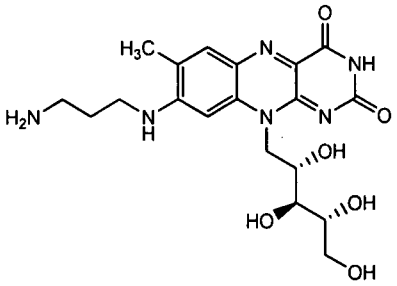
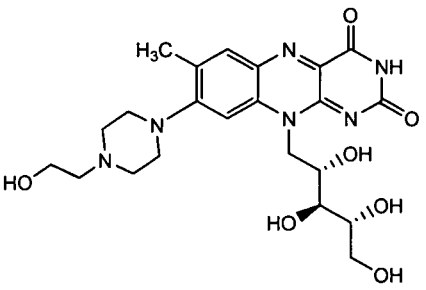
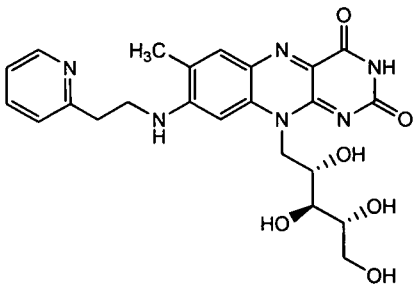
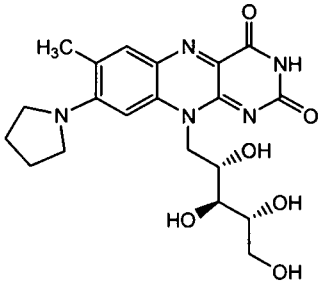
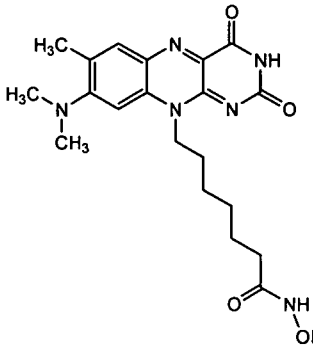
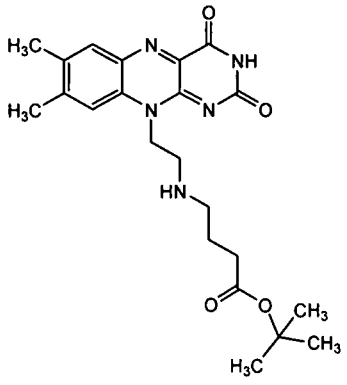
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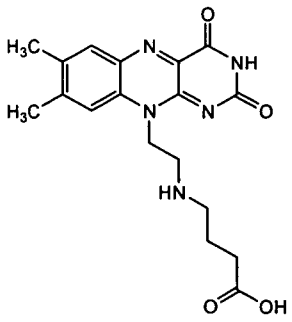
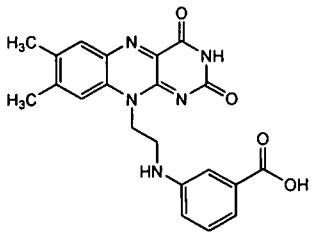
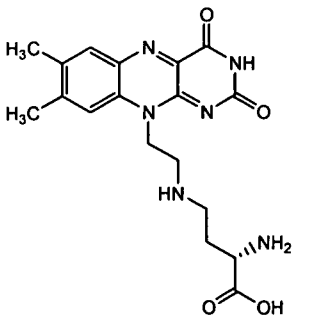
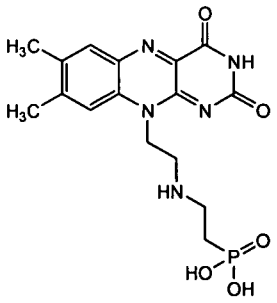
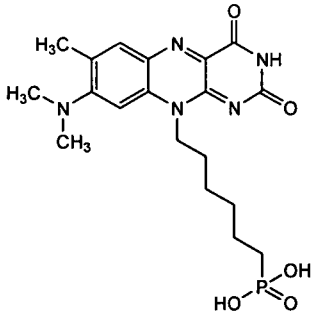
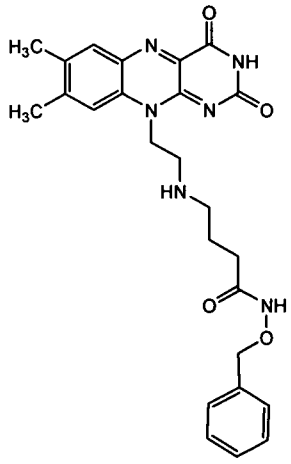
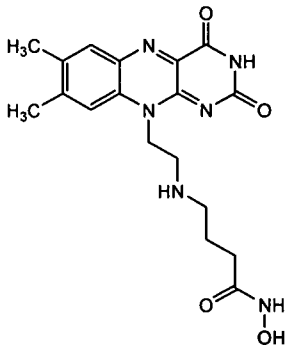
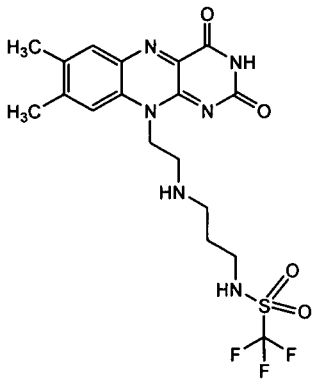
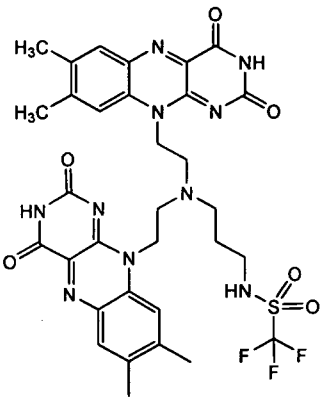
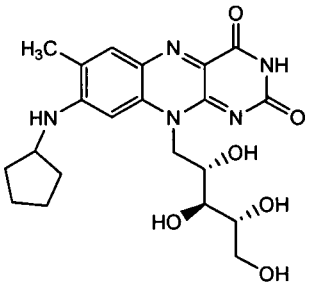
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and

in free or salt form.

[0050] In another embodiment, the riboswich ligand is preferably a compound selected from those set forth in formula 1.261 or 1.262, in free or salt form.

[0051] In another embodiment of the nineth aspect, the invention provides a riboswitch ligand which comprises a compound of Formula III, e.g., any of 3.1-3.27, preferably a compound selected from any of those set forth in formula 3.21, in free, salt or prodrug form. In another embodiment, the riboswitch ligand of the invention binds to FMN riboswitch, e.g., with an IC_{50} of less than or equal to 10μM, preferably less than 1μM, more preferably less than 100 nM, most preferably less than 10nM in a binding assay, for example, as described in Example 1.

[0052] In yet another embodiment of the nineth aspect, the invention provides a riboswitch ligand which comprises a compound of Formula IV, e.g., any of 4.1-4.22, preferably a compound selected from any of those set forth in formula 4.10, 4.12 or 4.21, in free, salt or prodrug form.

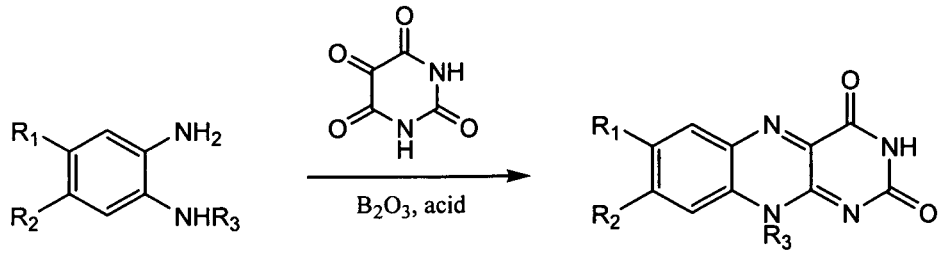
[0053] In still another embodiment of the nineth aspect, the invention provides a riboswitch ligand which comprises a compound of Formula V or VI, in free, salt or prodrug form.

[0054] In the tenth aspect, the invention provides a pharmaceutical composition comprising a compound of the invention, e.g., any of formula I, e.g., any of formulae 1.1- 1.212, or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, preferably formula 1.259-1.264, or formula II, e.g., any of 2.1-2.17, in free, pharmaceutically acceptable salt form, in admixture with a pharmaceutically acceptable diluent or carrier.

[0055] In another embodiment of the tenth aspect, the invention provides a pharmaceutical composition comprising a Compound of Formula III, e.g., any of 3.1-3.27, in free, pharmaceutically acceptable salt or prodrug form, in admixture with a pharmaceutically acceptable diluents or carrier. In still another embodiment of the tenth aspect, the invention provides a pharmaceutical composition comprising a Compound of Formula IV, e.g., any of 4.1-4.22, in free, pharmaceutically acceptable salt or prodrug form, in admixture with a pharmaceutically acceptable diluents or carrier. In yet another embodiment of the tenth aspect, the invention provides a pharmaceutical composition comprising a Compound of Formula V or VI, in free, pharmaceutically acceptable salt or prodrug form, in admixture with a pharmaceutically acceptable diluents or carrier.

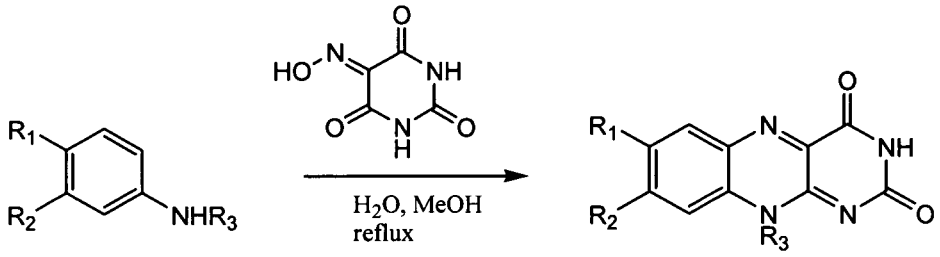
[0056] In still another aspect, the invention provides a method of preparing a Compound of formula I, e.g., any of formulae 1.1- 1.212, or any of formulae I(i)-I(v),

e.g., any of 1.213-1.265, or formula II comprising the step of reacting **Int-4** as described below with a pyrimidine-2,4,5,6(1*H*,3*H*)-tetrone in the presence of boron oxide and an acid, e.g., mineral acid, e.g., acetic acid.



Int-4 **Formula I-A**

[0057] In still another embodiment, the invention provides a method of preparing a compound of formula I or II comprising the step of reacting **Int-4A** as described below with a violuric acid at elevated temperature (e.g., greater than 25°C, e.g., about 95°C).



Int-4A **Formula I-A**

[0058] The invention further provides a method of preparing a compound of formula I or II as described below in Methods of Making Compounds of the Invention. In a further aspect, the invention provides a method of preparing a compound of formula I or II selected from any of the methods as described in any of Examples 2-92.

DETAILED DESCRIPTION OF THE INVENTION

[0059] The term "riboswitch" or "riboswitches" is an art recognized term and refers to an mRNA which comprises a natural aptamer that binds target metabolite and an expression platform which changes in the RNA structure to regulate genes. The term "FMN riboswitch" refers to a riboswitch that binds a metabolite such as flavin mono-nucleotide (FMN) or ligands such as various Compounds of Formula I or II, e.g., various compounds of formulae 1.1-1.212, 2.1-2.17, various compounds of formulae I(i)-I(v), e.g., various compounds of formulae 1.213-1.265, various Compounds of Formula III,

e.g., various compounds of formulae 3.1-3.27, various Compounds of Formula IV, e.g., various compounds of formulae 4.1-4.22, or various Compounds of Formula V or VI, e.g., any of the compounds in formulae 1.204, 1.210, 1.261, 1.262, 3.21, 4.10, 4.12 or 4.21, in free, salt or prodrug form and which affects downstream FMN biosynthesis and transport proteins.

[0060] "FMN riboswitch ligand" refers to any compound such as compounds of Formula I or II, e.g., various compounds of formulae 1.1-1.212, 2.1-2.17, formulae I(i)-I(v), e.g., various compounds of formulae 1.213-1.265, preferably formula 1.261 or 1.262, FMN or roseoflavin, or various compounds of Formula III, e.g., of formulae 3.1-3.27, various Compounds of Formula IV, e.g., of formulae of 4.1-4.22 or various Compounds of Formula V or VI, in free, salt or prodrug form which binds to the FMN riboswitch, e.g., via the FMN-binding aptamer called the RFN element, which is a highly conserved domain in the 5'-untranslated regions of prokaryotic mRNA. Without intended to be bound by any particular theory, it is believed the binding of the ligand to its riboswitch induces a conformational change in the bacterial mRNA such that the expression of the ORF is repressed, for example, such that the expression of enzymes responsible for riboflavin and FMN biosynthesis is repressed. This is achieved by inducing the mRNA to form (1) a terminator hairpin that halts RNA synthesis before the ORF can be synthesized or (2) a hairpin that sequesters the Shine-Dalgarno sequence and prevents the ribosome from binding to the mRNA so as to translate the ORF. Examples of FMN riboswitch ligands include, but are not limited to compounds of formulae 1.204, 1.210, 1.261, 1.262, 3.21, 4.10, 4.12 or 4.21, in free, salt or prodrug form.

[0061] The term "infection" encompasses any infection by bacteria and/or fungi In a particular embodiment, the term "infection" refers to a bacterial infection. In another embodiment, the infection is a Gram-positive or Gram-negative infection. In still another embodiment, the infection is an infection by one or more bacteria selected from a group consisting of *Moraxella catarrhalis, Klebsiella pneumoniae, Staphylococcus epidermidis, Streptococcus viridans, Enterococcus faecium, Staphylococcus aureus, Bacillus anthracis, Francisella tularensis, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Brucella melitensis, Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Salmonella enterica, Vibrio cholerae, Enterococcus faecalis* and *Yersinia pestis*. In addition, the infection is an infection by one or more bacteria selected from *Bacillus subtilis, Streptococcus pyogenes* and/or *Borrelia burgdorferi*. In a preferred

embodiment, the infection is a *Staphylococcus aureus* and/or *Staphylococcus epidermidis* infection. In a further embodiment, the infection is a *Staphylococcus aureus* infection. In a particular embodiment, the infection is an infection which is resistant to a drug which is not a riboswitch ligand. In a further aspect of this particular embodiment, the infection is an infection which is resistant to one or more drugs selected from a group consisting of penicillin, vancomycin, cephlorsporin and methicillin. In a particular embodiment, the infection is a methicillin-resistant *Staphylococcus aureus* (MRSA) infection.

[0062] In other aspect, the term "infection" refers to a fungal infection. Examples of a fungal infection include but are not limited to infection by Microsporum, Trichophyton, Epidermophyton, Tinea (e.g., tinea versicolor, tinea pedis, tinea corporis), Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatidis, Candida (e.g., Candida albicans), Aspergillus, Fumigatus and Sporothrix xchenckii fungi. Examples of conditions caused by a fungal infection include, but are not limited to mycoses such as superficial, cutaneous, subcutaneous or systemic mycosis, e.g., coccidioidomycosis, histoplasmosis, blastomycosis, candidiasis (e.g., yeast infection or moniliasis), sporotrichosis and ringworm (e.g., athlete's foot, jock itch, scalp ringworm, nail ringworm, body ringworm, beard ringworm).

[0063] The term "bacteria" or "bacterial" include, but are not limited to *Moraxella catarrhalis, Klebsiella pneumoniae, Staphylococcus epidermidis, Streptococcus viridans, Enterococcus faecium, Staphylococcus aureus, Bacillus anthracis, Francisella tularensis, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Brucella melitensis, Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Salmonella enterica, Vibrio cholerae, Enterococcus faecalis* and *Yersinia pestis*. The term "bacteria" refered to in the current invention also includes *Bacillus subtilis, Streptococcus pyogenes* and/or *Borrelia burgdorferi*. Preferably, the bacteria referred to in the current the invention include but not limited to *Moraxella catarrhalis, Klebsiella pneumoniae, Staphylococcus epidermidis, Streptococcus viridans, Enterococcus faecium, Staphylococcus aureus, Bacillus anthracis, Francisella tularensis, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Brucella melitensis, Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Salmonella enterica, Vibrio cholerae, Enterococcus faecalis, Yersinia pestis, Bacillus subtilis* and *Streptococcus pyogenes*. More preferably, the bacteria referred to in the current the invention include but not limited to *Staphylococcus aureus, Staphylococcus epidermidis,*

Bacillus subtilis, Enterococcus faecalis, Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Haemophilus influenzae, Acinetobacter baumannii, Most preferably, the bacteria referred to in the current the invention include *Staphylococcus aureus* and/or *Staphylococcus epidermidis*.

[0064] If not otherwise specified or clear from context, the following terms as used herein have the following meetings:

a. "Alkyl" as used herein is a saturated or unsaturated hydrocarbon moiety, preferably saturated, e.g., one to eight or one to four carbon atoms in length, which may be linear or branched (e.g., n-butyl or tert-butyl), and may be optionally substituted, e.g., mono-, di-, or tri-substituted on any one of the carbon atom, e.g., with alkyl (e.g., methyl), alkoxy, halogen (e.g., chloro or fluoro), haloalkyl (e.g., trifluoromethyl), hydroxy, and carboxy. For example, "C_1-C_8 alkyl" denotes alkyl having 1 to 8 carbon atoms. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, 3-methylpentyl, 4-methylpentyl, n-pentyl, n-hexyl and n-heptyl.

b. "Aryl" as used herein is a mono or bicyclic aromatic hydrocarbon, preferably phenyl or naphthyl, optionally substituted, e.g., with C_1-C_8alkyl (e.g., methyl), C_1-C_8alkoxy, halogen (e.g., chloro or fluoro), haloC_1-C_8alkyl (e.g., trifluoromethyl), hydroxy, carboxy, or an additional aryl or heteroaryl.

c. "Cycloalkyl" is intended to include monocyclic or polycyclic ring system comprising at least one aliphatic (non-aromatic) ring. Therefore, "cycloalkyl" may denote simply a cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl and the like.

d. Heterocycle as used herein refers to a monocyclic or polycyclic non-aromatic ring system wherein at least one carbon atom is replaced with a heteroatom selected from a group consisting of N, O, and S. Examples of heteroatom include morpholinyl (e.g., morpholin-4-yl), piperazinyl, piperidinyl, pyrolidinyl and the like. Heterocycle of the invention may optionally be substituted with $C_{1\text{-}8}$alkyl (e.g., methyl).

e. Heteroaryl as used herein refers to a mono or bicyclic aromatic ring system comprises at least one aromatic ring containing at least one heteroatom independently selected from the group consisting of N, O and S. The heteroaryl ring may be attached to its pendant group at any heteroatom or carbon atom which results in a stable structure. The heteoraryl rings described herein may be substituted on the carbon or on the nitrogen atom if the resulting compound is stable. Examples of heteroaryl group include, but are not limited to pyridinyl (e.g., pyridine-2-yl), imidazolyl, thiazolyl, pyrazinyl, pyrimidinyl, quinoxalinyl, and the like. The heteroaryl group may also be optionally substituted with C_{1-8}alkyl (e.g., methyl), C_{1-8}alkoxy, halogen, hydroxy, haloalkyl or carboxy.

[0065] The substituents on the Compounds of the Invention, e.g., R_1-R_{18} may be specifically or generally defined. Unless specified otherwise, R_1-R_{18} are defined as in Formula I, II, III or IV. In other instances, R_1-R_{18} are defined by the embodiment or claims to which it depends.

[0066] The Compounds of the Invention (e.g., Compounds of Formula I, e.g., any of 1.1-1.212 or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, as described in any of Methods I or II; Compounds of Formula II, or any of 2.1-2.17; a Compound of Formula III, e.g., any of 3.1-3.27; a Compound of Formula IV, e.g., any of 4.1-4.22, or a Compound of Formula V or VI, as hereinbefore described, or a compound in Examples 2-92, as hereinafter described) may exist in free or salt form, e.g., as acid addition salts. An acid-addition salt of a compound of the invention which is sufficiently basic, for example, an acid-addition salt with, for example, an inorganic or organic acid, for example hydrochloric, hydrobromic, sulphuric, phosphoric, acid acetic, trifluoroacetic, citric, maleic acid, toluene sulfonic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic acid, and the like. In addition a salt of a compound of the invention which is sufficiently acidic is an alkali metal salt, for example a sodium or potassium salt, an alkaline earth metal salt, for example a calcium or magnesium salt, an ammonium salt or a salt with an organic base which affords a physiologically-acceptable cation, for example a salt with methylamine, dimethylamine, trimethylamine, piperidine, morpholine or tris-(2-hydroxyethyl)amine.

[0067] In this specification, unless otherwise indicated, language such as Compounds of the Invention is to be understood as embracing such Compounds of Formula I (e.g., any of 1.1-1.212 or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, preferably formula 1.259, 1.260 or 1.261 as described in any of Methods I or II),Compounds of formula II (e.g., any of 2.1-2.17,), Compounds of Formula III (e.g., any of 3.1-3.27); a Compound of Formula IV (e.g., any of 4.1-4.22) or a Compound of Formula V or VI in any form, for example free or acid addition salt or prodrug form, or where the compounds contain acidic substituents, in base addition salt form. The Compounds of the Invention are intended for use as pharmaceuticals, therefore pharmaceutically acceptable salts are preferred.

[0068] Compounds of the Invention may or may not be used as pharmaceuticals. Therefore, salts which are unsuitable for pharmaceutical uses may be useful, for example, for the isolation or purification of free Compounds of the Invention or their pharmaceutically acceptable salts, and are therefore also included.

[0069] As Compounds of Formula II is a subset of Compounds of Formula I, Compounds of Formula II or any of 2.1-2.17 as hereinbefore described may also be useful for the same methods of use, e.g., any of Methods I, I-A to I-E, or II. In addition, the invention also encompases use of a Compound of Formula II or any of 2.1-2.17, a Compound of Formula III, e.g., any of formulae 3.1-3.27, a Compound of Formula IV, e.g., any of formulae 4.1-4.22, or a Compound of Formula V or VI, as hereinbefore described in the manufacture of a medicament for the treatment or prophylaxis of an infection as hereinbefore described in Method I, I-A to I-E, I(a)-A to I(a)-E, I(b)-A to I(b)-E, I(c)-A to I(c)-E, or II (e.g., bacterial or fungal infection) or II(a), II(b) or II(c). In still another embodiment, the invention also encompases a pharmaceutical composition comprising a Compound of Formula II or any of 2.1-2.17 as hereinbefore described, in free, pharmaceutically acceptable salt or prodrug form in an admixture with a pharmaceutically acceptable diluent or carrier.

[0070] The methods (Method I, I-A through I-E, I(a)-A through I(a)-E, I(b)-A through I(b)-E, I(c)-A through I(c)-E, Method II, II(a), II(b) and II(c)), use, pharmaceutical composition and riboswitch ligands of the current invention are intended to encompass all of the compounds of the invention, which includes any compounds of formula I, e.g, any of 1.1-1.212 or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, formula II, e.g., 2.1-2.17, Formula III, e.g., any of 3.1-3.27, Formula IV, e.g., any of 4.1-

4.22, or Formula IV or V, in free, salt or prodrug form. In one preferred embodiment, the compound is selected from any of those set forth in formula 1.261 or 1.262, in free, salt or prodrug form. In another preferred embodiment, the compound of Formula III is a compound selected from any one of those set forth in formula 3.21 or 3.22, in free, salt or prodrug form. In still another preferred embodiment, the compound of Formula IV is a compound selected from any one of those set forth in formula 4.10, 4.12 or 4.21, in free, salt or prodrug form.

[0071] The Compounds of the Invention may comprise one or more chiral carbon atoms. The compounds thus exist in individual isomeric, e.g., enantiomeric or diasteriomeric form or as mixtures of individual forms, e.g., racemic/diastereomeric mixtures. Any isomer may be present in which the asymmetric center is in the (*R*)-, (*S*)-, or (*R,S*)- configuration. The invention is to be understood as embracing both individual optically active isomers as well as mixtures (e.g., racemic/diasteromeric mixtures) thereof. Accordingly, the Compound of the Invention may be predominantly, e.g., in pure, or substantially pure, isomeric form, e.g., greater than 70% enantiomeric excess ("ee"), preferably greater than 80% ee, more preferably greater than 90% ee, most preferably greater than 95% ee. The purification of said isomers and the separation of said isomeric mixtures may be accomplished by standard techniques known in the art. Wherein R_3 is -2,3,4,5-tetrahydroxypentyl or 2,3,4-trihydroxypentyl-$OP(O)(OH)_2$ or 2,3,4-trihydroxypentyl-$P(O)(OH)_2$, the (2S,3S,4R) configuration is preferred. Therefore, in a particular embodiment of the invention, a compound of Formula I wherein R_3 is -2,3,4,5-tetrahydroxypentyl, the compound is predominantly pure in the (2S,3S,4R) form.

[0072] Geometric isomers by nature of substituents about a double bond or a ring may be present in cis (=*Z*-) or trans (=*E*-) form, and both isomeric forms are encompassed within the scope of this invention.

[0073] Compounds of the Invention may in some cases also exist in prodrug form. The term "prodrug" is an art recognized term and refers to a drug precursors prior to administration, but generate or release the active metabolite *in vivo* following administration, via some chemical or physiological process. For example, when the Compounds of the Invention (e.g., Formula I, e.g., 1.1-1.212 or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, as described in Method I or II, a Compound of Formula II, e.g., 2.1-2.17, a Compound of Formula III, e.g., any of 3.1-3.27, or Formula IV, e.g., any of 4.1-4.22) contain carboxy, phosphate or phosphonate substituents, these substituents may

be esterified to form physiologically hydrolysable and acceptable esters (e.g., carboxylic acid, phosphate or phosphonate esters, e.g., -C(O)OR_9, -OP(O)(OR_9)(OR_{17}), -OP(O)(OR_9)($NR_{13}R_{14}$)), -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$)). As used herein, "physiologically hydrolysable and acceptable esters" means esters of Compounds of the Present Invention which are hydrolysable under physiological conditions to yield acids, e.g., carboxylic acid, phosphonic or phosphoric acid (in the case of Compounds of the Invention which have carboxy, phosphonate or phosphate substituents) on the one hand and HOR_9 or HOR_{17} on the other hand, which are themselves physiologically tolerable at doses to be administered. Similarly, the invention encompasses a Compound of the Invention in, e.g., -OP(O)(OR_9)($NR_{13}R_{14}$), -OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -P(O)(OR_9)($NR_{13}R_{14}$) or -P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$) prodrug form, wherein the phosphoramidates and phosphonamidates are hydrolysed so as to release the phosphoric or phosphonic acid. In still another embodiment, the invention encompasses a Compound of the Invention which contains an alcohol substituent, e.g., R_3 is hydroxy$C_{1\text{-}8}$alkyl, wherein said compound is the prodrug and is phosphorylated *in vivo*, e.g., by a kinase to form an active phosphate derivative. As will be appreciated the term thus embraces conventional pharmaceutical prodrug forms.

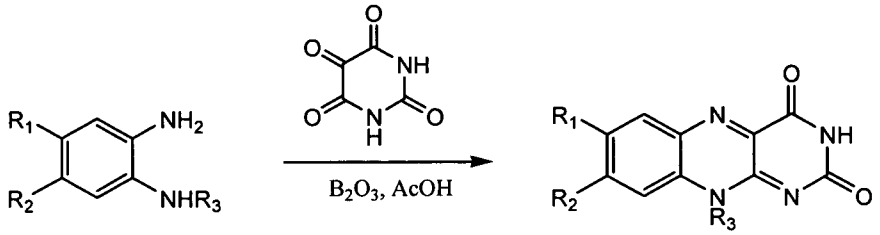
Methods of Making Compounds of the Invention

[0074] The compounds of the Formula I,II, III, IV, V and VI and their salts may be made using the methods as described and exemplified herein and by methods similar thereto and by methods known in the chemical art. Such methods include, but not limited to, those described below. In the description of the synthetic methods described herein, it is to be understood that all proposed reaction conditions, including choice of solvent, reaction atmosphere, reaction temperature, duration of the experiment and workup procedures, are chosen to be the conditions standard for that reaction, which should be readily recognized by one skilled in the art. Therefore, at times, the reaction may require to be run at elevated temperature or for a longer or shorter period of time. It is understood by one skilled in the art of organic synthesis that functionality present on various portions of the molecule must be compatible with the reagents and reactions proposed. If not commercially available, starting materials for these processes may be made by procedures, which are selected from the chemical art using techniques which are similar or analogous

to the synthesis of known compounds. All references cited herein are hereby incorporated in their entirety by reference.

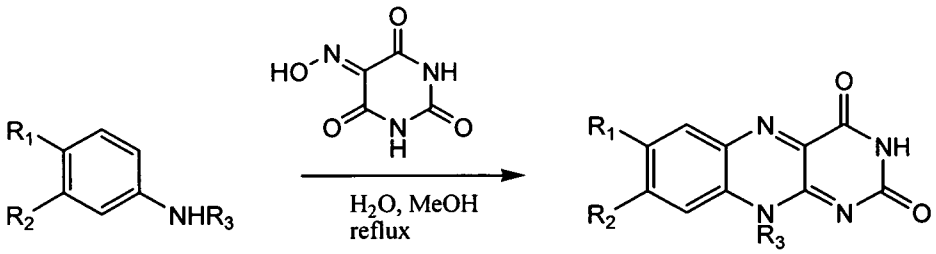
[0075] The synthetic methods for the Compounds of the Present Invention are illustrated below. The significances for the R groups are as set forth above for Formula I or II, unless otherwise indicated. In another embodiment, the significances of the substituents are as set forth in Formula III-VI unless otherwise indicated.

[0076] Compounds of Formula I or II may be prepared by reacting **Int-4** with alloxan (i.e., pyrimidine-2,4,5,6(1*H*,3*H*)-tetrone), in the presence boron oxide and acid, e.g., acetic acid.



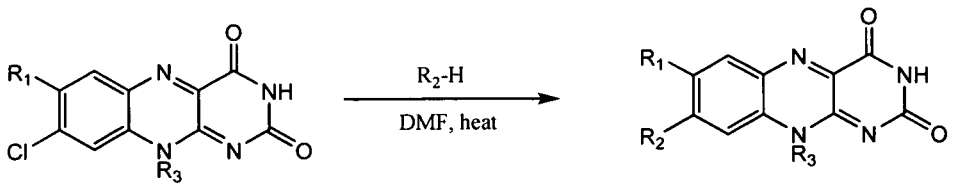
Int-4 **Formula I or II**

[0077] Alternatively, a compound of formula I or II may be prepared comprising the step of reacting **Int-4A** as described below with a violuric acid at elevated temperature (e.g., greater than 25°C, e.g., about 95°C).



Int-4A **Formula I or II**

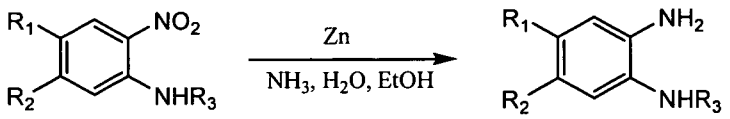
[0078] Wherein R_2 of Compound of Formula I or II is -N(R_4)(R_5), (e.g., methylamino, dimethylamino or other amino derivative), said compounds may also be prepared by reacting **Int-5** with R_2-H wherein R_2 is -N(R_4)(R_5). This reaction may require heating, e.g., greater than 30°C, e.g., 30°-153°C, e.g., 100°C.



Int-5

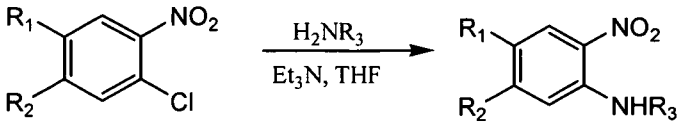
Formula I wherein
R_2 = -N(R_4)(R_5),
arylC_{1-6}alkyl-NH-,
-NH(CH_2)$_{2-6}$N(R_6)(R_7),
heteroarylC_{1-6}alkyl-NH-,
CO_2HC_{1-6}alkyl-NH-,
heterocycle,

[0079] In another embodiment, Compounds of Formula I or II may also be prepared by further comprising the step of reducing, prior to the preparation of **Int-5**, the nitro group of **Int-3** to an amine of **Int-4** by using metal (e.g., zinc, tin, iron or sodium borohydride) and acid (e.g., hydrochloric acid). For example, a Compound of Formula I or II may be prepared by further comprising the step of reacting **Int-3** with zinc and ammonia in a solvent such as water and ethanol.



Int-3 **Int-4**

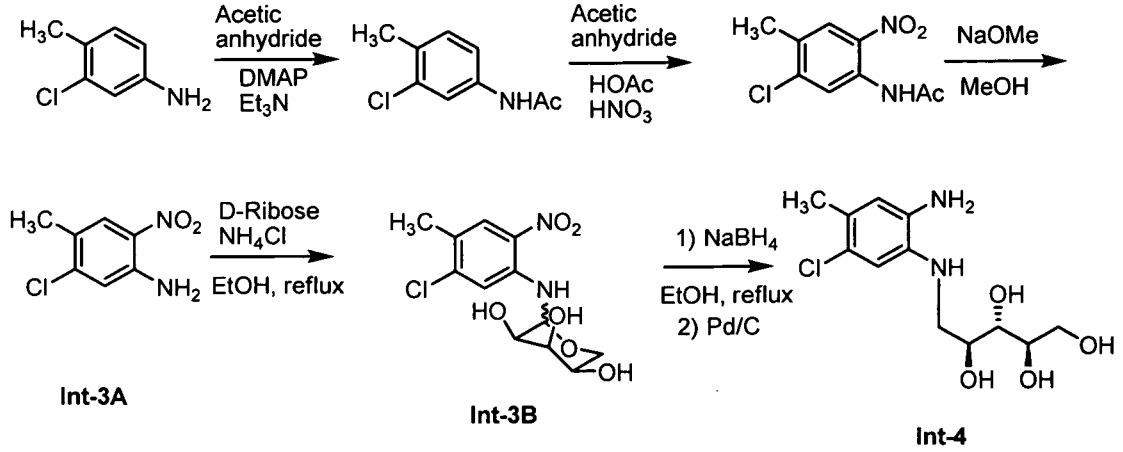
[0080] In a further embodiment, Compounds of Formula I may be prepared by further comprising, prior to the preparation of **Int-3**, the step of reacting **Int-2** with a primary amine, R_3NH_2 in the presence of a base such as triethylamine.



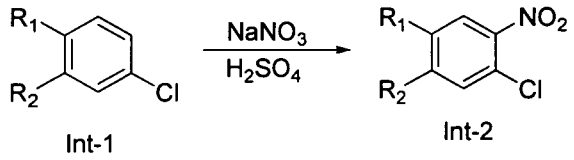
Int-2 **Int-3**

[0081] Alternatively, **Int-4** wherein R_3 is (2S,3S,4R)-2,3,4,5-tetrahydroxypentyl may be prepared by reacting 3-chloro-4-methyl-phenylamine with acetic anhydride, nitrating the ring using nitric acid in the presence of acetic acid and then reacting the resulting product with a strong base such as sodium methoxide to obtain 5-chloro-4-methyl-2-nitro-phenylamine (**Int-3A**). **Int-3A** is then reacted with D-ribose in the presence of ammonium chloride to obtain **Int-3B** wherein R_3 is ribose. The ribose may

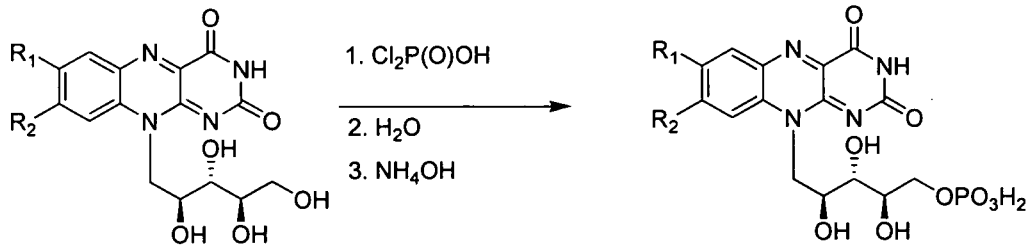
undergo ring opening and the nitro group may be reduced to an amine using sodium borohydride and palladium on carbon to yield **Int-4**.



[0082] In still a further embodiment, Compounds of Formula I or II may be prepared, by further comprising the step of nitrating, prior to the preparation of **Int-2**, Intermediate-1 (**Int-1**), e.g., with sodium nitrate in the presence of an acid, e.g., mineral acid, e.g., sulfuric acid.

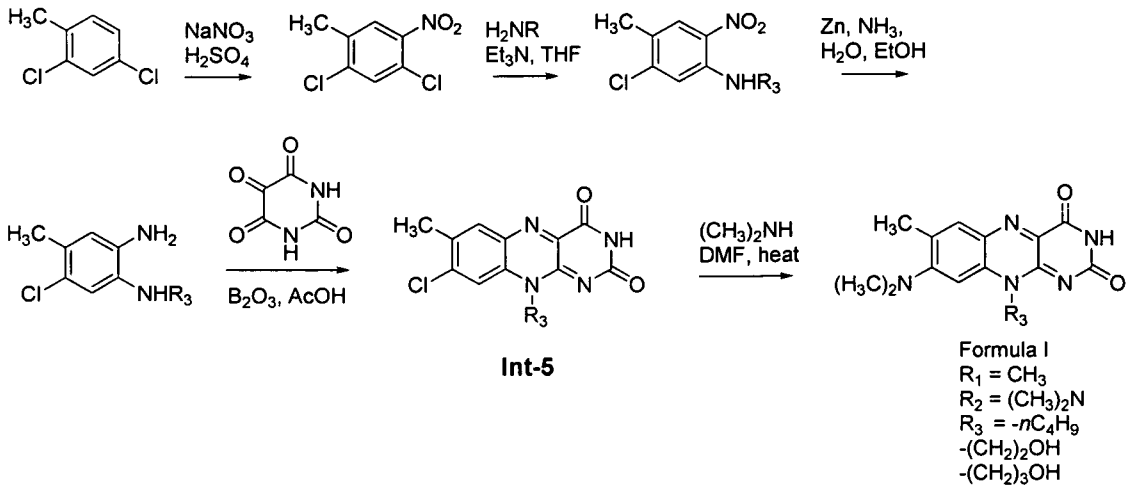


[0083] Phosphate derivatives of the Compounds of the Invention may be prepared by reacting a compound of formula I, wherein R_3 is C_{1-6} alkyl substituted with hydroxy, e.g., R_3 is (2S,3S,4R)-2,3,4,5-tetrahydroxypentyl, with dichlorophosphoric acid.



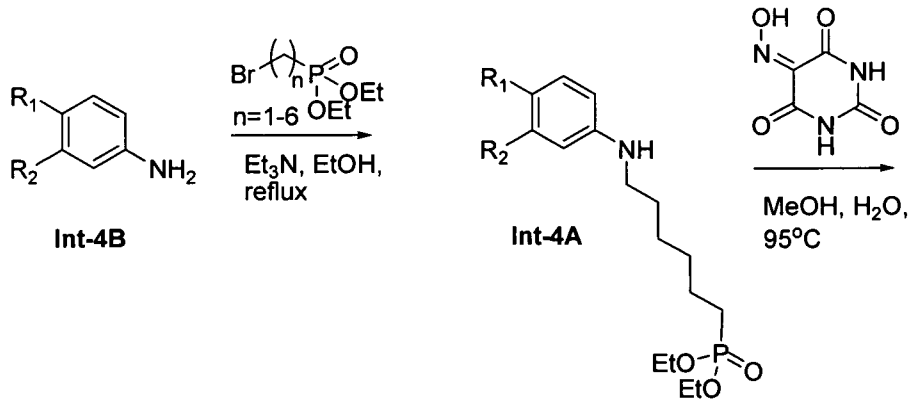
[0084] In a particular embodiment, Compounds of formula I or II, e.g., wherein R_1 is methyl, R_2 is dimethylamine and R_3 is $-nC_4H_9$, $-(CH_2)_2OH$, $-(CH_2)_3OH$, $-(CH_2)_4OH$ or $-(CH_2)_5OH$ may be prepared by (1) nitrating 2,4-dichloro-1-methylbenzene using sodium nitrate in the presence of sulfuric acid to yield 1,5-dichloro-2-methyl-4-nitrobenzene, which is then (2) reacted with R_3NH_2 in the presence of a base to yield 5-chloro-4-methyl-2-nitroaniline. This product is then (3) reacted with zinc and ammonium hydroxide in

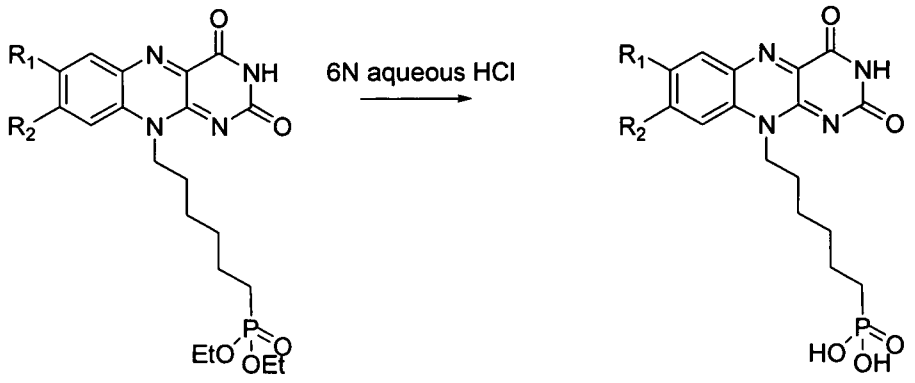
water/ethanol solvent to yield 4-chloro-5-methylbenzene-1,2-diamine, which is then (4) reacted with alloxan in the presence of borane oxide and acetic acid to obtain **Int-5**. Finally, a Compound of formula I or II as herein described is obtained by (5) reacting **Int-5** with dimethylamine in DMF at 100°C.



[0085] A Compound of Formula I or II having various R_2 substituents may be prepared by starting with a Compound of Formula I, wherein R_2 is halo (e.g., chloro) and reacting such compound with $HN(R_4)(R_5)$.

[0086] In a particular embodiment, Compounds of formula I wherein R_3 is a dihydrogen phosphate alkyl may be prepared by reacting **Int-4B** with diethyl bromoalkylphosphonate (e.g., diethyl 6-bromohexylphosphonate) to yield **Int-4A**. **Int-4A** may be converted to Compound of Formula I or II, wherein R_3 is alkylphosphonate dialkyl ester by reacting with violuric acid. The phosphonate ester may be hydrolyzed by using an acid, e.g, hydrochloric acid.

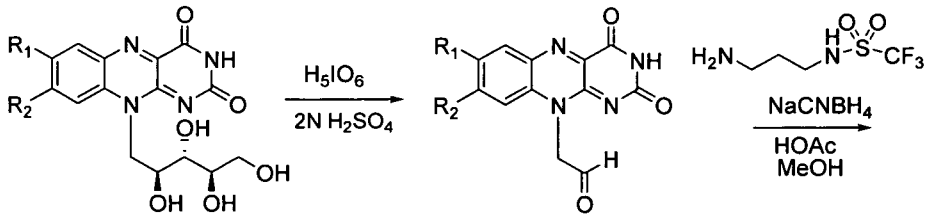




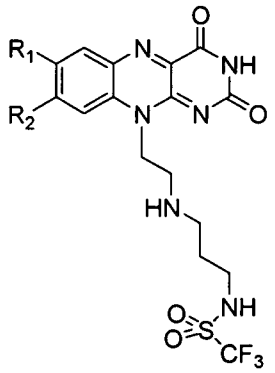
Formula I or II

Formula I or II

[0087] In a particular embodiment, Compounds of formula I, e.g., wherein R_3 is an alkyl amino-alkyltrifluoromethanesulfonamide (e.g. N-(3-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)propyl)-1,1,1-trifluoromethanesulfonamide) may be prepared by starting with a Compound of Formula I wherein R_3 is (2R,3S,4S)-2,3,4,5-tetrahydroxypentyl and reacting it with orthoperiodic acid and sulfuric acid to yield **Int-6**. **Int-6** may then be converted to a Compound of Formula I or II, wherein R_3 is an alkyl amino-alkyltrifluoromethanesulfonamide, by reductive amination reaction, e.g., reacting **Int-6** with N-(3-aminoalkyl)-trifluoromethanesulfonamide followed by a reducing agent, e.g., sodium cyanoborohydride to yield a sulfonamide derivative of a Compound of Forumla I.

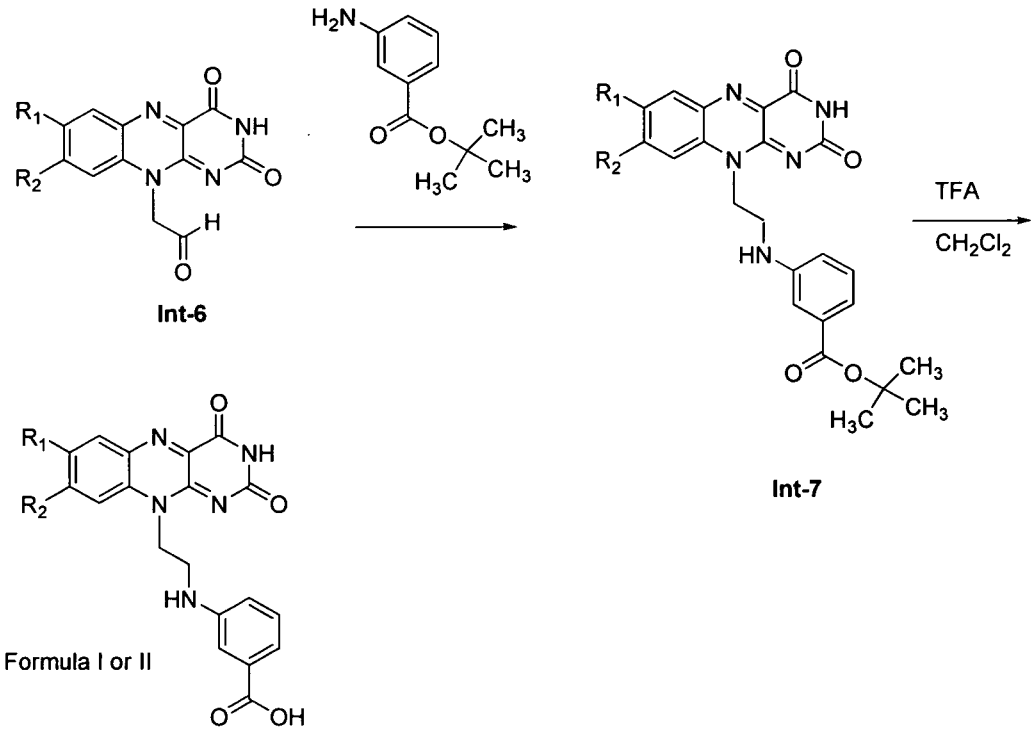


Int-6

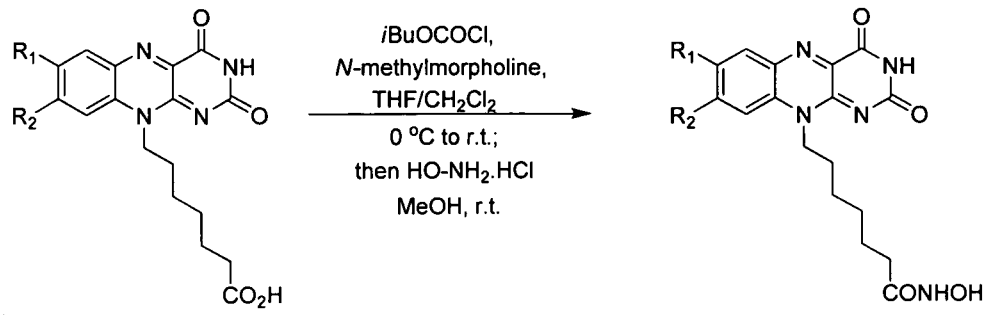


Formula I or II

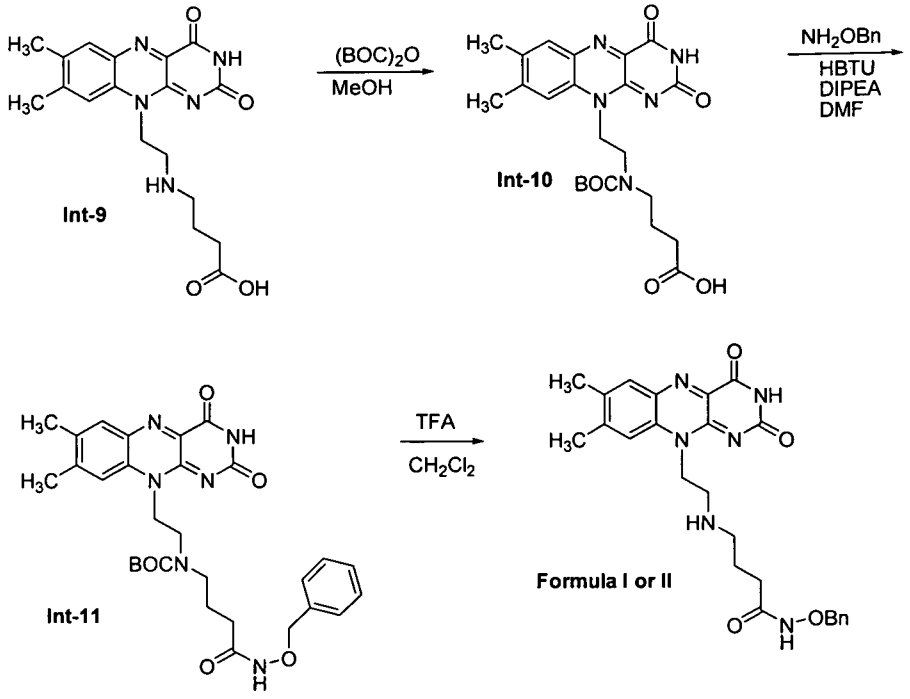
[0088] Similarly, Compounds of formula I, e.g., wherein R_3 is benzoic acid aminoalkyl (e.g., 3-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)benzoic acid) may be prepared by subjecting **Int-6** to a reductive amination reaction as described above by reacting **Int-6** with alkyl 3-aminobenzoate (e.g., t-butyl-3-aminobenzoate) followed by sodium cyanoborohydride to yield **Int-7** below. **Int-7** may be hydrolyzed using an acid, e.g., trifluoroacetic acid, to benzoic acid deriviative of Formula I below.



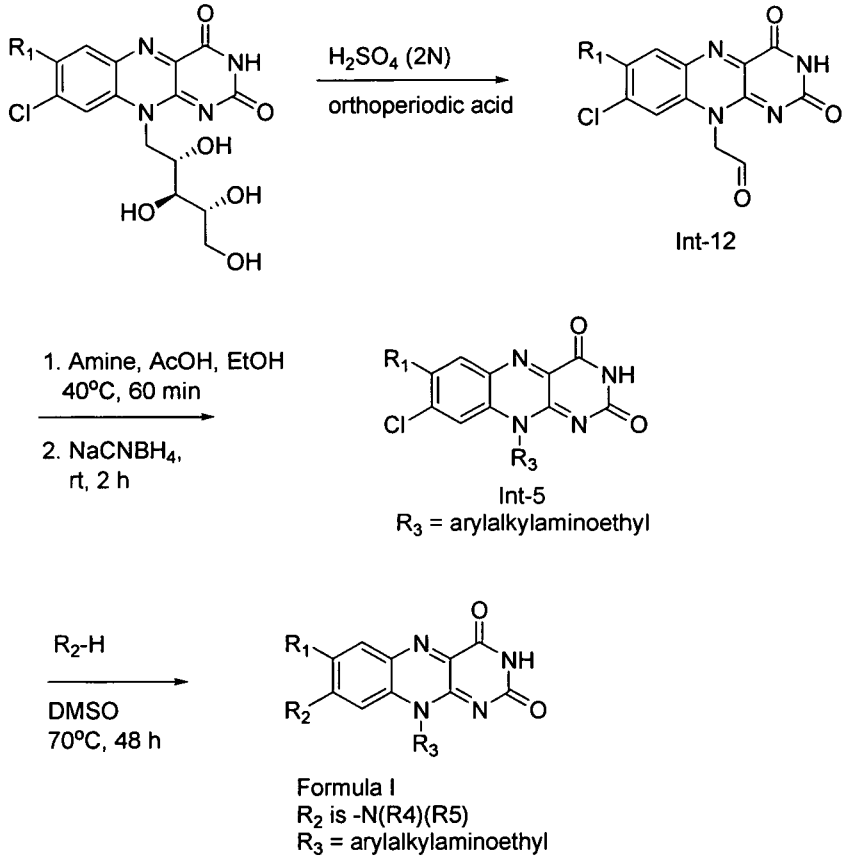
[0089] In a particular embodiment, Compounds of formula I, e.g., wherein R_3 is an –alkyl-CONHOH may be prepared by reacting a Compound of Formula I, wherein R_3 is an –alkyl-COOH with an alkyl chloroformate (e.g., isobutylchloroformate) and N-methylmorpholine followed by hydroxylamine hydroxychloride to yield the hydroxamide alkyl derivative.



[0090] In a particular embodiment, Compounds of formula I wherein R_3 is an alkyl-N(R_6)(R_7) wherein R_6 is –alkyl-CONHOalkyl and R_7 is H may be prepared by protecting the amine of **Int-9** with a protecting group, e.g. BOC anhydride to yield Int-10. Int-10 is then coupled with O-benzylhydroxylamine hydrochloride using HBTU and a base, e.g., diisopropylethylamine to yield **Int-11**, which is then deprotected using an acid, e.g, trifluoroacetic acid.



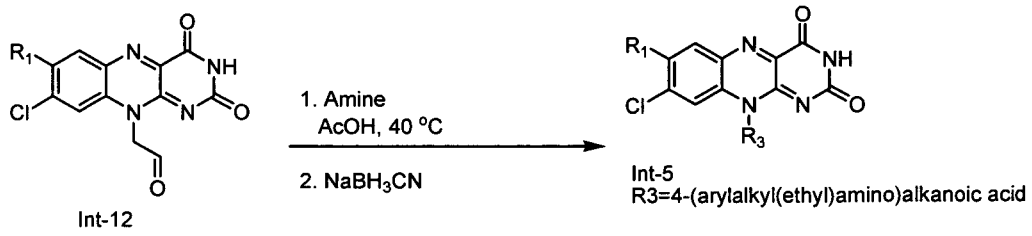
[0091] In certain aspect, the invention further provides methods of making the Compounds of the Invention, e.g., as setforth below. Compounds of formula I, wherein R_3 is arylalkylaminoethyl, R_2 is -N(R_4)(R_5) and R_1 is as hereinbefore described in Formula I, I(i)-I(v), II-VI, (e.g., 10-(2-(benzylamino)ethyl)-8-(cyclopropylamino)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione) may be prepared by subjecting **Int-12** to a reductive amination reaction, e.g., by reacting **Int-12** with an amine (e.g., phenylmethanamine) followed by a reduction reaction, e.g., using sodium borohydride or cyanoborohydride to yield **Int-5** below. **Int-5** may be reacted with R_2-H wherein R_2 is -N(R_4)(R_5) to give compounds of formula I below. This reaction may require heating, e.g., greater than 30°C, e.g., 30°-153°C, e.g., 70°C. **In-12** maybe prepared via oxidative cleavage of 8-chloro-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione using orthoperiodic acid and sulfuric acid.



[0092] Compounds of formula I, wherein R_3 is arylalkylaminoethyl, R_2 is -O-C_{3-7}cycloalkyl or C_{1-8}alkoxy and R_1 is as hereinbefore described in Formula I, I(i)-I(v), II-VI, (e.g., 10-(2-(benzylamino)ethyl)-8-(cyclopentyloxy)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione) may also be prepared from an intermediate such as **Int-5** in which the amino moiety of the arylalkylaminoethyl moiety is protected (e.g., carbamate group, e.g., BOC,) during the reaction of **Int-5** with R_2-H wherein R_2 is -O-C_{3-7}cycloalkyl. The reaction may require base (e.g. sodium hydride) and heating. The protecting group (e.g., carbamate group) may be removed using acid (e.g. HCl) to give compounds of formula I wherein R_3 is arylalkylaminoethyl and R_2 is -O-C_{3-7}cycloalkyl.

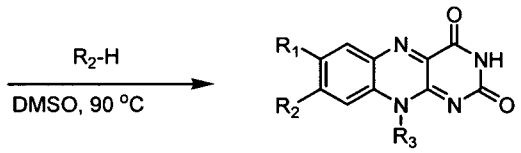
[0093] Similarly, compounds of formula I, wherein R_3 is 4-(arylalkyl(ethyl)amino)-alkanoic acid, R_2 is -N(R_4)(R_5) and R_1 is as hereinbefore described in Formula I, I(i)-I(v), II-VI, (e.g., 4-(benzyl(2-(8-(cyclopentylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)amino)butanoic acid) may also be prepared from **Int-12** by subjecting **Int-12** to a reductive amination reaction, e.g., by reacting **Int-12** with an appropriate amine (e.g., 4-(benzylamino)butanoic acid) followed by a reduction reaction, e.g., using sodium borohydride or cyanoborohydride to yield **Int-5** below (R_3 =

4-(arylalkyl(ethyl)amino)alkanoic acid). **Int-5** may be reacted with R_2-H wherein R_2 is -$N(R_4)(R_5)$ to give compounds of formula I. This reaction may require heating, e.g., greater than 30°C, e.g., 30°-153°C, e.g., 90°C.



Int-12

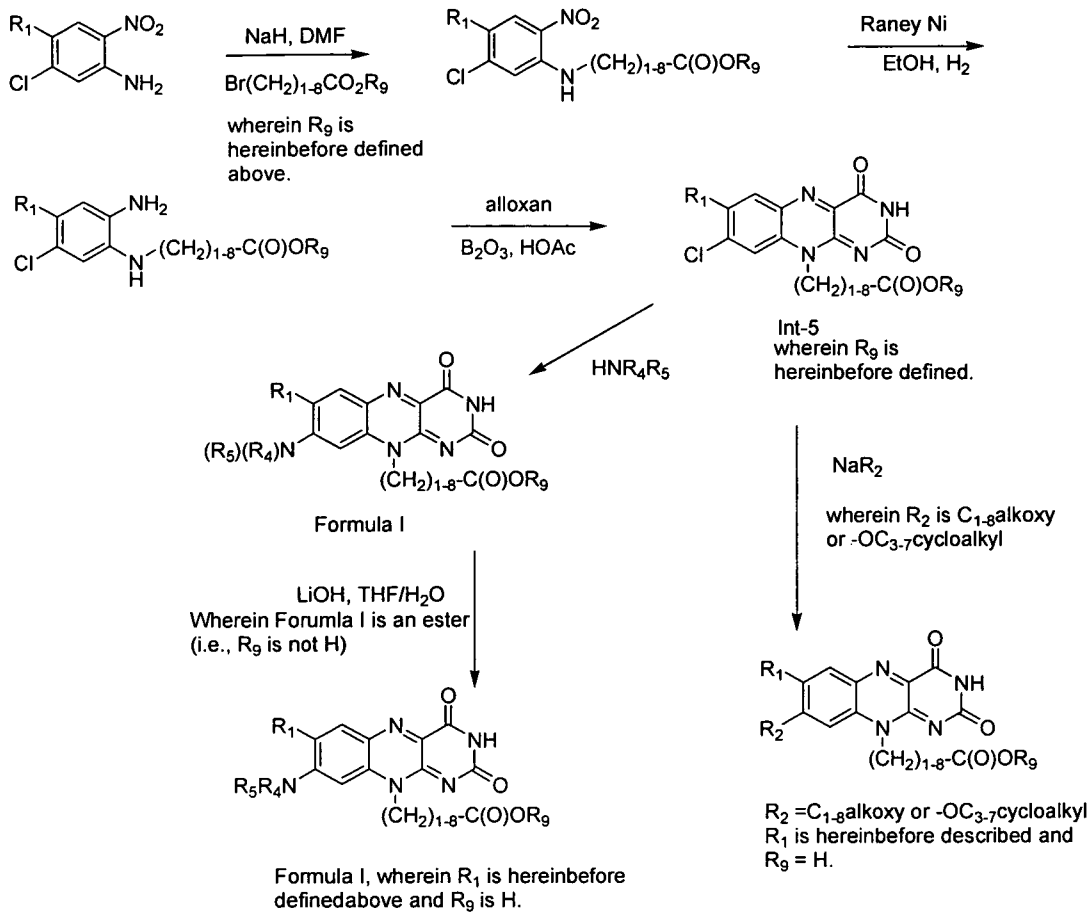
Int-5
R3=4-(arylalkyl(ethyl)amino)alkanoic acid



Formula I
R_2 is -N(R4)(R5)
R_3 = 4-(arylalkyl(ethyl)amino)alkanoic acid

[0094] In a particular embodiment, Compounds of formula I wherein R_3 is an alkyl ester or alkyl acid and R_2 is -$N(R_4)(R_5)$ and R_1 is as hereinbefore described in Formula I, I(i)-I(v), II-VI, (e.g., *tert*-butyl 7-[8-(cyclopropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate) may be prepared by reacting **Int-5** with R_2-H wherein R_2 is -$N(R_4)(R_5)$ to give compounds of formula I, wherein R_1 and R_9 are hereinbefore described. Wherein R_9 is not H (e.g., the compound is an ester), hydrolysis of the ester moiety using base (e.g. lithium hydroxide in THF/water) provides the corresponding acid of formula I below.

[0095] Similarly, reaction of **Int-5** (R_3=alkyl ester) with R_2-Na wherein R_2 is -O-C_{3-7}cycloalkyl or C_{1-8}alkoxy provides a compound of formula I (e.g., 7-(8-methoxy-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid) wherein R_2 is -O-C_{3-7}cycloalkyl or C_{1-8}alkoxy and R_3 is an alkyl acid.



[0096] Compounds of Formula I wherein R_3 is C_{1-8}alkyl substituted with -$P(O)(OR_9)(NR_{13}R_{14})$, -$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$P(O)(OR_9)(NR_{13}R_{14})$, or -$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$ may be prepared by methods known in the art. One method of preparing such phosphoramidates of Formula I is to, e.g., react a compound of Formula I containing a hydroxyl substitutent, e.g., Formula I wherein R_3 is C_{1-8}alkyl substituted with –OH, with Cl-$P(O)(OR_9)(NR_{13}R_{14})$, Cl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, e.g., phenyl methoxyalininyl phosphorocloridates, in the presence of a base, e.g., an amine base, e.g., N-methyl-imidazole, e.g., in a solvent such as dichloromethane or tetrahydrofuran. Preparation of Cl-$P(O)(OR_9)(NR_{13}R_{14})$, Cl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, e.g., phenyl methoxyalininyl phosphorocloridates, as well as other phosphoramidates, bis-phosphoramidates and phosphonamidates may be prepared by using similar methods as those described in McGuigan et al., *Antiviral Res.* (1992) 17:311-321, McGuigan et al., *Antiviral Res.* (1991) 15:255-263, Serafinowska et al., *J. Med. Chem.* (1995) 38:1372-1379, Mehellou et al., *Bioorg. Med. Chem. Lett.* (2007) 17:3666-3669, Jones et al. (1991) 2:35-39 and U.S. Pat. No. 7,071,176, the contents of each of which are herein incorporated

by reference in their entirety. Bis(phosphonamidates) of Compounds of Formula I can also be prepared by using methods similar to those described in WO 2006/023515 (the contents of which are incorporated by reference in their entirety), for example, activating the phosphonic acid substituent of a Compound of Formula I (e.g., wherein R_3 is alkyl substituted with $-P(O)(OH)_2$) with e.g., oxalyl chloride, and reacting the resulting compound with $HN(R_{13}R_{14})(R_{15}R_{16})$, e.g., methylalanine or methylalanine ethyl ester, in the presence of a base, e.g., an amine base, e.g., diethylisopropylamine or diisopropylethylamine, triethylamine or the like.

Methods of using Compounds of the Invention

[0097] The Compounds of the Present Invention are useful for the treatment of an infection, particularly an infection by bacteria including but not limited to *Moraxella catarrhalis, Klebsiella pneumoniae, Staphylococcus epidermidis, Streptococcus viridians, Enterococcus faecium, Staphylococcus aureus, Bacillus anthracis, Francisella tularensis, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Brucella melitensis, Escherichia coli, Haemophilus influenza, Listeria monocytogenes, Salmonella enterica, Vibrio choierae, Enterococcus faecalis* and *Yersinia pestis.* In addition to these bacteria, The Compounds of the Present Invention are useful for the treatment of an infection, particularly an infection by bacteria including but not limited to *Bacillus subtilis, Streptococcus pyogenes* and/or *Borrelia burgdorferi* bacteria. In a preferred embodiment, the bacteria is selected from any one of the following: *Staphylococcus aureus, Staphylococcus epidermidis, Bacillus subtilis, Enterococcus faecalis, Streptococcus pneumoniae, Streptococcus pyogenes, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Haemophilus influenzae, Acinetobacter baumannii.* In another preferred embodiment, the infection is by the *Staphylococcus aureus* and/or *Staphylococcus epidermidis* bacteria.

[0098] The invention therefore provides methods of treatment of any one or more of the following conditions: anthrax infection, staphylococcal scalded skin syndrome (staph infections), pneumonia, impetigo, boils, cellulitis folliculitis, furuncles, carbuncles, scalded skin syndrome, abscesses, meningitis, osteomyelitis endocarditis, Toxic Shock Syndrome (TSS), septicemia, acute sinusitis, otitis media, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, brain abscess, tularemia, urinary tract infection, empyema, food poisoning, diarrhea and conjunctivitis; comprising administering an

effective amount of a Compound of Formula I, e.g., any of 1.1-1.212, or any of formulae I(i)-I(v), e.g., any of 1.213-1.265, preferably formula 1.261 or 1.262, as described in Method I, or formula II, in free, pharmaceutically acceptable salt or prodrug form, to a human or animal patient in need thereof. In other embodiments, the invention provides methods of treatment of the conditions set forth above comprising administering an effective amount of a Compound of Formula III, e.g., any of 3.1-3.27; a Compound of Formula IV, e.g., any of 4.1-4.22, a Compound of Formula V or VI, in free, pharmaceutically acceptable salt or prodrug form.The words "treatment" and "treating" are to be understood accordingly as embracing prophylaxis and treatment or amelioration of symptoms of disease as well as treatment of the cause of the disease.

[0099] The term "patient" as used herein encompasses human or non-human (e.g., animal).

[00100] Dosages employed in practicing the present invention will of course vary depending, e.g. on the particular disease or condition to be treated, the particular Compound of the Invention used, the mode of administration, and the therapy desired. Administration of a therapeutically active amount of the therapeutic compositions is defined as an amount effective, at dosages and for periods of time necessary to achieve the desired result. For example, a therapeutically effective amount of a Compound of the Present Invention reactive with at least a portion of FMN riboswitch may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the compound to elicit a desired response in the individual. Dosage regiment may be adjusted to provide the optimum therapeutic response. For example, several divided doses may be administered daily or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation.

[0100] Pharmaceutical compositions comprising Compounds of the Present Invention may be prepared using conventional diluents or excipients and techniques known in the galenic art. Thus oral dosage forms may include tablets, capsules, solutions, suspensions and the like. The term "pharmaceutically acceptable carrier" as used herein is intended to include diluents such as saline and aqueous buffer solutions. The Compounds of the Present Invention may be administered in a convenient manner such as by injection such as subcutaneous, intravenous, by oral administration, inhalation, transdermal application, intravaginal application, topical application, intranasal, sublingual or rectal administration. Depending on the route of administration, the active compound may be

coated in a material to protect the compound from the degradation by enzymes, acids and other natural conditions that may inactivate the compound. In a preferred embodiment, the compound may be orally administered. In another embodiment, the compound is administered via topical application.

[0101] In certain embodiment, the Compounds of the Invention may be administered alone or in conjunction, e.g., at or about the same time, simultaneously and separately or simultaneously in an admixture, with another agent, e.g., an agent to facilitate entry or permeability of the Compounds of the Invention into the cell, e.g., an antimicrobial cationic peptide. Antimicrobial cationic peptides include peptides which contain (1) a disulfide-bonded β-sheet peptides; (2) amphipathic α-helical peptides; (3) extended peptides; or (4) loop-structured peptides. Examples of cationic peptide include but are not limited to defensins, cecropins, melittins, magainins, indolicidins, bactenecin and protegrins. Other examples of antimicrobial cationic peptides include but are not limited to human neutrophil defensin-1 (HNP-1), platelet microbicidal protein-1 (tPMP), inhibitors of DNA gyrase or protein synthesis, CP26, CP29, CP11CN, CP10A, Bac2A-NH_2 as disclosed in Friedrich et al., *Antimicrob. Agents Chemother.* (2000) 44(8):2086, the contents of which are hereby incorporated by reference in its entirety. Further examples of antibacterial cationic peptides include but are not limited to polymyxin e.g., polymixin B, polymyxin E or polymyxin nonapeptide. Therefore, in another embodiment, the Compounds of the Invention may be administered in conjunction with polymyxin, e.g., polymixin B, polymyxin E or polymyxin nonapeptide, preferably polymyxin B.

[0102] In still another embodiment, the Compounds of the Invention may be administered alone or in conjunction, e.g., at or about the same time, simultaneously and separately, or simultaneously in an admixture, with other antimicrobial agents, e.g., other antifungal or other systemic antibacterial (bactericidal or bacteriostatic) agents. Examples of bacterial agents include agents which inhibit bacterial cell wall synthesis (e.g., penicillins, cephalosporins, carbapenems, vancomycin), agents which damage cytoplasmic membrane (e.g., polymixins as discussed above), agents which modify the synthesis or metabolism of nucleic acids (e.g., quinolones, rifampin, nitrofurantoin), agents which inhibit protein synthesis (aminoglycosides, tetracyclines, chloramphenicol, erythomycin, clindamycin), agents which interfer with the folate synthesis (e.g., folate-inhibitors), agents which modify energy metabolism (e.g., sulfonamides, trimethoprim) and/or other antibiotics (beta-lactam antibiotic, beta-lactamase inhibitors). Specific anti-infective

agents, particularly antibacterial and antifungal agents, are discussed in Remington: The Science and Practice of Pharmacy, Chapter 90, pp. 1626-1684 (21st Ed., Lippincott Williams & Wilkins 2005), the contents of which are hereby incorporated by reference.

Binding of ligand to riboswitch:

Example 1:

[0103] An in-line probing assay, as described in Regulski and Breaker, "In-line probing analysis of riboswitches", (2008), *Methods in Molecular Biology,* Vol 419, pp 53-67, the contents of which are incorporated by reference in its entirety, is used to estimate the dissociation binding constants for the interaction of each of the ligands described herein with an FMN riboswitch amplified from the genome of *Bacillus subtilis*. Precursor mRNA leader molecules are prepared by in vitro transcription from templates generated by PCR and [5'-^{32}P]-labeling using methods described previously (Regulski and Breaker, In-line probing analysis of riboswitches (2008), *Methods in Molecular Biology* Vol 419, pp 53-67). Approximately 5 nM of labeled RNA precursor is incubated for 41 hours at 25°C in 20 mM $MgCl_2$, 50 mM Tris HCl (pH 8.3 at 25°C) in the presence or absence of increasing concentrations of each ligand. In-line cleavage products are separated on 10% polyacrylamide gel electrophoresis (PAGE), and the resulting gel is visualized using a Molecular Dynamics Phosphorimager. The location of products bands corresponding to cleavage are identified by comparison to a partial digest of the RNA with RNase T1 (G-specific cleavage) or alkali (nonspecific cleavage).

[0104] In-line probing exploits the natural ability of RNA to self-cleave at elevated pH and metal ion concentrations (pH $\approx$ 8.3, 25 mM $MgCl_2$) in a conformation-dependent manner. For self-cleavage to occur, the 2'-hydroxyl of the ribose must be "in-line" with the phosphate-oxygen bond of the internucleotide linkage, facilitating a S_N2P nucleophilic transesterification and strand cleavage. Typically, single-stranded regions of the Riboswitch are dynamic in the absence of an active ligand, and the internucleotide linkages in these regions can frequently access the required in-line conformation. Binding of an active ligand to the Riboswitch generally reduces the dynamics of these regions, thereby reducing the accessibility to the in-line conformation, resulting in fewer in-line cleavage events within those regions. These ligand-dependent changes in RNA cleavage can be readily detected by denaturing gel electrophoresis.

[0105] The experiments show that various Compounds of the invention, particularly 1.204, 1.210, 1.261, 1.262, 3.21, 4.10, 4.12 or 4.21, in free, salt or prodrug form, have a binding affinity to FMN riboswitch with an IC_{50} value of less than, or equal to, 10μM.

***Minimum Inhibitory Concentration*:**

Example 1A:

[0106] The MIC assays are carried out in a final volume of 100 μL in 96-well clear round-bottom plates according to methods established by the Clinical Laboratory Standards Institute (CLSI). Briefly, test compound suspended in 100 % DMSO (or another suitable solubilizing buffer) is added to an aliquot of media appropriate for a given pathogen to a total volume of 50 μL. This solution is serially diluted by 2-fold into successive tubes of the same media to give a range of test compound concentrations appropriate to the assay. To each dilution of test compound in media is added 50 μl of a bacterial suspension from an overnight culture growth in media appropriate to a given pathogen. Final bacterial inoculum is approximately 10^5-10^6 CFU/well. After growth for 18-24 hours at 37° C, the MIC is defined as the lowest concentration of antimicrobial agent that completely inhibits growth of the organism as detected by the unaided eye, relative to control for bacterial growth in the absence of added antibiotic. Ciprofloxacin is used as an antibiotic-positive control in each screening assay. Each of the bacterial cultures that are available from the American Type Culture Collection (ATCC, www.atcc.org) is identified by its ATCC number.

[0107] The experiments show that various compounds of the invention, e.g., various compounds set forth in formula 1.210, any of 1.259-1.264, e.g., 1.263, avrious compounds of formula III, e.g., various compounds of formula 3.20, various compounds of formulae 4.9-4.20, e.g., 4.11, have a minimum inhibitory concentration (MIC) of less than 128μg/mL and in some instances, less than 32μg/mL.

Synthesis of flavin derivatives of the invention:

[0108] Temperatures are given in degrees Celsius (°C); unless otherwise stated, operations are carried out at room or ambient temperature, that is, at a temperature in the range of 18-25 °C. Chromatography means flash chromatography on silica gel; thin layer chromatography (TLC) is carried out on silica gel plates. Samples were dissolved in

deuterated solvents for NMR spectroscopy. NMR data is in the delta values of major diagnostic protons, given in parts per million (ppm) relative to the appropriate solvent signals. Conventional abbreviations for signal shape are used. For mass spectra (MS), the lowest mass major ion is reported for molecules where isotope splitting results in multiple mass spectral peaks. Solvent mixture compositions are given as volume percentages or volume ratios. In cases where the NMR spectra are complex, only diagnostic signals are reported. The LC-MS method is as described in Method C of analytical HPLC analysis below.

General methods for analytical HPLC analysis:

Method A: Analytical HPLC is performed using a Luna Prep C_{18}, 100 Å 5 μm, 4.6 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is 0.1% TFA in acetonitrile. The elution profile is as follows: 95% aqueous (0 to 0.5 min); a gradient from 95% aqueous to 98% organic (0.5 to 10.5 min); 98% organic (2 min); a gradient from 98% organic to 95% aqueous (5.5 min); 95% aqueous (1 min).

Method B: Analytical HPLC is performed using a Luna Prep C_{18}, 100 Å 5 μm, 4.6 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is 0.1% TFA in acetonitrile. The elution profile is as follows: 95% aqueous (0 to 0.5 min); a gradient from 95% aqueous to 100% organic (0.5 to 10.5 min); a gradient from 100% organic to 95% aqueous (2 min); 95% aqueous (4 min).

Method C: Analytical LCMS is performed using a YMC Combiscreen ODS-AQ, 5 μm, 4.6 x 50 mm column. The aqueous phase is 1% 2 mM NH_4OAc in 90:10 IPA:H_2O, 0.03% TFA in USP water. The organic phase is 1% 2 mM NH_4OAc in 90:10 IPA:H_2O, 0.03% TFA in acetonitrile. The elution profile is as follows: a gradient from 95% aqueous to 100% organic (0 to 10 min); 100% organic (2 min); a gradient from 100% organic to 95% aqueous (0.1 min); 95% aqueous (3 min).

Method D: Analytical HPLC is performed using a Luna Prep C_{18}, 100 Å 5 μm, 4.6 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is 0.1% TFA in acetonitrile. The elution profile is as follows: a gradient from 95% aqueous to 75% aqueous (0 to 10 min); a second gradient from 75% aqueous to 98% organic (2.5 min); a third gradient to 95% aqueous (over 1 min).

Method E: Analytical HPLC is performed using a Luna Prep C_{18}, 100 Å 5 μm, 4.6 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is 0.1% TFA in acetonitrile. The elution profile is as follows: a gradient from 95% aqueous to 40 % aqueous (0 to 10 min); a second gradient from 40% aqueous to 2% aqueous (2 min); 2% aqueous (1 min); 2% aqueous to 95% aqueous (4 min).

Method F: Analytical HPLC is performed using a Luna Prep C_{18}, 100 Å 5 μm, 4.6 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is 0.1% TFA in acetonitrile. The elution profile is as follows: a gradient from 95% aqueous to 60 % aqueous (0 to 10 min); a second gradient from 60% aqueous to 2% aqueous (2 min); 2% aqueous (1 min); 2% aqueous to 95% aqueous (4 min).

System A: Agilent 1100 HPLC, Agilent Scalar C18 150 x 4.6 mm 5 micron column, 1.5 mL/min, Solvent A -Water (0.1% TFA), Solvent B-Acetonitrile (0.07% TFA), Gradient - 10 min 95%A to 95%B; 5min hold; then recycle, UV Detection @ 214 and 250nm.

System B: Agilent 1100 HPLC, Agilent XDB C8 150 x 4.6 mm 5 micron column, 1.5 mL/min, Solvent A-Water (0.1% TFA), Solvent B-Acetonitrile (0.07% TFA), Gradient - 10 min 95%A to 95%B; 5min hold; then recycle, UV Detection @ 214 and 250nm.

System C: Agilent 1100 HPLC, Agilent XDB C18 50 x 4.6 mm 1.8 micron column, 1.5 mL/min, Solvent A-Water (0.1% TFA), Solvent B -Acetonitrile (0.07% TFA), Gradient -7 min 95%A to 95%B; 1min hold; then recycle, UV Detection @ 214 and 254nm.

System D: Agilent 1100 HPLC, Agilent XDB C18 50 x 4.6 mm 1.8 micron column, 1.5 mL/min, Solvent A-Water (0.1% TFA), Solvent B -Acetonitrile (0.07% TFA), Gradient -5 min 95%A to 95%B; 1min hold; then recycle, UV Detection @ 214 and 254nm.

General procedure for preparative HPLC conditions.

Method 1: Preparatory HPLC is performed using a SunFire™ Prep C18 OBD™ 5 μm, 30 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is acetonitrile. The elution profile is as follows: 100% aqueous (0 to 3 min); a gradient from 100% aqueous to 98% organic (3 to 21 min); 98% organic (1 min); a gradient from 98% organic to 95% aqueous (1 min); 95% aqueous (1 min).

Method 2: Preparatory HPLC is performed using a SunFire™ Prep C18 OBD™ 5 μm, 30 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is acetonitrile. The elution profile is as follows: a gradient from 95% aqueous to 25%

organic (0 to 10 min); a second gradient from 25% organic to 98% organic (over 2.5 min min); a third gradient to 95% aqueous (over 1 min).

Method 3: Preparatory HPLC is performed using a SunFire™ Prep C18 OBD™ 5 μm, 30 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is acetonitrile. The elution profile is as follows: isocratic conditions of 20% organic (0-3 min); a gradient from 80% aqueous to 50% organic (3 to 16 min); isocratic conditions of 50% organic (16 to 18 min); a second gradient from 50% organic to 70% organic (from 18 to 25 min); a third gradient from 70% organic to 100% organic (over 0.5 min); then isocratic conditions of 100% organic (over 1 min); a fourth gradient from 100% organic to 95% aqueous (over 1min.).

Method 4: A SunFire™ Prep C18 OBD™ 5 μm, 30 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is acetonitrile. The elution profile is as follows: a gradient from 100% aqueous to 60% organic (0 to 29 min); then to 98% organic (29 to 31 min); 98% organic (2min); a gradient from 98% organic to 100% aqueous (2 min); 100% aqueous (2 min).

Method 5: Preparatory HPLC is performed using a SunFire™ Prep C18 OBD™ 5 μm, 30 x 100 mm column. The aqueous phase is 0.1% TFA in USP water. The organic phase is acetonitrile. The elution profile is as follows: isocratic conditions of 20% organic (0-3 min); a gradient from 80% aqueous to 50% organic (3 to 16 min); isocratic conditions of 50% organic (16 to 18 min); a second gradient from 50% organic to 70% organic (from 18 to 25 min); a third gradient from 70% organic to 100% organic (over 0.5 min); then isocratic conditions of 100% organic (over 1 min); a fourth gradient from 100% organic to 95% aqueous (over 1min.)

Method 6: Varian PrepStar, Phenomenex Luna(2) C18 250 x 21.2 mm 10 micron column, 20 mL/min, Solvent B-Water (0.1% TFA), Solvent A-Acetonitrile (0.07% TFA), Gradient- 10 min 5%A to 80%A; 5 min 80% A to 100 %A; 5 min hold; then recycle, UV Detection @ 254nm.

Terms and abbreviations:

Cat. = catalytic,

CAN = ammonium cerium (IV) nitrate,

CBzCl = benzyl chloroformate

D-ribose = (2R,3R,4R)-2,3,4,5-tetrahydroxypentane,

equiv. = equivalent(s),

h = hour(s),

HATU = 2-(1H-7-Azabenzotriazol-1-yl)-1,1,3,3-tetramethyl uronium hexafluorophosphate methanaminium,

HBTU=2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate,

ISCO = normal phase silica gel cartridges supplied by Teledyne ISCO,

Min. = minute(s)

PMB = p-methoxybenzyl,

POMCl = pivaloyloxymethylchloride,

PyBOP = benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate,

rt = room temperature,

RNase T1 = an endoribonuclease that specifically degrades single-stranded RNA at G residues,

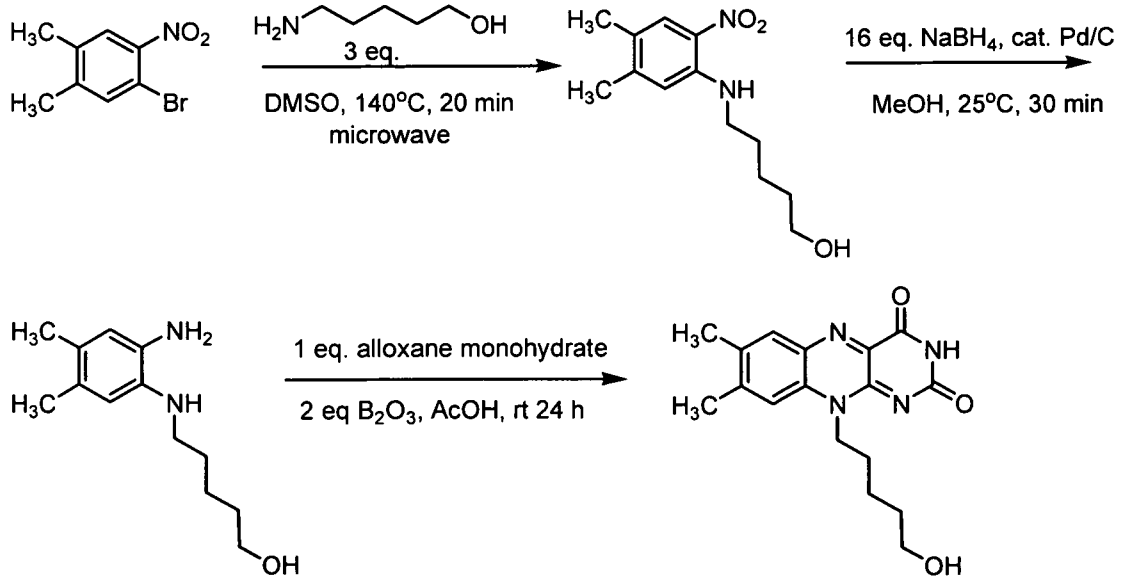
TBAI= tetrabutylammonium iodide,

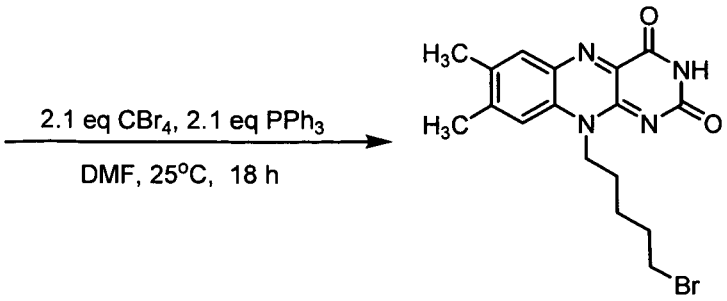
TLC = thin layer chromatography,

TMSBr= trimethylsilyl bromide,

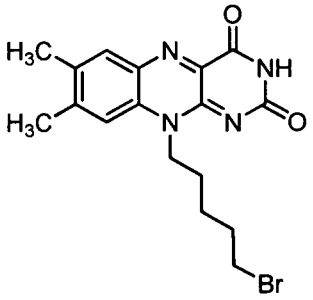
Tris HCl = Tris (hydroxymethyl) aminomethane hydrochloride

Intermediate 1

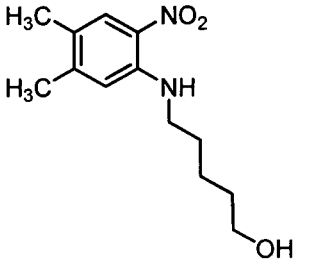




Preparation of 10-(6-bromopentyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione

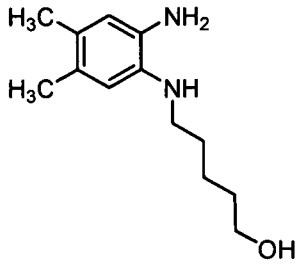


Step 1 Preparation 5-(4,5-dimethyl-2-nitrophenylamino)pentan-1-ol



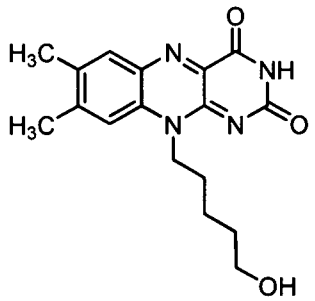
[0109] To a solution of 1-bromo-4,5-dimethyl-2-nitrobenzene (200 mg, 0.870 mmol) in anhydrous DMSO (1 mL), is added 5-aminopentan-1-ol (170 mg, 2.608 mmol). The reaction mixture is heated in a microwave at 140 °C for 20 min. The reaction mixture is concentrated under vacuum and diluted with water (5 mL) and the aqueous layer is extracted with DCM (3 x 5 mL). The organic layer is dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Desired product (147 mg) is isolated (yield: 67 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.55 (m, 2H), 1.66 (m, 2H), 1.79 (m, 2H), 2.20 (s, 3H), 2.29 (s, 3H), 2.38 (s, 2H), 3.32 (m, 2H), 3.71 (m, 2H), 6.64 (s, 1H), 7.95 (s, 1H).

Step 2 Preparation of 5-(2-amino-4,5-dimethylphenylamino)pentan-1-ol



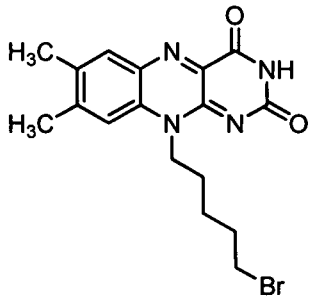
[0110] To a solution of 5-(4,5-dimethyl-2-nitrophenylamino)pentan-1-ol (147 mg, 0.583 mmol) in anhydrous MeOH (6 mL) under argon, is added Pd/C (8.4 mg) and sodium borohydride (64 mg, 1.68 mmol), the hydrogen atmosphere is retained with a balloon and the reaction mixture is stirred at room temperature for 30 min. The reaction mixture is filtered through celite, which is washed liberally with EtOH, and the solution is then concentrated to obtain the crude product as a clear, colourless oil which is used in the next step.

Step 3 Preparation of 10-(5-hydroxypentyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione



[0111] Crude 5-(2-amino-4,5-dimethylphenylamino)pentan-1-ol (0.583 mmol) is dissolved in glacial acetic acid (13 mL) under argon. Alloxan monohydrate (94 mg, 0.583 mmol) and boron oxide (81 mg, 1.165 mmol) are added to the stirring solution and the reaction is maintained under an argon atmosphere at 25°C with stirring for 2 h. The reaction mixture is evaporated under vacumm and the residue is dry loaded on silica gel using DCM as a solvent and purified by BIOTAGE flash column chromatography using a gradient from 0 to 10 % MeOH in DCM as eluent. Desired product (70 mg) is isolated (yield: 37 %). ^{1}H NMR (400 MHz, DMSO) δ 1.48 (m, 4H), 1.70 (m, 2H), 2.38 (s, 3H), 2.49 (s, 3H), 3.40 (m, 2H), 4.40 (t, 1H), 4.55 (m, 2H), 7.78, (s, 1H), 7.88 (s, 1H), 11.28 (s, 1H). ESI(+) $[M+Na]^+ = 351.2$.

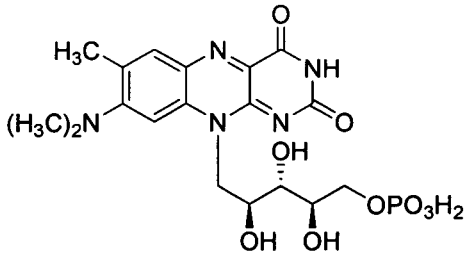
Step 4 Preparation of 10-(5-bromopentyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione



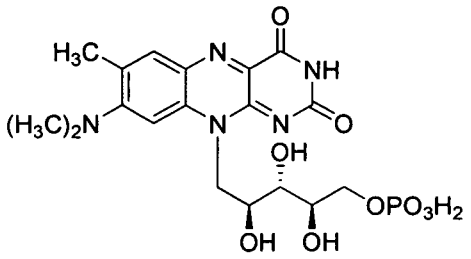
[0112] To a solution of 10-(5-hydroxypentyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (72 mg, 0.219 mmol) and carbon tetrabromide (80 mg, 0.241 mmol) in anhydrous DMF (5 mL) at 0°C, is added triphenyl phosphine (152 mg, 0.460 mmol) portion-wise. The reaction mixture is stirred at room temperature for 18 h. The reaction mixture is concentrated under reduced pressure and the residue is dry loaded on silica gel using DCM:MeOH (50:50) as a solvent and purified by BIOTAGE flash column chromatography using a gradient from 0 to 2% MeOH in DCM as eluent. Desired product (60 mg) is isolated (yield: 70 %). ^{1}H NMR (400 MHz, DMSO) δ 1.60 (m, 2H), 1.73 (m, 2H),1.90 (m, 2H), 2.40 (s, 3H), 2.50 (s, 3H), 3.58 (t, 2H), 4.59 (m, 2H), 7.80 (s, 1H), 7.90 (s, 1H), 11.31 (s, 1H). ESI(+) m/z = 391.1, 393.1.

Example 2:

(2R,3S,4S)-5-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-2,3,4-trihydroxypentyl dihydrogen phosphate



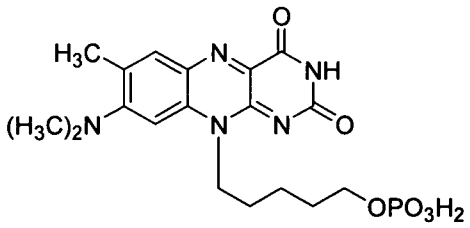
Step 1 Preparation of (2R,3S,4S)-5-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-2,3,4-trihydroxypentyl dihydrogen phosphate



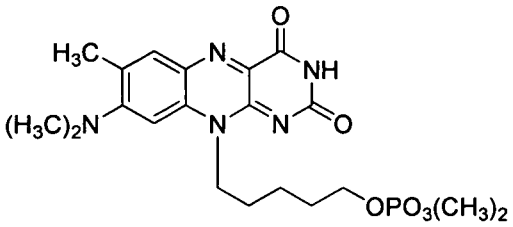
[0113] To roseoflavin (40 mg, 0.099 mmol) is added 0.3 mL of a solution of dichlorophosphoric acid (prepared by dropping water (7.2 mL, 400 mmol) over the course of 12 h to a flask containing phosphorus oxychloride (36.6 mL, 400 mmol), cooled to 0 °C). The mixture is stirred at room temperature for 4 h, at which point water (1 mL) is added. The solution quickly becomes warm. The solution is allowed to cool to room temperature, at which point it is neutralized with aqueous ammonium hydroxide. The reaction mixture is purified by preparative HPLC (Method 1). The desired product (23 mg) is isolated following lyophilization (Yield: 47.9%). ^{1}H NMR (400 MHz, D_2O) δ 2.39 (s, 3H), 3.17 (s, 6H), 3.97 (m, 3H), 4.33 (m, 2H), 4.86 (m, 2H), 6.66 (s, 1H), 7.35 (s, 1H); ESI(-) m/z = 484.1.

Example 3:

Phosphoric acid mono-[5-(8-dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentyl] ester



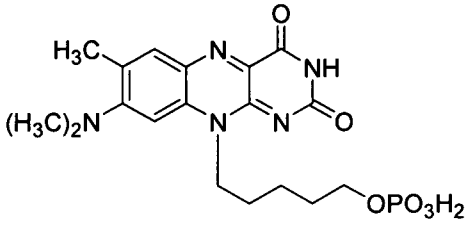
Step 1 Preparation of Phosphoric acid 5-(8-dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentyl ester dimethyl ester



[0114] 8-Dimethylamino-10-(5-hydroxy-pentyl)-7-methyl-10H-benzo[g]pteridine-2,4-dione (100 mg, 0.28 mmol) (prepared using the procedure described in example 10 steps 2-5 using 5-aminopentan-1-ol instead of butyl amine in step 2) is dissolved in dimethylchlorophosphate (2 mL), and the mixture heated to 50 °C while stirring. After 2 h, the reaction mixture is cooled to room temperature, and volatiles are removed under reduced pressure. The resulting residue is purified by preparative HPLC (Method 1). Phosphoric acid 5-(8-dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-

benzo[g]pteridin-10-yl)-pentyl ester dimethyl ester (30 mg) is isolated (Yield: 23.0%). LC-MS m/z 466.2 [M+H], retention time 3.00 min.

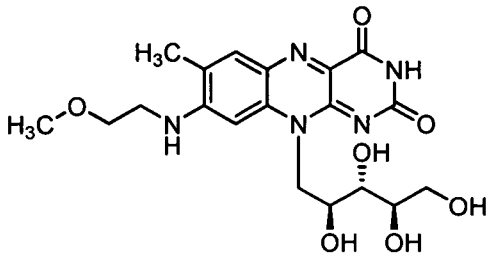
Step 2 Preparation of Phosphoric acid mono-[5-(8-dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentyl] ester



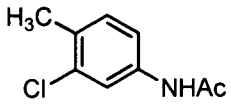
[0115] Phosphoric acid 5-(8-dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentyl ester dimethyl ester (30 mg, 0.064 mmol) is dissolved in anhydrous acetonitrile (15 mL), and the mixture is stirred at room temperature. Trimethylsilylbromide (80 μL, 0.60 mmol) is added dropwise to the stirring solution, and the reaction is stirred for 3 h at room temperature. The solution is concentrated under reduced pressure and the resulting residue is dissolved in 95:5 methanol:water (15 mL) and stirred at room temperature. After 1 h, 1.0 N aqueous HCl (5 mL) is added to the reaction, which is then stirred at room temperature for 12 h. The reaction mixture is purified by preparative HPLC (Method 1). Phosphoric acid mono-[5-(8-dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentyl] ester (14 mg) is isolated (Yield: 50.0%). LC-MS m/z 438.1 [M+H], retention time 2.07 min. ^{1}H NMR (400 MHz, CD_3OD) δ 1.69 (m, 2H), 1.83 (m, 2H), 1.93 (m, 2H), 2.55 (s, 3H), 3.22 (s, 6H), 4.05 (m, 2H), 4.72 (m, 2H), 6.86 (s, 1H), 7.80 (s, 1H).

Example 4:

8-(2-methoxyethylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione

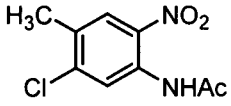


Step 1 Preparation of *N*-(3-Chloro-4-methyl-phenyl)-acetamide



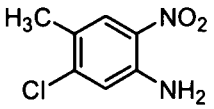
[0116] To a solution of 3-chloro-4-methyl-phenylamine (30 mL, 0.25 mol), Et_3N (104 mL, 0.75 mol), and DMAP (50 mg) in 750 mL of ethyl acetate at 0 °C, is added acetic anhydride (22.4 ml, 0.237 mol) in 100 mL of ethyl acetate, dropwise over 1h. Following completion of the addition, the reaction mixture is removed from the ice bath, and then stirred at room temperature for 5 h. The reaction is diluted with 200 mL of water and the organic layer is separated, and washed with brine. The organic layer is dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material is then triturated with hexanes and the solid filtered to yield 38.8 g of the desired product as an off-white solid (Yield: 84%).

Step 2 Preparation of *N*-(5-Chloro-4-methyl-2-nitro-phenyl)-acetamide



[0117] To a solution of N-(3-chloro-4-methyl-phenyl)-acetamide (38.8 g, 0.211 mol), in acetic anhydride (84 mL, 0.89 mol), and acetic acid (37 mL) cooled to -10 °C, is added nitric acid (17 mL) in 20 mL of acetic acid, dropwise over 0.5 h. Following completion of the addition, an additional 30 mL of acetic anhydride is added and the reaction mixture is removed from the ice bath, and then stirred at room temperature for 4.5 h. The reaction is poured into 300 mL of cold water and the solid is filtered, washed with water, ethanol, and ethyl ether. The crude is recrystallized from EtOH, filtered, and washed with cold ethanol to yield 23.7 g of the desired product as yellow solid (Yield: 49%).

Step 3 Preparation of 5-Chloro-4-methyl-2-nitro-phenylamine [Int-3A]

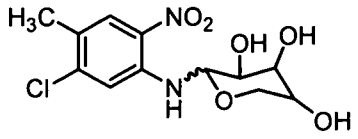


Int-3A

[0118] To a solution of *N*-(5-chloro-4-methyl-2-nitro-phenyl)-acetamide (23.7 g, 0.103 mol) in MeOH (80 mL) at room temperature is added sodium methoxide in methanol (25 weight percent, 20 mL). An additional 60 mL of MeOH is added for solubility and the solution is stirred for 5 h. The reaction is diluted with 500 mL of water

and the solid is filtered, washed with water, isopropanol, and hexanes to yield 19.8 g of the desired product **Int-3A** as an orange solid (Yield: 100%).

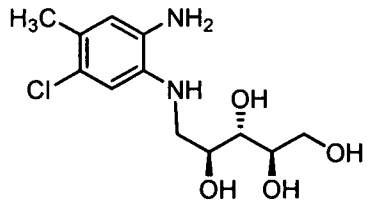
Step 4 Preparation of 2-(5-Chloro-4-methyl-2-nitro-phenylamino)-tetrahydro-pyran-3,4,5-triol [Int-3B]



Int-3B

[0119] A solution of 5-chloro-4-methyl-2-nitro-phenylamine **[Int-3A]** (19.8 g, 0.1 mol), ammonium chloride (100 mg), and D-ribose (15.9 g, 0.1 mol) in EtOH (200 mL) is set to reflux temperature under an argon atmosphere and stirred for 12 h. The solution is concentrated under reduced pressure, suspended in DCM:MeOH (1:1), and filtered to remove unreacted starting material. The mother liquor is dry loaded on silica gel (20% MeOH in DCM) and purified by ISCO flash column chromatography. Starting material is eluted using DCM, and the product is eluted using 20% MeOH/DCM. The desired product (7.7 g) **Int-3B** is isolated as a sticky orange solid (Yield: 24%). Unreacted starting material (12.6 g) is also recovered.

Step 5 Preparation of (2R,3S,4S)-5-(2-amino-5-chloro-4-methylphenylamino)-pentane-1,2,3,4-tetraol

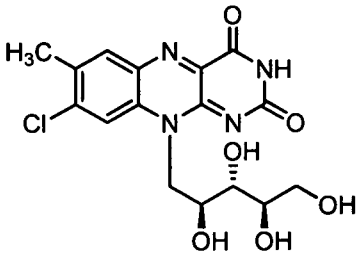


Int-4

[0120] To a solution of 2-(5-chloro-4-methyl-2-nitro-phenylamino)-tetrahydro-pyran-3,4,5-triol **[Int-3B]** (20 g, 0.63 mol) in EtOH (200 mL), is added sodium borohydride, portionwise, such that evolution of gas is not too vigorous. The resulting mixture is heated at reflux for 12 h. The reaction mixture is then cooled to 0 °C and palladium/carbon (400 mg) is added and the mixture is stirred at room temperature for 1 h. An additional portion of sodium borohydride (3.0 g) is added to complete the reduction, which is indicated by the reaction becoming colourless. The reaction mixture is filtered through Celite, which is washed liberally with MeOH, and the solution is then

concentrated to obtain the crude product **Int-4** as a clear, colourless oil to be used directly in the next step. LC-MS m/z 290.9 [M+H], retention time 1.38 min.

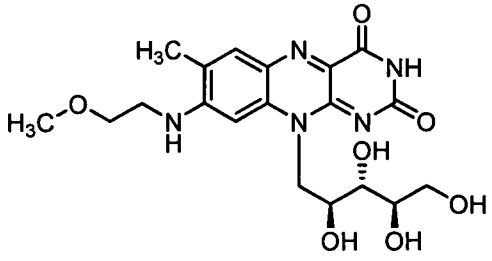
Step 6 Preparation of 8-chloro-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)-benzo[g]pteridine-2,4(3H,10H)-dione



Int 5

[0121] Crude 5-(2-amino-5-chloro-4-methyl-phenylamino)-pentane-1,2,3,4-tetraol (0.56 mmol) is dissolved in glacial acetic acid (6 mL) and stirred at room temperature. The flask is purged with argon for 20 min, following which alloxan monohydrate (90 mg, 0.56 mmol) and boron oxide (78 mg, 1.12 mmol) are added to the stirring solution. The reaction is maintained under an argon atmosphere and heated to 70 °C with stirring. After 14 h, the reaction is cooled to room temperature. Yellow precipitate is observed in solution. The solution is concentrated under reduced pressure, and the residue dissolved in DMSO (2 mL), filtered, and purified by preparatory HPLC (Method 1). 8-Chloro-7-methyl-10-(2,3,4,5-tetrahydroxy-pentyl)-10H-benzo[g]pteridine-2,4-dione (20 mg) is isolated following lyophilization of the appropriate fractions (Yield: 9 %). LC-MS m/z 397.1 [M+H], retention time 1.58 min. ^{1}H NMR (400 MHz, DMSO-d6) δ 2.51 (s, 3H), 3.46 (m, 1H), 3.64 (m, 2H), 4.23 (m, 1H), 4.49 (m, 1H), 4.67 (m, 1H), 4.78 (m, 2H), 4.88 (m, 1H), 5.15 (m, 2H), 8.13 (s, 1H), 8.20 (s, 1H), 11.47 (s, 1H).

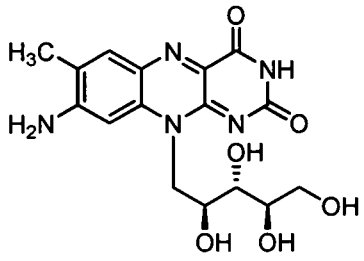
Step 7 Preparation of 8-(2-methoxyethylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione



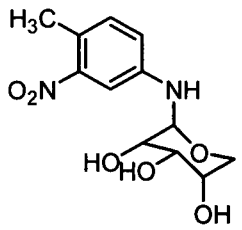
[0122] To a solution of 8-chloro-7-methyl-10-(2,3,4,5-tetrahydroxy-pentyl)-10H-benzo[g]pteridine-2,4-dione (50 mg, 0.13 mmol) in DMSO (2 mL) at room temperature, is added 2-methoxyethylamine (47 mg, 0.63 mmol), and the solution is stirred at 70 °C for 12 h. The reaction is cooled to room temperature, diluted with 3 mL of water, and purified by preparatory HPLC (Method 1). The desired product (45 mg) is isolated as a fluffy red solid (Yield: 82 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.99 (S, 1H), 7.67 (S, 1H), 7.10 (br, 1H), 6.87 (S, 1H), 5.00 (br, 2H), 4.50 (br, 2H), 4.24 (br, 2H), 3.3-3.6 (m, 11H), 2.27 (s, 3H); LC-MS *m/z* 436.3 (M+H), retention time 4.32 min.

Example 5:

8-amino-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]-pteridine-2,4(3H,10H)-dione

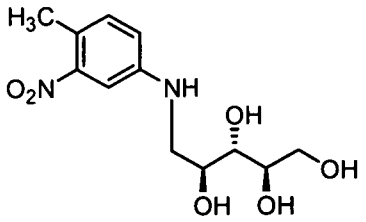


Step 1 Preparation of 2-(4-Methyl-3-nitro-phenylamino)-tetrahydro-pyran-3,4,5-triol



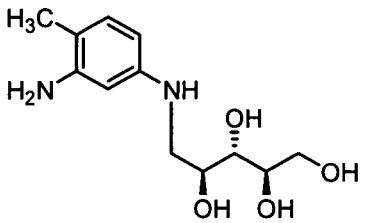
[0123] A solution of 4-methyl-3-nitro-phenylamine (2.0 g, 13.14 mmol), ammonium chloride (30 mg), and D-ribose (1.973 g, 13.14 mmol) in EtOH (75 mL) is refluxed under an argon atmosphere for 12 h. The solution is concentrated under reduced pressure. The residue is dry loaded on silica gel (20% MeOH in DCM) and purified by ISCO flash column chromatography using 20% MeOH in dichloromethane as eluent. Desired product (1.8 g) is isolated (Yield: 48 %).

Step 2 Preparation of 5-(4-Methyl-3-nitro-phenylamino)-pentane-1,2,3,4-tetraol



[0124] To an ice cooled solution of 2-(4-methyl-3-nitro-phenylamino)-tetrahydro-pyran-3,4,5-triol (1.8 g, 6.3 mmol) in EtOH (15 mL), is added sodium borohydride (1.7 g, 44 mmol). The reaction mixture is heated to reflux for 2.5 h. The reaction is cooled to room temperature and excess sodium borohydride is quenched using 1 M aqueous HCl. The mixture is neutralized using saturated, aqueous $NaHCO_3$ solution, and concentrated under reduced pressure. The residue is purified by flash column chromatography using methanol/tetrahydrofuran (0%-20%) as eluent to afford 1.2 g of the desired product. (Yield: 66 %) LC-MS *m/z* 287.1 (M+H), retention time 1.95 min.

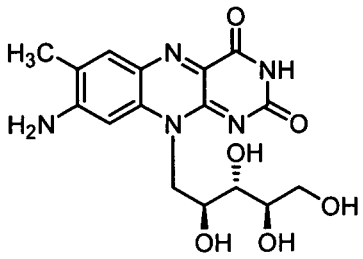
Step 3 Preparation of 5-(3-Amino-4-methyl-phenylamino)-pentane-1,2,3,4-tetraol



Int-4A

[0125] To a suspension of 5-(4-methyl-3-nitro-phenylamino)-pentane-1,2,3,4-tetraol (1.2 g, 4.2 mmol) in 25 mL of 30 % aqueous ammonia and 10 ml ethanol cooled to 0° C, is added zinc dust (1.37 g, 21.0 mmol). The reaction mixture is stirred at 0 °C for 30 min., and then at room temperature for 5 h. After the reaction is complete (monitored by TLC) the mixture is filtered through a Celite pad, and the pad is rinsed with dichloromethane. The filtrate is concentrated under reduced pressure and the resulting material used in the next step without further purification. LC-MS *m/z* 257.1 (M+H), retention time 0.74 min.

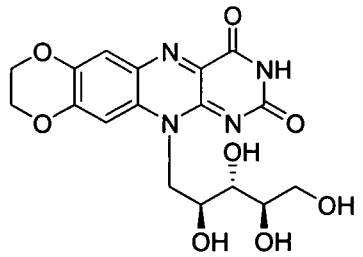
Step 4 Preparation of 8-Amino-7-methyl-10-(2,3,4,5-tetrahydroxy-pentyl)-10H-benzo[g]pteridine-2,4-dione



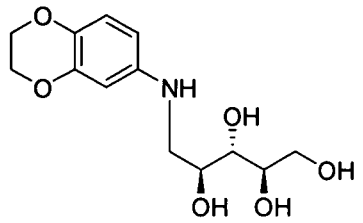
[0126] To a solution of 5-(3-amino-4-methyl-phenylamino)-pentane-1,2,3,4-tetraol [**Int-4A**] (crude product from step 3) in 20 mL MeOH, is added violuric acid monohydrate (740 mg, 4.20 mmol). The reaction mixture is heated to 70 °C for 18 hours. The solid is removed by filtration and the filtrate is concentrated and the resulting material is purified by preparatory HPLC (Method 1) to obtain 4.0 mg of the desired product (2 % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.24 (s, 3H), 3.56 (dd, 1H), 3.67 (m, 2H), 4.26 (d, 1H), 4.49 (d, 2H), 4.76 (t, 2H), 6.96 (s, 1H), 7.18 (br, 1H), 7.66 (s, 1H), 10.97 (s, 1H); LC-MS *m/z* 378.1 (M+H), retention time 1.00 min.

Example 6:

12-(2S,3S,4R,5-Tetrahydroxy-pentyl)-8,9-dihydro-12H-7,10-dioxa-1,3,5,12-tetraaza-napthacene-2,4-dione



Step 1 Preparation of 5-(2,3-Dihydro-benzo[1,4]dioxin-6-ylamino)-pentane-1,2R,3S,4S-tetraol

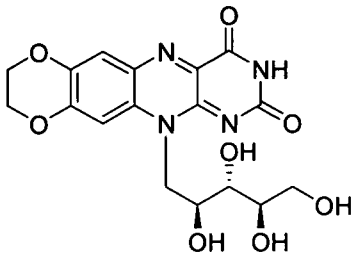


Int-4A

[0127] To a solution of 1,4-benzodioxan-6-amine (1.152 g, 7.620 mmol) in MeOH (15 mL) is added D-ribose (2.287 g, 15.24 mmol) and sodium cyanoborohydride (0.957 g, 15.24 mmol) and the mixture is heated to 70 °C for 2 h. The reaction is cooled to room

temperature and 1 M aqueous HCl is added causing evolution of gas. The mixture is neutralized with saturated $NaHCO_3$ solution (10 mL). The product is extracted using EtOAc (5 x 30 mL). The organic layer is dried over Na_2SO_4, filtered, and concentrated to dryness. The crude product is used in the following step without further purification. LC-MS m/z 286.3 (M+H), retention time 0.71 min.

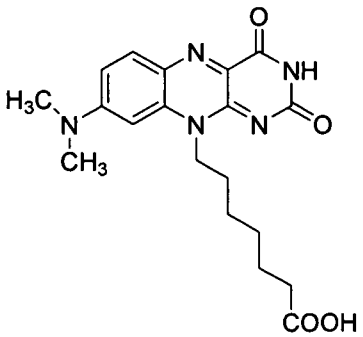
Step 2 Preparation of 12-(2,3,4,5-Tetrahydroxy-pentyl)-8,9-dihydro-12*H*-7,10-dioxa-1,3,5,12-tetraaza-napthacene-2,4-dione



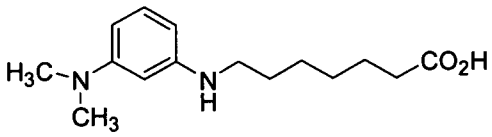
[0128] The crude compound obtained from the previous step, **Int-4A**, is dissolved in EtOH/H_2O (8 mL/8 mL) and violuric acid monohydrate (945 mg, 5.4 mmol) is added to the mixture, which is then heated to 110 °C for 18 hours. A precipitate forms and is filtered. The filtrate is concentrated, dissolved in 9 mL water and 1 mL DMSO, and purified by preparative HPLC (Method 1). After purification, 66.2 mg of desired product is isolated (2 % yield, 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.47 (br, 4H), 3.66 (m, 2H), 4.26 (m, 1H), 4.44 (m, 2H), 4.53 (m, 2H), 4.65 (d, 2H), 4.83 (t, 2H), 7.60 (s, 1H), 7.63 (s, 1H), 11.33 (s, 1H); LC-MS m/z 286.1 (M+H), retention time 1.15 min.

Example 7:

7-(8-Dimethylamino-2,4-dioxo-3,4-dihydro-2*H*-benzo[*g*]pteridin-10-yl)-heptanoic acid



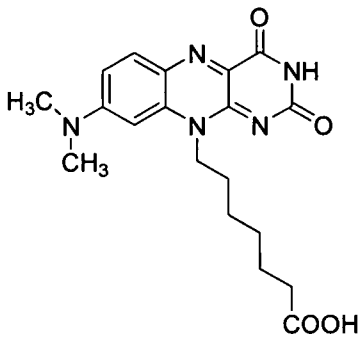
Step 1 Preparation of 7-(3-Dimethylamino-phenylamino)-heptanoic acid [Int-4A]



Int-4A

[0129] To a mixture of *N,N*-dimethyl-*m*-phenylenediamine dihydrochloride (663 mg, 3.17 mmol) and 7-bromoheptanoic acid (662 mg, 3.17 mmol) in 10 mL EtOH is added triethylamine (2.2 mL, 16 mmol). The reaction mixture becomes homogenous and is stirred at 90 °C for 21 h. The reaction is cooled to room temperature and solvent is removed under reduced pressure. The crude product **Int-4A** is used directly in the following step. LC-MS m/z 265.2 (M+H), retention time 2.33 min.

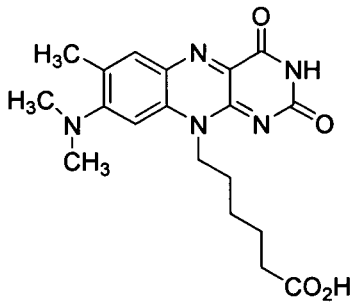
Step 2 Preparation of 7-(8-Dimethylamino-2,4-dioxo-3,4-dihydro-2*H*-benzo[*g*]pteridin-10yl)-heptanoic acid



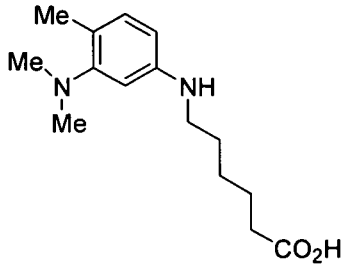
[0130] Violuric acid monohydrate (164 mg, 0.94 mmol) and crude 7-(3-dimethylamino-phenylamino)-heptanoic acid (250 mg, 0.940 mol) are dissolved in MeOH/H_2O (5 mL/5 mL) and the solution is heated to 70 °C for 18 h. The solvent is concentrated to dryness. The crude residue is dissolved in 6 mL of DMSO and purified by preparatory HPLC (Method 1). The product precipitates as a red solid in collected fractions. The solid is filtered, and washed with water and diethyl ether. Residual solvent is removed under vacuum and 6.91 mg of desired product is obtained (2% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.58-1.35 (m, 6H), 1.73 (br, 2H), 2.22 (m, 2H), 3.25 (s, 3H), 3.27 (s, 3H), 4.56 (br, 2H), 6.54 (s, 1H), 7.25 (br, 1H), 7.84 (m, 1H), 10.98 (s, 1H), 11.98 (s, 1H); LC-MS m/z 385.9 (M+H), retention time 2.54 min.

Example 8:

6-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2*H*-benzo[*g*]pteridin-10-yl)-hexanoic acid



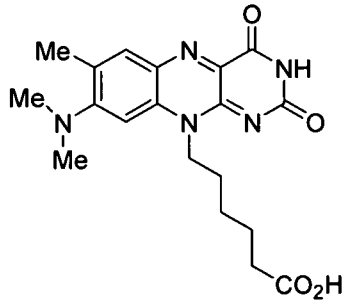
Step 1 Preparation of 6-(3-Dimethylamino-4-methyl-phenylamino)-hexanoic acid



Int-4A

[0131] N^1,N^1,6-trimethylbenzene-1,3-diamine (794 mg, 5.28 mmol) and 6-bromo-hexanoic acid (1.030 g, 5.28 mmol) are dissolved in 10 mL EtOH, following which triethylamine (3.7 mL, 26.4 mmol) is added to this solution. The reaction mixture is then stirred at 95-100 °C. After 4 h, 225 mg of 6-bromo-hexanoic acid is added to complete the reaction. Heating is continued for 3 more hours, following which the solution is cooled and kept at room temperature overnight. LC-MS analysis indicates the mixture contains approximately 20% dialkylated product. Solvent is removed and the crude residue **Int-4A** is dissolved in 15 mL MeOH and 15 mL water. Half of this mixture is used in the following step. LC-MS m/z 265.1 (M+H), retention time 1.59 min.

Step 2 Preparation of 6-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2*H*-benzo[*g*]pteridin-10-yl)-hexanoic acid

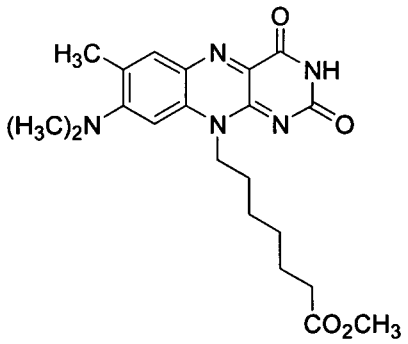


[0132] Into a 15 mL (1:1 MeOH:H_2O) solution containing the crude product from the previous step is added violuric acid monohydrate (462 mg, 4.64 mmol) and the

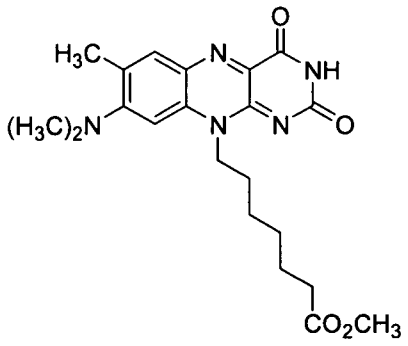
mixture is heated to 95 °C for 6 hours. The reaction is cooled to room temperature and kept at that temperature for 2 days. A red solid precipitates in the reaction mixture, which is filtered, and the precipitate is washed with water (10 mL) and ether (10 mL). Recrystallization of the precipitate is performed by dissolving the solid in 5 mL of hot MeOH and crashing out the product by adding 2 mL of water. The solid is filtered, washed with 30 mL water and then 20 mL Et_2O. The red solid is dried under vacuum and 178.4 mg of desired product is isolated. The filtrate is concentrated, dissolved in 9 mL of DMSO, and purified by preparative HPLC to produce 19.2 mg of the desired product. A total of 197.6 mg of the desired product is isolated (24% yield). ^1H NMR (400 MHz, DMSO-d_6) δ 1.48 (m, 2H), 1.62 (m, 2H), 1.75 (m, 2H), 2.25 (t, 2H), 2.46 (s, 3H), 3.06 (s, 6H), 4.59 (br, 2H), 6.86 (S, 1H), 7.80 (s, 1H), 11.10 (s, 1H), 12.01 (s, 1H); LC-MS m/z 385.9 (M+H), retention time 2.64 min.

Example 9:

7-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid methyl ester



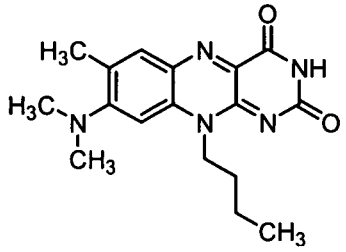
Step 1 Preparation of 7-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid methyl ester



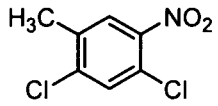
[0133] To a solution of 7-(8-dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid (20 mg, 0.050 mmol) in anhydrous methanol (3 mL) is added concentrated sulfuric acid (30 μL). The reaction mixture is heated to reflux and stirred for 14 h and then cooled to room temperature and neutralized with triethylamine. The solution is filtered and purified by preparative HPLC (Method 1). 7-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid methyl ester (12 mg) is isolated following lyophilization (Yield: 58.0%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.42 (m, 4H), 1.56 (m, 2H), 1.73 (m, 2H), 2.30 (m, 2H), 2.45 (s, 3H), 3.06 (s, 6H), 3.58 (s, 3H), 4.58 (m, 2H), 6.86 (s, 1H), 7.80 (s, 1H), 11.11 (s, 1H); LC-MS m/z 414.2 [M+H], retention time 3.63 min.

Example 10:

10-Butyl-8-dimethylamino-7-methyl-10H-benzo[g]pteridine-2,4-dione

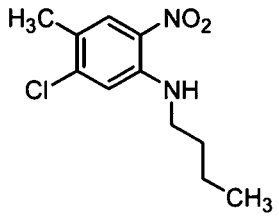


Step 1 Preparation of 1,5-Dichloro-2-methyl-4-nitro-benzene



[0134] To a solution of 2,4-dichloro-1-methyl-benzene (10.3 g, 0.064 mol) in 60 mL of concentrated sulfuric acid at -10 °C, is added nitric acid (2 mL, 0.06 mol) dropwise over 0.5 h, maintaining the reaction temperature at or below -10 °C. After the reaction is complete, as monitored by TLC, the reaction mixture is poured into 200 mL of ice and the solid is filtered and washed with water. The crude is recrystallized from hexane and filtered to yield 10.4 g of the desired product as a yellow solid (Yield: 80%).

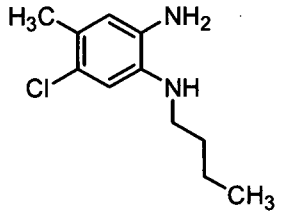
Step 2 Preparation of Butyl-(5-chloro-4-methyl-2-nitro-phenyl)-amine [Int-3]



Int-3

[0135] To a solution of 1,5-dichloro-2-methyl-4-nitro-benzene (900 mg, 4.37 mmol) in 50 mL of THF is added n-butylamine (1.6 g, 2.18 mL, 21.8 mmol) and triethylamine (660 mg, 0.9 mL, 6.56 mmol). The reaction mixture is heated to reflux for 15 h. The reaction mixture is concentrated under reduced pressure and the crude product purified by flash column chromatography using dichlomethane/hexanes (10%-30%) as eluent to yield 844 mg of the desired **Int-3** product (Yield: 80%). LC-MS *m/z* 243.1 (M+H), retention time 6.90 min.

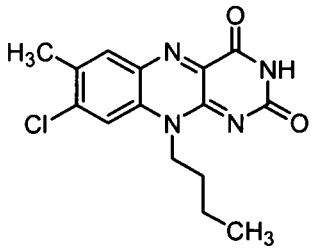
Step 3 Preparation of N^2-Butyl-4-chloro-5-methyl-benzene-1,2-diamine



Int-4

[0136] To a suspension of butyl-(5-chloro-4-methyl-2-nitro-phenyl)-amine **[Int-3]** (1.1 g, 4.53 mmol) in 10 mL of 30 % aqueous ammonia and 10 mL of ethanol at 0 °C, is added zinc dust (1.5 g, 22.8 mmol). The reaction is stirred at 0 °C for 15 min, at which point the ice bath is removed, and the reaction is stirred at room temperature for 5 h. After the reaction is complete, as monitored by TLC, the reaction mixture is filtered through a Celite pad, and rinsed with dichloromethane. The filtrate is concentrated under reduced pressure and purified by flash column chromatography using dichloromethane/hexanes (10%-100%) as eluent to yield 624 mg of the desired **Int-4** product (Yield: 71 %). LC-MS *m/z* 213.1 (M+H), retention time 3.34 min.

Step 4 Preparation of 10-Butyl-8-chloro-7-methyl-10*H*-benzo[*g*]pteridine-2,4-dione

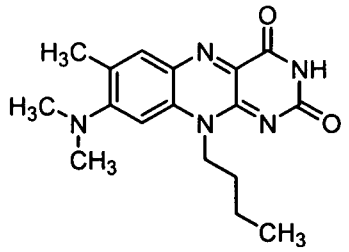


Int-5

[0137] To a solution of N^2-butyl-4-chloro-5-methyl-benzene-1,2-diamine **[Int-4]** (624 mg, 3.14 mmol) in 15 mL of acetic acid, under an argon atmosphere, is added alloxan monohydrate (503 mg, 3.14 mmol) and boron oxide (437 mg, 6.28 mmol). The reaction

mixture is stirred at 60 °C for 3 h, cooled to room temperature, and stirred for 16 h. The reaction mixture is diluted with 50 mL water, neutralized with aqueous sodium bicarbonate, and extracted with dichloromethane (3 x 50 mL). The organic layers are combined, dried over magnesium sulfate, and concentrated under reduced pressure. The crude **Int-5** product is purified by flash column chromatography using methanol/dichloromethane (0%-10%) as eluent to yield 600 mg of the desired **Int-5** product (Yield: 60 %). LC-MS *m/z* 319.1 (M+H), retention time 3.59 min.

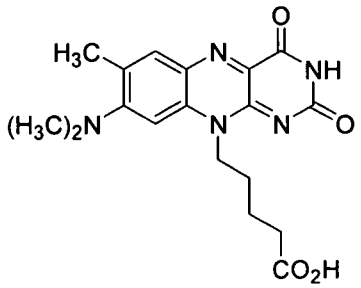
Step 5 Preparation of 10-Butyl-8-dimethylamino-7-methyl-10*H*-benzo[*g*]pteridine-2,4-dione



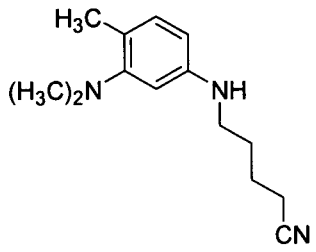
[0138] To a solution of 10-butyl-8-chloro-7-methyl-10*H*-benzo[*g*]pteridine-2,4-dione **[Int-5]** (80 mg, 0.25 mmol) in 3 mL of DMF is added N,N-dimethylamine (0.32 mL, 2M solution in THF, 0.63 mmol). The reaction mixture is heated at 100 °C for 12 h, cooled to room temperature, and purified by preparative HPLC (Method 1) to yield 12 mg of the desired product (Yield: 15 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.99 (t, 3H), 1.46 (m, 2H), 1.73 (m, 2H), 2.45 (s, 3H), 3.06 (s, 6H), 4.5-4.7 (br, 2H), 6.86 (s, 1H), 7.80 (s, 1H), 11.13 (s, 1H); LC-MS *m/z* 328.3 (M+H), retention time 3.23 min.

Example 11:

5-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentanoic acid



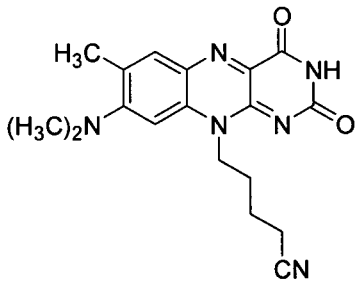
Step 1 Preparation of 5-(3-Dimethylamino-4-methyl-phenylamino)-pentanenitrile



Int-4A

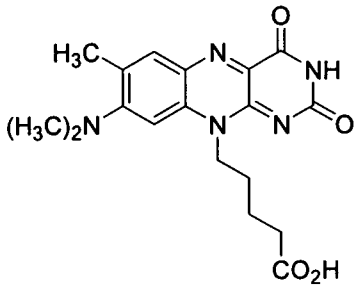
[0139] To a solution of 3-dimethylamino-4-methylaniline (632 mg, 4.21 mmol) in anhydrous ethanol (10 mL) is added triethylamine (1.76 mL, 12.63 mmol) and 5-bromovaleronitrile (682 mg, 4.21 mmol). The stirring solution is heated at reflux for 14 h. The solution is concentrated, and the crude product **Int-4A** is used directly in the following step. LC-MS m/z 232.1 [M+H], retention time 1.52 min.

Step 2 Preparation of 5-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentanenitrile



[0140] Crude 5-(3-dimethylamino-4-methyl-phenylamino)-pentanenitrile **[Int-4A]** (2 mmol) is dissolved in methanol (8 mL). Violuric acid monohydrate (350 mg, 2 mmol) is dissolved in water (8 mL) in a separate flask, and heated at 60 °C with stirring. The solution of 5-(3-dimethylamino-4-methyl-phenylamino)-pentanenitrile in methanol is added to the aqueous solution of violuric acid, and the mixture heated at 60 °C with stirring. After 6 h, the reaction mixture is removed from the heat, and the mixture is stored at room temperature in the dark for 16 h. The reaction mixture is concentrated, and the precipitate is filtered. The mother liquor is diluted with DMSO (5 mL) and purified by preparative HPLC (Method 1). The precipitate (38 mg) is also dissolved in DMSO and purified by preparative HPLC (Method 1). Lyophilization of combined fractions from the two preparative HPLC runs affords 713 mg (2.02 mmol) of desired product (Yield: 48.0% for two steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.75 (m, 2H), 1.88 (m, 2H), 2.46 (s, 3H), 2.64 (m, 2H), 3.07 (s, 6H), 4.65 (m, 2H), 6.89 (s, 1H), 7.81 (s, 1H), 11.11 (s, 1H); ESI(+) *m/z* 353.3 [M+H].

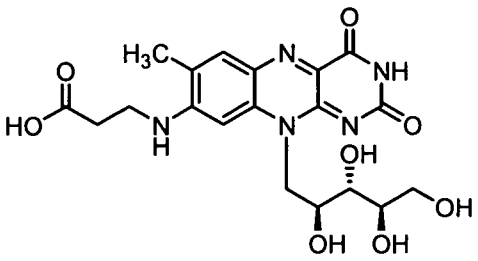
Step 3 Preparation of 5-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentanoic acid



[0141] 5-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentanenitrile (514 mg, 1.46 mmol) is dissolved in 6 N aqueous HCl (8 mL), and the solution is heated at reflux with stirring. After 5 h, TLC indicates consumption of the starting material. The reaction mixture is cooled to room temperature and neutralized with triethylamine. The mixture is then filtered and purified by preparative HPLC (Method 1). HPLC fractions are allowed to stand in the dark at room temperature for 24 h. Fractions containing product (as indicated by TLC 10 % MeOH in dichloromethane) are filtered, and the precipitate washed with water and air-dried. 5-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-pentanoic acid (10 mg) is isolated (Yield: 1.8%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.67 (m, 2H), 1.76 (m, 2H), 2.34 (t, 2H), 2.45 (s, 3H), 3.06 (s, 6H), 4.59 (m, 2H), 6.86 (s, 1H), 7.79 (s, 1H), 11.12 (s, 1H), 12.11 (br s, 1H); LC-MS m/z 372.2[M+H], retention time 2.32 min.

Example 12:

Preparation of 3-[7-Methyl-2,4-dioxo-10-(2,3,4,5-tetrahydroxy-pentyl)-2,3,4,10-tetrahydro-benzo[g]pteridin-8-ylamino]-propionic acid

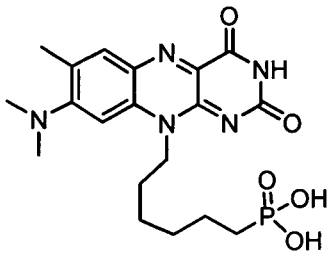


[0142] To a solution of 3-[7-methyl-2,4-dioxo-10-(2,3,4,5-tetrahydroxy-pentyl)-2,3,4,10-tetrahydro-benzo[g]pteridin-8-ylamino]-propionic acid tert-butyl ester (15 mg, 0.03 mmol) (prepared using the procedure for example 4, step 7) in DCM (2 mL) at room temperature is added TFA (2 mL), and the solution is stirred for 2 h. The solution is

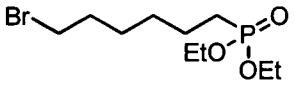
concentrated under reduced pressure, dissolved in ACN/water, and lyophilized to yield 5.3 mg of the product as a fluffy orange solid (Yield: 41 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.36 (s, 1H), 10.96 (s, 1H), 7.07 (s, 1H), 6.86 (S, 1H), 5.4-4.2 (m, 7H), 3.63 (m, 2H), 2.68 (m, 2H), 2.26 (s, 3H); LC-MS *m/z* 450.3 (M+H), retention time 4.24 min.

Example 13:

[6-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-hexyl]-phosphonic acid

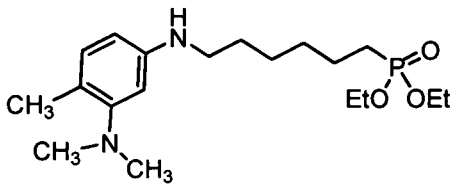


Step 1 Preparation of Diethyl 6-bromohexylphosphonate



[0143] 1,6-Dibromohexane (2 g, 8.2 mmol) and $P(OEt)_3$ (6.81 g, 4.1 mmol) are combined neat in a round bottom flask (25 mL). The mixture is then heated in an oil bath at 150 °C. The progress of the reaction is monitored by LC-MS and the reaction is complete after 3 h. A mixture of monophosphonate and bisphosphonate is obtained. The desired compound is found by LC-MS to have m/z 302.9 (M+H), and retention time 4.84 min. The undesired product has LC-MS m/z 359.1 (M+H), and retention time 4.21 min. The compounds are visualized on TLC (100 % hexane) by staining with phosphomolybdic acid solution. Crude product is used directly in the following step.

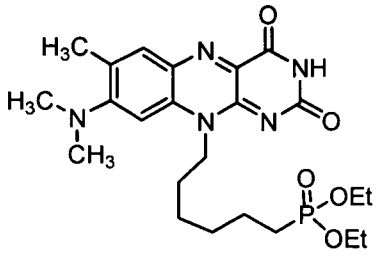
Step 2 Preparation of Diethyl 6-(3-(dimethylamino)-4 methylphenylamino)-hexylphosphonate.



[0144] This compound is prepared using the procedure of Example 8, Step 1 and using diethyl 6-bromohexylphosphonate (1.23 g, 4.1 mmol) and N^1,N^1,6-trimethylbenzene-1,3-diamine (616 mg, 4.1 mmol). The monoalkylated product has LC-

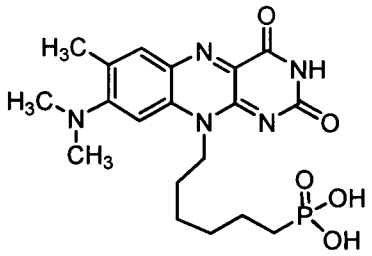
MS m/z 371.2 (M+H), retention time 3.18 min. The dialkylated product has LC-MS m/z 591.3 (M+H), retention time 4.38 min. The crude product is used in the next step without purification.

Step 3 Preparation of Diethyl 6-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexylphosphonate



[0145] This compound is prepared using the procedure of Example 8, Step 2 and using diethyl 6-(3-(dimethylamino)-4 methylphenylamino)hexylphosphonate from step 2 and violuric acid monohydrate (718 mg, 4.4 mmol). The product is isolated by preparative HPLC (Method 1) as a red solid with 2.5% overall yield (50 mg, 0.1 mmol) for the 3 steps. ^{1}H NMR (300 MHz, CD_3OD) δ 7.83 (1H, s), 6.89 (1H, s),), 4.75 (2H, m), 4.10 (4H, m), 3.20 (6H, s), 2.54 (3H, s), 1.85 (4H, m), 1.63 (6H, m), 1.33 (6H, t); LC-MS m/z 492.2 (M+H), retention time 3.72 min.

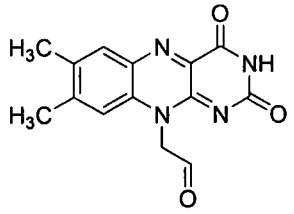
Step 4 Preparation of 6-(8-(Dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexylphosphonic acid



[0146] Diethyl 6-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]-pteridin-10(2H)-yl)hexylphosphonate (10 mg, 0.02 mmol) is dissolved in 6N aqueous HCl (5 mL) in a round bottom flask (10 mL) and heated at 100 °C in an oil bath for 12 hours. The reaction is monitored by LC-MS. Solvent is removed under reduced pressure and the residual solid is purified by HPLC (Preparative Method 2) and the desired product is isolated in 35% yield as a red solid (3.5 mg), LC-MS m/z 436.2 (M+H), retention time 2.53 min.

Example 14:

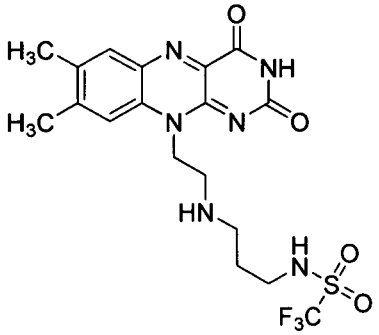
(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde



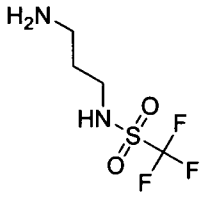
[0147] To a suspension of riboflavin (2.85 g, 7.5 mmol) in 2 N aqueous sulfuric acid (75 mL), cooled to 0 °C in a flask covered with tinfoil, is added orthoperiodic acid (6.3 g, 27.5 mmol). After 30 min, the reaction is allowed to warm to room temperature. After 2 h, the pH of the reaction solution is adjusted carefully to 1.5 by addition of solid sodium carbonate. The precipitate is then filtered off and the filtrate is basified (using solid sodium carbonate) to pH = 3.9. The precipitate is filtered, washed liberally with cold water, ethanol, and diethyl ether to yield 2.0 g of the desired product as an orange solid (Yield: 94%). LC-MS m/z 285.1 [M+H].

Example 15:

[0148] ***N*-(3-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)propyl)-1,1,1-trifluoromethanesulfonamide**



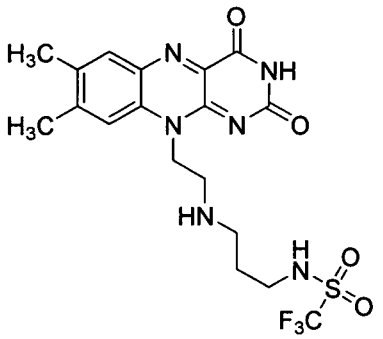
Step 1 *N*-(3-aminopropyl)-1,1,1-trifluoromethanesulfonamide



[0149] To a solution of 1,3-diaminopropane (2 mL, 24 mmol) and triethylamine (3.3 mL, 24 mmol) in anhydrous CH_2Cl_2 (10 mL) at 0 °C, is added trifluoromethanesulfonic anhydride (0.8 mL, 5 mmol) dropwise over 10 min. After

completion of the addition, the reaction mixture is removed from the ice bath, and then stirred at room temperature for 7 h. The reaction is diluted with water (20 mL) and the organic layer is separated, and washed with brine (20 mL). The organic layer is dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue is then triturated with diethyl ether:ethyl acetate (1:1) and the solid is removed by filtration. The filtrate is concentrated and purified via silica gel chromatography (ISCO) (100% CH_2Cl_2 to 10% MeOH/CH_2Cl_2) over 15 minutes to obtain a yield of 163 mg of desired product as a white semi-solid (Yield: 17%). LC-MS m/z 207.0 [M+H].

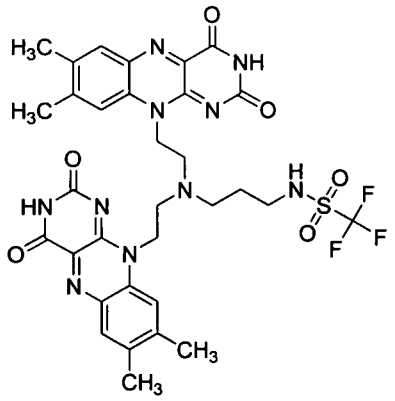
Step 2 Preparation of N-{3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-propyl}-C,C,C-trifluoromethanesulfonamide



[0150] To a suspension of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (100 mg, 0.35 mmol) in methanol (7 mL) is added *N*-(3-amino-propyl)-C,C,C-trifluoro-methanesulfonamide (72 mg, 0.35 mmol)) and acetic acid (0.1 mL) at room temperature. After 30 min., sodium cyanoborohydride (48 mg, 0.77 mmol) is added, and the solution is stirred for 16 h. The reaction mixture is concentrated, and the residue is dissolved in DMF/water, filtered, and purified by preparative HPLC (Method 1). *N*-{3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-propyl}-C,C,C-trifluoromethanesulfonamide (21 mg) is isolated following lyophilization of the appropriate fractions (Yield: 13%). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.82 (t, 2H), 2.43 (s, 3H), 2.54 (s, 3H), 3.13 (m, 2H), 3.25 (m, 2H), 4.94(m, 2H), 7.81 (d, 1H), 7.99 (m, 1H), 8.63 (brs, 1H), 9.56 (brs, 1H), 11.49 (s, 1H). LC-MS m/z 475.2 [M-H].

Example 16:

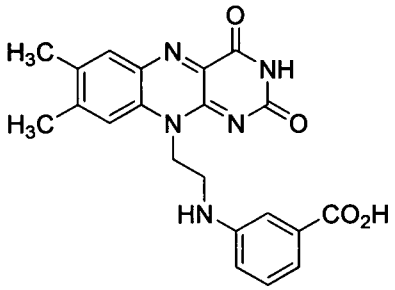
N-(3-{Bis-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-amino}-propyl)-C,C,C-trifluoro-methanesulfonamide



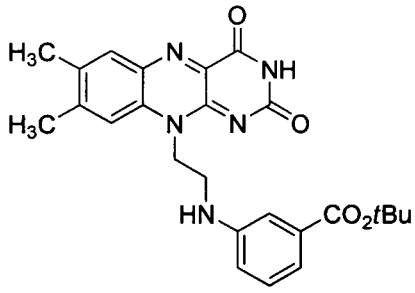
[0151] This is a byproduct of the above reaction and isolated from the HPLC run as described in example 15. The product (17 mg) is obtained as an orange solid (Yield: 10%). LC-MS m/z 743.3 [M+H].

Example 17:

3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-benzoic acid

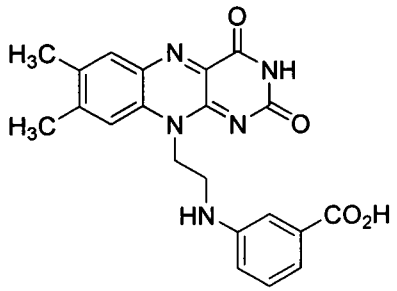


Step 1 Preparation of 3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-benzoic acid t-butyl ester



[0152] This product is prepared using the procedure of Example 15, Step 2 except (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (100 mg, 0.35 mmol) and tert-butyl 3-aminobenzoate (51 mg, 0.26 mmol) are used to obtain a yield of 22 mg of the desired product as a red powder (Yield: 18.3%). MS m/z 461.9 [M+H].

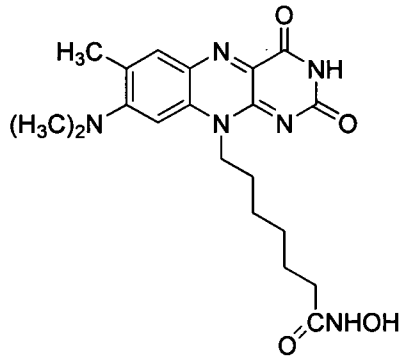
Step 2 Preparation of 3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-benzoic acid



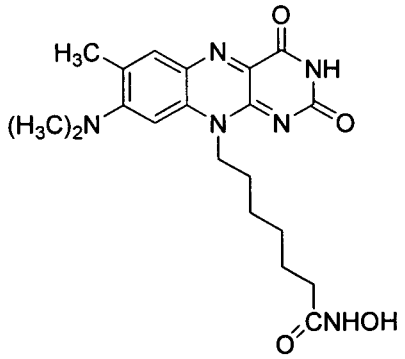
[0153] To a suspension of 3-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-benzoic acid t-butyl ester (22 mg, 0.05 mmol) in CH_2Cl_2 (2 mL) is added trifluoroacetic acid (2 mL) at room temperature. After 2 h, the reaction mixture is concentrated and the residual material is dissolved in water/acetonitrile and lyophilized. 3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-benzoic acid (17 mg) is isolated (Yield: 83.9%). ^{1}H NMR (400 MHz, DMSO-d6) δ 2.29 (s, 3H), 2.36 (s, 3H), 3.60 (m, 2H), 4.74 (m, 2H), 6.90 (d, 1H), 7.07 (s, 1H), 7.16 (m, 2H), 7.53 (s, 1H), 7.86 (s, 1H), 11.36 (s, 1H), LC-MS m/z 404.1 [M-H].

Example 18:

7-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]-pteridin-10-yl)-heptanoic acid hydroxyamide



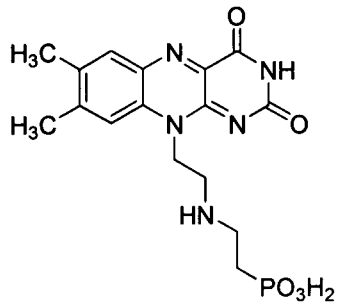
Step 1 Preparation of 7-(8-Dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid hydroxyamide



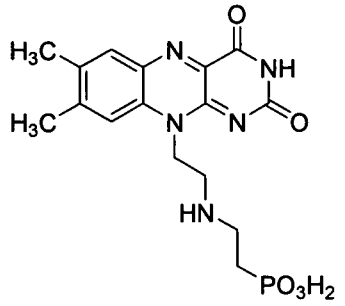
[0154] To a solution of 7-(8-dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid (20 mg, 0.05 mmol) (prepared using a similar procedure to that of Example 8 using the appropriate starting materials) in a mixture of anhydrous THF (15 mL) and anhydrous CH_2Cl_2 (3 mL) at 0 °C (ice/water bath) under an argon atmosphere is added *N*-methylmorpholine (22 μL, 0.20 mmol) and isobutylchloroformate (26 μL, 0.20 mmol). The ice bath is removed and the solution stirred at room temperature for 2 h. Hydroxylamine hydrochloride (7 mg, 0.10 mmol) is added to the stirring solution at room temperature, and after stirring for 2 h, methanol (2 mL) is added to aid solubility. The solution is stirred for an additional 18 h. The solution is concentrated, and the residue dissolved in a 1:1 mixture of DMSO:water (4 mL). Crude product is purified by preparative HPLC (Method 1). Following lyophilization of appropriate fractions, 7-(8-dimethylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid hydroxyamide (6.0 mg, 0.0145 mmol) is isolated (Yield: 29 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.49 (m, 6H), 1.74 (m, 2H), 1.97 (t, 2H), 2.46 (s, 3H), 3.06 (s, 6H), 4.58 (m, 2H), 6.86 (s, 1H), 7.81 (s, 1H), 8.67 (s, 1H), 10.36 (s, 1H), 11.13 (s, 1H); LC-MS m/z 415.1[M+H], retention time 4.32 min.

Example 19:

{2-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-ethyl}-phosphonic acid



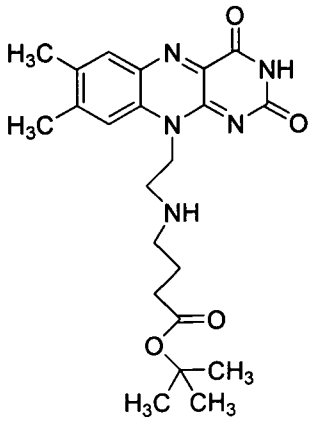
Step 1 Preparation of {2-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-ethyl}-phosphonic acid



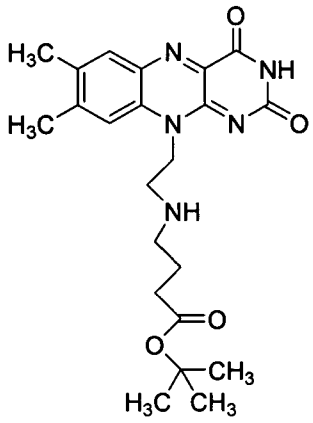
[0155] To a suspension of {2-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-ethyl}-phosphonic acid diethyl ester (50 mg, 0.11 mmol) (prepared by reductive amination using a procedure similar to that of Example 15, Step 2 using (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (140 mg, 0.49 mmol) and (2-amino-ethyl)-phosphonic acid diethyl ester (71 mg, 0.39 mmol)) in anhydrous dichloromethane (2 mL) is added bromotrimethylsilane (0.5 mL). The reaction mixture is stirred at room temperature for 16 hours. After completion of the reaction (as monitored by TLC and LC/MS), the reaction is quenched by the addition of water (2 mL) at room temperature. After the solution is stirred for 15 min., methanol is added until the solution becomes homogeneous. The solution is stirred for an additional 15 min, and then concentrated under reduced pressure. The remaining residue is purified by preparative HPLC (Method 1). {2-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-ethyl}-phosphonic acid (11.0 mg, 0.0280 mmol) is isolated following lyophilization of appropriate fractions (Yield: 25 %). ^{1}H NMR (400 MHz, CD_3OD) δ 2.11 (m, 2H), 2.50 (s, 3H), 2.62 (s, 3H), 3.65 (m, 2H), 5.07 (m, 2H), 7.81 (s, 1H), 8.04 (s, 1H); LC-MS m/z 394.0 [M+H], retention time 1.40 min.

Example 20:

[0156] **4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyric acid tert-butyl ester**



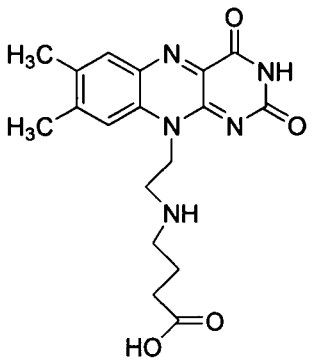
Step 1 Preparation of 4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyric acid tert-butyl ester



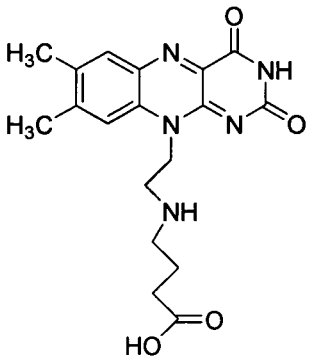
[0157] The reductive amination method of Example 15, step 2 is used starting with (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (403 mg, 1.62 mmol) and tert-butyl 4-aminobutanoate (349 mg, 1.78 mmol). The isolated yield of the desired product is 27 %. ^{1}H NMR (400 MHz, d_6-DMSO) δ 1.41 (s, 9H), 1.76 (m, 2H), 2.32 (t, 2H), 2.43 (s, 3H), 2.53 (s, 3H), 3.07 (bm, 2H), 4.93 (t, 2H), 7.81 (s, 1H), 7.98 (s, 1H), 8.54 (bs, 2H), 11.48 (s, 1H), LC-MS m/z 428.2 [M+H] retention time 2.67 min.

Example 21:

4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyric acid



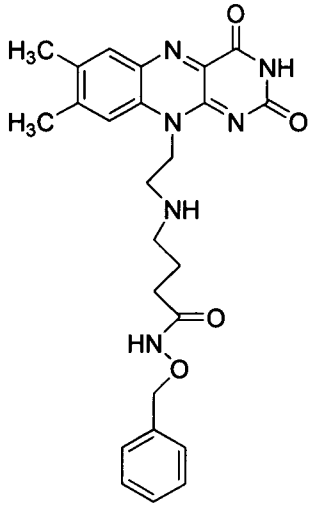
Step 1 Preparation of 4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyric acid



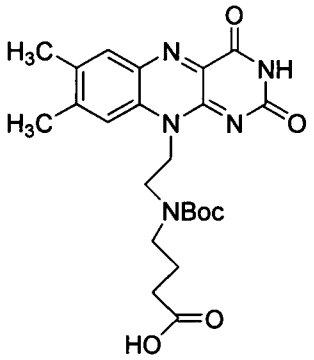
[0158] 4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyric acid is prepared by following the procedure of Example 17, Step 2 starting with 4-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyric acid tert-butyl ester (120 mg, 0.280 mmol) and trifluoroacetic acid (3 mL) in dichloromethane (5 mL) . The isolated yield of the desired product is 86%. ^{1}H NMR (400 MHz, CD_3OD) δ 2.00 (m, 2H), 2.50 (m, 2H), 2.51 (s, 3H), 2.64 (s, 3H), 3.22 (t, 2H), 3.64 (t, 2H), 5.09 (t, 2H), 7.81 (s, 1H), 8.03 (s, 1H). LC-MS m/z 372.2 [M+H] retention time 1.40 min.

Example 22:

***N*-Benzyloxy-4-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]-pteridin-10-yl)-ethylamino]-butyramide**

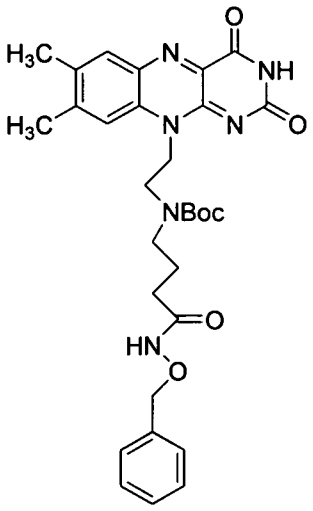


Step 1 Preparation of 4-{tert-Butoxycarbonyl-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-amino}-butyric acid



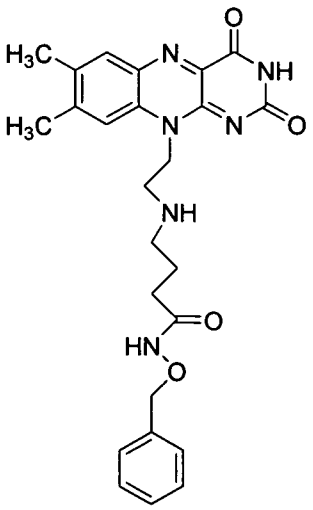
[0159] 4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyric acid (Example 21) (234 mg, 0.63 mmol) is dissolved in MeOH (6 mL), triethylamine (0.5 mL) and di-tert-butyl-dicarbonate (206 mg, 0.945 mmol) is added. The reaction mixture is stirred at room temperature for 1 h. Upon completion of the reaction (as monitored by TLC), solvent is removed and the crude product is used in the following step without any purification LC-MS m/z 472.0 [M+H], retention time 3.31 min.

Step 2 Preparation of (3-Benzyloxycarbamoyl-propyl)-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-carbamic acid tert-butyl ester



[0160] 4-{*tert*-Butoxycarbonyl-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-amino}-butyric acid is dissolved in DMF (3 mL). *O*-benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluroniumhexafluoro phosphate (358 mg, 0.945 mmol) is added to this solution and stirred at room temperature for 5 minutes. *O*-benzylhydroxylamine hydrochloride (201 mg, 1.26 mmol) is added along with diisopropylethylamine (0.5 mL) and the mixture is stirred for 3.5 h. The reaction mixture is diluted with water (6 mL) and purified by preparative HPLC (Method 1). After lyophilization, 161 mg of the desired product is isolated (44% yield). LC-MS m/z 577.0 [M+H], retention time 4.14 min.

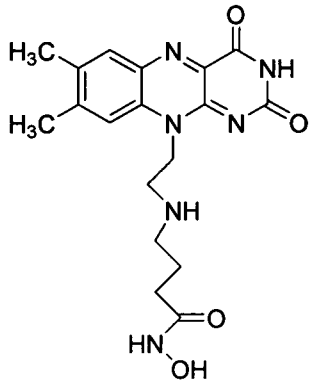
Step 3 Preparation of N-Benzyloxy-4-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyramide



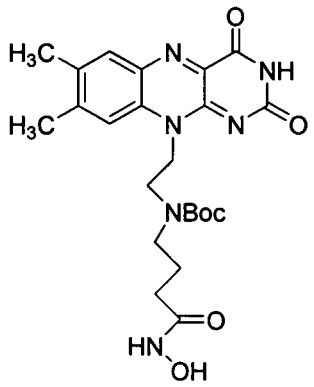
[0161] To a solution of (3-benzyloxycarbamoyl-propyl)-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-carbamic acid tert-butyl ester (12.9 mg, 0.022 mmol) in dichloromethane (0.5 mL) is added trifluoroacetic acid (0.3 mL). After 3 h of stirring at room temperature, all of the starting material is consumed (as indicated by TLC). The reaction mixture is concentrated under reduced pressure and the residue is dried using a vacuum pump, affording 6.6 mg of the desired product as the TFA salt (63% yield). ^{1}H NMR (400 MHz, CD_3OD) δ 1.96 (m, 2H), 2.25 (t, 2H), 2.49 (s, 3H), 2.63 (s, 3H), 3.19 (t, 2H), 3.65 (t, 2H), 4.78 (s, 2H), 5.11 (t, 2H), 7.37 (s, 5H), 7.82 (s, 1H), 7.98 (s, 1H), LC-MS m/z 477.0 [M+H], retention time 2.20 min.

Example 23:

4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-N-hydroxy-butyramide



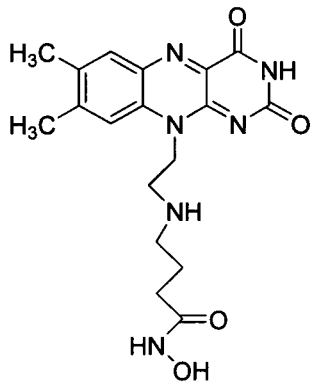
Step 1 Preparation of [2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-(3-hydroxycarbamoyl-propyl)-carbamic acid tert-butyl ester



[0162] (3-Benzyloxycarbamoyl-propyl)-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-carbamic acid tert-butyl ester (150 mg, 0.26 mmol) is

dissolved in MeOH (10 mL). The reacton mixture is purged with argon, following which palladium/carbon (10 weight percent, 30 mg) is added. The reaction mixture is placed under an atmosphere of hydrogen at room temperature using a balloon filled with hydrogen. After completion of the reaction (as monitored by TLC) the mixture is filtered through a Celite pad and the Celite is washed with methanol (30 mL). The filtrate is concentrated under reduced pressure and the crude product is used in the final step. LC-MS m/z 486.9 [M+H], retention time 2.48 min.

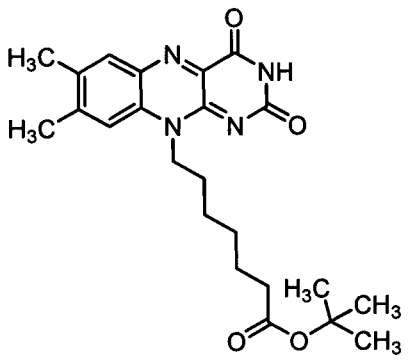
Step 2 Preparation of 4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-N-hydroxy-butyramide



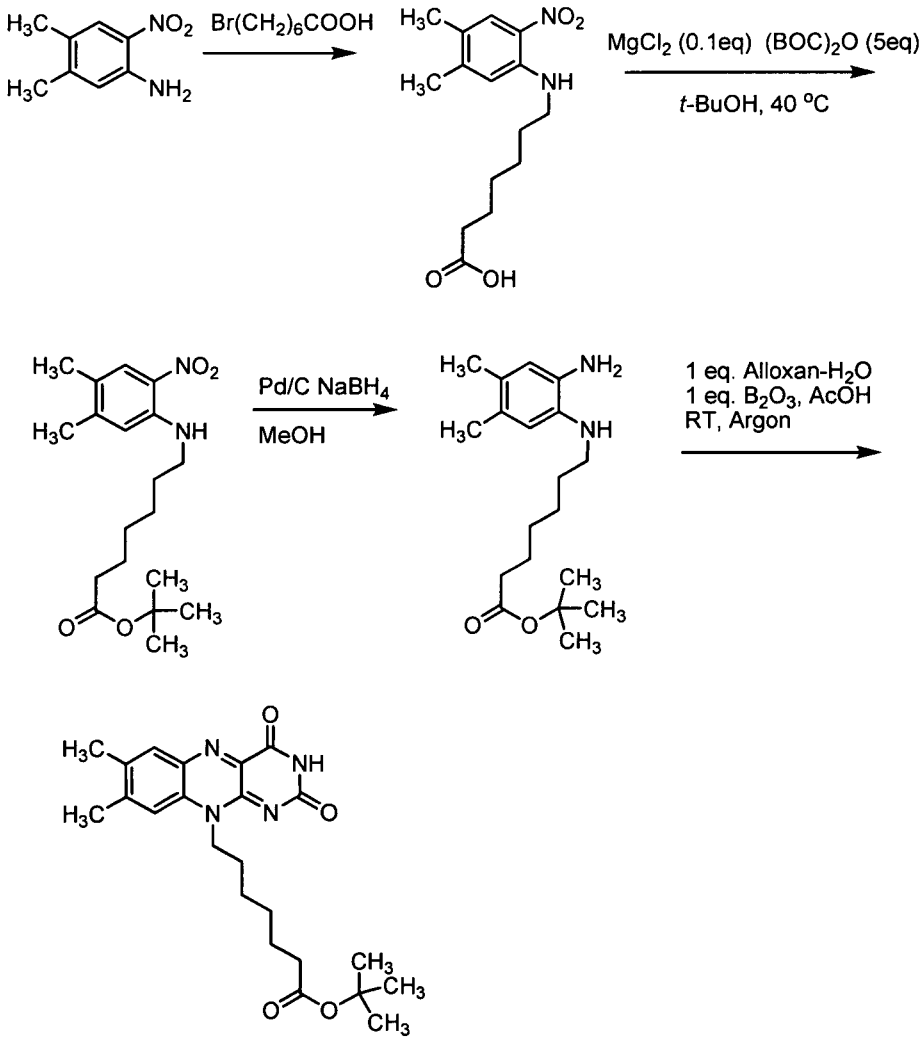
[0163] [2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-(3-hydroxycarbamoyl-propyl)-carbamic acid tert-butyl ester is dissolved in dichloromethane (3.5 mL) and trifluoroacetic acid (1 mL) is added. The mixture is stirred at room temperature for 2 h. The reaction mixture is concentrated under reduced pressure and the crude product is dissolved in water (6 mL) and purified by preparative HPLC (Method 1). The yield of this reaction is 68 mg (68%) after two steps. ^{1}H NMR (400 MHz, CD_3OD) δ 1.96 (m, 2H), 2.31 (t, 2H), 2.51 (s, 3H), 2.64 (s, 3H), 3.23 (t, 2H), 3.64 (t, 2H), 5.11 (t, 2H), 7.82 (s, 1H), 8.03 (s, 1H), LC-MS m/z 387.1 [M+H], retention time 1.38 min.

Example 24

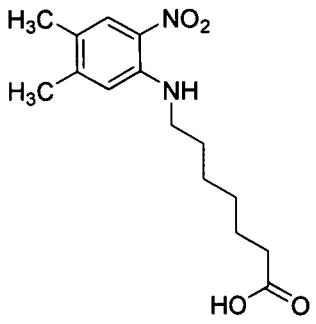
Preparation of 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid tert-butyl ester



Scheme 1:

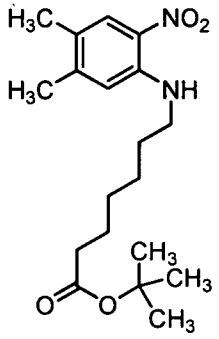


Step 1 Preparation of 7-(4,5-Dimethyl-2-nitro-phenylamino)-heptanoic acid



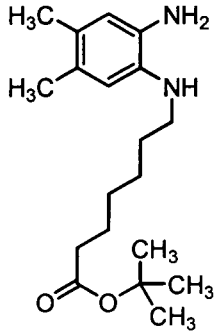
[0164] 4,5-Dimethyl-2-nitro-phenylamine (2.4 g, 14 mmol) is dissolved in DMF (40 mL) and stirred at 0°C. Sodium hydride (0.57 g, 14 mmol) is added and the reaction mixture is warmed to rt. After 30 min, the mixture is cooled to 0 °C at which point a solution of 7-bromoheptanoic acid (1.0 g, 4.8 mmol) in DMF (2 mL) is added dropwise. The mixture is then allowed to warm to rt slowly over 4 h. The reaction mixture is stirred with water (20 mL) for 30 min then concentrated under vacuum. The solid is then dry loaded on silica gel and ISCO flash column purification is performed using 0 to 10 % methanol in DCM over 15 minutes as the mobile phase to afford the crude product as an orange oil. Purification using preparative HPLC Method 1 afforded 7-(4,5-dimethyl-2-nitro-phenylamino)-heptanoic acid (506 mg) as an orange oil (yield: 49 %). LC-MS m/z 295.0 [M+H], retention time = 3.94 min.

Step 2: Preparation of 7-(4,5-Dimethyl-2-nitro-phenylamino)-heptanoic acid tert-butyl ester



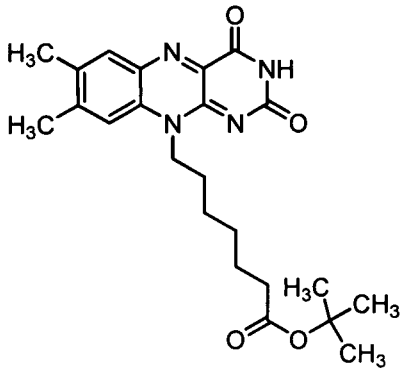
[0165] 7-(4,5-Dimethyl-2-nitro-phenylamino)-heptanoic acid (2.7 g, 0.0092 mol) is dissolved in t-BuOH (40 mL) with stirring at 40 °C. tert-Butoxycarbonyl anhydride (10.04 g, 0.046 mol) and magnesium chloride (0.09 g, 0.0009 mol) are added and the reaction mixture is kept under argon and allowed to stir at 40 °C for 48 h. The mixture is lyophilized and the crude is dissolved in water and extracted with ethyl acetate. The organic layer is dried with sodium sulfate and concentrated to give 3.1 g of an orange oil (crude yield = 97 %). LC-MS m/z 350.9 $[M + H]^+$, retention time 7.66 min.

Step 3: Preparation of 7-(2-Amino-4,5-dimethyl-phenylamino)-heptanoic acid tert-butyl ester



[0166] Prepared using a similar procedure to that of **Example 25**, step 2.

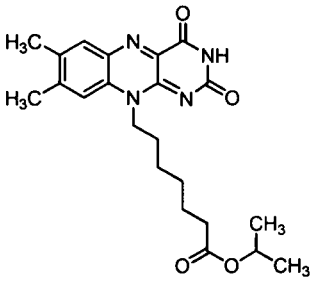
Step 4: Preparation of 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid tert-butyl ester



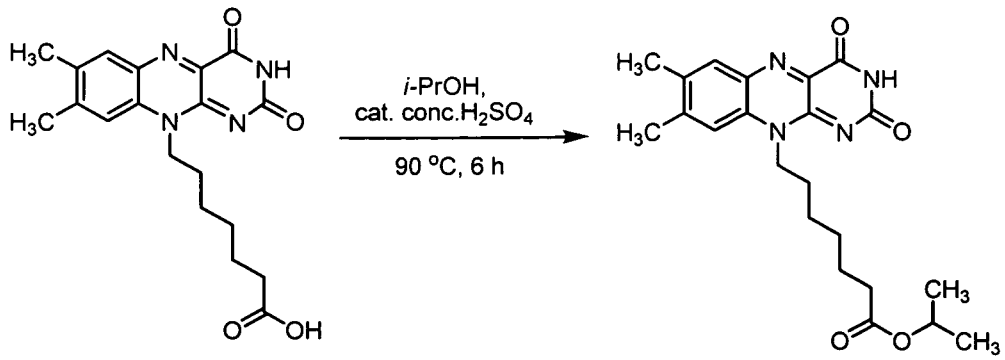
[0167] Prepared using a similar procedure to that of **Example 25**, step 3. Purified by preparative HPLC (Method 3). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.3-1.38 (m, 3H), 1.39 (s, 9H), 1.4-1.53 (m, 5H), 1.68 (m, 2H), 2.2 (t, 2H), 2.39 (s, 3H), 4.54 (m, 2H), 7.76 (s, 1H), 7.86 (s, 1H), 11.3 (s, 1H). LC-MS m/z 427.19 $[M + H]^+$, retention time 8.44 min.

Example 25:

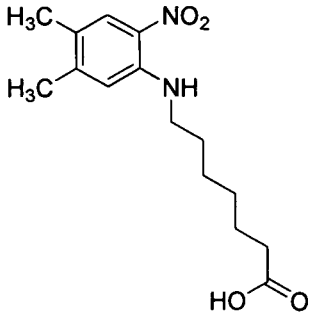
Isopropyl 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



Scheme 2:

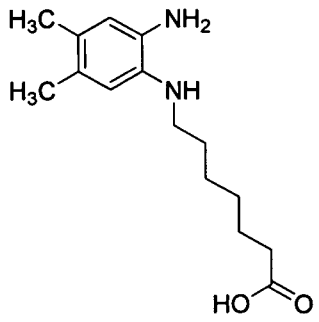


Step 1 Preparation of 7-(4,5-Dimethyl-2-nitro-phenylamino)-heptanoic acid



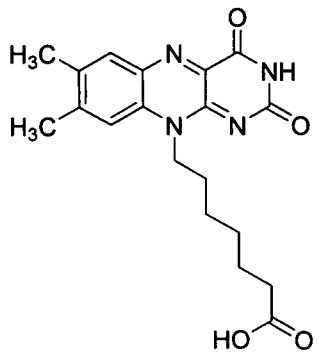
[0168] 4,5-Dimethyl-2-nitro-phenylamine (2.4 g, 14 mmol) is dissolved in DMF (40 mL) and stirred at 0 °C. Sodium hydride (0.57 g, 14 mmol) is added and the reaction mixture is warmed to rt. After 30 min. the mixture is cooled to 0 °C at which point a solution of 7-aminoheptanoic acid (1.0 g, 4.8 mmol) in DMF (2 mL) is added dropwise. The mixture is then allowed to warm to rt slowly over 4 h. The reaction mixture is stirred with water (20 mL) for 30 min and then concentrated under vacuum. The solid is then dry loaded onto silica gel and passed through a ISCO flash column using 0 to 10 % methanol in DCM over 15 minutes as the mobile phase to afford the crude product as an orange oil. This oil is then purified using preparative HPLC (method 1) to obtain 7-(4,5-dimethyl-2-nitro-phenylamino)-heptanoic acid (506 mg) as an orange oil (yield: 49%). LC-MS m/z 295.0 [M+H], retention time = 3.94 min.

Step 2 Preparation of 7-(2-Amino-4,5-dimethyl-phenylamino)-heptanoic acid



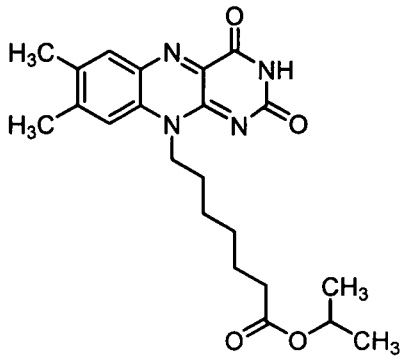
[0169] 7-(4,5-Dimethyl-2-nitro-phenylamino)-heptanoic acid (70 mg, 0.24 mmol) is dissolved in methanol (5 mL) and palladium/carbon (20 mg) is added followed by sodium borohydride (91 mg, 2.4 mmol) with stirring at RT. The reaction mixture is filtered through celite after 1 h and washed with methanol. The filtrate is concentrated under vacuum to obtain the product (63 mg) as a slightly brown oil (yield: 100%).

Step 3 Preparation of 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid



[0170] 7-(2-Amino-4,5-dimethyl-phenylamino)-heptanoic acid (64 mg, 0.24 mmol) is dissolved in acetic acid (5 mL) followed by addition of boron trioxide (33 mg, 0.48 mmol) and alloxan monohydrate (38 mg, 0.24 mmol). After 3 h the reaction mixture is concentrated under vacuum and purified using preparative HPLC (method 1). 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid (24 mg) is isolated following lyophilization of the appropriate fractions (yield: 27%). ^{1}H NMR (400 MHz, DMSO-d6) δ 11,37 (s, 1H), 7.92 (s, 1H), 7.83(s, 1H), 4.55 (m, 2H), 2.40 (s, 3H), 2.19 (m, 2H), 1.68 (m, 2H), 1.47 (m, 4H), 1.33 (m, 2H). MS m/z 369.3 [M-H]$^-$, retention time = 6.12 min.

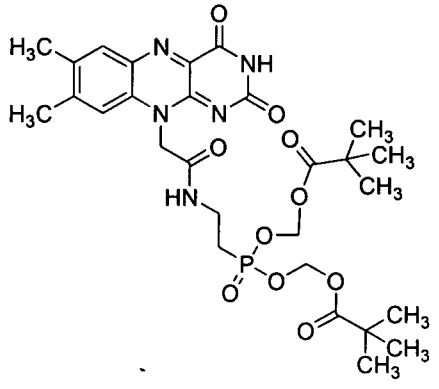
Step 4 Preparation of Isopropyl 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



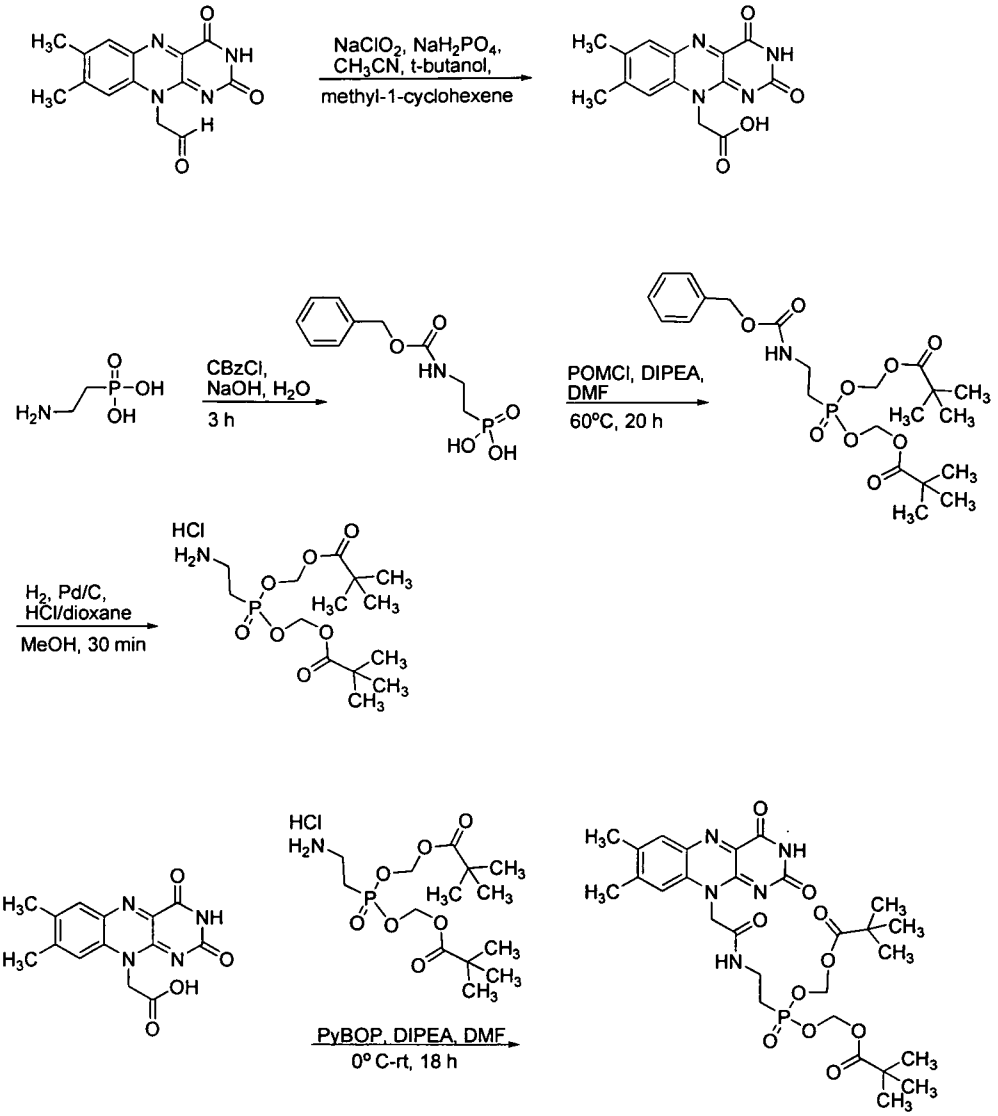
[0171] To a solution of 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl) heptanoic acid (from step 3) (1g, 2.70 mmol) is added anhydrous isopropanol (60 mL) followed by concentrated sulfuric acid (0.5 mL). The reaction mixture is stirred at 90 °C for 6 h. The reaction mixture is neutralized with solid sodium bicarbonate, filtered and concentrated under vacuum at 25 °C, and the residue is dry loaded onto silica gel using DCM as a solvent and purified by column chromatography (silica) using gradient elution (from 0% to 50% acetone in DCM). The desired product is isolated by evaporation, under vacuum at 25°C, of the fractions following of lyophilization (966 mg, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.25 (d, 6H), 1.46 (m, 2H), 1.58 (m, 2H), 1.68 (m, 2H), 1.89 (m, 2H), 2.31 (t, 2H), 2.48 (s, 3H), 2.59 (s, 3H), 4.71, (m, 2H), 5.02 (m, 1H), 7.43 (s, 1H), 8.09 (s, 1H), 8.43 (s, 1H). ESI(+) m/z = 413.1.

Example 26:

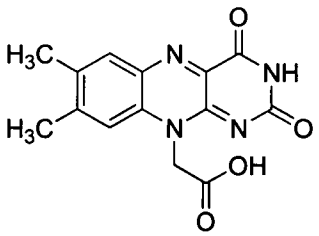
((2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetamido)ethyl)phosphoryl)bis(oxy)bis(methylene) bis(2,2-dimethylpropanoate)



Scheme 3:



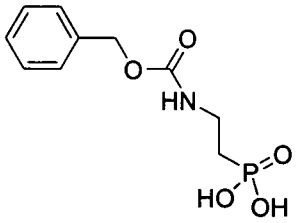
Step 1 Preparation of (7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetic acid



[0172] To a suspension of (7, 8-dimethyl-2, 4-dioxo-3, 4-dihydro-2H-benzo[g]pteridin-10-yl)- acetaldehyde (prepared by the method of **Example 14**) (50 mg, 0.18 mmol) in acetonitrile (2 ml), tert-butanol (8 mL), and methyl-1-cyclohexene (3 mL) at 0 °C, a solution of sodium chlorite (122 mg, 1.35 mmol) and sodium dihydrogen

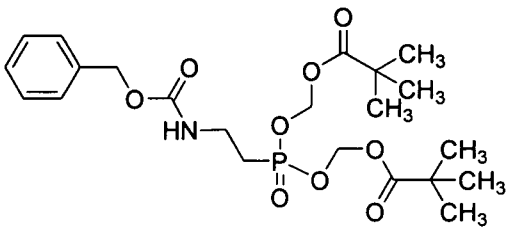
phosphate (148 mg, 1.23 mmol) in water (2 mL) is added dropwise over 5 min. After 2 h, the reaction mixture is diluted with water and the organic layer is discarded. The aqueous phase is concentrated under vacuum and the resultant crude mixture is purified via preparative HPLC. (7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetic acid (36 mg) is isolated following lyophilization of the appropriate fractions (yield: 68%). LC-MS m/z 301.1 [M+H], retention time = 1.68 min.

Step 2 Preparation of 2-(benzyloxycarbonylamino)ethylphosphonic acid



[0173] To a stirred solution of sodium hydroxide (5.76 g, 14.4 mmol) in water (40 mL) is added aminoethyl phosphonic acid (6 g, 4.8 mmol). Benzyl chloroformate (10.64 g, 6.2 mmol) is added in several portions controlling the temperature at approximately 40 °C. The reaction mixture is stirred at RT for 3 h. The mixture is extracted twice with diethyl ether (2 X 20 mL) to remove benzyl chloroformate. The aqueous layer is acidified with concentrated HCl to pH 1-2. A white solid crashed out. The solid is collected by filtration and washed with acetonitrile. The solid is dissolved in methanol (20 mL) and treated with Dowex H^+ resin (16 g) that has been prewashed with water and methanol. The mixture is stirred at rt for 2 h, filtered and rinsed with methanol. The filtrate is concentrated to obtain 2-(benzyloxycarbonylamino)ethylphosphonic acid (8.7 g) as a thick oil (yield 70%). LC-MS m/z 259.9 [M+H], retention time = 1.76 min.

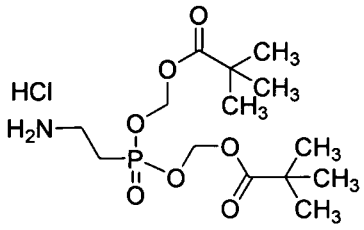
Step 3 Preparation of ((2-(benzyloxycarbonylamino)phosphoryl)bis(oxy)bis (methylene)bis(2,2-dimethylpropanoate)



[0174] To a stirred solution of 2-(benzyloxycarbonylamino)ethylphosphonic acid (4.3 g, 1.6 mmol) in anhydrous DMF (20 mL), is added DIPEA (6.4 g, 4.9 mmol) followed by chloromethyl pivalate (7.5 g, 4.9 mmol). The reaction mixture is stirred at 60

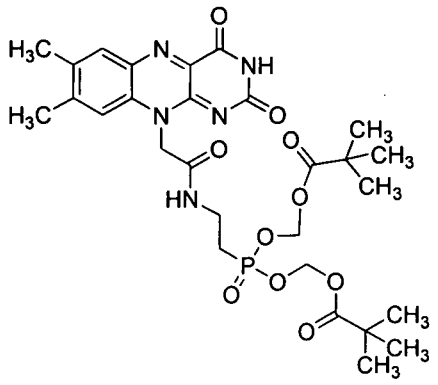
°C for 20 h. The reaction mixture is concentrated in vacuo, the residue is diluted with water (20 mL) followed by extraction with ethyl acetate (3 X 25 mL). The combined organic fractions are dried over sodium sulfate and filtered. The filtrate is concentrated to obtain ((2-(benzyloxycarbonylamino)phosphoryl) bis(oxy)bis(methylene)bis(2,2-dimethylpropanoate) (7.2 g) (yield: 29 %). LC-MS m/z 488.0 [M+H], retention time = 4.94 min.

Step 4 Preparation of ((2-aminoethyl)phosphoryl)bis(oxy)bis(methylene) bis(2,2-dimethylpropanoate) hydrochloride



[0175] A solution of ((2-(benzyloxycarbonylamino)phosphoryl) bis(oxy)bis(methylene)bis(2,2-dimethylpropanoate) (2.01 g, 4.12 mmol) in methanol (100 ml) is purged with argon for 10 min. Then, 4N HCl/dioxane (0.8 mL, 4.94 mmol) is added followed by palladium/carbon (500 mg) and the reaction mixture is placed under an atmosphere of hydrogen for 30 min. The reaction mixture is filtered through a celite pad and the filtrate is concentrated under reduced pressure to dryness. The residue is redissolved in DCM (5 mL). Hexanes are added to precipitate out the desired product which is filtered to obtain ((2-aminoethyl)phosphoryl)bis(oxy) bis(methylene)bis(2,2-dimethylpropanoate)hydrochloride (1.41 g, 88%). LC-MS m/z 354.0 [(M-HCl)+H], retention time = 2.82 min.

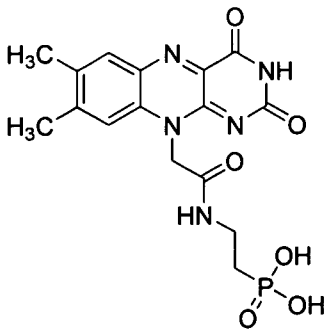
Step 5 Preparation of ((2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetamido)ethyl)phosphoryl)bis(oxy)bis(methylene) bis(2,2-dimethylpropanoate)



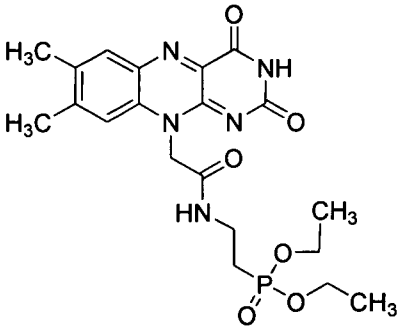
[0176] A suspension of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetic acid (560 mg, 1.86 mmol) (from step 1) and ((2-aminoethyl)phosphoryl)bis(oxy)bis(methylene)-bis(2,2-dimethylpropanoate) hydrochloride (from step 4) (799 mg, 2.05 mmol) in DMF (35 mL), is stirred at 0 °C and purged with argon for 10 min and DIPEA (0.65 mL, 3.73 mmol) is added to the reaction mixture. PyBOP (874 mg, 1.68 mmol) is added in three portions (at 30 min intervals) while maintaining the reaction mixture at 0 °C. The reaction mixture is allowed to warm to room temperature and stirred for 18 h. The reaction mixture is concentrated and the residue is diluted with water (20 mL) and extracted with ethyl acetate (3 X 25 mL). The combined organic fractions are dried over sodium sulfate and filtered. The filtrate is concentrated and the crude is purified by silica gel chromatography (ISCO) using 100% DCM to 10% MeOH/DCM as eluent to obtain ((2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetamido)ethyl) phosphoryl)bis(oxy)bis(methylene)bis-(2,2-dimethylpropanoate) (209 mg, 18 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.24 (s, 18H), 2.12 (m, 2H), 2.45 (s, 3H), 2.56 (s, 3H), 3.58 (m, 2H), 5.48 (s, 2H), 5.64 (m, 4H), 7.56 (t, 1H), 7.58 (s, 1H), 8.03 (s, 1H), 8.98 (s, 1H); LC-MS m/z 636.1 [M+H], retention time = 5.36 min.

Example 27

2-(2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetamido)ethylphosphonic acid

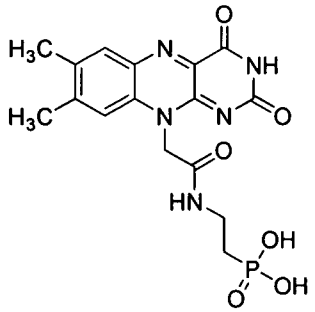


Step 1 Preparation of diethyl 2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetamido)ethylphosphonate



[0177] A suspension of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetic acid (23 mg, 0.077 mmol) and diethyl 2-aminoethylphosphonate (27.9 mg, 0.154 mmol) in DMF (1 mL), is stirred at rt under argon for 10 min and DIPEA (0.1 mL) is added to the reaction mixture. HATU (58.5 mg, 0.154 mmol) is added and the mixture is stirred for 18 h at rt. Water (6 mL) is added to dissolve the mixture and the mixture was filtered and purified using preparative HPLC (method 1) to give the desired product (6.5 mg). LC-MS m/z 464.0 [M+H], retention time = 2.22 min.

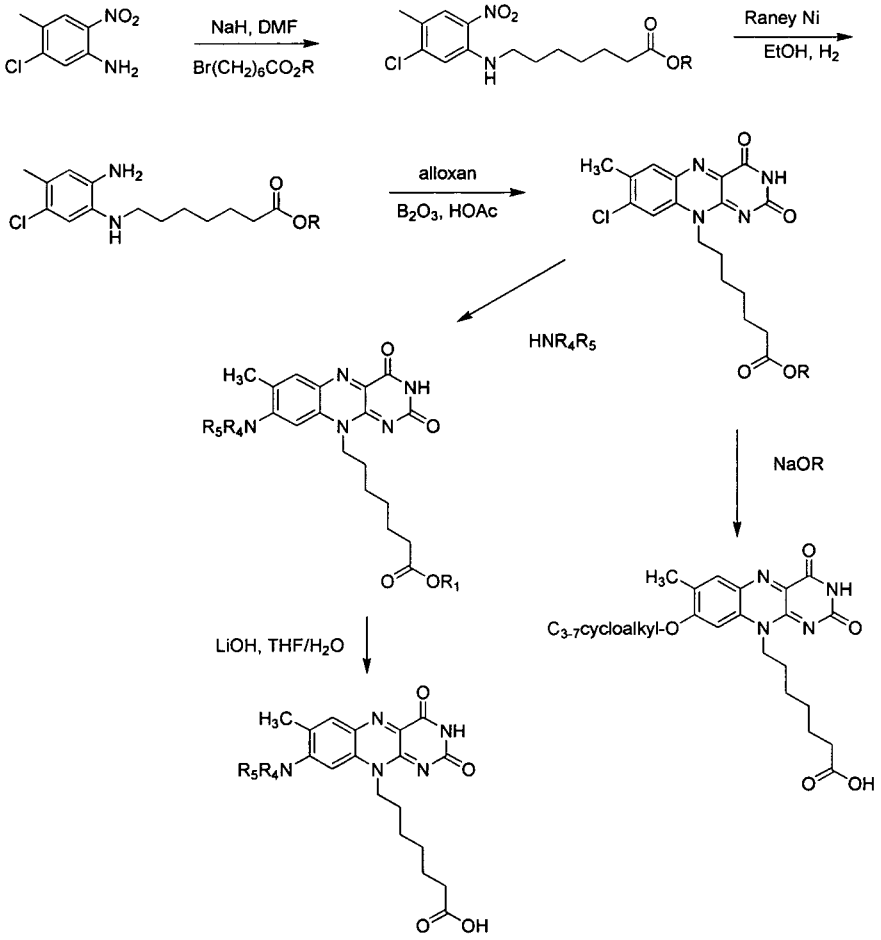
Step 2 Preparation of 2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetamido)ethylphosphonic acid



[0178] Diethyl 2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetamido)ethylphosphonate is deprotected using a similar procedure to that of

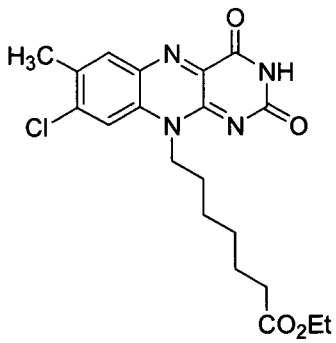
Example 19 using bromotrimethylsilane to give 2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetamido)ethylphosphonic acid. LC-MS m/z 406.1 $[M-H]^-$, retention time = 3.52 min.

Scheme 4:

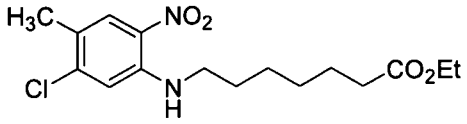


Example 28:

Ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate

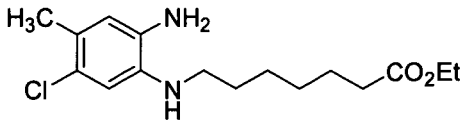


Step 1 Preparation of Ethyl 7-(5-chloro-4-methyl-2-nitro-phenylamino)-heptanoate



[0179] A solution of 4-amino-2-chloro-5-nitrotoluene (0.507 g, 2.72 mmol) in dry DMF (10 mL, 0.2 mol) is cooled at 0 °C under nitrogen and sodium hydride (109 mg, 60%, 2.72 mmol) is added as a solid. Hydrogen evolution was observed and the mixture is allowed to warm to rt and stirred for 30 min. Ethyl 7-bromoheptanoate (0.635 mL, 3.26 mmol) is then added drop wise via syringe and stirring continued at rt for 3h. The reaction was concentrated *in vacuo* to remove DMF and the residue partitioned between DCM and saturated ammonium chloride. The layers are separated, the aqueous is extracted with DCM, and the organics are combined, dried with anhydrous sodium sulfate and concentrated. Chromatography on silica gel (Whatman, 230-400 mesh, 90 g, elution with 5% EtOAc/hexane) gave 605 mg (65%) of desired product as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (3 H, t), 1.43 (4 H, m), 1.65 (2 H, m), 1.73 (2 H, m), 2.28 (3 H, s), 2.32 (2 H, t), 3.25 (2 H, m), 4.13 (2 H, q), 6.86 (1 H, s), 7.88 (1 H, m), 8.04 (1 H, s); MS (ESI+) for $C_{16}H_{23}ClN_2O_4$ *m/z* 343.2 (M+H)+; HPLC retention time: 9.55 min. (System A).

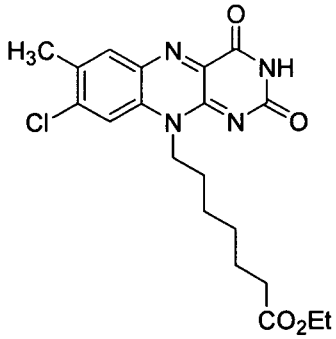
Step 2 Preparation of Ethyl 7-(2-Amino-5-chloro-4-methyl-phenylamino)-heptanoate.



[0180] A solution of ethyl 7-(5-chloro-4-methyl-2-nitro-phenylamino)-heptanoate (64.0 mg, 0.19 mmol) in ethanol (4.0 mL) is stirred at rt and activated (wet) Raney Nickel (6.4 mg, 0.11 mmol) is added. The reaction is placed under an atmospheric pressure of hydrogen, evacuated & purged (4x) and stirred at rt. After complete (1h), the reaction was diluted with ethyl acetate, filtered through Celite and concentrated to give 55 mg (94%) of

desired product as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (3 H, t), 1.41 (4 H, m), 1.66 (4 H, m), 2.22 (3 H, s), 2.31 (2 H, t), 3.04 (2 H, t), 3.24 (3 H, br. s.), 4.13 (2 H, q), 6.56 (1 H, s), 6.60 (1 H, s); MS (ESI+) for $C_{16}H_{25}ClN_2O_2$ *m/z* 313.2 (M+H)+; HPLC retention time: 6.55 min. (System A).

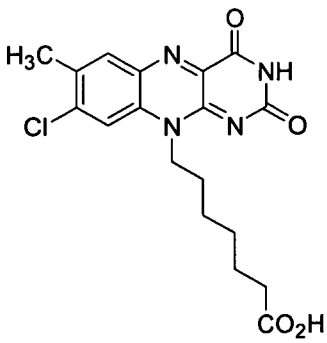
Step 3 Preparation of Ethyl 7-(8-Chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



[0181] To a well-stirred solution of ethyl 7-(2-amino-5-chloro-4-methyl-phenylamino)-heptanoate (260.0 mg, 0.83 mmol) in acetic acid (4.0 mL) at rt under nitrogen is added alloxan (133.0 mg, 0.83 mmol) and boron oxide (62.53 mg, 1.7 mmol). The reaction is heated at 60°C for 3h, cooled to rt and concentrated. The residue is partitioned between saturated aqueous sodium bicarbonate solution and DCM (50 mL each) and extracted with DCM (3 x 25mL). The organics are combined, dried with anhydrous sodium sulfate and is concentrated. Chromatography of the residue on silica gel (Silicycle, 230-400 mesh prepack, 40 g, elution with 10, 15 and 20% acetone/DCM) provided 151 mg (43%) of the desired product as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (3 H, t), 1.44 (2 H, m), 1.56 (2 H, m), 1.67 (2 H, m), 1.87 (2 H, m), 2.33 (2 H, t), 2.57 (3 H, s), 4.13 (2 H, q), 4.64 (2 H, m), 7.65 (1 H, s), 8.18 (1 H, s), 8.67 (1 H, br s.); MS (ESI+) for $C_{20}H_{23}ClN_4O_4$ *m/z* 419.1 (M+H)+; HPLC retention time: 5.71 min. (System B).

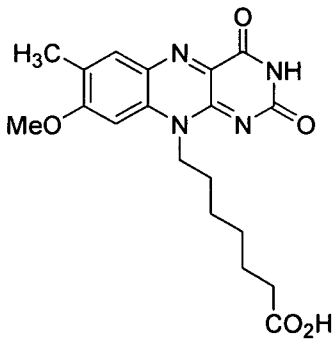
Example 29:

7-(8-Chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



[0182] To a well-stirred slurry of ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (35 mg, 0.084 mmol) in THF (2.0 mL, 25 mmol) at rt is added 1.0 M LiOH in water (1.0 mL). The reaction is allowed to stir for 3h and is quenched with acetic acid (57 μL, 1.0 mmol). The mixture is allowed to stir for 1h, the precipitate collected, washed with water and air dried to give 21 mg (64%) of the desired product as an amorphous yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 1.34 (2 H, m), 1.45 (2 H, m), 1.51 (2 H, m), 1.67 (2 H, m), 2.21 (2 H, t), 4.53 (2 H, t), 8.11 (1 H, s), 8.13 (1 H, s), 11.39 (1 H, s), 11.99 (1 H, br s.); MS (ESI+) for $C_{18}H_{19}ClN_4O_4$ *m/z* 391.1 (M+H)+; HPLC retention time: 4.70 min. (System B).

Example 30: 7-(8-Methoxy-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid

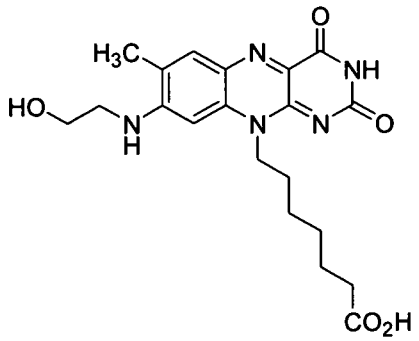


[0183] A 25 mL sealed tube is charged with ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (51 mg, 0.12 mmol), sodium methoxide, 25% wt in MeOH (0.5 mL) and methanol (3.0 mL). The reaction is sealed under dry nitrogen and heated at 80 °C for 18 h. The reaction is cooled, concentrated, re-suspended in water and acidified with acetic acid (0.1 mL, 2 mmol). The precipitate that forms is collected and air dried to provide 25 mg (53%) of desired product as a yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 1.36 (2 H, m), 1.46 (2 H, m), 1.52 (2 H, m), 1.73

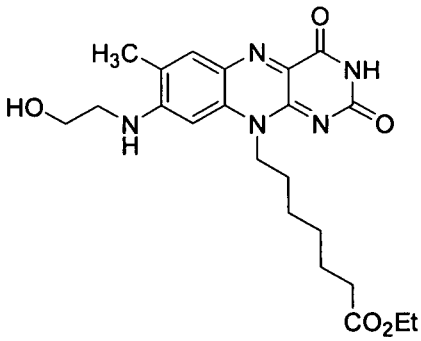
(2 H, m), 2.21 (2 H, t), 2.30 (3 H, s), 4.09 (3 H, s), 4.65 (2 H, br s), 7.16 (1 H, s), 7.92 (1 H, s), 11.23 (1 H, s), 11.99 (1 H, s); MS (ESI+) for $C_{19}H_{22}N_4O_5$ *m/z* 387.1 (M+H)+. HPLC retention time: 4.44 min. (System B).

Example 31:

7-[8-(2-Hydroxy-ethylamino)-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl]-heptanoic acid

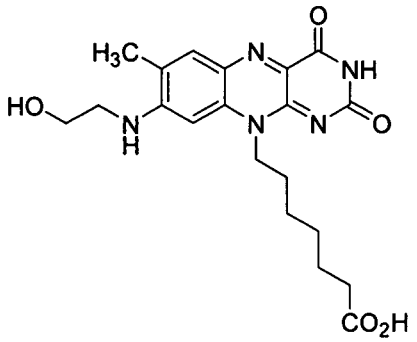


Step 1 Preparation of Ethyl 7-8-[(2-hydroxyethyl)amino]-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-ylheptanoate



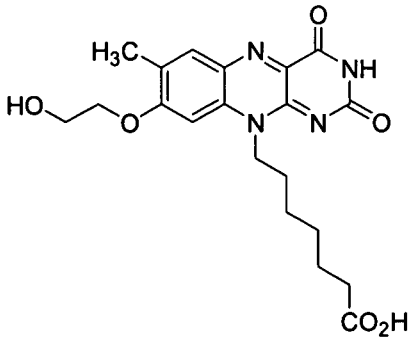
[0184] To a well-stirred slurry of ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (81.0 mg, 0.193 mmol) in dry DMF (3.0 mL) at rt under nitrogen is added ethanolamine (0.115 mL, 1.91 mmol). The reaction is heated at 60 °C for 18 h, cooled to rt and concentrated *in vacuo*. The red residue is subjected to preparative reverse phase chromatography to give 31mg (36%) of desired product as a red amorphous solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 1.16 (3 H, t), 1.35 (2 H, m), 1.442 (2 H, m), 1.54 (2 H, m), 1.70 (2 H, m), 2.28 (5 H, m), 3.52 (2 H, m), 3.68 (2 H, t), 4.03 (2 H, q), 4.54 (2 H, m), 6.59 (1 H, s), 7.10 (1 H, m), 7.66 (1 H, s), 10.95 (1 H, s); MS (ESI+) for $C_{22}H_{29}N_5O_5$ *m/z* 444.2 (M+H)+; HPLC retention time: 4.31 min. (System B).

Step 2 Preparation of 7-[8-(2-Hydroxy-ethylamino)-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl]-heptanoic Acid



[0185] To a well stirred slurry of ethyl 7-8-[(2-hydroxyethyl)amino]-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-ylheptanoate (25.0 mg, 0.06 mmol), water (1.0 mL) and THF (3.0 mL) at rt is added 1.0 M LiOH in water (0.5 mL). The reaction is stirred at rt for 1 h and quenched with acetic acid (30 uL, 0.5 mmol). This mixture is concentrated and re-suspended in water (5mL). The precipitate is collected and dried under vacuum to give 15 mg (64%) of a red solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 1.35 (2 H, m), 1.43 (2 H, m), 1.50 (2 H, m), 1.70 (2 H, m), 2.20 (2 H, t), 2.26 (3 H, s), 3.51 (2 H, q), 3.68 (2 H, t), 4.54 (2 H, m), 6.59 (1 H, s), 7.07 (1 H, t), 7.65 (1 H, s), 10.92 (1 H, s); MS (ESI+) for $C_{20}H_{25}N_5O_5$ *m/z* 416.2 (M+H)+; HPLC retention time: 4.60 min. (System A).

Example 32:
7-[8-(2-Hydroxy-ethoxy)-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl]-heptanoic acid

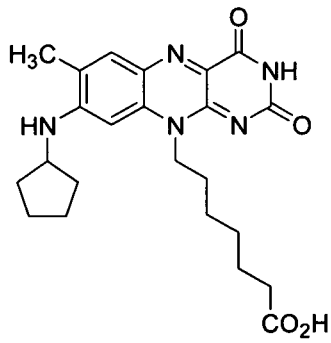


[0186] To a well-stirred slurry of sodium hydride (97.4 mg, 60%, 2.44 mmol) in dry THF (6.0 mL) at rt under dry nitrogen is added 1,2-ethanediol (0.136 mL, 2.44 mmol) slowly via syringe. Gas evolution is observed and this mixture is stirred at rt for 1 h.

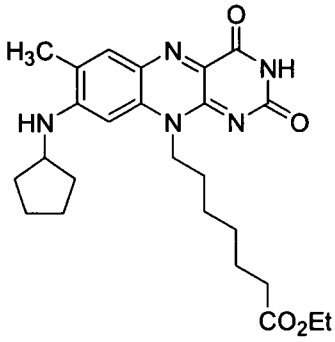
Solid ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (51 mg, 0.12 mmol) is then added and this mixture is stirred at rt under dry nitrogen for 3 days. Acetic acid (0.25 mL), is added and the reaction mixture is concentrated and subjected to preparative reverse phase chromatography which provided 10 mg (20%) of desired product as a yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 1.35 (2 H, m), 1.44 (2 H, m), 1.51 (2 H, m), 1.72 (2 H, m), 2.19 (2 H, m), 2.32 (3 H, s), 3.84 (2 H, m), 4.34 (2 H, m), 4.62 (2 H, m), 5.03 (1 H, br s), 7.19 (1 H, s), 7.92 (1 H, s), 11.24 (1 H, br s), 11.98 (1 H, br s); MS (ESI+) for $C_{20}H_{24}N_4O_6$ *m/z* 417.0 (M+H)+; HPLC retention time: 4.84 min. (System A).

Example 33:

7-(8-Cyclopentylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid



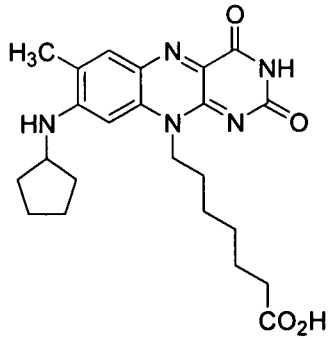
Step 1 Preparation of ethyl 7-[8-(cyclopentylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate



[0187] To a well-stirred slurry of ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]-pteridin-10(2H)-yl)heptanoate (60.0 mg, 0.143 mmol) in dry DMF (4.0 mL) at rt under nitrogen is added cyclopentylamine (141 μL, 1.43 mmol). The reaction is heated at 60 °C for 18, cooled to rt and concentrated *in vacuo*. The red residue was

subjected to preparative reverse phase chromatography to give 31 mg of a red amorphous solid that is then re-chromatographed on silica gel (ISCO Redi-Sep 12g, elution with DCM then 1,2,3 and 4% MeOH/DCM) to give 10.2 mg (15%) of desired product as a red solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 1.15 (3 H, t), 1.36 (2 H, m), 1.45 (2 H, m), 1.54 (2 H, m), 1.61 (2 H, m), 1.73 (6 H, m), 2.07 (2 H, d), 2.28 (5 H, m), 4.03 (2 H, q), 4.16 (1 H, m), 4.56 (2 H, br s), 6.49 (1 H, s), 6.68 (1 H, d), 7.65 (1 H, s), 10.93 (1 H, s); MS (ESI+) for $C_{25}H_{33}N_5O_4$ *m/z* 468.1 (M+H)+; HPLC retention time: 3.59 min. (System C).

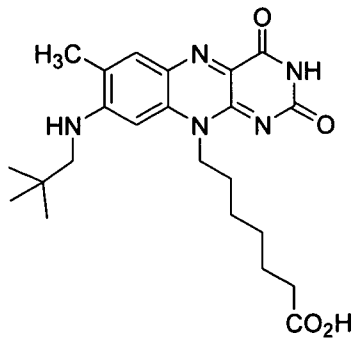
Step 2 Preparation of 7-(8-Cyclopentylamino-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic Acid



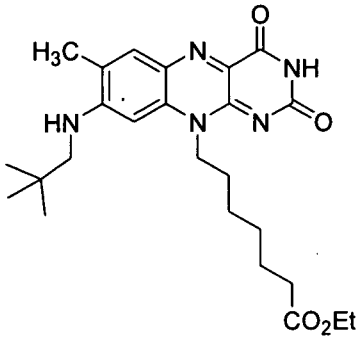
[0188] A mixture of ethyl 7-[8-(cyclopentylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo-[g]pteridin-10(2H)-yl]heptanoate (50.0 mg, 0.096 mmol) and 1.0 M LiOH in 4:1 THF/water (5 mL) is stirred at rt for 3 h. Acetic acid (0.2 mL, 4 mmol) is added and the reaction mixture is concentrated. The residue is purified by preparative reverse phase chromatography to give 16 mg (37 %) of desired product as a red amorphous solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 1.37 (2 H, m), 1.48 (4 H, m), 1.62 (2 H, m), 1.72 (6 H, m), 2.07 (2 H, m), 2.20 (2 H, t), 2.28 (3 H, s), 4.17 (1 H, m), 4.56 (2 H, m), 6.49 (1 H, s), 6.67 (1 H, d), 7.65 (1 H, s), 10.93 (1 H, s), 11.99 (1 H, br s); MS (ESI+) for $C_{23}H_{29}N_5O_4$ *m/z* 440.2 (M+H)+. HPLC retention time: 6.04 min. (System A).

Example 34:

7-8-[(2,2-Dimethylpropyl)amino]-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-ylheptanoic acid

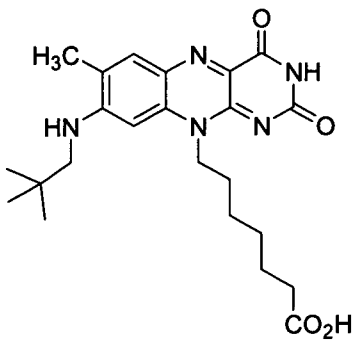


Step 1 Preparation of Ethyl 7-8-[(2,2-dimethylpropyl)amino]-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-ylheptanoate



[0189] To a well-stirred slurry of ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo-[g]pteridin-10(2H)-yl)heptanoate (90.0 mg, 0.215 mmol) in dry DMF (6.0 mL) at rt under nitrogen is added neopentylamine (0.251 mL, 2.15 mmol). The reaction mixture is heated at 80 °C for 18 h, cooled to rt and concentrated *in vacuo*. The red residue was purified by chromatography on silica gel (Silicycle, 230-400 mesh, 40 g, elution with DCM then 2, and 3% MeOH/DCM) to give 45 mg (44%) of a red solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (9 H, s), 1.26 (3 H, t), 1.28 (2 H, m), 1.44 (2 H, m), 1.67 (2 H, m), 1.87 (2 H, m), 2.32 (5 H, m), 3.17 (2 H, d), 4.12 (2 H), 4.65 (2 H, m), 4.97 (1 H, m), 6.41 (1 H, s), 7.88 (1 H, s), 8.25 (1 H, s); MS (ESI+) for $C_{25}H_{35}N_5O_4$ *m/z* 470.2 (M+H)+. HPLC retention time: 3.66 min. (System C).

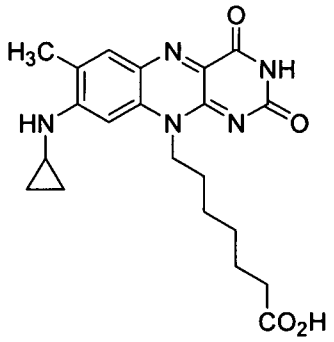
Step 2 Preparation of 7-8-[(2,2-Dimethylpropyl)amino]-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-ylheptanoic acid



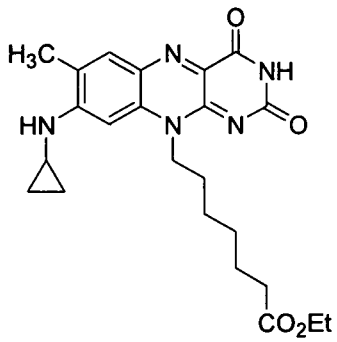
[0190] To a well stirred slurry of ethyl 7-8-[(2,2-dimethylpropyl)amino]-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-ylheptanoate (29.0 mg, 0.062 mmol) and water (1.0 mL) in THF (3.0 mL) at rt was added 1.0 M LiOH in water (0.5 mL). The reaction mixture is stirred at rt for 1h and quenched with acetic acid (50 uL, 0.09 mmol). This mixture is concentrated and re-suspended in water (5mL). The precipitate is collected and dried under vacuum to give 24 mg (88%) of desired product as a red solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 0.98 (9 H, s), 1.19 (2 H, m), 1.35 (2 H, m), 1.50 (4 H, m), 1.65 (2 H, m), 2.20 (2 H), 2.30 (3 H, s), 4.56 (2 H, br. s.), 6.61 (1 H, s), 6.91 (1 H), 7.65 (1 H, s), 10.91 (1 H, s), 11.99 (1 H, s); MS (ESI+) for $C_{23}H_{31}N_5O_4$ *m/z* 442.1 (M+H)+. HPLC retention time: 3.01 min. (System C).

Example 35:

7-[8-(Cyclopropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoic acid

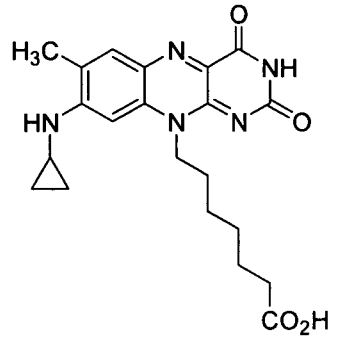


Step 1 Preparation of Ethyl 7-[8-(Cyclopropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate



[0191] To a well-stirred slurry of ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo-[g]pteridin-10(2H)-yl)heptanoate (72 mg, 0.17 mmol) in dry DMF (3.1 mL) at rt under nitrogen is added cyclopropylamine (0.119 mL, 1.72 mmol). The reaction is heated at 60 °C for 24 h, cooled to rt and concentrated *in vacuo*. Chromatography of the residue on silica gel (Silicycle, 230-400 mesh, 40 g, elution with DCM then 2 and 3% MeOH/DCM) provides 31 mg (41%) of desired material as a red solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.75 (2 H, m), 1.04 (2 H, m), 1.25 (3 H), 1.54 (2 H, m), 1.60 (2 H, br s), 1.66 (2 H, m), 1.91 (2 H, m), 2.27 (3 H, s), 2.31 (2 H), 2.72 (1 H, m), 4.12 (2 H), 4.68 (2 H, m), 6.90 (1 H, s), 7.86 (1 H, s), 8.34 (1 H, s); MS (ESI+) for $C_{23}H_{29}N_5O_4$ *m/z* 440.1 (M+H)+. HPLC retention time: 3.01 min. (System C).

Step 2 Preparation of 7-[8-(Cyclopropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoic acid

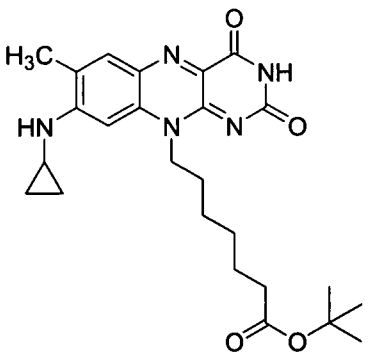


[0192] To a well stirred slurry of ethyl 7-[8-(cyclopropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate (27.1 mg, 0.062 mmol) and water (1.0 mL) in THF (3.0 mL) at rt was added 1.0 M LiOH in water (0.5 mL). The reaction is stirred at rt for 1 h and acetic acid (50 uL, 0.9 mol) is then added. The mixture is concentrated and re-suspended in water (5mL). The precipitate is collected and dried under vacuum to give 18 mg (70%) of desired product as a red solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 0.66 (2 H, m), 0.92 (2 H, m), 1.38 (2 H, m), 1.52 (4 H, m), 1.76 (2 H, m),

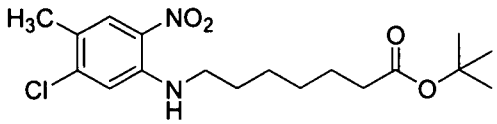
2.20 (2 H, m), 2.23 (3 H, s), 2.71 (1 H, br s), 4.54 (2 H, br s), 6.88 (1 H, s), 7.43 (1 H, s), 7.66 (1 H, s), 10.97 (1 H, s), 12.00 (1 H, br s); MS (ESI+) for $C_{21}H_{25}N_5O_4$ *m/z* 412.1 (M+H)+. HPLC retention time: 2.58 min. (System D).

Example 36:

***tert*-Butyl 7-[8-(Cyclopropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate**

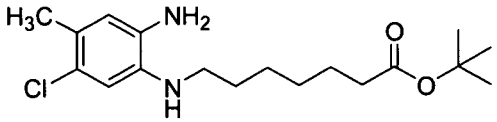


Step 1 Preparation of *tert*-Butyl 7-[(5-chloro-4-methyl-2-nitrophenyl)amino]-heptanoate



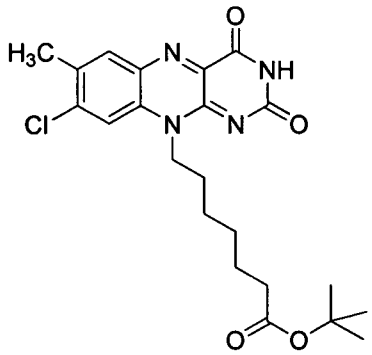
[0193] A solution of 4-amino-2-chloro-5-nitrotoluene (0.762 g, 4.1 mmol) in dry DMF (20 mL) is cooled at 0 °C under nitrogen and sodium hydride (163 mg, 60%, 4.1 mmol) is added as a solid. Hydrogen evolution is observed and the mixture is allowed to warm to rt and is stirred for 30 min. *tert*-Butyl 7-bromoheptanoate (1.30 g, 0.00490 mol) is then added dropwise via syringe and stirring is continued at rt for 6h. The reaction is concentrated *in vacuo* and the residue is partitioned between DCM and saturated, aqueous ammounium chloride (100 mL each). The layers are separated, the aqueous extracted with DCM, and the organics combined, dried with anhydrous sodium sulfate and concentrated. Chromatography on silica gel (Silicycle, 230-400 mesh, 350 g, elution with 5-10% EtOAc/hexane) provides 1.52 g (62 %) of desired product as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (9 H, 3), 1.43 (4 H, m), 1.61 (2 H, m), 1.73 (2 H, m), 2.23 (2 H, t), 2.28 (3 H, s), 3.25 (2 H, m), 6.86 (1 H, s), 7.89 (1 H, m), 8.04 (1 H, s); MS (ESI+) for $C_{18}H_{27}ClN_2O_4$ *m/z* 393.1 (M+Na)+. HPLC retention time: 6.14 min. (System D).

Step 2 Preparation of *tert*-Butyl 7-[(2-Amino-5-chloro-4-methylphenyl)amino]-heptanoate



[0194] A well-stirred slurry of *tert*-butyl 7-[(5-chloro-4-methyl-2-nitrophenyl)amino]heptanoate (940.0 mg, 2.53 mmol) and Raney nickel (80 mg, 1.0 mol) in ethanol (15 mL) are exposed to 1 atm of hydrogen (balloon) for 6 h. The reaction is colorless when complete. The mixture is filtered through Celite and the filtrate concentrated *in vacuo* to provide 864 mg (98%) of the desired product as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (2 H, m), 1.44 (9 H, s), 1.63 (4 H, m), 2.22 (3H, s), 2.23 (2 H, m), 3.04 (2 H), 3.23 (3 H, m), 6.56 (1 H, s), 6.60 (1 H, s); MS (ESI+) for $C_{18}H_{27}ClN_2O_2$ *m/z* 341.1 (M+H)+. HPLC retention time: 3.98 min. (System D).

Step 3 Preparation of *tert*-Butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate

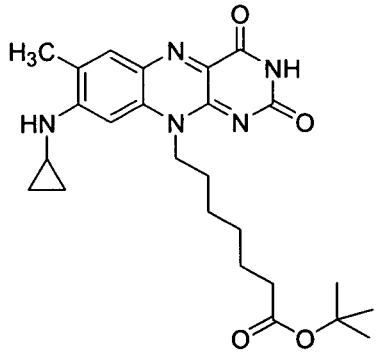


[0195] To a well-stirred mixture of *tert*-butyl 7-[(2-amino-5-chloro-4-methylphenyl)amino]heptanoate (860.0 mg, 2.52 mmol) and boron oxide (0.019mg, 5.04 mmol) in acetic acid (10 mL) at rt under nitrogen is added alloxan (404 mg, 2.52 mmol) and the reaction is heated at 60 °C for 30 min. The residue is partitioned between DCM and saturated, aqueous sodium bicarbonate solution (100 mL each) and the layers are separated. The aqueous layer is extracted with DCM (3x30mL) and the organics are combined, dried and concentrated. Chromatography of the residue on silica gel (Silicycle, 230-400 mesh, 150 g, elution with 2 and 4 % EtOH in chloroform) provides 328 mg (29 %) of the desired product as an amorphous yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 1.33 (2 H, m), 1.38 (9 H, s), 1.44 (2 H, m), 1.50 (2 H, m), 1.66 (2 H, m), 2.18 (2 H), 4.53

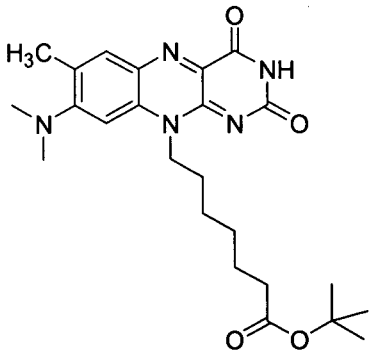
(2 H), 8.10 (1 H, s), 8.13 (1 H, s), 11.39 (1 H, s); MS (ESI+) for $C_{22}H_{27}ClN_4O_4$ *m/z* 447.0 (M+H)+; HPLC retention time: 4.16 min. (System D)

Step 4 Preparation of *tert*-Butyl 7-[8-(cyclopropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate (I)

and *tert*-Butyl 7-[8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate (II)



(I)

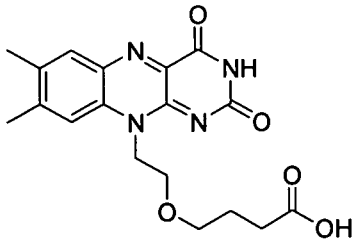


(II)

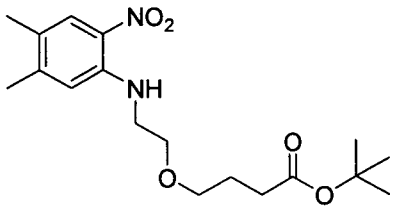
[0196] To a well-stirred slurry of *tert*-butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (51.0 mg, 0.114 mmol) in dry DMF (3.0 mL) at rt under nitrogen is added cyclopropylamine (0.10 mL, 1.4 mmol) . The reaction is heated at 60 °C for 18 h, cooled to rt and concentrated *in vacuo*. The red residue is purified by chromatography on silica gel (Silicycle, 230-400 mesh, 40 g, elution with DCM then 2,3 then 4% MeOH/DCM) to give 27 mg (50 %) of *tert*-butyl 7-[8-(cyclopropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate (I) as a red solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 0.66 (2 H, m), 0.91 (2 H, m), 1.33 (2 H, m), 1.36 (9 H, s), 1.50 (4 H, m), 1.75 (2 H, m), 2.18 (2 H2.23 (3 H, s), 2.72 (1 H, m), 4.54 (2 H, m), 6.88 (1 H, s), 7.43 (1 H, s), 7.66 (1 H, s), 10.97 (1 H, s); MS (ESI+) for $C_{25}H_{33}N_5O_4$ *m/z* 468.1 (M+H)+; HPLC retention time: 3.63 min. (System C).

[0197] In addition, 23 mg (44%) of *tert*-butyl 7-[8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate (II) was isolated from this column as the result of dimethylamine being present or generated during the reaction. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (2 H, m), 1.45 (9 H, s), 1.55 (2 H, m), 1.62 (2 H, m), 1.89 (2 H, m), 2.23 (2 H), 2.49 (3 H, s), 3.12 (6 H, s), 4.65 (2 H, m), 6.70 (1 H, s), 7.95 (1 H, s), 8.29 (1 H, br s); MS (ESI+) for $C_{24}H_{33}N_5O_4$ *m/z* 456.1 (M+H)+. HPLC retention time: 3.74 min. (System C).

Example 37: 4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2*H*)-yl)ethoxy]butanoic acid

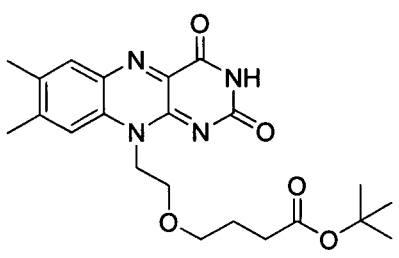


Step 1 Preparation of *tert*-Butyl 4-{2-[(4,5-dimethyl-2-nitrophenyl)amino]ethoxy} butanoate

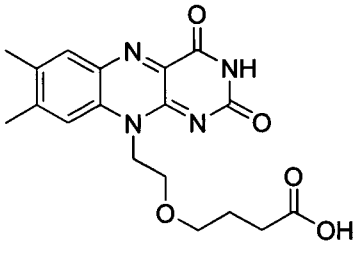


[0198] A solution of 1-bromo-4,5-dimethyl-2-nitrobenzene (0.163 g, 0.708 mmol) and *tert*-butyl 4-(2-aminoethoxy)butanoate [prepared using a procedure similar to that described in EP0655439A2(1994)] in DMSO (1.4 mL) is heated at 100 °C under an atmosphere of nitrogen. After 20 hours, the orange solution is partitioned between ethyl acetate and aqueous sodium bicarbonate. The organic layer is washed twice more with aqueous sodium bicarbonate and then brine; it is dried with sodium sulfate, filtered, and concentrated *in vacuo*. The red residue is flash chromatographed on a 20x80 mm silica gel column eluted with 50% chloroform/hexanes and 100% chloroform, then 5% methanol/chloroform. The methanol/chloroform fraction is chromatographed again, eluted with 5% ethyl acetate/ hexanes and 10% ethyl acetate/ hexanes to give 0.11 g of desired product as an orange oil. (Yield: 44%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (br s, 1 H), 7.95 (s, 1 H), 6.67 (s, 1 H), 3.72 (t, 2 H), 3.55 (t, 2 H), 3.49 (m, 2 H), 2.35 (t, 2 H), 2.29 (s, 3 H), 2.20 (s, 3 H), 1.91 (m, 2 H), 1.46 (s, 9 H). HPLC retention time 5.30 min. (System D).

Step 2 Preparation of *tert*-Butyl 4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethoxy)butanoate (I) and 4-(2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethoxy)butanoic acid (II)



(I)



(II)

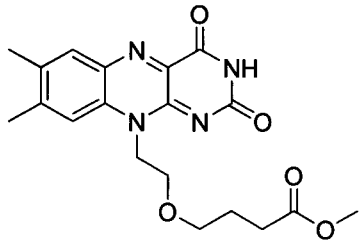
[0199] A well-stirred slurry of Raney nickel (25 mg, 0.43 mmol) and *tert*-butyl 4-{2-[(4,5-dimethyl-2-nitrophenyl)aminoethoxy} butanoate (0.110 g, 0.312 mmol) in ethanol (3 mL) is alternately evacuated then covered with 1 atm hydrogen (3x) (balloon). After stirring overnight at rt, the mixture is filtered through Celite®, and concentrated then azeotroped with toluene to give a brown oil, 0.117 g. The brown oil intermediate is dissolved in acetic acid (3 mL) and alloxan monohydrate (50.0 mg, 0.312 mmol) is added. The mixture is heated at 80 °C under an atmosphere of nitrogen and after an hour, diboron trioxide (43.4 mg, 0.624 mmol) is added and heating continued for 3 hours at 80 °C and 60 °C for another 13 hours. The reaction mixture consisted of both the *tert*-butyl ester and the corresponding carboxylic acid. The reaction was concentrated *in vacuo* and the residue is flash chromatographed on a 28x80 mm silica gel column, eluted with 1% to 5% methanol/ methylene chloride and 5% of (10% formic acid in methanol)/ methylene chloride (200 mL) and 10% methanol/ methylene chloride (200 mL). Fractions with product were combined and concentrated *in vacuo* to give 18 mg of *tert*-butyl 4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethoxy)butanoate (I) as an amorphous orange solid. (Yield: 13%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.33 (s, 1 H), 7.89 (s, 1 H), 7.88 (s, 1H), 4.79 (m, 2 H), 3.79 (t, 2 H), 3.38 (t, 2 H), 2.50 (s, 3H), 2.41 (s, 3 H), 2.07 (t, 2 H), 1.59 (m, 2 H), 1.35 (s, 9 H). Mass spec (ESI+) for $C_{22}H_{28}N_4O_5$ *m/z* 429.1 $(M+H)^+$. HPLC retention time 3.52 min. (System D).

Late, impure chromatography fractions were subjected to preparative plate silica chromatography (20 x 20 cm plates silica gel 60 F254, 0.5 mm thickness, eluted with 10% ethanol/ chloroform). The appropriate yellow band is removed, slurried with methanol/ dichloromethane, and filtered through Celite®. Solvent is removed *in vacuo* to give 6.4 mg of 4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethoxy)butanoic acid (II) as an amorphous yellow solid. (Yield: 5.5%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.32 (br s, 1 H), 7.89 (s, 2 H), 4.79 (t, 2 H), 3.78 (t, 2 H), 3.39 (m, 2

H), 2.50 (s, 3 H), 2.40 (s, 3 H), 2.05 (t, 2 H), 1.61 (m, 2 H). Mass spec (ESI+) for $C_{18}H_{20}N_4O_5$ *m/z* 373.0 $(M+H)^+$. HPLC retention time 2.38 min. (System D).

Example 38:

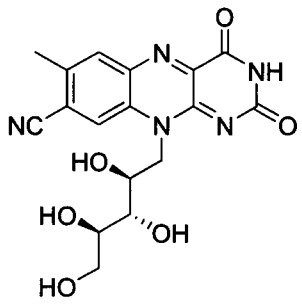
Methyl 4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethoxy)butanoate



[0200] *tert*-Butyl-4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethoxy)butanoate (11 mg, 0.026 mmol) was dissolved in methanol (5 mL) and cooled on an ice bath. Methanol (5.0 mL,) was cooled in an ice bath and acetyl chloride (1.0 mL, 14 mmol) was added. After 10 minutes, it was added to the above solution and the ice bath was removed. After stirring 2 days, concentration *in vacuo* gave brown oil. Preparative plate silica chromatography (20 x20 cm plates silica gel 60 F254, 0.5 mm thickness), eluted with 10% ethanol/ chloroform gave 6.1 mg yellow solid. (Yield: 61%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.33 (s, 1 H), 7.89 (s, 1 H), 7.87 (s, 1 H), 4.78 (t, 2 H), 3.78 (t, 2 H), 3.53 (s, 3H), 3.39 (m, 2 H), 2.49 (s, 3 H), 2.40 (s, 3 H), 2.18 (t, 2 H), 1.64 (m, 2 H). Mass spec (ESI+) for $C_{19}H_{22}N_4O_5$ *m/z* 387.1 $(M+H)^+$. HPLC retention time 2.78 minutes (System D).

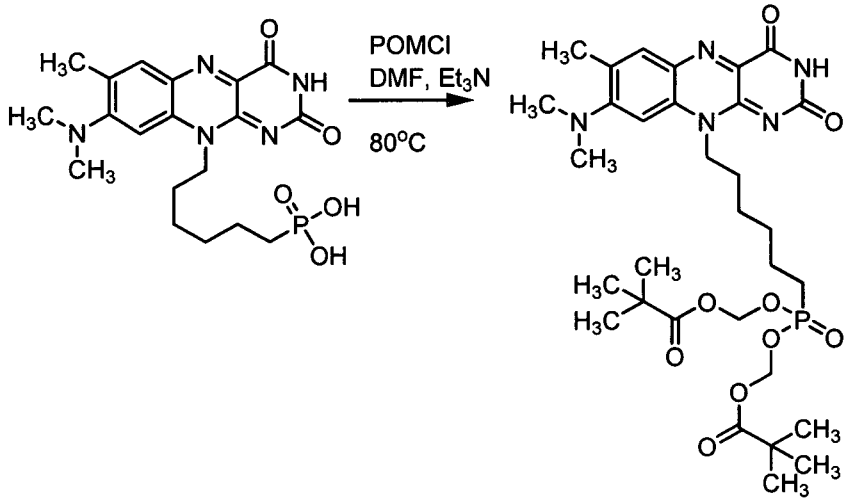
Example 39:

7-Methyl-2,4-dioxo-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)-2,3,4,10-tetrahydrobenzo[g]pteridine-8-carbonitrile

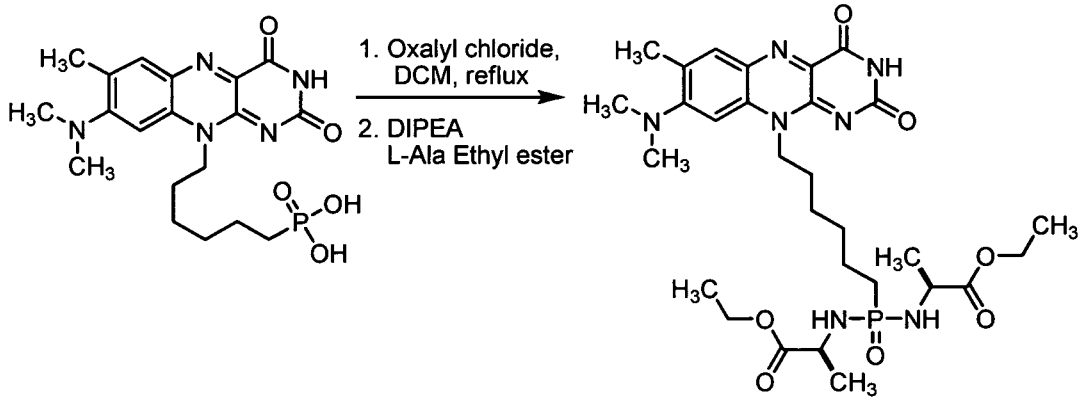


[0201] Prepared using a procedure similar to that described in *The Journal of Biological Chemistry* (**1998**), 273, 8975-8982, Yerramilli V. S. N. Murthy and Vincent Massey. ^{1}H NMR (400 MHz, D_2O) δ 8.31 (s, 1 H), 8.01 (s, 1 H), 4.78 (m, 2 H), 4.28 (m, 1 H), 3.86 (m, 1 H), 3.78 (m, 1H), 3.75 (m, 1H), 3.61 (m, 1H), 2.57 (m, 3H). Mass spec (ESI+) for $C_{17}H_{17}N_5O_6$ *m/z* 388.1 $(M+H)^+$, 410.1 $(M+Na)^+$. HPLC retention time 1.98 min. (System D).

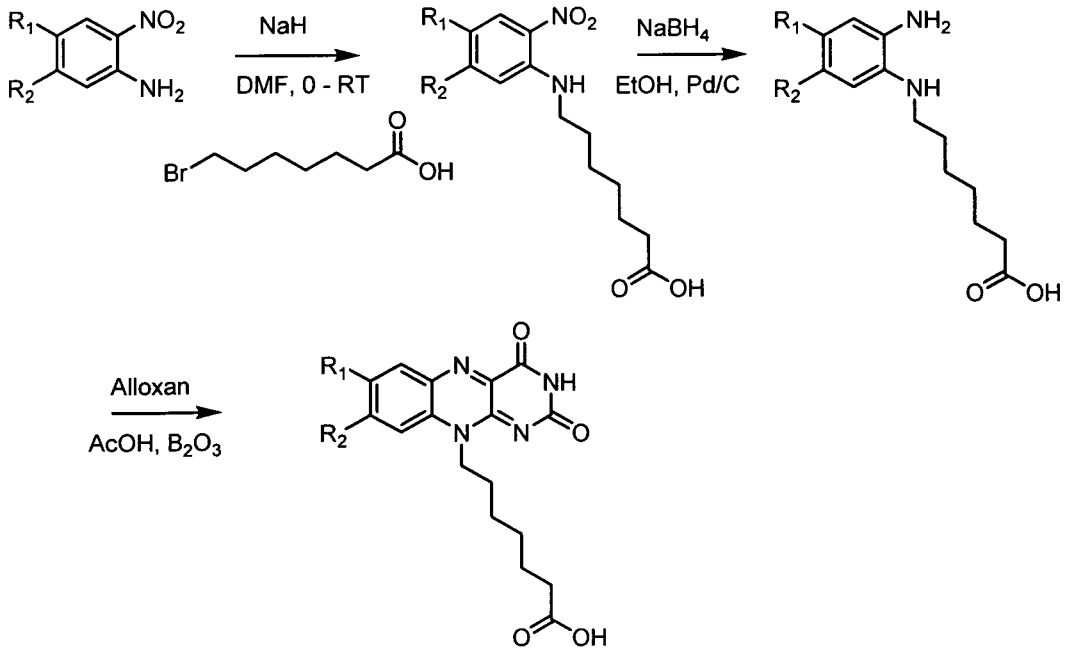
Scheme 5:



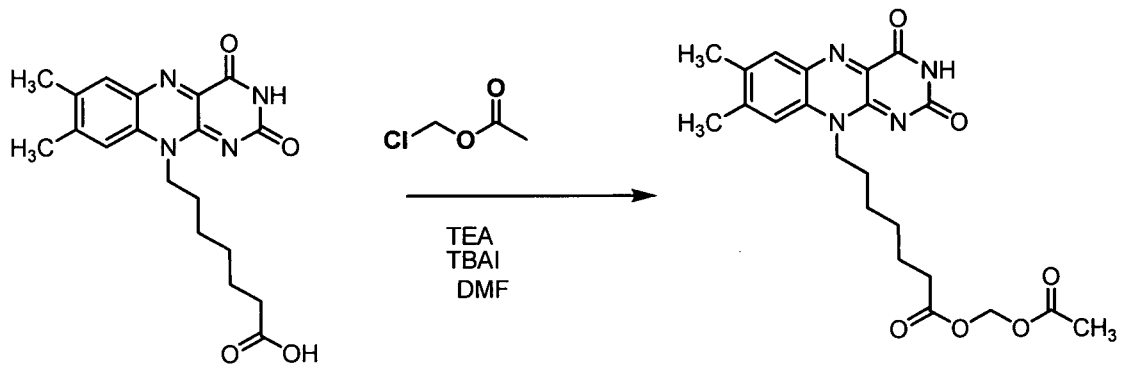
Scheme 6:



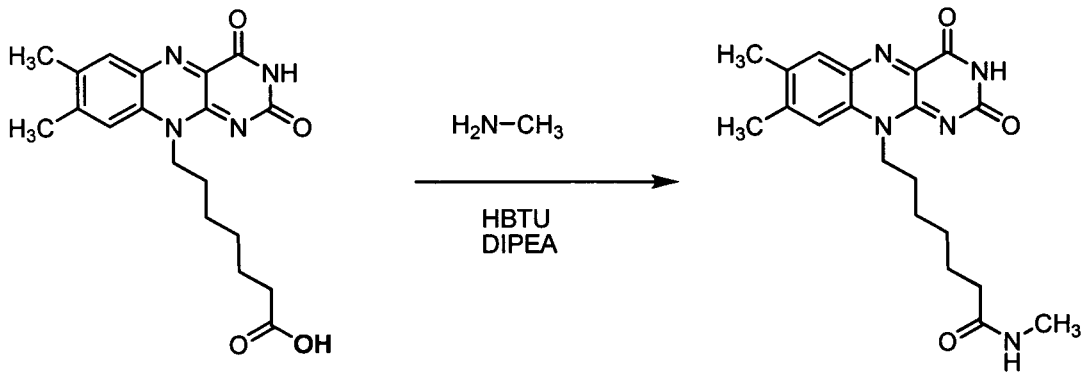
Scheme 7:



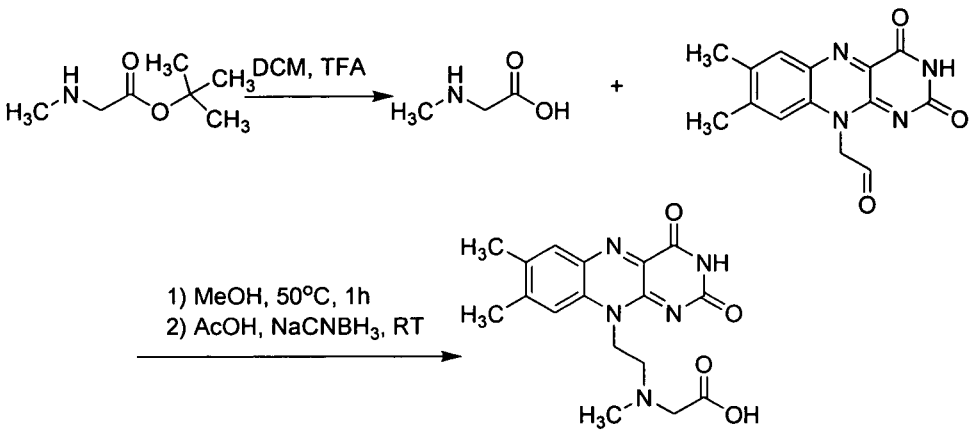
Scheme 8:



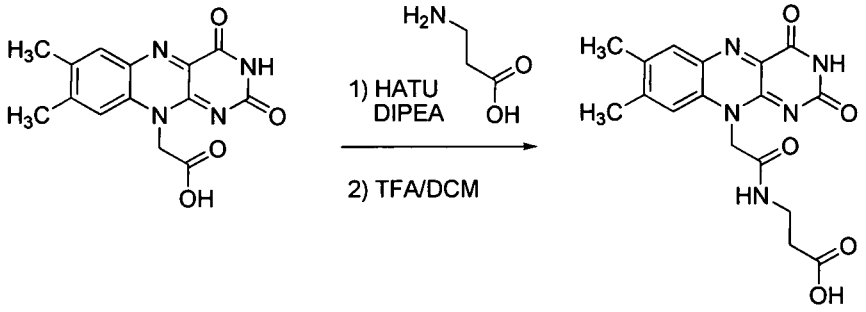
Scheme 9:



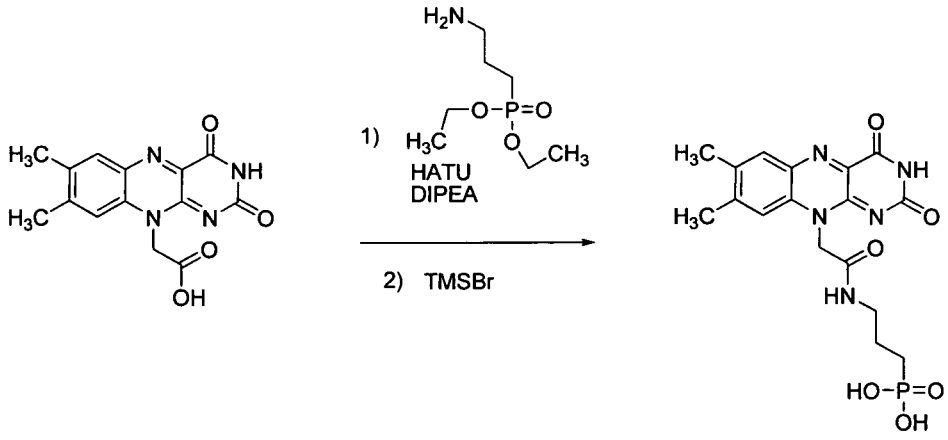
Scheme 10:



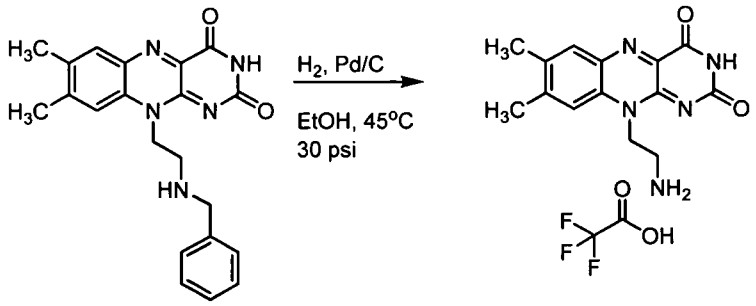
Scheme 11:



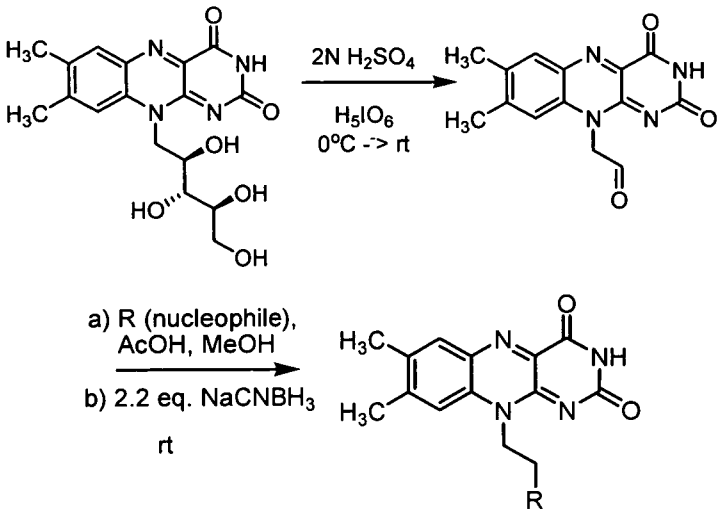
Scheme 12:



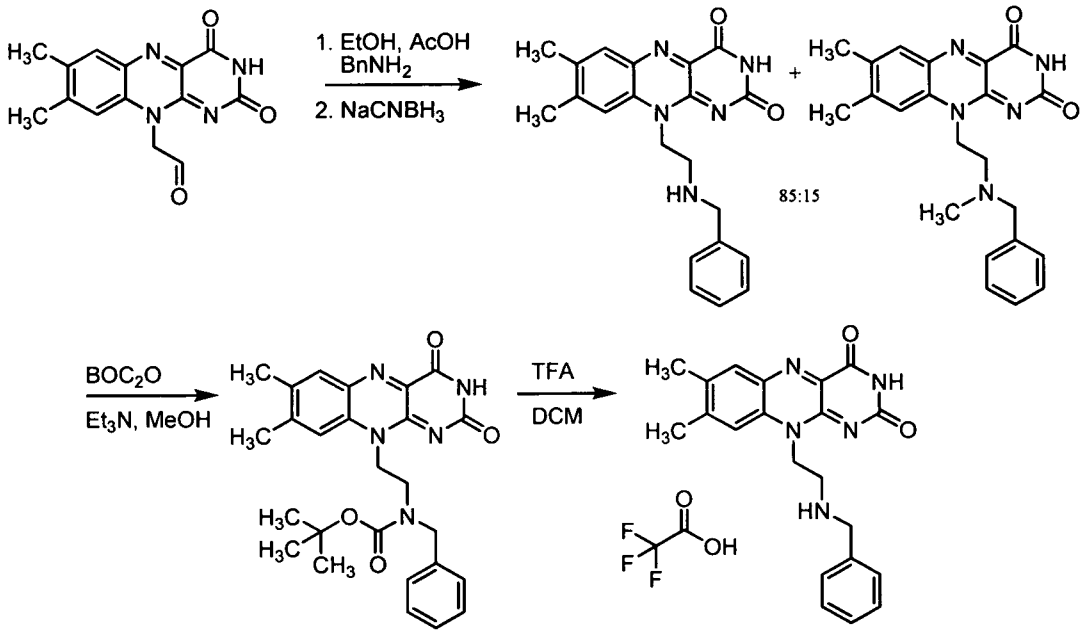
Scheme 13:



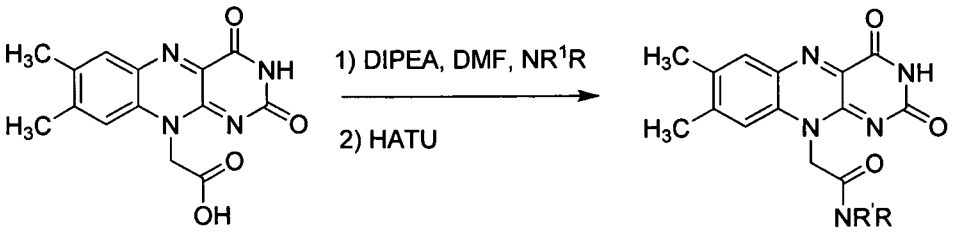
Scheme 14:



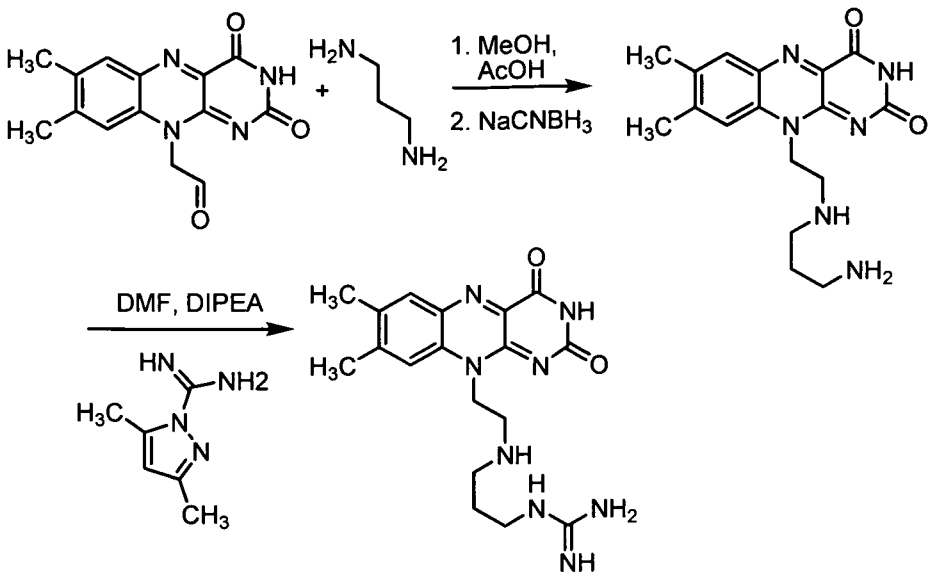
Scheme 15:



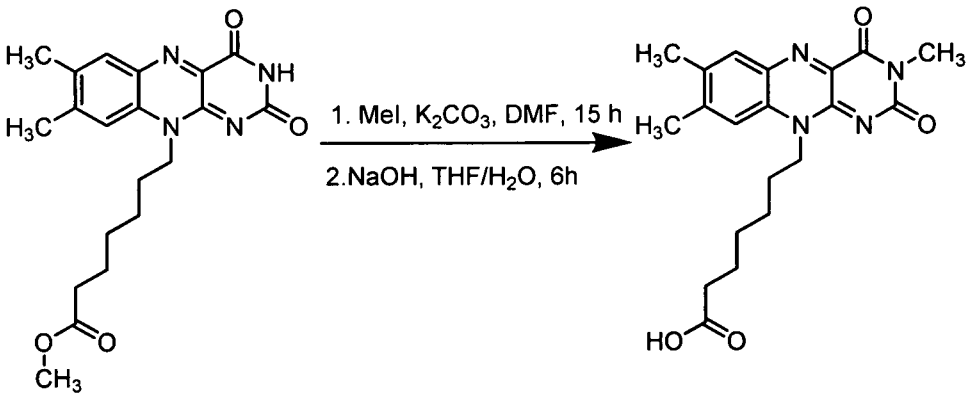
Scheme 16:



Scheme 17:

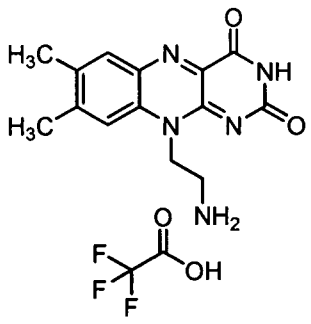


Scheme 18:



Example 40:

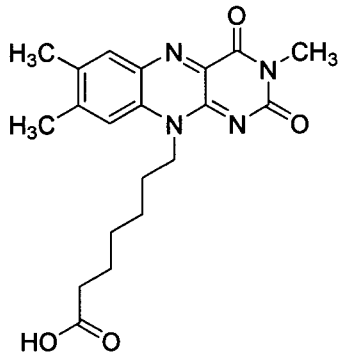
10-(2-Aminoethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione-2,2,2-trifluoroacetate salt



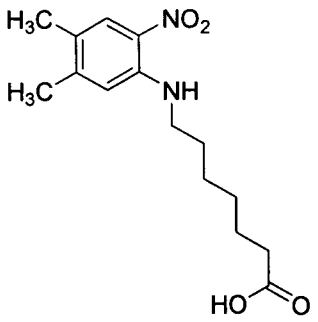
[0202] A solution of 10-(2-(benzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (see Example 55 for preparation) (395 mg, 1.05 mmol) and Pd/C (75 mg) in absolute EtOH (100 ml) is stirred under an atmosphere of hydrogen at 30 psi and 45 °C overnight. The mixture is filtered through a celite pad. The filtrate is concentrated under reduced pressure to dryness to obtain a crude product (230 mg, 77%). Crude product (19.5 mg, 0.07 mmol) is dissolved in MeOH (8 ml) and purified by preparative HPLC (Method 2). Lyophilization of the combined fractions affords desired product (5.0 mg, 14%) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.42 (s, 3H), 2.50 (s, 3H), 4.20 (m, 2H), 4.87 (m, 2H), 7.81 (s, 1H), 7.88 (m, 3H), 7.97 (s, 1H), 11.45 (s, 1H).

Example 41:

7-(3,7,8-Trimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid



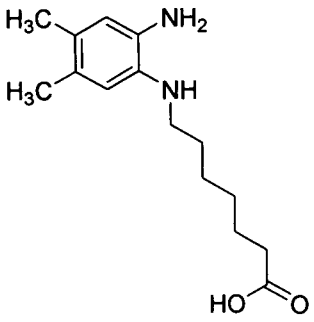
Step 1 Preparation of 7-(4,5-Dimethyl-2-nitro-phenylamino)-heptanoic acid



[0203] 4,5-Dimethyl-2-nitro-phenylamine (2.4 g, 14 mmol) was dissolved in DMF (40 mL) and set to 0°C with stirring and then sodium hydride (0.57 g, 14 mmol) was added and the reaction mixture was warmed to room temperature. After 30 min. the mixture was cooled to 0°C at which point a solution of 7-aminoheptanoic acid (1.0 g, 4.8 mmol) in DMF (2 mL) was added dropwise. The mixture is then allowed to warm to room

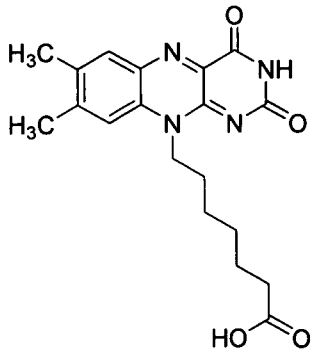
temperature slowly over 4 h. The reaction mixture is stirred with water (20 mL) for 30 min. and then concentrated under vacuum. The solid is then dry loaded onto silica gel gel and ISCO flash column purification is performed (0 to 10 % methanol in DCM) as the mobile phase to afford the crude product as an orange oil. The crude product is then purified using preparative HPLC (Method 1) to obtain 7-(4,5-dimethyl-2-nitro-phenylamino)-heptanoic acid (506 mg) as an orange oil (Yield: 49%). LC-MS m/z 295.0 [M+H], retention time = 3.94 min.

Step 2 Preparation of 7-(2-Amino-4,5-dimethyl-phenylamino)-heptanoic acid



[0204] 7-(4,5-Dimethyl-2-nitro-phenylamino)-heptanoic acid (70 mg, 0.24 mmol) is dissolved in methanol (5 mL) and Pd/C (20mg) is added followed by sodium borohydride (91 mg, 2.4 mmol) with stirring. The reaction mixture is filtered through celite after 1 h and is washed with methanol. The filtrate is concentrated under vacuum to obtain the product (63 mg) as a slightly brown oil (Yield: 100%).

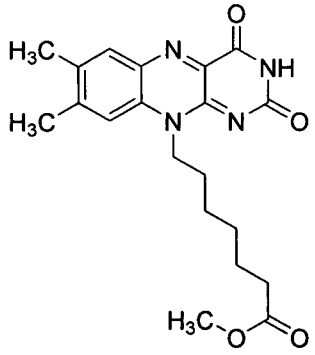
Step 3 Preparation of 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid



[0205] 7-(2-Amino-4,5-dimethyl-phenylamino)-heptanoic acid (64 mg, 0.24 mmol) is dissolved in acetic acid (5 mL) and then boron trioxide (33 mg, 0.48 mmol) and alloxan monohydrate (38 mg, 0.24 mmol) are added. After 3 h, the reaction mixture is

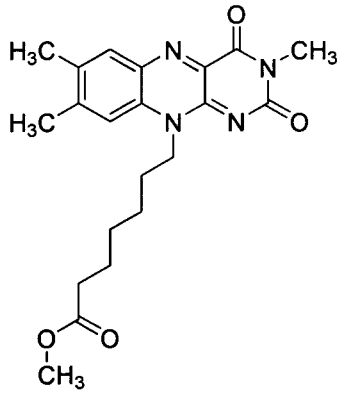
concentrated under vacuum and purified using preparative HPLC (Method 1). 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid (24 mg) is isolated following lyophilization of the appropriate fractions (Yield: 27%). ^{1}H NMR (400 MHz, DMSO-d6) δ 11.37 (s, 1H), 7.92 (s, 1H), 7.83 (s, 1H), 4.55 (m, 2H), 2.40 (s, 3H), 2.19 (m, 2H), 1.68 (m, 2H), 1.47 (m, 4H), 1.33 (m, 2H). MS m/z 369.3 $[M-H]^-$, retention time = 6.12 min.

Step 4 Preparation of Methyl 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



[0206] The preparation of this compound is similar to that of Example 25 using the acid from the previous step and methanol as a substitute for *i*-PrOH.

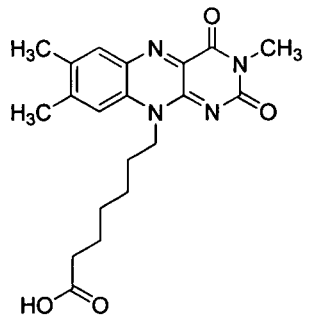
Step 5 Preparation of 7-(3,7,8-Trimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid methyl ester



[0207] 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid methyl ester (from the previous step) (350 mg, 0.91 mmol) is dissolved in DMF (2 mL). Methyl iodide (2 mL) and K_2CO_3 (251 mg, 182 mmol) are added to the reaction mixture and the mixture is stirred at rt for 15 h. The reaction mixture is filtered and the solid is washed with MeOH (10 mL). The filtrate is evaporated to a volume of 6.5 mL. The solution is diluted with water (1 mL) and purified by preparative HPLC (Method

1). The desired product is isolated in 12% (45 mg) yield after lyophilization. This product is used in the following step without further purification.

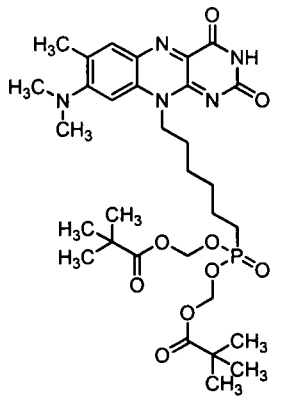
Step 6 Preparation of 7-(3,7,8-Trimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid



[0208] 7-(3,7,8-Trimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid methyl ester (24.5 mg, 0.061 mmol) is suspended in H_2O (1.5 mL) and NaOH (26 mg, 0.61 mmol) is added to this suspension. THF (0.1 mL) is added to dissolve the rest of the acid. The reaction mixture is stirred at room temperature for 6 h When the reaction is complete (as monitored by LCMS, ~5 h), the pH of the reaction is adjusted to 1 by 1M aqueous HCl and is stirred for 30 min. The reaction mixture is filtered and purified by preparative HPLC (Method 4). After lyophilization, the desired compound (3.9 mg) is isolated in 17% yield. ^{1}H NMR (400 MHz, MeOD-d4) δ 1.48 (m, 2H), 1.58 (m, 2H), 1.67 (m, 2H), 1.90 (m, 2H), 2.34 (m, 2H), 2.50 (s, 3H), 2.62 (s, 3H), 3.48 (3H), 4.78 (t, 2H), 7.81 (s, 1H), 8.02 (s, 1H).

Example 42:

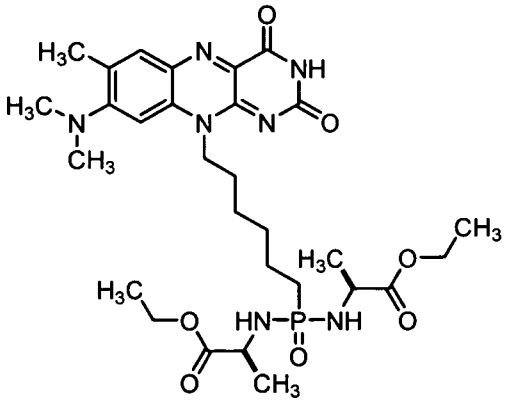
((6-(8-(Dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]-pteridin-10(2H)-yl)hexyl)phosphoryl)bis(oxy)bis(methylene) bis(2,2-dimethylpropanoate)



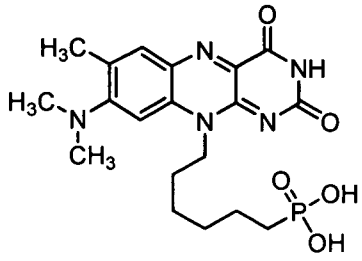
[0209] POMCl (327 mg, 2.17 mmol) is added to a suspension of 6-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexylphosphonic acid (122 mg, 0.28 mmol) and Et_3N (2 ml) in anhydrous DMF (10 ml). The reaction mixture is heated at 80 °C under an argon atmosphere for 24 h. Et_2O (20 ml) is added and the mixture is stirred at rt. The resulting solid is filtered off and the filtrate is concentrated under reduced pressure, dissolved in ACN (6 ml)/water (2 ml) and purified by preparative HPLC (Method 2). Lyophilization of combined fractions (LCMS) affords 11.4 mg (0.008 mmol) of desired product as a red solid. The product is further purified via preparative TLC (10% MeOH in DCM) to afford desired product (9.0 mg, 4.8%) as a red solid. ^1H NMR (400 MHz, DMSO-d_6) δ 1.14 (s, 18H), 1.44 (m, 6H), 1.71 (m, 2H), 1.80 (m, 2H), 2.45 (s, 3H), 3.05 (s, 6H), 4.58 (m, 2H), 5.58 (m, 4H), 6.86 (s, 1H), 7.81 (s, 1H), 11.12 (s, 1H).

Example 43:

(2S,2'S)-Diethyl-2,2'-((6-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexyl)phosphoryl)bis(azanediyl)dipropanoate

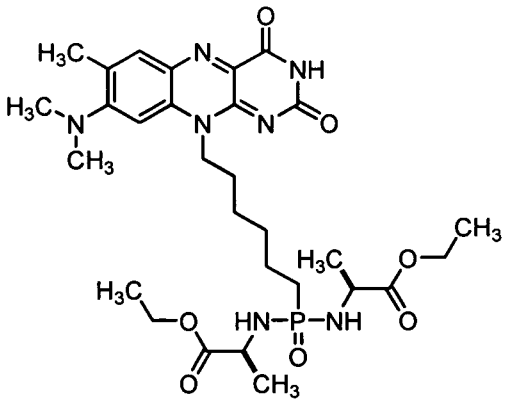


Step 1 Preparation of 6-(8-(Dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexylphosphonic acid



[0210] The above compound is prepared as in Example 13

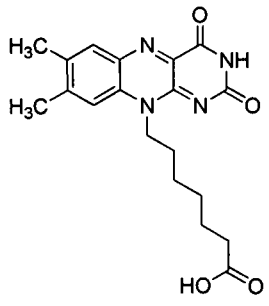
Step 2 Preparation of (2S,2'S)-Diethyl-2,2'-((6-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)yl)hexyl)phosphoryl)bis(azanediyl) dipropanoate



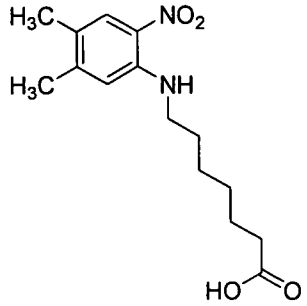
[0211] Oxalyl chloride (140 mg, 1.1 mmol) is added to a suspension of 6-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexylphosphonic acid (40 mg, 0.09 mmol) in anhydrous DCM (10 ml) followed by DMF (0.2 ml). The reaction mixture becomes homogenous and is refluxed under an argon atmosphere for 2 h. The solvent is concentrated to dryness. The resulting solid is dissolved in anhydrous DCM (10 ml), cooled to 0 °C, then L-alanine ethyl ester (152 mg, 0.98 mmol) is added, followed by DIPEA (0.2 ml, 1.2 mmol). The reaction is warmed to rt with stirring for 1 h. The solution is concentrated under reduced pressure, dissolved in ACN (6 ml)/water (2 ml) and purified by preparative HPLC (Method 2). Lyophilization of combined fractions (LCMS) affords desired product (5.4 mg, 9.2%) of as a purple solid. ^{1}H NMR (400 MHz, MeOD-d4) δ 1.31 (m, 6H), 1.65 (m, 14H), 1.93 (m, 2H), 2.62 (d, 3H) and 2.63 (d, 3H), 3.31 (s, 6H), 4.25 (m, 4H), 4.67 (m, 2H), 4.60-4.74 (m,1H), 4.80-5.80 (m, 1H), and 6.94 (s, 1H), 7.94 and 7.98 (s, 1H).

Example 44:

7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid

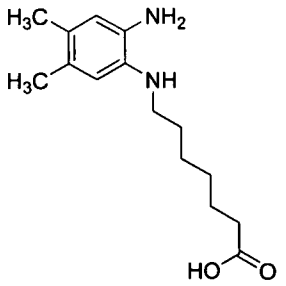


Step 1 Preparation of 7-(4,5-Dimethyl-2-nitro-phenylamino)-heptanoic acid



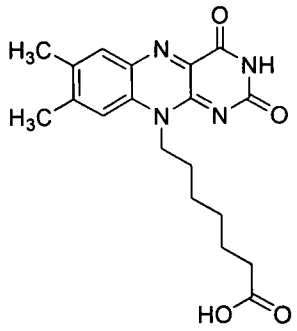
[0212] 4,5-Dimethyl-2-nitro-phenylamine (2.4 g, 14 mmol) is dissolved in DMF (40 mL) and stirred at 0°C and then sodium hydride (0.57 g, 14 mmol) is added and the reaction mixture is warmed to room temperature. After 30 min., the mixture is cooled to 0°C at which point a solution of 7-aminoheptanoic acid (1.0 g, 4.8 mmol) in DMF (2 mL) is added dropwise. The mixture is then allowed to warm to room temperature slowly over 4 h. The reaction mixture is stirred with water (20 mL) for 30 min. then concentrated under vacuum. The solid is then dry loaded onto silicagel and ISCO flash column purification is performed (0 to 10 % methanol in DCM) as the mobile phase to afford the desired product as an orange oil 7-(4,5-dimethyl-2-nitro-phenylamino)-heptanoic acid (506 mg) (Yield: 49%). LC-MS m/z 295.0 [M+H], retention time = 3.94 min.

Step 2 Preparation of 7-(2-Amino-4,5-dimethyl-phenylamino)-heptanoic acid



[0213] 7-(4,5-Dimethyl-2-nitro-phenylamino)-heptanoic acid (70 mg, 0.24 mmol) is dissolved in methanol (5 mL) and Pd/C (20 mg) is added followed by sodium borohydride (91 mg, 2.4 mmol) with stirring. The reaction mixture is filtered through celite after 1 h and the celite is washed with methanol. The filtrate is concentrated under vacuum to obtain the desired product (63 mg) as a slightly brown oil (Yield: 100%).

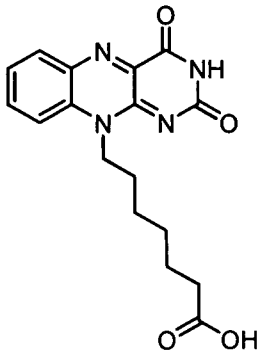
Step 3 Preparation of 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid



[0214] 7-(2-Amino-4,5-dimethyl-phenylamino)-heptanoic acid (64 mg, 0.24 mmol) is dissolved in acetic acid (5 mL) then boron trioxide (33 mg, 0.48 mmol) and alloxan monohydrate (38 mg, 0.24 mmol) are added. After 3 h, the reaction mixture is concentrated under vacuum and purified using preparative HPLC (Method 1). 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-heptanoic acid (24 mg) is isolated following lyophilization of the appropriate fractions (Yield: 27%). ^{1}H NMR (400 MHz, DMSO-d6) δ 11.37 (s, 1H), 7.92 (s, 1H), 7.83(s, 1H), 4.55 (m, 2H), 2.40 (s, 3H), 2.19 (m, 2H), 1.68 (m, 2H), 1.47 (m, 4H), 1.33 (m, 2H). MS m/z 369.3 [M-H]$^-$, retention time = 6.12 min.

Example 45:

7-(2,4-Dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid

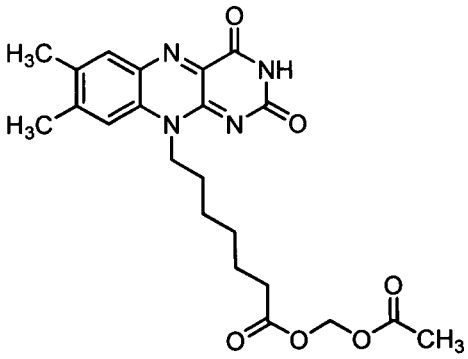


[0215] 7-(2,4-Dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid is synthesized from 7-(2-aminophenylamino)heptanoic acid (382 mg, 1.62 mmol) and alloxan (260 mg, 1.61 mmol) following the procedure described for Example 44. The reaction mixture is concentrated under vacuum and the resulting residue is purified by column chromatography (silica gel) using gradient elution (0 to 10% MeOH in DCM). The desired product is isolated following evaporation under vacuum (288 mg, 52% yield). ^{1}H NMR (400 MHz, DMSO) δ 1.33 (m, 2H), 1.45 (m, 4H), 1.69 (m, 2H), 2.03 (t, 2H),

4.54 (m, 2H), 7.62 (m, 1H), 7.91 (m, 2H), 8.11 (d, 1H), 11.37 (bs, 2H); ESI(+) m/z = 343.0.

Example 46:

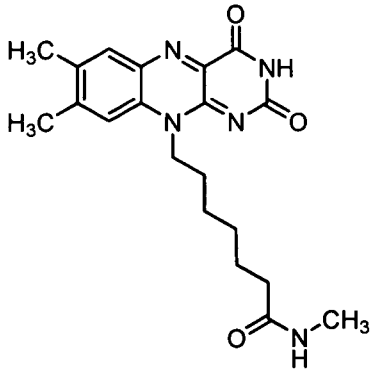
Acetoxymethyl 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



[0216] A mixture of 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (30 mg, 0.081 mmol), chloromethylacetate (44 mg, 0.405 mmol), triethylamine (45 μL, 0.324 mmol), and tetrabutylammonium iodide (150 mg, 0.405 mmol) in 2 mL of anhydrous DMF (2 mL) were stirred at 25°C for 24 h. The reaction mixture is concentrated under vacuum and the residue is dry loaded on silica gel using DCM as solvent and purified by BIOTAGE flash column chromatography using gradient from 1 to 5% MeOH in DCM as eluent. Desired product (11 mg) is isolated in 29 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (m, 2H), 1.54 (m, 2H), 1.69 (m, 2H), 1.87 (m, 2H), 2.04 (s, 3H), 2.39 (m, 2H), 2.45 (s, 3H), 2.57 (s, 3H), 4.69 (m, 2H), 5.69 (s, 2H), 7.40 (s, 1H), 8.07 (s, 1H), 8.36 (s, 1H); ESI(+) m/z = 443.0.

Example 47:

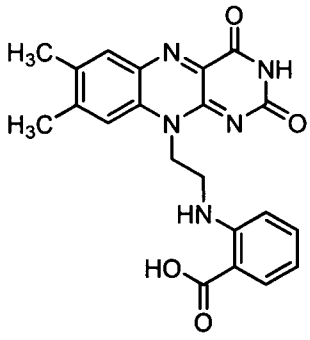
7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-N-methylheptanamide



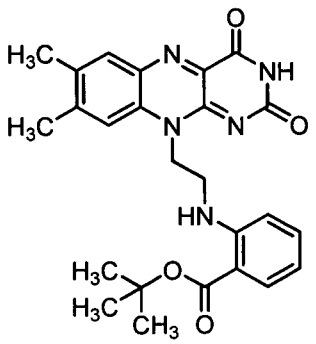
[0217] A mixture of 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (30 mg, 0.081 mmol), HBTU (31 mg, 0.081 mmol), DIPEA (42 μL, 0.243 mmol), and 2M methylamine in THF solution (405 μL, 0.81 mmol) in 2 mL of anhydrous DMF (2 mL) were stirred at 25°C for 16 h. The reaction mixture is concentrated under vacuum and the residue is dry loaded on silica gel and purified by BIOTAGE flash column chromatography using a gradient from 1 to 2% MeOH in DCM as eluent. Desired product (21 mg) is isolated in 68 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (m, 2H), 1.56 (m, 2H), 1.72 (m, 2H), 1.87 (m, 2H), 2.22 (t, 2H), 2.46 (s, 3H), 2.58 (s, 3H), 2.80 (d, 3H), 4,68 (m, 2H), 5.89 (bs, 1H), 7.42 (s, 1H), 8.07 (s, 1H) 8.41 (s, 1H); ESI(+) m/z = 384.1.

Example 48:

2-(2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)benzoic acid

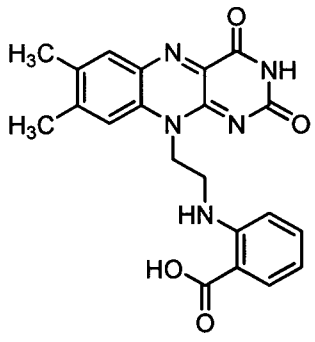


Step 1 Preparation of *tert*-Butyl 2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)



[0218] To a solution of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde from Example 14 (50 mg, 0.176 mmol) in methanol (5 mL) are added *tert*-butyl 2-aminobenzoate (37 mg, 0.193 mmol) and AcOH (75μL) at room temperature. The reaction is stirred at 50°C for 30 min. The reaction is cooled to room temperature and sodium cyanoborohydride (25 mg, 0.39 mmol) is added and the reaction mixture is stirred at 50°C for 24 h. The product precipitates from the reacton mixture and is filtered and washed with MeOH (10mL) and dried overnight under vacuum (49 mg, 61% yield). ^{1}H NMR (400 MHz, DMSO) δ 1.45 (s, 9H), 2.29 (s, 3H), 2.36 (s, 3H), 3.34 (bs, 1H), 3.72 (m, 2H), 4.74 (m, 2H), 6.62 (t, 1H), 7.31 (d, 1H), 7.41 (t, 1H), 7.60 (s, 1H), 7.74 (d, 1H), 7.86 (s, 1H), 11.35 (bs, 1H) ESI(+) m/z = 462.0.

Step 2 Preparation of 2-(2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)benzoic acid



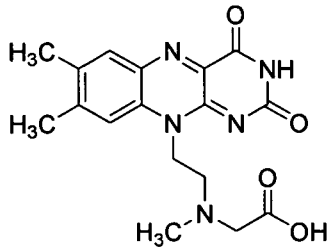
[0219]

[0220] To a solution of *tert*-butyl 2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)benzoate (29 mg, 0.063 mmol) in anhydrous DCM (2 mL) is added TFA (500 μL, 6.45 mmol) and the mixture is stirred at 40°C for 16 h. The solution is concentrated under reduced pressure, and the residue is dissolved in DMSO (1 mL), filtered, and purified by preparatory HPLC (Method 1). The desired product (14.0 mg) is isolated following lyophilization (Yield: 55%). ^{1}H NMR (400 MHz, DMSO) δ 2.33 (s, 3H), 2.37 (s, 3H), 3.72 (m, 2H), 4.75 (m, 2H), 6.60 (t, 1H),

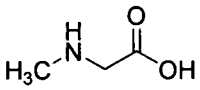
7.31 (d, 1H), 7.39 (m, 1H), 7. 7 (s, 1H), 7.76 (dd, 1H), 7.86 (s, 1H), 11.36 (s, 1H), 12.50 (b s, 1H)ESI(+) m/z = 370.0.

Example 49:

{[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-methyl-amino}-acetic acid

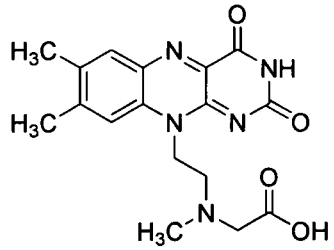


Step 1 Preparation of 2-(Methylamino)acetic acid



[0221] tert-Butyl 2-(methylamino)acetate (250 mg, 1.4 mmol) is dissolved in DCM (2 mL) and TFA (2 mL) is added at room temperature and stirred for 2 h. The reaction mixture is then concentrated to dryness. The residue is mixed with TEA (0.5 mL) and again concentrated to dryness to afford the product as a clear oil and is used directly in the next step.

Step 2 Preparation of {[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-methyl-amino}-acetic acid

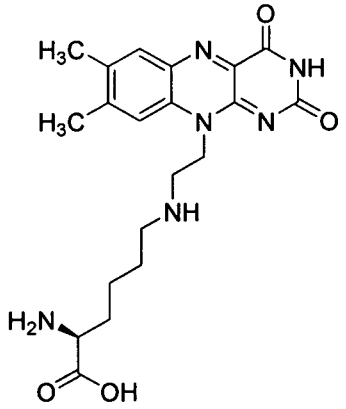


[0222] Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (100 mg, 0.35 mmol) from Example 14 and 2-(methylamino)acetic acid (133 mg, 1.0 mmol) are suspended in methanol (15 mL) and stirred at 50°C. After one hour, the mixture is cooled to room temperature and acetic acid (0.1 mL) is added, followed by sodium cyanoborohydride (55 mg, 0.9 mmol). The resulting mixture was stirred for 16 h. Dilute with water (3 mL) and purify via prep HPLC (Method 1) to obtain the product (62

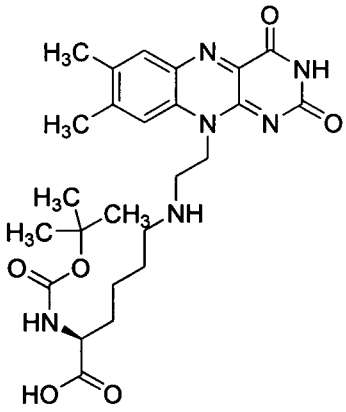
mg) as a yellow solid (Yield: 50 %). LCMS m/z 358.13 $[M+H]^+$, retention time = 5.13 min

Example 50:

(S)-2-Amino-6-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-hexanoic acid

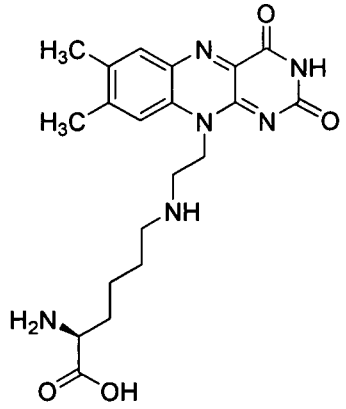


Step 1 Preparation of (S)-2-*tert*-Butoxycarbonylamino-6-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-hexanoic acid



[0223] Into a suspension of 2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (68 mg, 0.239 mmol) in MeOH (2.5 mL) are added (S)-6-amino-2-*tert*-butoxycarbonylamino-hexanoic acid (65 mg, 0.263 mol), $NaCNBH_3$ (18 mg, 0.287 mmol), and AcOH (0.1 mL) respectively and stirred at room temperature for 24 h. The reaction mixture is heated at 40 °C for 16 h. The solvent is removed under vacuum and the crude is used in the following step without further purification.

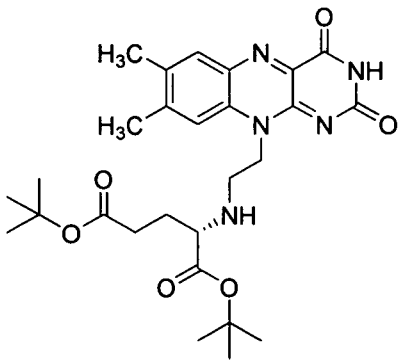
Step 2 Preparation of (S)-2-Amino-6-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-hexanoic acid



[0224] The crude product from step 1 is dissolved in TFA (2 mL) and DCM (2 mL) and stirred at room temperature for 24 h. The solvent is removed and the crude product is dissolved in H_2O (8 mL) and purified by preparative HPLC (Method 2). After lyophilization the desired compound (26 mg) is obtained in 26% yield after two steps. ^1H NMR (400 MHz, MeOH-d4) δ 1.36 (s, 2H), 1.61 (m, 2H), 1.82 (m, 2H), 2.00 (m, 2H), 2.48 (s, 3H), 2.61 (s, 3H), 3.22 (t, 2H), 3.67 (t, 2H), 3.99 (t, 1H) 5.10 (t, 2H), 7.81 (s, 1H), 7.91 (s, 1H).

Example 51:

2-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-pentanedioic acid di-*tert*-butyl ester

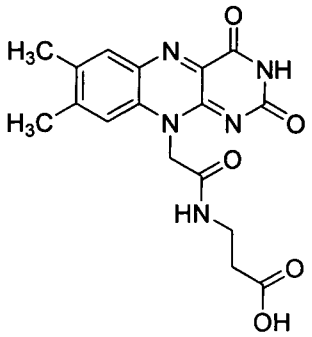


[0225] To a suspension of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (see Example 14) (100 mg, 0.352 mmol) in methanol (5 mL) is added L-glutamic acid di-*tert*-butyl ester hydrochloride (104 mg, 0.352 mmol) at room temperature followed by glacial acetic acid (0.1 mL). The reaction mixture is heated to 40°C and stirred for 1 h. Then sodium cyanoborohydride (49 mg,

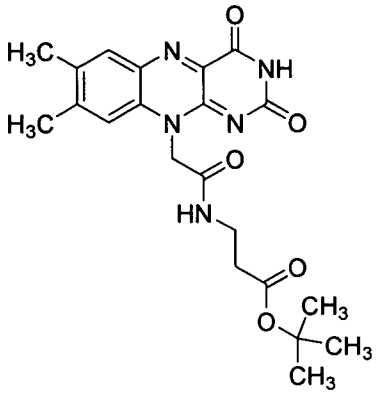
0.775 mmol) is added, and the solution is stirred for 16 h at 20°C. The reaction mixture is concentrated; the residue is dissolved in DMF/water (1/3) and purified by preparative HPLC (Method 1). 2-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-pentanedioic acid di-*tert*-butyl ester (30 mg) is isolated following lyophilization of the appropriate fractions (Yield: 16%). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.40 (s, 9H), 1.46 (s, 9H), 1.94 (m, 1H), 2.05 (m, 1H), 2.29 (m, 1H), 2.42 (s, 3H), 2.53 (s, 3H), 3.36 (m, 2H), 4.14 (m, 1H), 4.86 (m, 1H), 5.00 (m, 1H), 7.82 (s, 1H), 7.86 (s, 1H), 9.30 (br s, 1H), 11.46 (s, 1H).

Example 52:

3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propionic acid



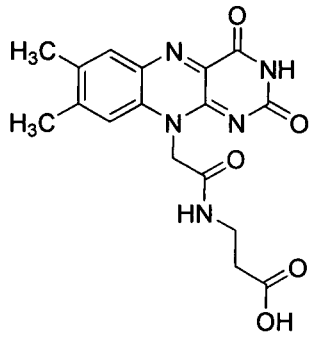
Step 1 Preparation of 3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propionic acid *tert*-butyl ester



[0226] To a suspension of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetic acid (100 mg, 0.34 mmol) and 3-amino-propionic acid *tert*-butyl ester (99 mg, 0.68 mmol) in DMF (3 mL), DIPEA (0.13 mL, 0.68 mmol) and HATU (128 mg, 0.68 mmol) are added sequentially at room temperature. The temperature is then increased to 40°C and the reaction mixture is stirred for 18 h. The reaction mixture is

cooled to room temperature, diluted with water (3 mL) and purified using preparative HPLC purification (Method 1). 3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propionic acid *tert*-butyl ester (16 mg) is isolated following lyophilization of the appropriate fractions (Yield: 11 %). LC-MS m/z 428.0 $[M+H]^+$. Retention time = 2.75 min.

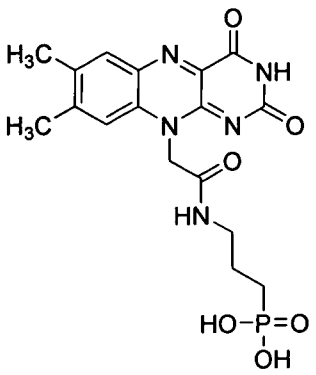
Step 2 Preparation of 3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propionic acid



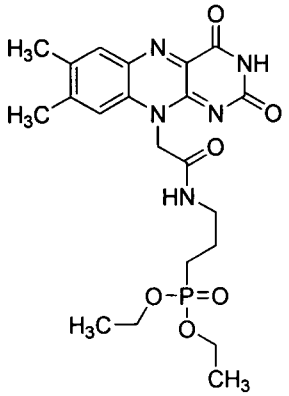
[0227] To a suspension of 3-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propionic acid *tert*-butyl ester (7 mg, 0.02 mmol) in DCM (2 mL) is added trifluoroacetic acid (2 mL) at room temperature. After 2 h, the reaction mixture is concentrated and the residual material is purified using prep HPLC (Method 1) and the appropriate fractions were lyophilized to obtain 3-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propionic acid (3.2 mg) as a yellow solid (Yield: 53 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 11.42 (s, 1H), 8.41 (s, 1H), 7.93 (s, 1H), 7.49 (s, 1H), 5.71 (s, 1H), 5.28 (m, 2H), 2.46 (s, 3H), 2.40 (s, 3H), MS m/z 371.9 $[M+H]^+$, retention time = 6.24 min.

Example 53:

{3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propyl}-phosphonic acid

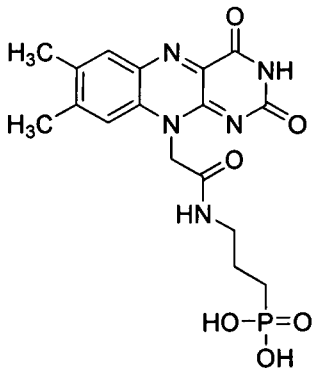


Step 1 Preparation of {3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propyl}-phosphonic acid diethyl ester



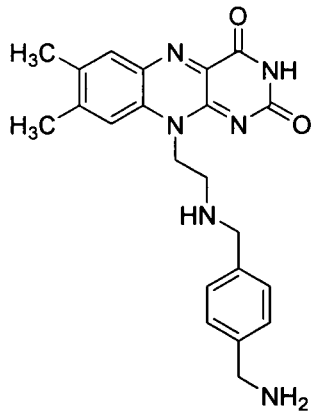
[0228] To a suspension of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetic acid (50 mg, 0.17 mmol) and (3-amino-propyl)-phosphonic acid diethyl ester (33 mg, 0.17 mmol) in DMF (5 mL), DIPEA (0.09 mL, 0.34 mmol) and HATU (64 mg, 0.17 mmol) are added sequentially at room temperature. After 18 h the reaction mixture is diluted with water (3 mL) and purified using preparative HPLC purification (Method 1). {3-[2-(7, 8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propyl}-phosphonic acid diethyl ester (20 mg) is isolated following lyophilization of the appropriate fractions (Yield: 25 %). LC-MS m/z 478.0 [M+H], retention time = 2.48 min.

Step 2 Preparation of {3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propyl}-phosphonic acid

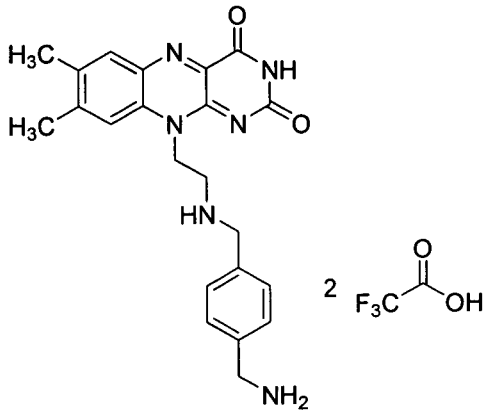


[0229] {3-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propyl}-phosphonic acid diethyl ester (20 mg, 0.04 mmol) is dissolved in DCM (3 mL) and then trimethylsilylbromide is added (0.5 mL) at room temperature and the solution is stirred for 2 days. The solution is then concentrated under vacuum and purified using prep HPLC (Method 1) to obtain {3-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetylamino]-propyl}-phosphonic acid (4.2 mg) as a yellow solid (Yield: 24 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 11.41 (s, 1H), 8.29 (s, 1H), 7.94 (s, 1H), 7.58 (s, 1H), 5.29 (m, 2H), 2.47 (s, 3H), 2.40 (s, 3H), 1.60 (m, 2H), 1.47 (m, 2H), MS m/z 420.4 $[M-H]^-$, retention time = 4.34 min.

Example 54:
10-(2-(4-(aminomethyl)benzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione

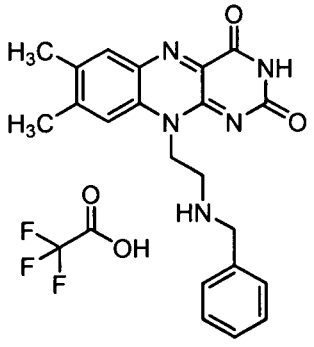


Step 1 Preparation of 10-(2-(4-(Aminomethyl)benzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione

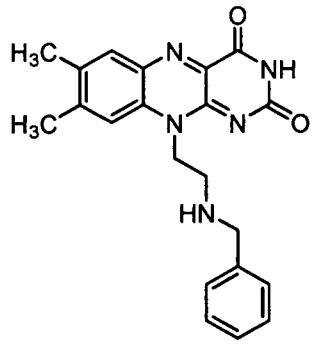


[0230] To a suspension of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (Example 14) (50 mg, 0.18 mmol) in methanol (5 mL) at room temperature is added 1,4-phenylenedimethanamine (48 mg, 0.35 mmol), acetic acid (0.075 mL) and sodium cyanoborohydride (24 mg, 0.39 mmol), and the solution is stirred at room temperature for 72 h. The reaction mixture is mixed with silica gel, concentrated, and purified by column chromatography (CH_2Cl_2/MeOH/Et_3N, 90:10:1). The resulting mixture is further purified by preparative HPLC (Method 1). 10-(2-(4-(Aminomethyl)benzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (16 mg) is isolated following lyophilization of the appropriate fractions (Yield: 23 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 2.42 (s, 3H), 2.54 (d, 3H), 4.07 (s, 2H), 4.36 (s, 2H), 5.10 (s, 2H), 7.50 (d, 2H), 7.56 (d, 2H), 7.89 (s, 1H), 7.96 (s, 1H), 8.32 (br s, 3H) 9.29 (br s, 2H), 11.45 (s, 1H). LC-MS m/z 405.1 [M-H], retention time 4.16 min.

Example 55:
10-(2-(Benzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione 2,2,2-trifluoroacetate

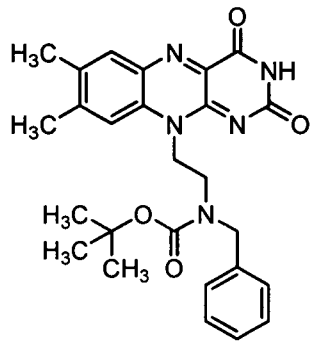


Step 1 Preparation of 10-(2-(Benzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione.



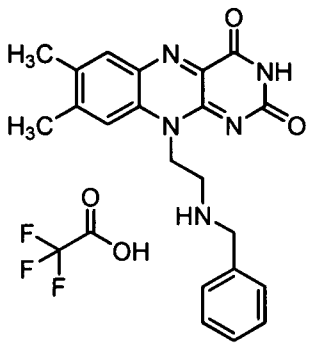
[0231] Crude material is prepared by reductive amination using a procedure similar to that of Step 2, Example 15 using 2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetaldehyde (Example 14) and benzylamine. This product is contaminated with 10-(2-(benzyl(methyl)amino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione. The next two steps are performed to isolate desired product.

Step 2 Preparation of *tert*-Butyl benzyl(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)carbamate



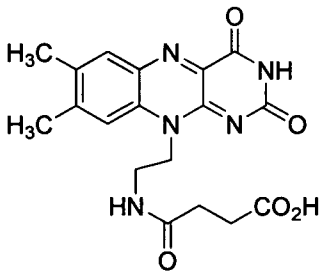
[0232] To a solution of crude 10-(2-(benzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (7.53 mmol) in MeOH (200 mL) is added di-*tert*-butyl dicarbonate (5.2 g, 23.8 mmol) and Et_3N (4 ml). The reaction was concentrated under reduced pressure and purified via silica gel chromatography (ISCO) (100% DCM to 10% MeOH/DCM) over 1 h to obtain desired product (1.85 g, 54%) as a brown solid.

Step 3 Preparation of 10-(2-(Benzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione 2,2,2-trifluoroacetate



[0233] To a solution of *tert*-butyl benzyl(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)carbamate (50 mg, 0.11 mmol) in DCM (2 mL) is added TFA (2 mL) at rt. After 2 h, the reaction mixture is concentrated and the residual material is dissolved in MeOH (10 ml) and purified by preparative HPLC (Method 2). Lyophilization of combined fractions affords desired product (33.6 mg, 65%) as a brown solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.42 (s, 3H), 2.53 (s, 3H), 4.35 (s, 2H), 5.00 (m, 2H), 7.43 (m, 3H), 7.52 (m, 2H), 7.83 (s, 1H), 7.96 (s, 1H), 9.02 (s, 2H), 11.49 (s, 1H).

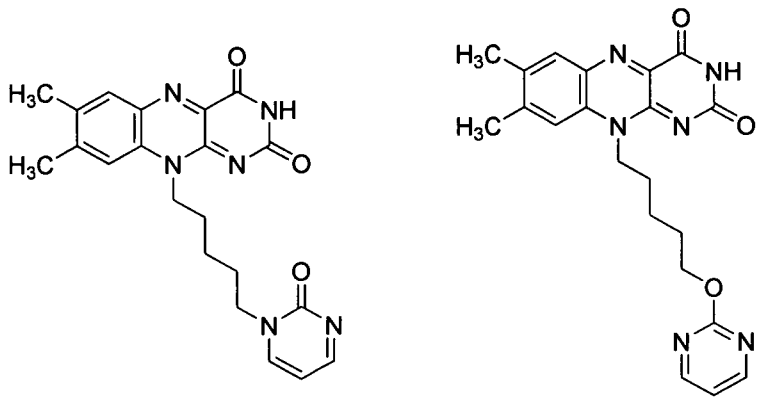
Example 56:
N-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-succinamic acid



[0234] The mixture of 10-(2-aminoethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (15 mg, 0.053 mmol) (see Example 40)) and succinic anhydride (15 mg, 0.15 mmol) in pyridine (2 mL) is stirred at room temperature for 5 h. The reaction mixture is concentrated to dryness, dissolved in DMF/water (1/3) and purified by preparative HPLC (Method 4) to give, after isolation and lyophilization, *N*-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-succinamic acid (3.4 mg, yield: 17%). ^{1}H NMR (400 MHz, DMSO-d6) δ 2.18 (m, 2H), 2.34 (m, 2H), 2.40 (s, 3H), 3.47 (m, 2H), 4.46 (m, 2H), 7.87 (s, 1H), 7.91 (s, 1H), 8.11 (m, 1H), 11.35 (s, 1H), 12.10 (br.s. 1H).

Example 57:

7,8-Dimethyl-10-(5-(2-oxopyrimidin-1(2H)-yl)pentyl)benzo[g]pteridine-2,4(3H,10H)-dione (I) and 7,8-dimethyl-10-(5-(pyrimidin-2-yloxy)pentyl)benzo[g]pteridine-2,4(3H,10H)-dione (II)

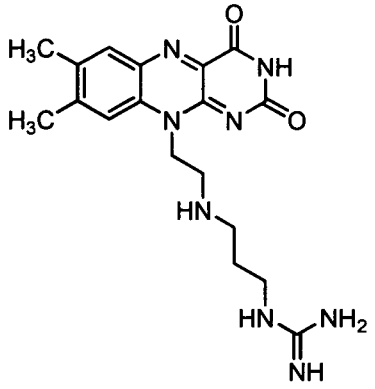


(I) (II)

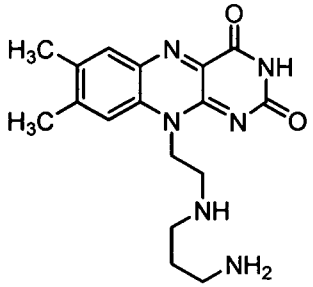
[0235] To a suspension of pyrimidin-2(1H)-one hydrochloride (100 mg, 0.755 mmol) and potassium carbonate (104 mg, 0.755 mmol) in anhydrous DMF (5 mL) is added 10-(5-bromopentyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (see Intermediate 1 for preparation) (50 mg, 0.128 mmol) at room temperature. The mixture is then heated to 50°C and stirred for 8 h, concentrated (50°C), dissolved in DMF/water (1/3) and purified by preparative HPLC (Method 1) to give, after lyophilization,, 7,8-dimethyl-10-[5-(2-oxo-2H-pyrimidin-1-yl)-pentyl]-10H-benzo[g]pteridine-2,4-dione (I) (10.9 mg, yield: 21%). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.45 (m, 2H), 1.76 (m, 4H), 2.39 (s, 3H), 2.51 (s, 3H), 3.95 (m, 2H), 4.57 (m, 2H), 6.58 (dd, 1H), 7.83 (s, 1H), 7.90 (s, 1H), 8.50 (dd, 1H), 8.61 (m, 1H), 11.31 (s, 1H); LC-MS m/z 407.1 $[M + H]^+$ and 7,8-Dimethyl-10-[5-(pyrimidin-2-yloxy)-pentyl]-10H-benzo[g]pteridine-2,4-dione (II) (4 mg, yield: 7.7%). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.59 (m, 2H), 1.81 (m, 4H), 2.40 (s, 3H), 4.32 (m, 2H), 4.61 (m, 2H), 7.12 (m, 1H), 7.83 (s, 1H), 7.91 (s, 1H), 8.58 (d, 2H), 11.30 (s, 1H).

Example 58:

1-(3-(2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)propyl)guanidine

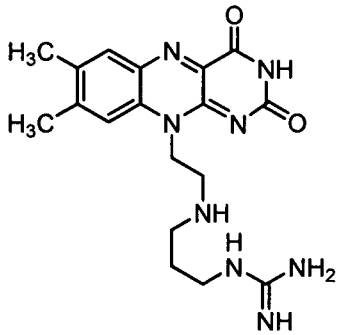


Step 1 Preparation of 10-(2-(3-Aminopropylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione



[0236] Prepared by reductive amination using a procedure similar to that of Example 15, step 2, using 2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetaldehyde (Example 14)) and propane-1,3-diamine (15 equivalents) as starting materials.

Step 2 Preparation of 1-(3-(2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)propyl)guanidine

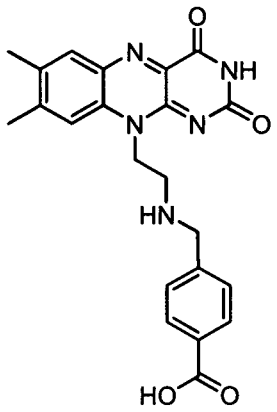


[0237] A mixture of 10-(2-(3-aminopropylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (66 mg, 0.19 mmol), 3,5-dimethyl-1H-pyrazole-1-carboximidamide (33 mg, 0.16) and DIPEA (45 mg, 0.348 mmol) in DMF (3 ml) are stirred at rt for 16 h. The reaction is concentrated under reduced pressure, dissolved in ACN (5 ml)/water (2 ml) and purified by preparative HPLC (Method 2).

Lyophilization of combined fractions affords desired product (30.5 mg, 41%). ^{1}H NMR (400 MHz, CD_3OD) δ 2.03 (m, 2H), 2.50 (s, 3H), 2.62 (s, 3H), 3.37 (m, 4H), 3.67 (m, 2H), 5.11 (m, 2H), 7.83 (s, 1H), 8.00 (s, 1H).

Example 59:

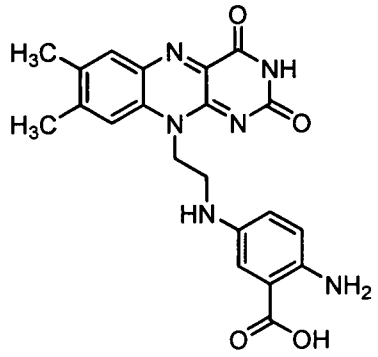
4-((2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)methyl)benzoic acid



[0238] To a solution of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (Example 14)) (50 mg, 0.176 mmol) in methanol (5 mL) are added 4-(aminomethyl)benzoic acid (26.6 mg, 0.176 mmol) and acetic acid (75 μL) at rt. The reaction is stirred at 50 °C for 30 min. The reaction is cooled to room temperature and sodium cyanoborohydride (25 mg, 0.39 mmol) is added and the reaction mixture is stirred at 50 °C for 24 h. The product precipitates from the reacton mixture and is filtered and washed with MeOH (10 mL) and dried overnight under vacuum (50.0 mg, 69% yield). ^{1}H NMR (400 MHz, DMSO) δ 2.38 (s, 3H), 2.46 (s, 3H), 2.91 (m, 2H), 3.84 (s, 2H), 4.70 (m, 2H), 7.39 (d, 2H), 7.82 (m, 4H), 11.30 (s, 1H). ESI(-) m/z = 418.5

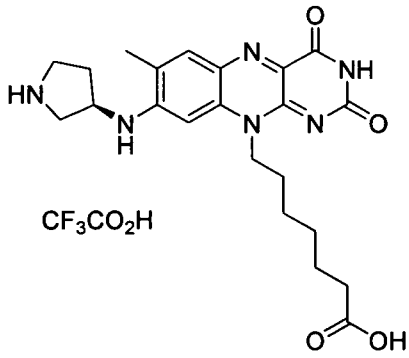
Example 60:

2-Amino-5-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)benzoic acid

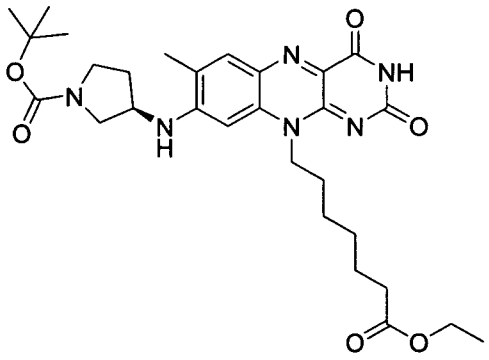


[0239] 2-Amino-5-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)benzoic acid is synthesized from (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (Example 14) (50 mg, 0.176 mmol) and 2,5-diaminobenzoic acid dihydrochloride (44 mg, 0.195 mmol) following the procedure described for Example 59. The solution is concentrated under reduced pressure, and the residue dissolved in DMSO (1 mL), filtered, and purified by preparatory HPLC (Method 2). The desired product (12.7 mg) is isolated after lyophilization of the fractions (yield: 18.6%). ^{1}H NMR (400 MHz, DMSO) δ 2.30 (s, 3H), 2.38 (s, 3H), 2.56 (m, 2H), 4.72 (m, 2H), 6.18 (m, 1H), 6.73 (m, 2H), 7.44 (m, 2H), 7.53 (s, 1H), 7.89 (s, 1H), 11.38 (s, 1H) ESI(-) m/z = 419.1.

Example 61: 7-{7-methyl-2,4-dioxo-8-[(3*R*)-pyrrolidin-3-ylamino]-3,4-dihydrobenzo[g]pteridin-10(2H)-yl}heptanoic acid trifluoroacetate salt

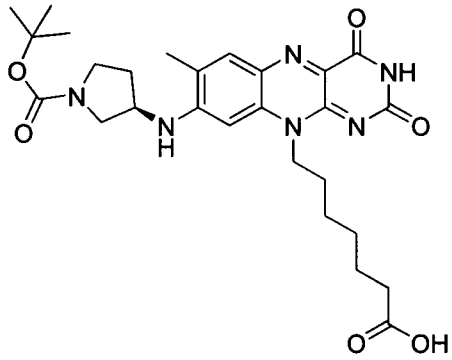


Step 1 Preparation of *tert*-Butyl (3*R*)-3-{[10-(7-ethoxy-7-oxoheptyl)-7-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl]amino}pyrrolidine-1-carboxylate



[0240] A sealed 20 mL scintillation vial containing a solution of ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (103 mg, 0.24 mmol), *tert*-butyl (3R)-3-aminopyrrolidine-1-carboxylate (229 mg, 1.23 mmol) and NMP (5.0 mL) is stirred at 90 °C for 24 h. The reaction is cooled to rt and partitioned between saturated sodium bicarbonate and DCM (50 mL each). The layers are separated and the aqueous extracted with DCM (3x25 mL). The organics are combined, dried with anhydrous sodium sulfate and concentrated. The residue is subjected to preparative reverse phase chromatography to give 34 mg (24%) of desired product as an amorphous red solid after lyophilization. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.0 (1H, s), 7.70 (1H, s), 6.79 (1H, m), 6.58 (1H, s), 4.01 (2H, q), 2.30 (3H, s), 1.41 & 1.39 (9H, s), 1.16 (3H, t). MS (ESI+) for $C_{29}H_{40}N_6O_6$ m/z 569.1 (M+H)+, retention time: 3.63 min (System C).

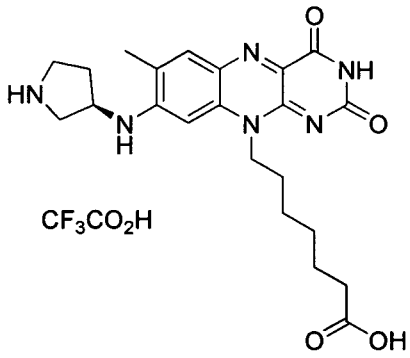
Step 2 Preparation of 7-[8-{[(3*R*)-1-I-Butoxycarbonyl)pyrrolidin-3-yl]amino}-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoic acid



[0241] A solution of *tert*-butyl (3R)-3-{[10-(7-ethoxy-7-oxoheptyl)-7-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl]amino}pyrrolidine-1-carboxylate (89.0 mg, 0.156 mmol) and 1.0 M lithium hydroxide (0.5 mL, 0. 5 mmol) in THF (2.0 mL,) and water (0.5 mL) is stirred at rt for 2 h. Acetic acid (0.10 mL, 1.8 mmol) is added and the reaction mixture is concentrated. The red residue is suspended in water (5 mL), filtered, washed with water and dried in vacuo to give 52 mg (61%) of the desired product as a red

solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.0 (1H, s), 7.69 (1H, s), 6.78 (m, 1H), 6.58 (1H, s), 2.29 (3H, s), 1.41 and 1.39 (9H, s). MS (ESI+) for $C_{27}H_{36}N_6O_6$ m/z 541.2 (M+H)+, retention time: 3.07 min (System C).

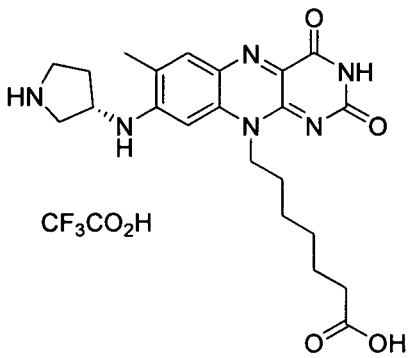
Step 3 Preparation of 7-{7-Methyl-2,4-dioxo-8-[(3*R*)-pyrrolidin-3-ylamino]-3,4-dihydrobenzo[g]pteridin-10(2H)-yl}heptanoic acid trifluoroacetate salt



[0242] A slurry of 7-[8-{[(3R)-1-(*tert*-butoxycarbonyl)pyrrolidin-3-yl]amino}-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoic acid (35.0 mg, 0.065 mmol) in TFA (0.9 mL) and water (6.0 mL) is stirred at rt for 18h. This solution is then lyophilized to give 34 mg (94 %) of desired product as a red solid. ^{1}H NMR (400 MHz, D_2O) δ 7.30 (1H, s), 6.11 (1H, s), 4.47 (1H, m), 4.38 (1H, m), 4.29 (1H, m), 3.68 (1H, m), 3.55-3.46 (3H, m), 2.45 (1H, M), 2.28 (3H, m), 2.14 (3H, s), 1.63 (2H, m), 1.51 (2H, m) 1.38-1.30 (4H, m). MS (ESI+) for $C_{22}H_{28}N_6O_4$ m/z 441.2 (M+H)+, retention time: 1.99 min (System C).

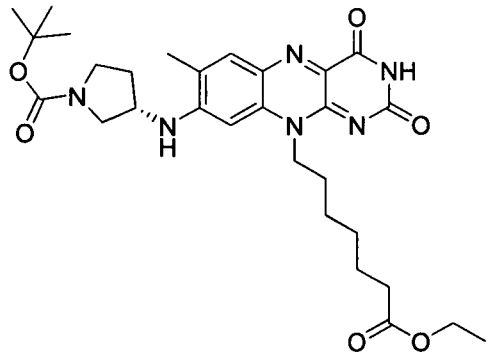
Example 62:

7-{7-Methyl-2,4-dioxo-8-[(3*S*)-pyrrolidin-3-ylamino]-3,4-dihydrobenzo[g]pteridin-10(2H)-yl}heptanoic acid trifluoroacetate salt



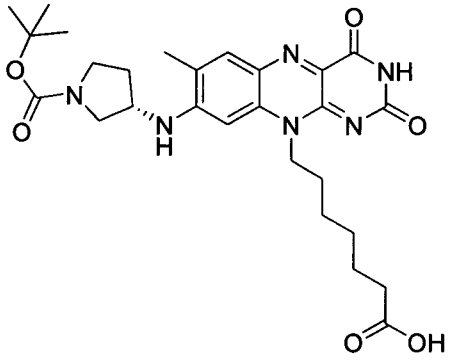
Step 1 Preparation of *tert*-Butyl (3*S*)-3-{[10-(7-ethoxy-7-oxoheptyl)-7-methyl-2,4-

dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl]amino}pyrrolidine-1-carboxylate



[0243] A sealed 20 mL scintillation vial containing a solution of ethyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (50.0 mg, 0.12 mmol) and *tert*-butyl (3S)-3-aminopyrrolidine-1-carboxylate (100 mg, 0. 6 mmol) in NMP (3.0 mL) is stirred at 90 °C for 48 h. The reaction is concentrated and subjected to preparative reverse phase chromatography to provide 20 mg (30%) of the desired product as a red solid after lyophilization. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.0 (1H, s), 7.70 (1H, s), 6.79 (1H, m), 6.58 (1H, s), 4.01 (2H, q), 2.30 (3H, s), 1.39 (9H, s), 1.16 (3H, t). MS (ESI+) for $C_{29}H_{40}N_6O_6$ m/z 569.1 (M+H)+, retention time: 3.65 min (System C).

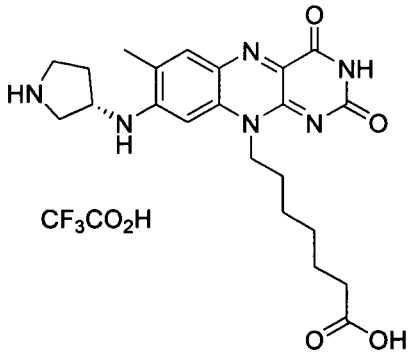
Step 2 Preparation of 7-[8-{[(3*S*)-1-I-Butoxycarbonyl)pyrrolidin-3-yl]amino}-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoic acid



[0244] To a well-stirred slurry of *tert*-butyl (3S)-3-{[10-(7-ethoxy-7-oxoheptyl)-7-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl]amino}pyrrolidine-1-carboxylate (20.0 mg, 0.04 mmol) and water (1.0 mL) in THF (3.0 mL,) at rt is added 1.0 M lithium hydroxide (0.50 mL). The reaction is stirred at rt for 1h and quenched with acetic acid (50 uL). This mixture is concentrated and re-suspended in water (5mL). The precipitate is collected and dried *in vacuo* to give 11 mg (58%) of desired product as a red solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.9 (1H, br s), 11.0 (1H, s), 7.69 (1H, s), 6.79

(m, 1H), 6.58 (1H, s), 2.29 (3H, s), 1.41 & 1.39 (9H, s). MS (ESI+) for $C_{27}H_{36}N_6O_6$ m/z 541.0 (M+H)+, retention time: 3.07 min (System C).

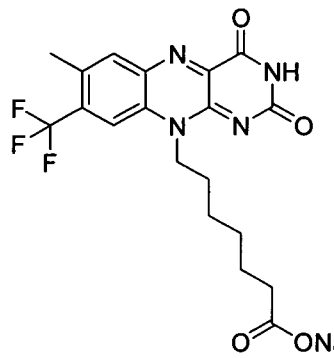
Step 3 Preparation of 7-{7-Methyl-2,4-dioxo-8-[(3S)-pyrrolidin-3-ylamino]-3,4-dihydrobenzo[g]pteridin-10(2H)-yl}heptanoic acid trifluoroacetate salt



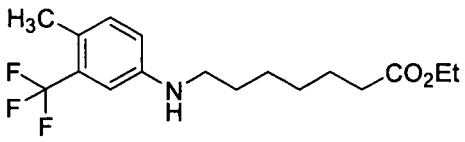
[0245] A slurry of 7-[8-{[(3S)-1-(*tert*-butoxycarbonyl)pyrrolidin-3-yl]amino}-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoic acid (34.5 mg, 0.064 mmol) in TFA (0.3 mL) and water (2.0 mL) is stirred at rt for 18 h. The solution is lyophilized to give 33 mg of desired product as a red solid (93%). ^{1}H NMR (400 MHz, D_2O) δ 7.30 (1H, s), 6.11 (1H, s), 4.47 (1H, m), 4.38 (1H, m), 4.29 (1H, m), 3.68 (1H, m), 3.55-3.46 (3H, m), 2.45 (1H, M), 2.28 (3H, m), 2.14 (3H, s), 1.63 (2H, m), 1.51 (2H, m), 1.38-1.30 (4H, m). MS (ESI+) for $C_{22}H_{28}N_6O_4$ m/z 441.2 (M+H)+, retention time: 1.99 min (System C).

Example 63:

Sodium 7-[7-methyl-2,4-dioxo-8-(trifluoromethyl)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate

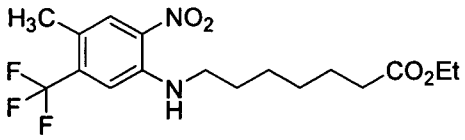


Step 1 Preparation of Ethyl 7-{[4-methyl-3-(trifluoromethyl)phenyl]amino}-heptanoate



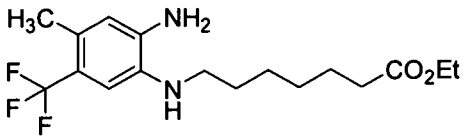
[0246] An N_2 flushed solution of ethyl 7-bromoheptanoate (1.3 mL, 6.7 mmol), 4-methyl-3-(trifluoromethyl)aniline (1.3 mL, 9.0 mmol), and DIPEA (2.0 mL, 11 mmol) is shaken at 70°C. After 18 h, the mixture is removed from heat, diluted with heptane (10ml) and is allowed to stand at room temperature for 5 days. The mixture is then filtered (5x10 mL heptane rinses). The heptane layer is washed with water (50 mL), stripped to dryness, and then chromatographed on silica gel using a gradient from heptane to 20% CH_2Cl_2/heptane. This provides desired product as a colorless oil (1.66 g, 75% yield). MS (ESI+) for $C_{17}H_{24}F_3NO_2$ *m/z* 332.15 $(M+H)^+$, retention time 6.44 min (System B).

Step 2 Preparation of Ethyl 7-{[4-methyl-2-nitro-5-(trifluoromethyl)phenyl]amino} heptanoate



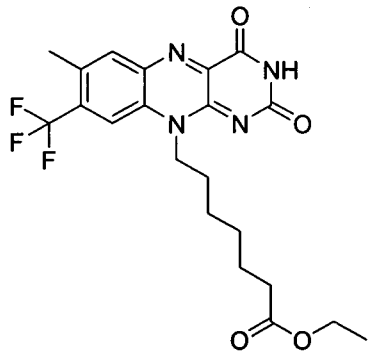
[0247] A well-stirred mixture of ethyl 7-{[4-methyl-3-(trifluoromethyl)phenyl]amino}-heptanoate (0.333 g, 1.00 mmol) and acetic acid (4 mL, 70 mmol) is cooled to 10-12 °C (internally monitored). To this mixture is added nitric acid (0.0936 mL, 2.01 mmol) dropwise followed by acetic anhydride (1.0 mL, 1.0E1 mmol) and the cooling bath is removed. After 72 h, the mixture is mixed with ice (5 mL), diluted with water (10 mL), saturated aqueous $NaHCO_3$(10 mL), and heptanes (30 mL). More saturated aqueous $NaHCO_3$ is added until the mixture is basic, then the organic layer is isolated, washed with water and concentrated *in vacuo* to a reddish oil. The residue is chromatographed on silica gel using 2% EtOAc/heptane to give the desired product as a red oil (0.080 g, 21% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (3 H, t), 1.36 - 1.53 (4 H, m), 1.60 - 1.81 (4 H, m), 2.32 (2 H, t), 2.38 (3 H, br s), 3.27 - 3.35 (2 H, m), 4.14 (2 H, q), 7.12 (1 H, s), 7.90 (1 H, br s), 8.08 (1 H, s). MS (ESI+) for $C_{17}H_{23}F_3N_2O_4$ *m/z* 377.0 $(M+H)^+$, retention time 7.87min (System B).

Step 3 Preparation of Ethyl 7-{[2amino-4-methyl-5-(trifluoromethyl)phenyl]amino} heptanoate



[0248] An N_2 flushed mixture of ethyl 7-{[4-methyl-2-nitro-5-(trifluoromethyl)phenyl]amino}-heptanoate (73 mg, 0.19 mmol) and Raney nickel (0.03 mL in H_2O) in EtOH (2mL) is stirred under an H_2 balloon. After overnight stirring, additional Raney nickel(0.03 mL in H_2O) is added and stirring under H_2 is continued. After 72h, the mixture is filtered through a 1cm silica gel column (1mL EtOH rinse), fresh Raney nickel (0.03 mL in H_2O) is added and stirring under H_2 is resumed. After 2 hr, the reaction mixture is filtered and stripped to provide the desired product as an oil (65 mg, 83% yield). MS (ESI+) for $C_{17}H_{25}F_3N_2O_2$ *m/z* 347.1 $(M+H)^+$, retention time 5.65 min (System B).

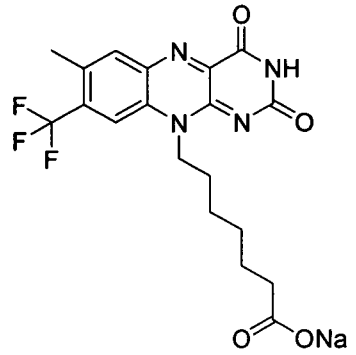
Step 4 Preparation of Ethyl 7-[7-methyl-2,4-dioxo-8-(trifluoromethyl)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate



[0249] An N_2 flushed mixture of ethyl 7-{[2-amino-4-methyl-5-(trifluoromethyl)phenyl]-amino}heptanoate (62 mg, 0.12 mmol), alloxan monohydrate (0.015 g, 0.094 mmol) and boric acid (0.03 g, 0.5 mmol) in acetic acid (1.5mL) is stirred at rt. After 18h, additional boric acid (0.03 g, 0.5 mmol) is added and stirring is continued. After another 18h, additional alloxan monohydrate (0.020 g, 0.12 mmol) is added and the mixture is heated to 50 °C for 24h. The mixture is concentrated and chromatographed on silica gel using a gradient from 20 to 50% EtOAc/DCM. This provided 70 mg of a semi-purified solid that is subjected to preparative silica gel chromatography (divided onto two 0.1mm prep silica gel plates and elution with 5% EtOH/DCM). This provides 14 mg (17 %) of the desired product as a yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.16 (3 H, t), 1.29 - 1.48 (4 H, m), 1.49 - 1.58 (2 H, m), 1.63 - 1.76 (2 H, m), 2.18 - 2.36 (2 H, m),

2.59 (3 H, s), 3.94 - 4.10 (2 H, m), 4.62 (2 H, br s), 8.06 (1 H, s), 8.22 (1 H, s), 11.49 (1 H, br s). MS (ESI-) for $C_{21}H_{23}F_3N_4O_4$ *m/z* 451.1 $(M-H)^-$, retention time: 5.83min (System B).

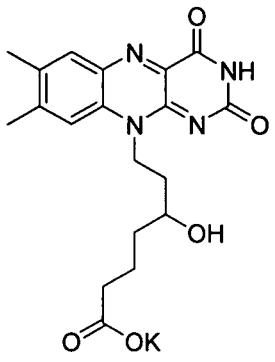
Step 5 Preparation of Sodium 7-[7-methyl-2,4-dioxo-8-(trifluoromethyl)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate



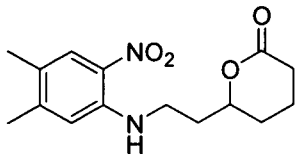
[0250] To a solution of ethyl 7-[7-methyl-2,4-dioxo-8-(trifluoromethyl)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl]heptanoate (13.5 mg, 0.0239 mmol) in THF(0.5 mL) is added 12 M aqueous HCl (0.010 mL, 0.12 mmol). After 4 days, additional 12 M aqueous HCl (0.002 mL, 0.02 mmol) is added. After 5 days, the mixture is cooled in ice, diluted with 1/2 mL of ice and brought to pH 8-9 with aqueous $NaHCO_3$ at which point two layers formed. The layers are separated and the aqueous layer is washed with EtOAc (4x1 mL) and purified on reverse phase silica (C18, elution with water then methanol). Concentration provides the desired product as an orange solid (6 mg, 47%). ^1H NMR (400 MHz, DMSO-d_6) δ 1.18 - 1.47 (7 H, m), 1.65 (2 H, br s), 1.76 - 1.88 (2 H, m), 2.55 (3 H, br s), 4.51 (2 H, br s), 7.92 (1 H, br s), 8.10 (1 H, br s). MS (ESI-) for $C_{19}H_{18}F_3N_4NaO_4$ *m/z* 423.0 $(M-H)^-$, retention time 4.92min (System B).

Example 64:

Potassium 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-5-hydroxyheptanoate

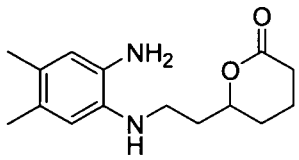


Step 1 Preparation of 6-{2-[(4,5-Dimethyl-2-nitrophenyl)amino]ethyl}tetrahydro-2H-pyran-2-one



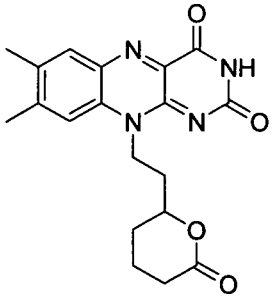
[0251] A mixture of 4,5-dimethyl-2-nitroaniline (0.16 g, 0.97 mmol), 6-(2-bromoethyl)-tetrahydro-2H-pyran-2-one (0.167 g, 0.806 mmol) [Molander, G.A.; McKie, J.A. *J. Org. Chem.* **1993** *58*, 7216], and DIPEA (3 mL, 20 mmol) in a capped vial is shaken at 120 °C. After 6 h 40 minutes, the reaction mixture is cooled, concentrated and chromatographed on silica gel (DCM followed by 0.3% MeOH/DCM) giving desired product as an orange/red solid (0.110 g , 46% yield). MS (ESI+) for $C_{15}H_{20}N_2O_4$ *m/z* 293.3 $(M+H)^+$, retention time 5.99 min (System B).

Step 2 Preparation of 6-{2-[(2-Amino-4,5-dimethylphenyl)amino]ethyl}tetrahydro-2H-pyran-2-one



[0252] An N_2 flushed mixture of 6-{2-[(4,5-dimethyl-2-nitrophenyl)amino]ethyl}tetrahydro-2H-pyran-2-one (0.108 g, 0.369 mmol) and Raney nickel(0.03 mL in H_2O) in EtOH (30 mL) is stirred under H_2 (balloon). After 18 h, additional Raney nickel (0.03 mL in H_2O) is added and stirring under H_2 is continued. After 3 ch, the reaction mixture is filtered and concentrated to an oil (95 mg, 98%). MS (ESI+) for $C_{15}H_{22}N_2O_2$ *m/z* 263.16 $(M+H)^+$, retention time 4.11min (System B).

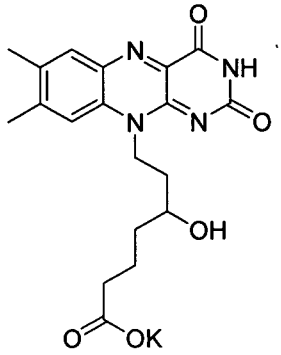
Step 3 Preparation of 7,8-Dimethyl-10-[2-(6-oxotetrahydro-2H-pyran-2-yl)ethyl]benzo[g]pteridine-2,4(3H,10H)-dione



[0253] An N_2 flushed mixture of 6-{2-[(2-amino-4,5-dimethylphenyl)amino]ethyl}tetrahydro-2H-pyran-2-one (0.120 g, 0.274 mmol), alloxan

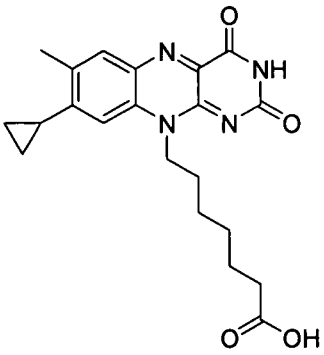
monohydrate (0.066 g, 0.41 mmol) and boric acid (0.1 g, 2 mmol) in acetic acid (3mL) is stirred at room temperature. After 18h, additional alloxan monohydrate (0.0330 g, 0.206 mmol) is added. After 2days, the reaction mixture is concentrated to a dark red solid. The solid is suspended in water (5 mL) and extracted with DCM (3x3 mL). The combined organic layers are stripped to dryness, mixed with THF (5mL) and filtered (2x1 mL THF washes). The filtered solid is washed with MeOH (3x2mL) and dried under high vacuum overnight to give a yellow-orange solid (11 mg, 31% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.50 - 1.64 (1 H, m), 1.92 - 2.10 (3 H, m), 2.40 (3 H, s), 4.46 - 4.84 (3 H, m), 7.78 (1 H, s), 7.92 (1 H, s), 11.32 (1 H, br s). MS (ESI-) for $C_{19}H_{20}N_4O_4$ *m/z* 367.0 $(M-H)^-$, retention time: 4.14 min (System B).

Step 4 Preparation of Potassium 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-5-hydroxyheptanoate

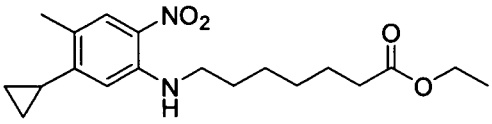


[0254] A mixture of 7,8-dimethyl-10-[2-(6-oxotetrahydro-2H-pyran-2-yl)ethyl]benzo[g]pteridine-2,4(3H,10H)-dione (6 mg, 0.01 mmol) and potassium hydroxide (1.2 mg, 0.018 mmol) in water (1.2mL) is stirred at room temperature for 1 h. The orange solution is transferred (in water) to a 0.5 g C18 reverse phase silica gel column and eluted with water (5 mL fractions being collected). The product containing fractions are combined and concentrated to give desired product as an orange solid (6.0 mg, 86%). ^{1}H NMR (400 MHz, D_2O) δ 1.38 - 2.03 (7 H, m), 2.34 - 2.37 (8 H, m), 2.48 (3 H, s), 3.76 (1 H, br s), 7.61 (1 H, br s), 7.66 (1 H, s). MS (ESI+) for $C_{19}H_{21}KN_4O_5$ *m/z* 424.88 $(M)^+$, retention time: 3.87 min (System B).

Example 65: 7-(8-Cyclopropyl-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)]heptanoic acid

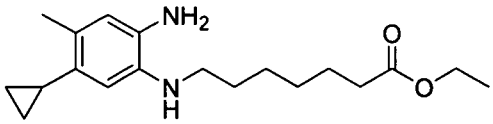


Step 1 Preparation of Ethyl 7-[(5-cyclopropyl-4-methyl-2-nitrophenyl)amino]-heptanoate



[0255] A mixture of ethyl 7-[(5-chloro-4-methyl-2-nitrophenyl)amino] heptanoate (218 mg, 0.636 mmol), cyclopropylboronic acid) (81.9 mg, 0.954 mmol), [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane (1:1) (31 mg, 0.038 mmol), and cesium carbonate (622 mg, 1.91 mmol) in N,N-dimethylacetamide (4.38 mL), rapidly stirred under nitrogen, is placed into a preheated 150 °C bath for 15 minutes. The reaction is allowed to cool to room temperature, stir open to air for 24 hours, and is then partitioned between aqueous sodium bicarbonate and DCM. The organic layer is washed with aqueous sodium bicarbonate then brine and is dried with anhydrous sodium sulfate. After concentration, the residue is subjected to flash chromatography on a 40 x95 mm silica gel column (Silicycle, 230-400 mesh, elution with 75% DCM/ hexanes) to give 85.2 mg of desired product as orange oil. MS (ESI+) for $C_{19}H_{28}N_2O_4$ m/z 349.2 (M+H)+, retention time: 5.62 min (System D).

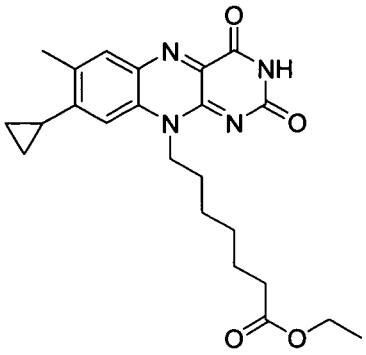
Step 2 Preparation of Ethyl 7-[(2-amino-5-cyclopropyl-4-methylphenyl)amino]-heptanoate



[0256] A well-stirred mixture of Raney nickel (50 mg, 0.85 mmol) and ethyl 7-[(5-cyclopropyl-4-methyl-2-nitrophenyl)amino]heptanoate (99 mg, 0.28 mmol) in ethanol (6 mL) is alternately evacuated then covered with 1 atmosphere of hydrogen (3x) (balloon). After an hour at room temperature, the mixture is filtered through Celite® and

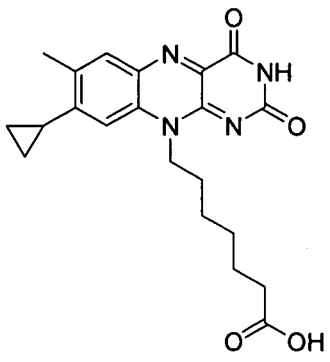
concentrated to give 90 mg (98%) as an oil. MS (ESI+) for $C_{19}H_{30}N_2O_2$ m/z 319.3 (M+H)+, retention time: 3.60 min (System D).

Step 3 Preparation of Ethyl 7-(8-cyclopropyl-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)]heptanoate



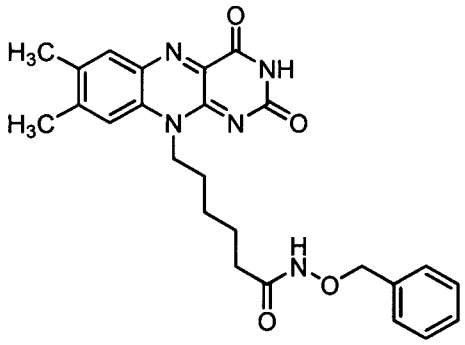
[0257] Ethyl 7-[(2-amino-5-cyclopropyl-4-methylphenyl)amino]heptan-oate (90 mg, 0.28 mmol) is dissolved in acetic acid (5 mL) and concentrated to dryness. The residue is dissolved in acetic acid (3 mL), and boric acid (87.8 mg, 1.42 mmol) is added followed by alloxan monohydrate (50.0 mg, 0.312 mmol). The flask is wrapped in aluminum foil and the solution is stirred at room temperature under nitrogen for 3 hours. The reaction is concentrated *in vacuo* and the residue is flash chromatographed on a C 18 reverse phase silica gel column eluted with acetonitrile/ water. This provided a mixture that is concentrated and flash chromatographed on a 28 x75 mm silica gel column (Silicycle, 230-400 mesh, elution with 50% and 80% ethyl acetate/ DCM) to give 68 mg (56%) of product as yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (m, 2 H), 1.28 (m, 5 H), 1.46 (m, 2 H), 1.56 (m, 2 H), 1.69 (m, 2 H), 1.88 (m, 2 H), 2.18 (m, 1 H), 2.35 (t, 2 H), 2.62 (s, 3 H), 4.15 (m, 2 H), 4.71 (br s, 2 H), 7.15 (s, 1 H), 8.09 (s, 1 H), 8.43 (s, 1 H). MS (ESI+) for $C_{24}H_{29}N_4O_4$ m/z 425.2 (M+H)+, retention time: 3.70 min (System D).

Step 4 Preparation of 7-(8-Cyclopropyl-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)]heptanoic acid



[0258] 7-(8-Cyclopropyl-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)]heptanoate (4) (45.0 mg, 0.106 mmol) is suspended in THF (3.0 mL) with rapid stirring. Lithium hydroxide (aqueous 1.0M, 1.06 mL) is added at room temperature, and after 1 hour the reaction is quenched with acetic acid (0.060 mL, 1.06 mmol). The mixture is concentrated *in vacuo* and re-suspended in water. The solid is collected by filtration, washed with water, and dried under vacuum to give 34.0 mg of desired product as yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.94 (m, 2 H), 1.15 (m, 2 H), 1.37 (m, 2 H), 1.44 (m, 2 H), 1.52 (m, 2 H), 1.68 (m, 2 H), 2.21 (m, 3 H), 2.55 (s, 3 H), 4.62 (m, 2 H), 7.23 (s, 1 H), 7.92 (s, 1 H), 11.3 (s, 1 H), 12.0 (s, 1 H). MS (ESI+) for $C_{21}H_{24}N_4O_4$ m/z 397.1 (M+H)+, retention time: 3.10 min (System D).

Example 66 N-(Benzyloxy)-6-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexanamide

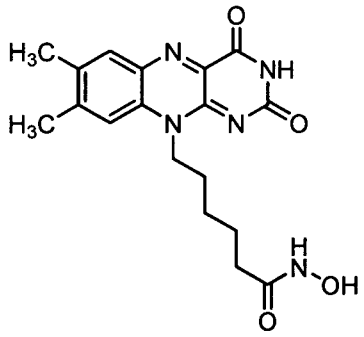


[0259] To a stirred suspension of 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexanoic acid (80 mg, 0.16 mmol) (prepared using the synthesis of steps 1-3 of Example 25) in DCM (1 mL), at 0 °C under argon, thionyl chloride (2 mL) is added. The reaction mixture is stirred for 10 min, warmed to room temperature, and stirred for 30 min at room temperature. The reaction mixture is concentrated under vacuo. The residue is dissolved in DCM (5 mL) and TEA (0.5 mL). DMAP (5 mg) and O-benzylhydroxylamine hydrochloride (107 mg, 0.67 mmol) is added under argon. The reaction mixture is stirred at rt overnight. The reaction mixture is concentrated under vacuo and purified by silica gel column chromatography using 0 to 10% MeOH in DCM as eluent. N-(benzyloxy)-6-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexanamide (71mg, 69%) is obtained as a yellow solid after concentrating the desired fractions under vacuo. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.66 (m, 2H), 1.90 (m, 4H), 2.34 (m, 2H), 2.49 (s, 3H), 2.61 (s, 3H), 4.60 (m, 2H), 5.0 (s, 2H),

5.42 (s, 1H), 7.34 (m, 2H), 7.45 (m, 3H), 8.11 (s, 1H), 8.51 (s, 1H), 10.00 (s, 1H). LC-MS m/z 462.1 $[M+H]^+$, retention time 4.33 min.

Example 67

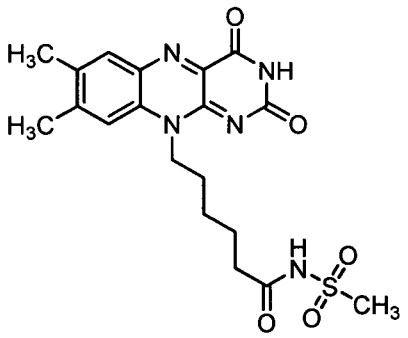
6-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-N-hydroxyhexanamide



[0260] N-(benzyloxy)-6-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl) hexanamide (52 mg, 0.11mmol) (Example above) is dissolved in methanol (5 mL), purged with argon for 10 min. Palladium on carbon (10%, 20 mg) is added, followed by hydrogen (via balloon). The reaction mixture is stirred under hydrogen at rt overnight. The reaction mixture is filtered through celite and the celite is washed with methanol (10 mL). The filtrate is concentrated under vacuo to obtain crude 6-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-N-hydroxyhexanamide (48 mg). The residue is purified by preparative TLC using 10% methanol in DCM as eluent to afford desired 6-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-N-hydroxyhexanamide (12.0 mg, 30%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 1.63 (m, 2H), 1.77 (m, 2H), 1.92 (m, 2H), 2.21 (t, 2H), 2.49 (s, 3H), 2.61 (s, 3H), 4.73 (t, 2H), 7.76 (s, 1H), 7.94 (s, 1H). LC-MS m/z 372.0 $[M+H]^+$, retention time 3.56 min.

Example 68

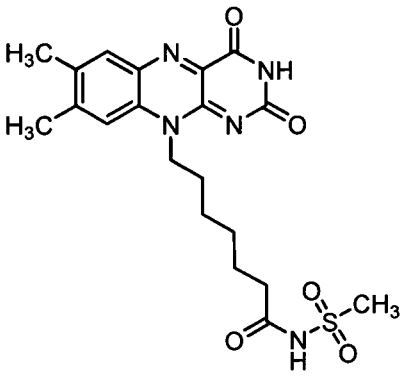
7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-N-(methyl sulfonyl)hexanamide



[0261] To a stirred suspension of 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexanoic acid (prepared using the synthesis of steps 1-3 of Example 25) (57 mg, 0.16 mmol) in DCM (1 mL), at 0 °C under argon, thionyl chloride (2 mL) is added. The reaction mixture is stirred, warmed to room temperature, and stirred for 30 min at room temperature. The reaction mixture is concentrated under vacuo. In the meantime, to a stirred solution of methanesulfonamide (23 mg, 0.24 mmol) in anhydrous THF (5 mL) is added sodium hydride (5 mg, 0.32 mmol) under argon. The reaction mixture is stirred at rt for 30 min and then transferred to the acid chloride prepared earlier. The reaction mixture is stirred at rt overnight. The reaction mixture is concentrated under vacuum and purified by preparative HPLC (Method 2). Lyophilization of the combined desired fractions affords 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-N-(methylsulfonyl)hexanamide (7.4 mg, 11%) as a yellow solid. ^{1}H NMR (400 MHz, MeOH-d_4) δ 1.53 (m, 2H), 1.68 (m, 2H), 1.85 (m, 2H), 2.16 (t, 2H), 2.44 (s, 3H), 2.57 (s, 3H), 2.92 (s, 3H), 4.71 (t, 2H), 7.75 (s, 1H), 7.92 (s, 1H). LC-MS m/z 434.1 $[M+H]^+$, retention time 2.48 min.

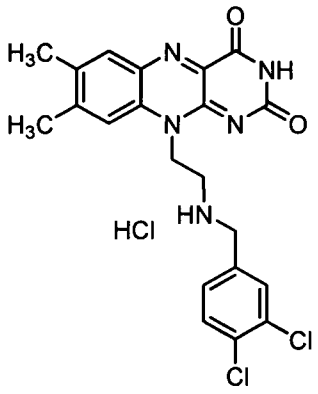
Example 69

7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-N-(methylsulfonyl)heptanamide

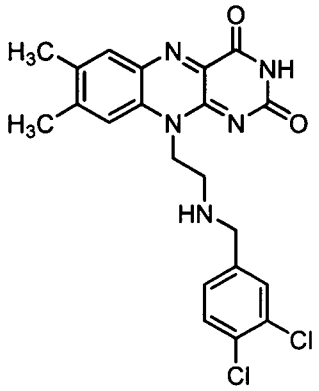


[0262] A mixture of 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (52 mg, 0.14 mmol) (prepared using the synthesis of step 3 of Example 25), HATU (70 mg, 0.18 mmol), DIPEA (0.1, 0.57 mmol), and methanesulfonamide (40 mg, 0.42 mmol) in anhydrous DMF (5 mL) are stirred at 25 °C for 3 h. The reaction mixture is concentrated under vacuum and purified by preparative HPLC (Method 2). Lyophilization of the combined desired fractions affords desired product (6.5 mg, 11%) as a yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.32 (m, 2H), 1.47 (m, 4H), 1.71 (m, 2H), 2.05 (t, 2H), 2.40 (s, 3H), 2.53 (s, 3H), 2.80 (s, 3H), 4.56 (t, 2H), 7.82 (s, 1H), 7.90 (s, 1H), 11.28 (s, 1H). LC-MS m/z 447.9 $[M+H]^+$, retention time 4.02 min.

Example 70
10-(2-(3,4-Dichlorobenzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione hydrochloride

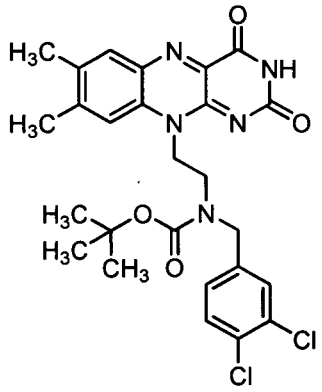


Step 1 Preparation of 10-(2-(3,4-Dichlorobenzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione



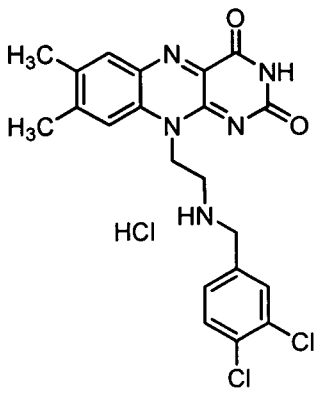
[0263] To a solution of (7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (Example 14) (44 mg, 0.176 mmol) in ethanol (5 mL) are added (3,4-dichlorophenyl)methanamine (0.1 ml, 0.75 mmol) and AcOH (0.1 ml) at room temperature. The reaction is stirred at 40 °C for 60 min. The reaction mixture is cooled to room temperature and sodium cyanoborohydride (28 mg, 0.44 mmol) is added and the reaction mixture is stirred at rt for 2 h. The solvent is removed under vacuum and the crude is used in the following step without further purification.

Step 2 Preparation of *tert*-Butyl 3,4-dichlorobenzyl(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)carbamate



[0264] Into a suspension of 10-(2-(3,4-dichlorobenzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione in MeOH (5 mL) is added di-*tert*-butyl dicarbonate (150 mg, 0.69 mmol), and triethylamine (0.1 mL, 0.72 mmol) and the mixture is stirred at room temperature for 16 h. The solvent is removed under vacuum and the crude is purified by preparative TLC (5% MeOH in DCM) to afford desired product (54 mg) as a yellow solid (63% over three steps). LC-MS m/z 543.9 $[M+H]^+$, retention time 6.12 min.

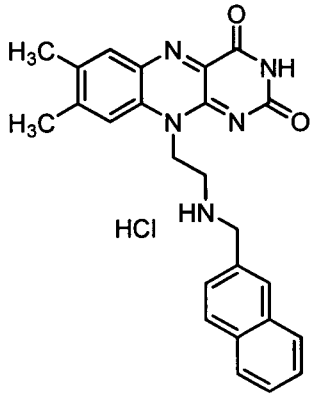
Step 3 Preparation of 10-(2-(3,4-Dichlorobenzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione hydrochloride



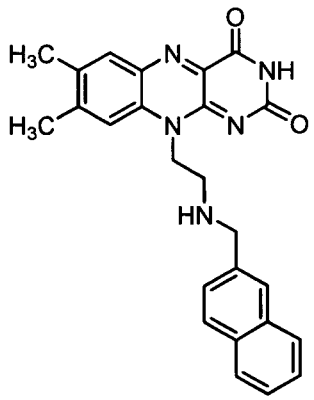
[0265] To *tert*-butyl 3,4-dichlorobenzyl(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)carbamate (54 mg) is added 4 N HCl in dioxane (1 ml) and the mixture is stirred for 2 h at rt. The reaction is monitored by LCMS (Method C). Once the reaction is complete, Et_2O (3 ml) is added and the solid is collected by filtration. The desired product (15.5 mg) is isolated as an HCl salt (Yield: 33%). ^1H NMR (400 MHz, DMSO-$_{d6}$) δ 2.42 (s, 3H), 2.55 (s, 3H), 3.17 (s, 2H), 4.35 (s, 2H), 4.99 (s, 2H), 7.61 (d, 1H), 7.72 (d, 1H), 7.91 (m, 1H), 7.95 (s, 1H), 8.08 (dd, 1H), 9.55 (s, 2H), 11.46 (s, 1H). LC-MS m/z 443.9 $[(M-HCl)+H]^+$, retention time 4.41 min.

Example 71

7,8-Dimethyl-10-(2-(naphthalen-2-ylmethylamino)ethyl)benzo[g]pteridine-2,4(3H,10H)-dione hydrochloride

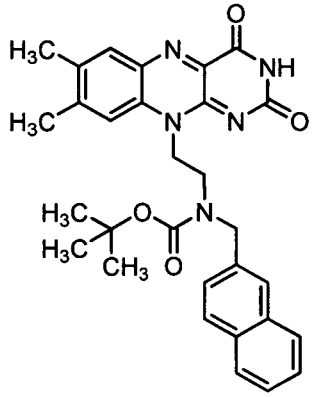


Step 1 Preparation of 7,8-Dimethyl-10-(2-(naphthalen-2-ylmethylamino)ethyl)benzo[g]pteridine-2,4(3H,10H)-dione



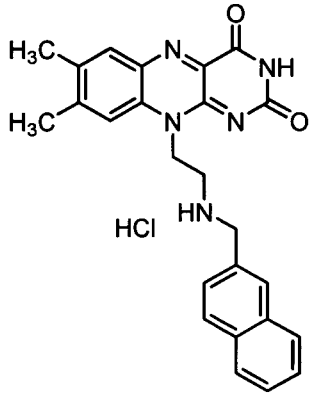
[0266] The preparation of this compound is similar to that of Example 70 using 10-(2-aminoethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (Example 40) and 2-naphthaldehyde.

Step 2 Preparation of 7 *tert*-Butyl 2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl(naphthalen-2-ylmethyl)carbamate



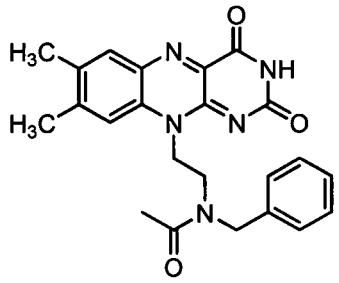
[0267] The preparation of this compound is similar to that of Example 70, Step 2.

Step 3 Preparation of 7,8-Dimethyl-10-(2-(naphthalen-2-ylmethylamino)ethyl)benzo[g]pteridine-2,4(3H,10H)-dione hydrochloride



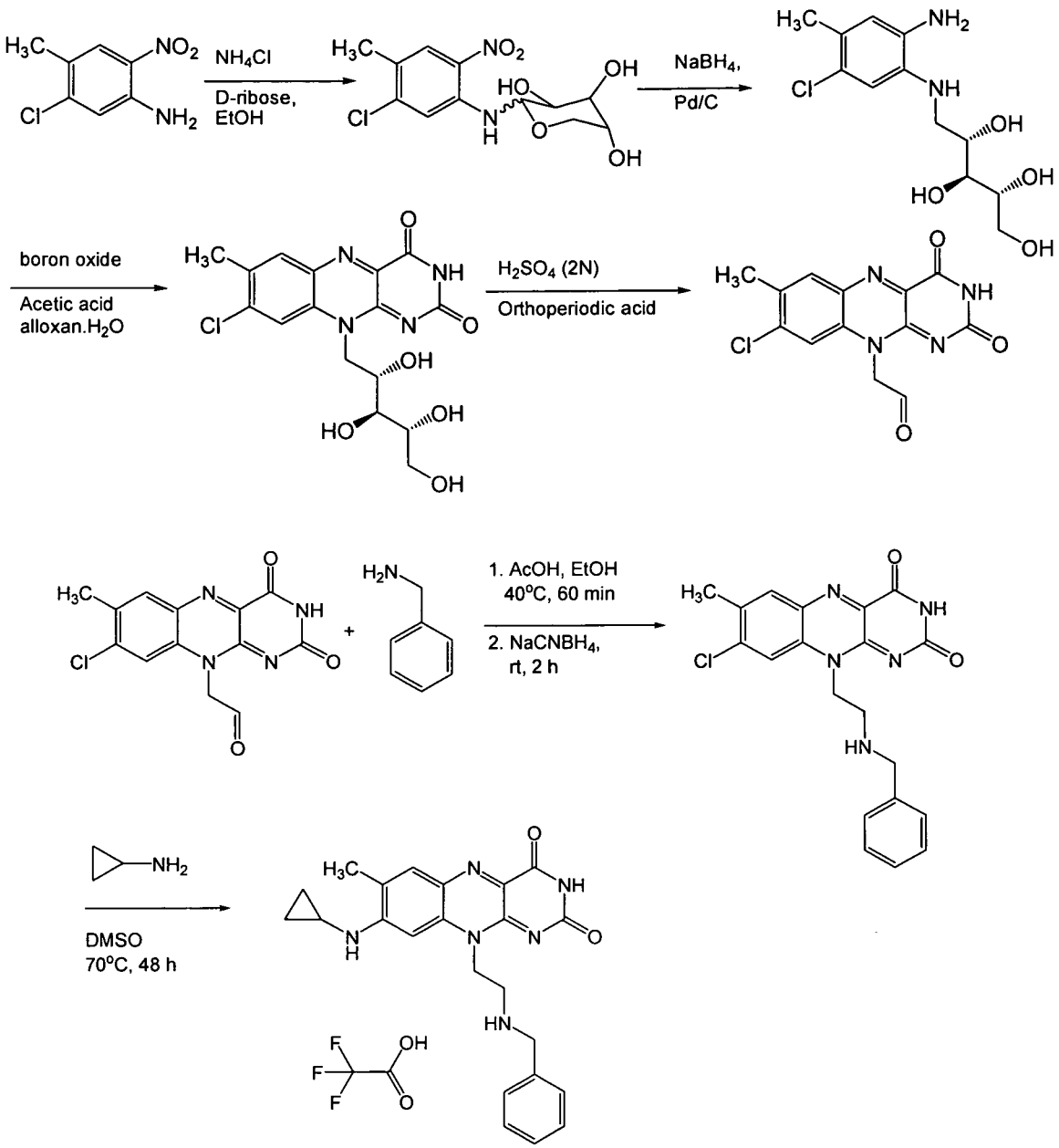
[0268] The preparation of this compound is similar to that of Example 70, Step 3. ^{1}H NMR (400 MHz, DMSO-$_{d6}$) δ 2.41 (s, 3H), 2.54 (s, 3H), 3.40 (s, 2H), 4.48 (s, 2H), 5.05 (s, 2H), 7.55-7.60 (m, 2H), 7.75 (d, 1H), 7.88-8.10 (m, 4H), 8.13 (m, 1H), 8.18 (s, 1H), 9.76 (s, 2H), 11.46 (s, 1H). LC-MS m/z 426.0 $[(M-HCl)+H]^+$, retention time 3.87 min.

Example 72
N-Benzyl-N-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)acetamide



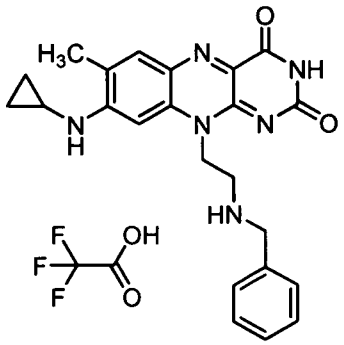
[0269] To a solution of 10-(2-(benzylamino)ethyl)-7,8-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (314 mg, 0.83 mmol) (Example 55) in DCM (10 ml) is added DIPEA (0.45 ml, 2.5 mmol) and acetic anhydride (0.15 ml, 1.58 mmol). The mixture is stirred at rt for 10 min. Solvent is concentrated under reduced pressure to obtain a crude product (147 mg). Crude product (31 mg) is dissolved in MeOH (8 ml) and purified by preparative HPLC (Method 2). Lyophilization of the combined desired fractions affords desired product (13.2 mg, 18% overall yield) as a yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.95 (s) and 2.22 (s) (rotamers, total of 3H), 2.40 (s) and 2.41 (s) (rotamers, total of 3H), 2.50 (s, 3H), 3.54 (t) and 3.66 (t) (rotamers, total of 2H), 4.55 (s) and 4.70 (s) (rotamers, total of 2H), 4.74 (s, 2H), 7.00-7.40 (m, 5H), 7.65 (s) and 7.85 (s) (rotamers, total of 1H), 7.89 (s, 1H), 11.34 (s) and 11.39 (s) (rotamers, total of 1H). LC-MS m/z 417.9 $[M+H]^+$, retention time 4.56 min.

Scheme 19:

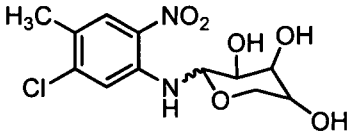


Example 73

10-(2-(Benzylamino)ethyl)-8-(cyclopropylamino)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione 2,2,2-trifluoroacetate

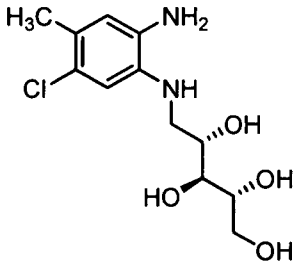


Step 1 Preparation of 2-(5-Chloro-4-methyl-2-nitro-phenylamino)-tetrahydro-pyran-3,4,5-triol



[0270] A solution of 5-chloro-4-methyl-2-nitro-phenylamine (19.8 g, 0.1 mol), ammonium chloride (0.1 g), and D-ribose (15.9 g, 0.1 mol) in EtOH (200 mL) is refluxed and stirred over night. The reaction mixture is concentrated under reduced pressure and resuspended in DCM:MeOH (1:1) and the precipitated unreacted staring material is removed by filtration. The mother liquor is dry loaded on silica gel using DCM:MeOH (1:1) and ISCO flash column chromatography is performed. 100% DCM is used until the first peak elutes, then 20% MeOH/DCM is used to elute the 11.5 g of orange product as a sticky solid (Yield: 40%) and 9.58 g of unreacted starting material is recovered. LC-MS m/z 318.7 [M+H], retention time 2.83 min. The product is used in the next step without further purification.

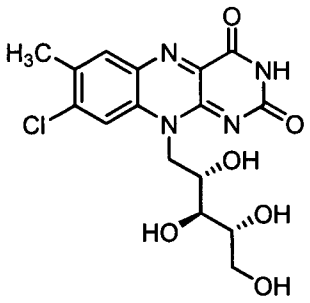
Step 2 Preparation of 5-(5-Chloro-4-methyl-2-amino-phenylamino)-pentane-1,2,3,4-tetraol



[0271] To a solution of 2-(5-chloro-4-methyl-2-nitro-phenylamino)-tetrahydro-pyran-3,4,5-triol (6.87 g, 0.02 mol) in EtOH (125 mL) is added sodium borohydride (1.65 g, 0.043 mol) portionwise such that evolution of gas is controlled to not overflow the contents of the flask. The resulting mixture is heated at reflux for 4 h. The reaction

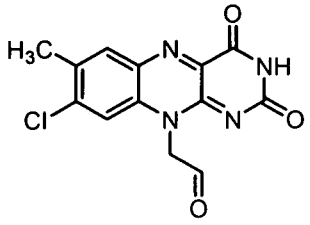
mixture is then cooled to 0 °C at which point Pd/C (300 mg) is added along with additional sodium borohydride (1.65 g, 0.043 mol). The reaction mixture is then allowed to stir at room temperature for 2 h. The reaction is complete when it is observed that the reaction has become colourless. The reaction mixture is filtered through celite and washed liberally with MeOH, and finally concentrated to obtain the crude product, (as a clear purple oil) to be used directly in the next step. LC-MS: m/z 290.9 [M+H], retention time 1.38 min.

Step 3 Preparation of 8-Chloro-7-methyl-10-(2,3,4,5-tetrahydroxy-pentyl)-10H-benzo[g]pteridine-2,4-dione



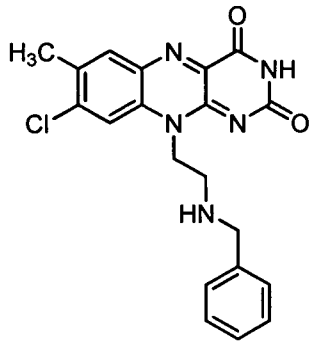
[0272] Crude 5-(2-amino-5-chloro-4-methyl-phenylamino)-pentane-1,2,3,4-tetraol (0.022 mol) is dissolved in glacial acetic acid (80 mL), covered in foil, and stirred at room temperature. At which point, the flask is purged with argon for 20 min, and alloxan monohydrate (3.45g, 0.022 mol), boron trioxide (1.35 g, 0.022 mol) are added to the stirring solution. The reaction is maintained under an argon atmosphere and left to react at room temperature for 3 h and a yellow precipitate is observed in solution. The solution is concentrated under reduced pressure and the residue is dissolved in water (300 mL), put in an ice bath, and the precipitate formed in solution is filtered. The resulting filtrate is purified by preparatory HPLC in 10 mL segments (30 injections) using Method 1. 8-Chloro-7-methyl-10-(2,3,4,5-tetrahydroxy-pentyl)-10H-benzo[g]pteridine-2,4-dione (455 mg) is isolated following lyophilization of the appropriate fractions (Yield: 5.3%). LC-MS m/z 397.1 [M+H], retention time 1.58 min. ^{1}H NMR (400 MHz, DMSO-d6) δ 2.51 (s, 3 H), 3.46 (m, 1 H), 3.64 (m, 2 H), 4.23 (m, 1 H), 4.49 (m, 1 H), 4.67 (m, 1 H), 4.78 (m, 2 H), 4.88 (m, 1 H), 5.15 (m, 2 H), 8.13 (s, 1 H), 8.20 (s, 1 H), 11.47 (s, 1 H).

Step 4 Preparation of (8-Chloro-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde



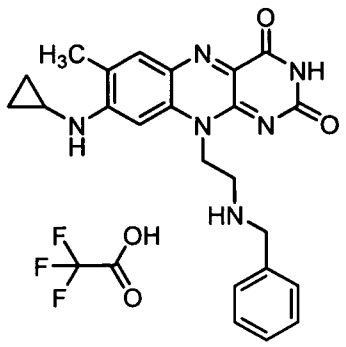
[0273] To a cooled suspension (0 °C) of 8-chloro-7-methyl-10-(2,3,4,5-tetrahydroxy-pentyl)-10H-benzo[g]pteridine-2,4-dione (0.235 g, 0.0006 mol) in 2 N aqueous sulfuric acid (60 mL), (in a flask covered with foil), is added (dropwise) orthoperiodic acid (0.41 g, 0.0018 mol), which is dissolved in water (25 mL). After 30 min, the reaction is allowed to warm to rt and is stirred until it becomes a clear, yellow solution. The pH of the reaction solution is then adjusted carefully to 3.8-3.9 (using a pH meter) by addition of solid sodium carbonate [it is extremely important that the pH is monitored carefully, otherwise going over a pH of 3.9 does not allow for the product to precipitate out of solution]. The precipitate is then filtered off and washed liberally with cold water, ethanol, and diethyl ether to yield 0.089 g of the desired product as an orange solid (Yield: 49%). LC-MS m/z 305.1 [M+H] retention time: 1.69 min.

Step 5 Preparation of 10-(2-(Benzylamino)ethyl)-8-chloro-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione



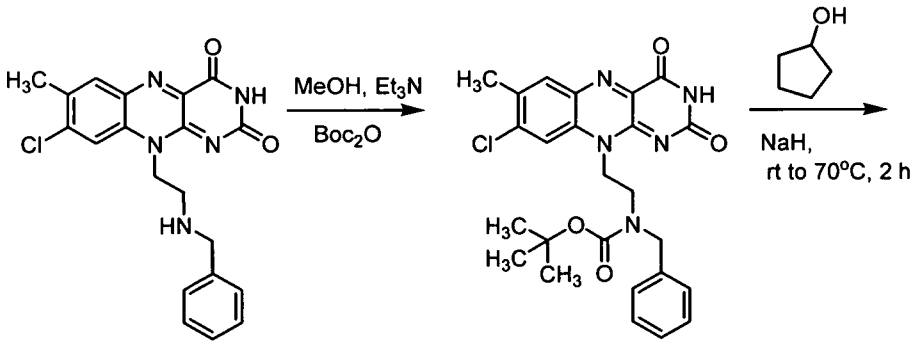
[0274] To a solution of (2-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)acetaldehyde (157 mg, 0.51 mmol) in ethanol (5 mL) is added phenylmethanamine (0.3 ml, 2.75 mmol) and AcOH (0.3 ml) at room temperature. The reaction is stirred at 40 °C for 60 min. The reaction is cooled to room temperature and sodium cyanoborohydride (95 mg, 1.53 mmol) is added and the reaction mixture is stirred at rt for 2 h. The solvent is removed under vacuum and the crudem material (166 mg) is used in the following step without further purification.

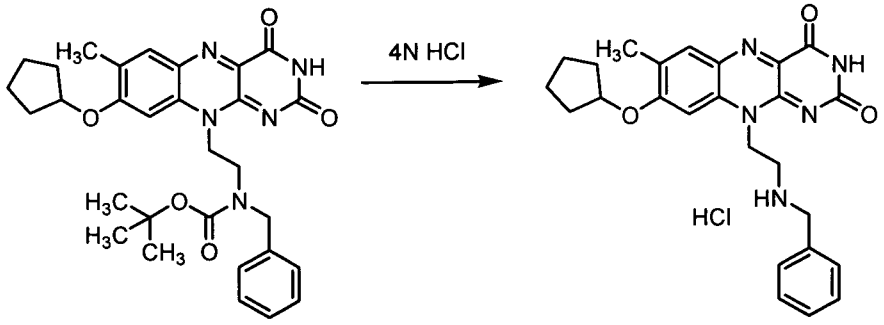
Step 6 Preparation of 10-(2-(Benzylamino)ethyl)-8-(cyclopropylamino)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione 2,2,2-trifluoroacetate



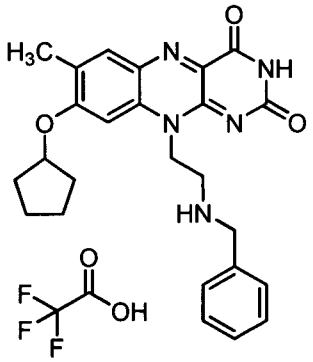
[0275] 10-(2-(Benzylamino)ethyl)-8-chloro-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione (27 mg, 0.68 mmol) is dissolved in DMSO (4 mL) and then cyclopropylamine (73 mg, 1.28 mmol) is added. The reaction is stirred at 70 °C for 48 h. The reaction mixture is concentrated under vacuum and purified using preparative HPLC (Method 3). 10-(2-(benzylamino)ethyl)-8-(cyclopropylamino)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione (2.21 mg) is isolated following lyophilization of the appropriate fractions (Yield: 9%). ^{1}H NMR (400 MHz, CD_3OD) δ 0.83 (m, 2 H), 1.10 (m, 2 H), 2.21 (s, 3 H), 2.82 (m, 1 H), 3.89 (s, 2 H), 4.48 (s, 2 H), 5.11 (s, 2 H), 6.90 (s, 1 H), 7.01 (s, 1 H), 7.43 (m, 3 H), 7.55 (m, 2 H). LC-MS m/z 417.0 $[(M\text{-}TFA)+H]^+$, retention time 3.51 min.

Scheme 20:

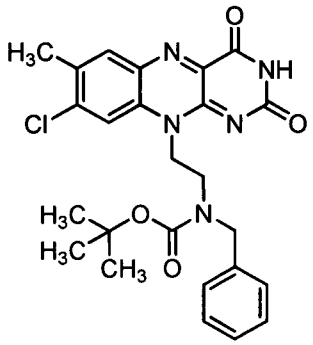




Example 74
10-(2-(benzylamino)ethyl)-8-(cyclopentyloxy)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione



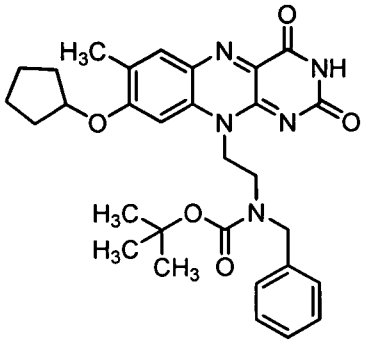
Step 1 Preparation of *tert*-Butyl benzyl(2-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)carbamate



[0276] To a solution of crude 10-(2-(benzylamino)ethyl)-8-chloro-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione (Step 5, Example 73) (84 mg, 0.28 mmol) in MeOH (200 mL) is added di-*tert*-butyl dicarbonate (200 mg, 0.96 mmol) and Et_3N (0.1 mL). The mixture is stirred for 2 h at rt. The reaction is concentrated under reduced pressure and purified via silica gel chromatography (ISCO) (100% DCM to 10%

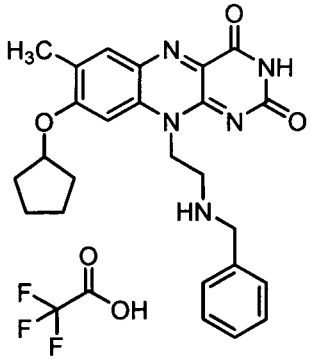
MeOH/DCM) over 1 h to obtain the desired product (45 mg, 43%) as a solid. LC-MS m/z 495.9 $[M+H]^+$, retention time 5.19 min.

Step 2 Preparation of *tert*-Butyl benzyl(2-(8-(cyclopentyloxy)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)carbamate



[0277] To a solution of NaH (26 mg, 0.65 mmol) in cyclopentanol (3 ml) is added *tert*-butyl benzyl(2-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)carbamate (43 mg, 0.086 mmol) in cyclopentanol (1 mL). The reaction is stirred at 70°C for 2 h. The reaction is concentrated under reduced pressure and purified via preparative TLC (5% MeOH in DCM) to afford the desired product (12 mg, 26%) as a solid. LC-MS m/z 545.9 $[M+H]^+$, retention time 5.97 min.

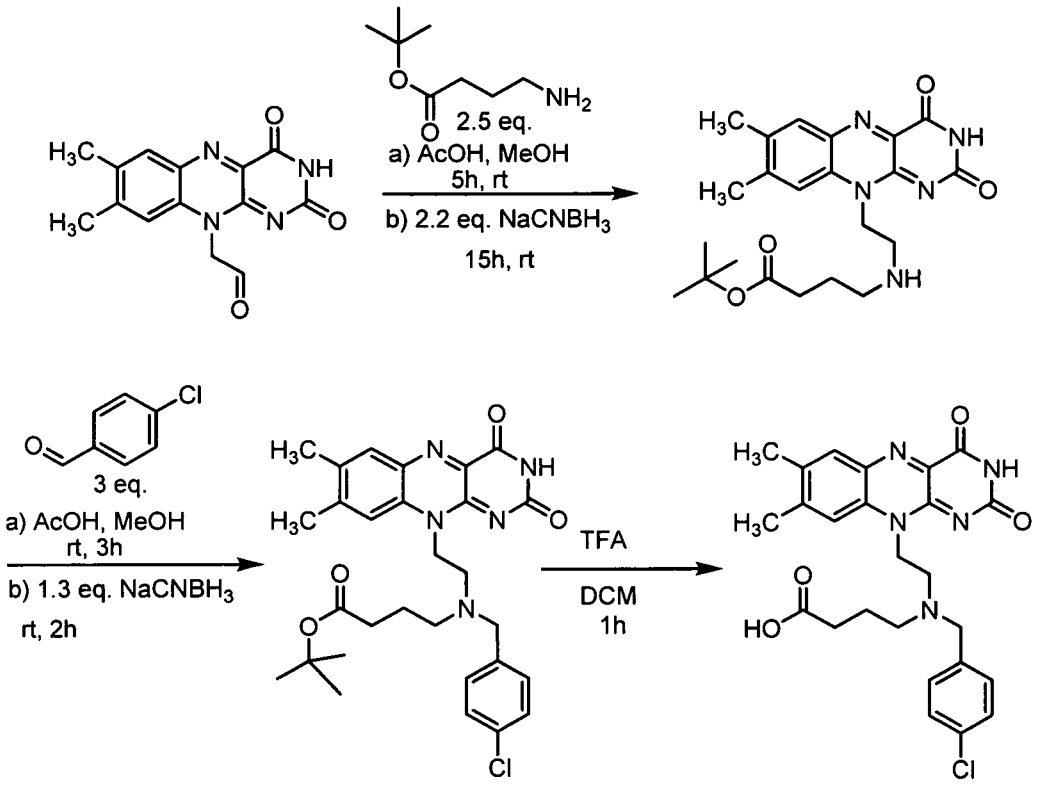
Step 3 Preparation of 10-(2-(benzylamino)ethyl)-8-(cyclopentyloxy)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione



[0278] To *tert*-butyl benzyl(2-(8-(cyclopentyloxy)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)carbamate (12 mg) is added 4 N HCl in dioxane (2 ml) and the mixture is stirred for 2 h at rt. The reaction is monitored by LCMS (Method C). Once the reaction is completed, Et_2O (3 mL) is added and the solid is collected by filtration. The solid is further purified by preparative HPLC (Method 3). Desired product (3.9 mg) is isolated as a yellow solid following lyophilization of the appropriate fractions (Yield: 32%). ^1H NMR (400 MHz, CD_3OD) δ 1.72-1.84 (m, 2 H),

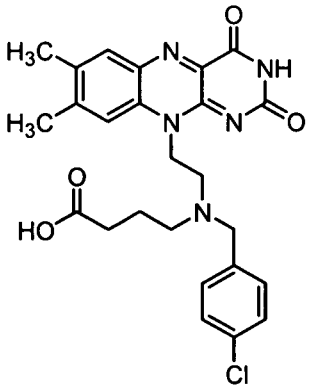
1.84-2.04 (m, 4 H), 2.08-2.20 (m, 2 H), 2.33 (s, 3 H), 3.71 (t, 2 H), 4.41 (s, 2 H), 5.15 (t, 2 H), 5.30 (s, 1 H), 7.08 (s, 1 H), 7.44 (m, 3 H), 7.53 (m, 2 H), 7.76 (s, 1 H). LC-MS m/z 446.1 $[(M\text{-}TFA)+H]^+$, retention time 4.35 min.

Scheme 21:

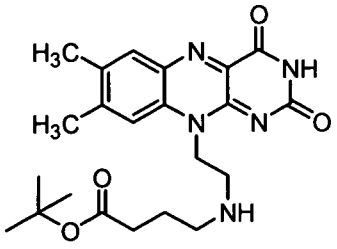


Example 75

4-{(4-Chloro-benzyl)-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-amino}-butyric acid

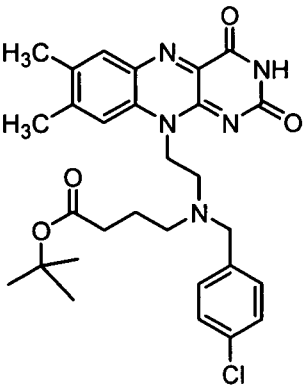


Step 1: Preparation of 4-[2-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyric acid *tert* butyl ester



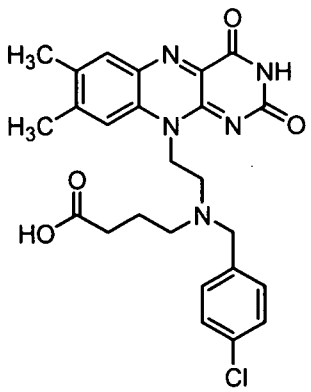
[0279] Prepared similarly to Example 20.

Step 2: Preparation of 4-{(4-Chloro-benzyl)-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-amino}-butyric acid *tert*-butyl ester



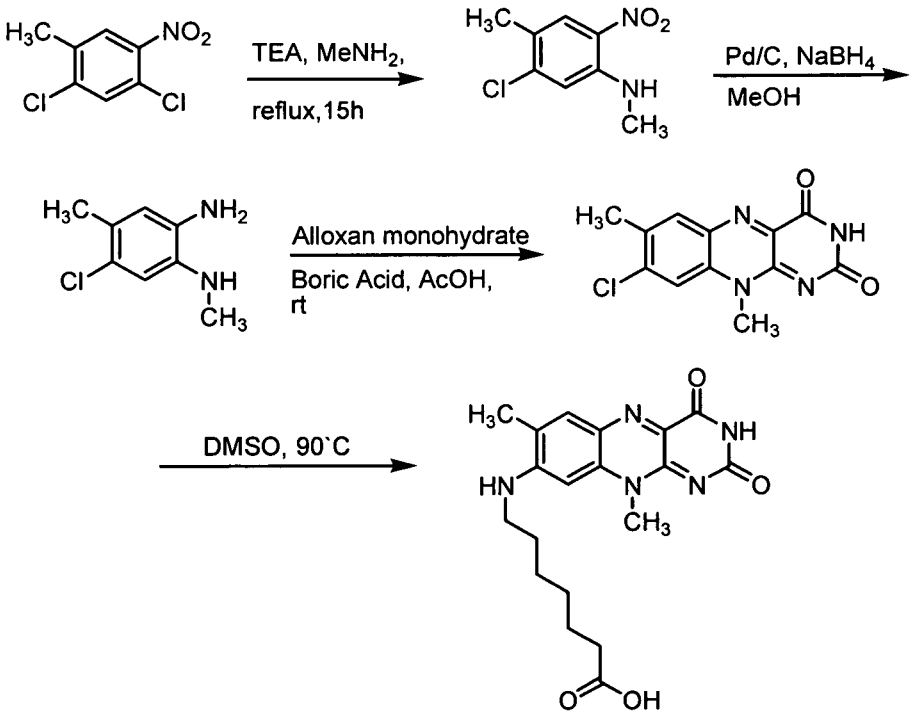
[0280] To a suspension of 4-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethylamino]-butyric acid *tert* butyl ester (95 mg, 0.22 mmol) in methanol (30 mL) is added 4-chloro-benzaldehyde (94 mg, 0.7 mmol) at room temperature. Glacial acetic acid (10 drops) is added and allowed to stir at room temperature for 3 h. Sodium cyanoborohydride (28 mg, 0.44 mmol) is added, and the solution is stirred for 4 h. The reaction mixture is concentrated, and the residue is dissolved in DMSO, filtered, and purified by preparative HPLC (Method 1). 4-{(4-Chloro-benzyl)-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-amino}-butyric acid *tert*-butyl ester (5.7 mg) is isolated following lyophilization of the appropriate fractions (Yield: 4.0%). ^{1}H NMR (400 MHz, CD_3OD) δ 1.45 (s, 9 H), 1.68 (m, 2 H), 2.23 (t, 2 H), 2.49 (s, 6 H), 2.68 (t, 2 H), 2.91 (m, 2 H), 3.46 (s, 2 H), 4.8 (m, 2 H), 6.78 (d, 2 H), 6.96 (d, 2 H), 7.56 (s, 1 H), 7.93 (s, 1H). LC-MS m/z 552.0 $[M + H]^+$, retention time 4.59 min.

Step 3: Preparation of 4-{(4-Chloro-benzyl)-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-amino}-butyric acid



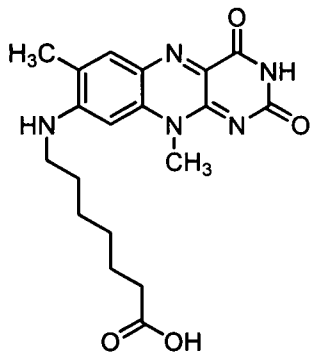
[0281] 4-{(4-Chloro-benzyl)-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-amino}-butyric acid *tert*-butyl ester (4.6 mg, 0.00832 mmol) is dissolved in a 1:1 mixture of DCM/TFA (3 mL) and allowed to stir at rt for 1h. The reaction mixture is concentrated and lyophilized without further purification to give 4-{(4-Chloro-benzyl)-[2-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-amino}-butyric acid (3.82 mg, Yield: 93%) as a yellow powder. LC-MS m/z 495.9 $[M + H]^+$, retention time 3.88 min. ^1H NMR (400 MHz, CD_3OD) δ 2.29 (m, 2 H), 2.49 (m, 5 H), 2.60 (s, 3 H), 3.41 (m, 2H), 3.73 (m, 2 H), 4.54 (s, 2 H), 5.06 (m, 2 H), 7.40 (d, 2 H), 7.58 (d, 2H), 7.72 (s, 1 H), 7.92 (s, 1H).

Scheme 22:

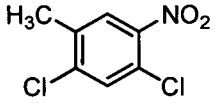


Example 76

Preparation of 7-(7,10-Dimethyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-ylamino)heptanoic acid

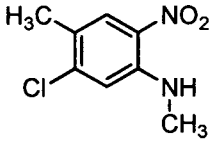


Step 1 Preparation of 1,5-Dichloro-2-methyl-4-nitro-benzene



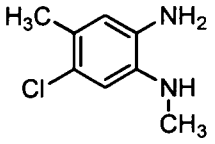
[0282] To a solution of 2,4-dichloro-1-methyl-benzene (10.3 g, 0.064 mol) in concentrated sulfuric acid (60 mL) at -10 °C, is added nitric acid (2 mL, 0.06 mol) dropwise over 0.5 h, maintaining the reaction temperature at or below -10 °C. After the reaction is complete, as monitored by TLC, the reaction mixture is poured into ice (200 mL) and the solid is filtered and washed with water. The crude is recrystallized from hexane and filtered to yield the desired product (10.4 g) as a yellow solid (Yield: 80%).

Step 2 Preparation of 5-Chloro-N,4-dimethyl-2-nitroaniline



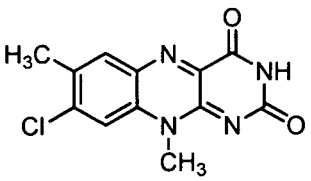
[0283] To a solution of 1,5-dichloro-2-methyl-4-nitro-benzene 3.0 g, 13 mmol) in THF (50 mL) is added methylamine hydrochloride (0.94 g, 14 mmol) and triethylamine (10 mL). The reaction mixture is heated to reflux in a sealed flask for 15 h. The reaction mixture is concentrated under reduced pressure and the crude product is purified by flash column chromatography using dichlomethane/hexanes (20%) to DCM (over 20 min) as eluent to yield the desired product (800 mg, 31%). LC-MS *m/z* 201.1 (M+H), retention time 4.76 min.

Step 3 Preparation of 5-Chloro-N1,4-dimethylbenzene-1,2-diamine



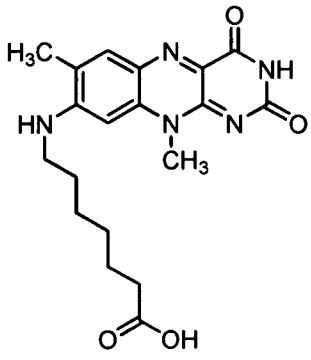
[0284] To a suspension of 5-chloro-N,4-dimethyl-2-nitroaniline (0.8 g, 4 mmol) in methanol (40 mL) at room temperature under Ar, is added 10 % Pd/C (100 mg), followed by the portionwise addition of sodium borohydride (750 mg, 20 mmol). The reaction is stirred at room temperature for 30 min. After the reaction is complete, as monitored by TLC, the reaction mixture is filtered through a celite pad, which is rinsed with methanol. The filtrate is concentrated under reduced pressure and the residue is used in the next step.

Step 4 Preparation of 8-Chloro-7,10-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione



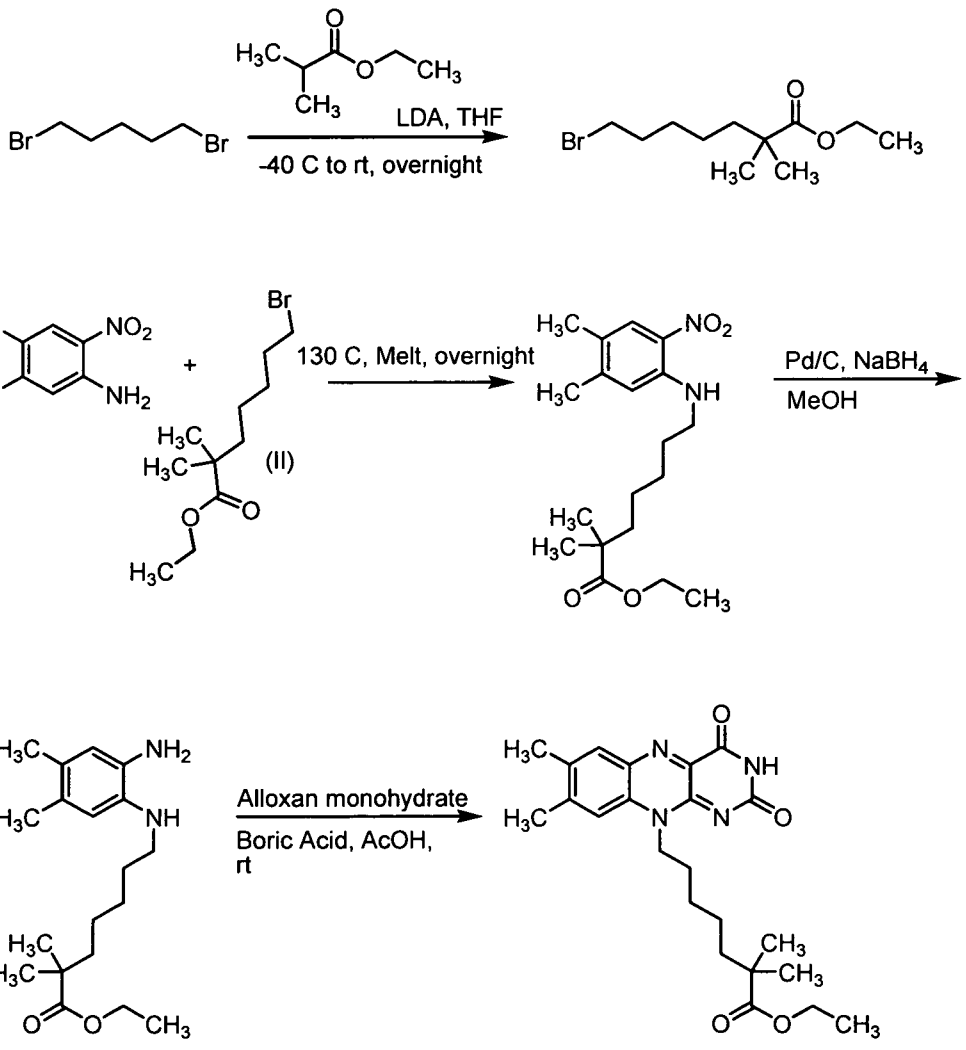
[0285] To a solution of 5-chloro-N1,4-dimethylbenzene-1,2-diamine (678 mg, 4 mmol) in acetic acid (25 mL), under an argon atmosphere, is added alloxan monohydrate (640 mg, 4 mmol) and boric acid (494 mg, 8 mmol). The reaction mixture is stirred at rt for 16 h and then is concentrated under reduced pressure. The solid is then suspended in a 1/1 mixture of methanol/water (100 mL) and the precipitate is collected via suction filtration. The precipitate is washed with water (10 mL), isopropanol (10 mL), then diethyl ether (10 mL) to afford crude product (596 mg) by LCMS. The crude product is purified by preparative HPLC (Method 1) to obtain the desired product. LC-MS *m/z* 277.1 (M+H), retention time 2.33 min.

Step 5 Preparation of 7-(7,10-Dimethyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]-pteridin-8-ylamino)heptanoic acid



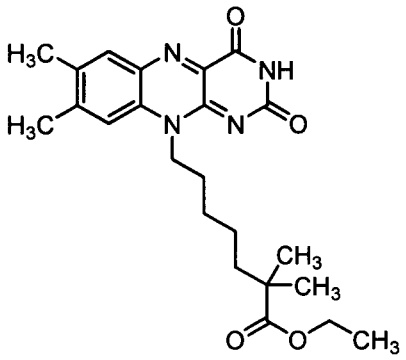
[0286] To a solution of 8-chloro-7,10-dimethylbenzo[g]pteridine-2,4(3H,10H)-dione (25 mg, 0.09 mmol) in DMF (5 mL) is added 7-aminoheptanoic acid (78 mg, 0.54 mmol). The reaction mixture is heated at 70 °C for 2 h, then at 90 °C for a further 16 h. The product is purified first using prep TLC (5% MeOH/DCM) then by preparative HPLC (Method 1) to yield the desired product (7.2 mg, 21 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.38 (m, 4 H), 1.54 (m, 2 H), 1.69 (m, 2 H), 2.23 (m, 5 H), 3.43 (m, 2 H), 3.92 (s, 3 H), 6.50 (s, 1 H), 7.16 (t, 1 H), 7.65 (s, 1 H), 10.90 (s, 1 H), 11.99 (s, 1 H). LC-MS *m/z* 386.3 (M+H), retention time 2.55 min.

Scheme 23:

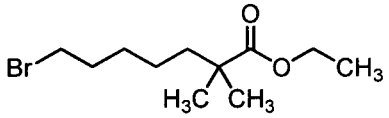


Example 77

Ethyl 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-2,2-dimethylheptanoate

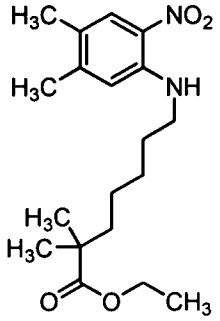


Step 1 Preparation of Ethyl 7-bromo-2,2-dimethylheptanoate



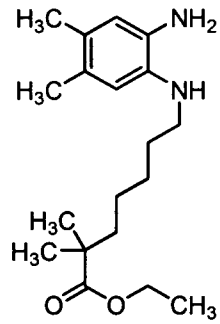
[0287] To a stirred solution of ethyl isobutyrate (1.4 g, 12.05 mmol) in anhydrous THF (30 mL) under argon, at -40 °C, is added dropwise a solution of lithium diisopropylamide (2.0 M solution in THF, 6.0 mL, 12.05 mmol). After 1 h, dibromopentane (3.95 g, 17.2 mmol) is added. The mixture is stirred for 30 min at -40 °C and then allowed to warm to room temperature and stirred overnight. The reaction is quenched with ice cold water (5 mL). The THF is removed under reduced pressure. The residue is extracted with ethyl acetate (3 x 20 mL). The combined organic layers are washed with brine, dried over anhydrous Na_2SO_4 and concentrated to afford a crude yellow oil (5.3g). The residue is purified by silica gel column chromatography using a gradient from hexanes to EtOAc/hexanes (10/90). Desired ethyl 7-bromo-2,2-dimethylheptanoate (2.13 g, Yield: 67%) is obtained as an oil after concentrating the desired fractions under vacuo. ^1H NMR ($CDCl_3$) δ 1.46 (s, 6 H), 1.24 (m, 5 H), 1.41 (m, 2H), 1.51 (m, 2H), 1.84 (m, 2H), 3.83 (t, 2H), 4.10 (q, 2H).

Step 2 Preparation of Ethyl 7-(4,5-dimethyl-2-nitrophenylamino)-2,2-dimethylheptanoate



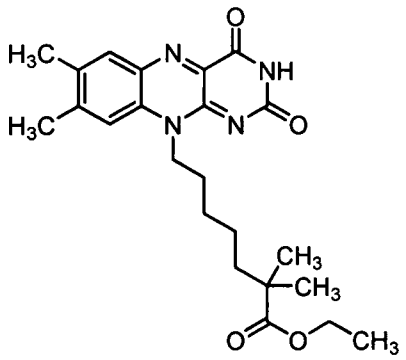
[0288] 4,5-Dimethyl-2-nitro-phenylamine (332 mg, 2.0 mmol) was melted with ethyl 7-bromo-2,2-dimethylheptanoate (530 mg, 2.0 mmol) in a vial at 130 °C overnight. The reaction is monitored by LCMS. The reaction mixture is dissolved in DCM and purified by silica gel column chromatography using 0 to 30% EtOAc in hexanes as eluent. Desired ethyl 7-(4,5-dimethyl-2-nitrophenylamino)-2,2-dimethylheptanoate (376 mg) is obtained after concentrating the desired fractions under vacuo (Yield: 54%). LC-MS m/z 351.0 [M+H], retention time = 6.76 min.

Step 3 Preparation of Ethyl 7-(2-amino-4,5-dimethylphenylamino)-2,2-dimethylheptanoate



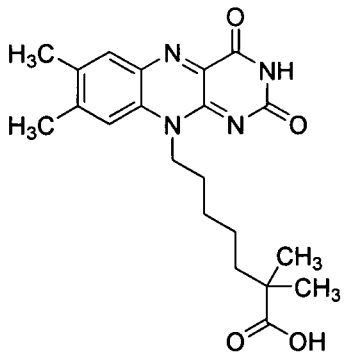
[0289] Ethyl 7-(4,5-dimethyl-2-nitrophenylamino)-2,2-dimethylheptanoate (376 mg, 1.07 mmol) is dissolved in methanol (10 mL) and palladium on carbon (10%, 50 mg) is added followed by sodium borohydride (122 mg, 3.22 mmol) with stirring at rt. The reaction mixture is filtered through celite after 30 min and the celite is washed with methanol (10 mL). The filtrate is concentrated under vacuum. The residue is dissolved in water (20 mL), followed by extraction with EtOAc (2 x 15 mL). The organic layers are combined, dried over sodium sulfate, and filtered. The filtrate is concentrated under vacuo to obtain ethyl 7-(2-amino-4,5-dimethylphenylamino)-2,2-dimethylheptanoate (272 mg) as desired compound (Yield: 80%). LC-MS m/z 321.0 [M+H], retention time = 3.73 min.

Step 4 Preparation of Ethyl 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-2,2-dimethylheptanoate



[0290] Ethyl 7-(2-amino-4,5-dimethylphenylamino)-2,2-dimethylheptanoate (272 mg, 0.85 mmol) is dissolved in acetic acid (5 mL) followed by addition of boric acid (52 mg, 0.85 mmol) and alloxan monohydrate (136 mg, 0.85 mmol). After 30 min, the reaction mixture is concentrated under vacuum and purified by silica gel column chromatography using 0 to 5% MeOH in DCM as eluent. Ethyl 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-2,2-dimethylheptanoate (178 mg, 49%) is obtained after concentrating the desired fractions under vacuo. ^{1}H NMR ($CDCl_3$) δ 1.26 (s, 6 H), 1.26 (t, 3 H), 1.28 (m, 2 H), 1.55 (m, 4H), 1.89 (m, 2 H), 2.48 (s, 3 H), 2.60 (s, 3 H), 4.14 (q, 2 H), 4.70 (m, 2 H), 7.44 (s, 1 H), 8.09 (s, 1 H), 8.47(s, 1 H). LC-MS m/z 427.1 [M+H], retention time = 5.05 min.

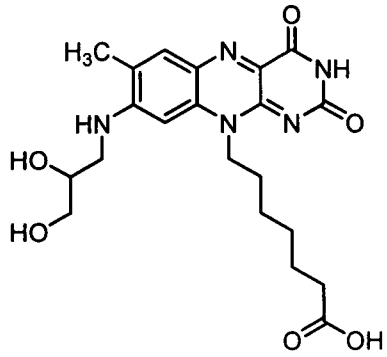
Example 78
7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-2,2-dimethylheptanoic acid



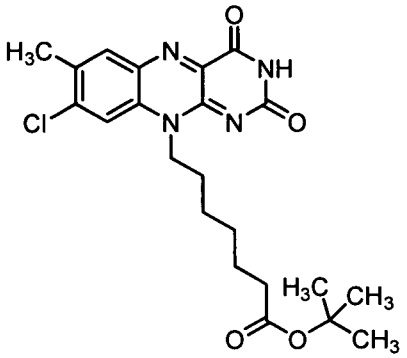
[0291] To a solution of ethyl 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-2,2-dimethylheptanoate (Example above) (21 mg, 0.049 mmol) in water (2 mL) is added concentrated hydrochloric acid (2 mL). The reaction mixture is stirred at 85 °C for 2 h and then cooled to room temperature, and concentrated under vacuo. The residue is purified by preparative TLC using 15% acetone

in DCM as eluent. 7-(7,8-Dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-2,2-dimethylheptanoic acid (14.7 mg, 75%) is isolated by preparative TLC. ^{1}H NMR (400 MHz, MeOH-d_4) δ 1.18 (s, 6 H), 1.42 (m, 2 H), 1.60 (m, 4 H), 1.94 (m, 2 H), 2.57 (s, 3 H), 2.70 (s, 3 H), 4.86 (m, 2 H), 8.08 (s, 1 H), 8.15 (s, 1H); LC-MS m/z 399.1 [M+H], retention time 3.07 min.

Example 79
7-(8-(2,3-Dihydroxypropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid

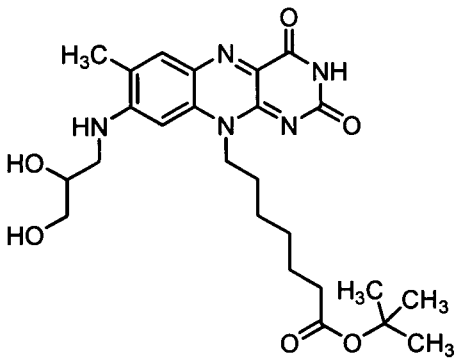


Step 1 Preparation of *tert*-Butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



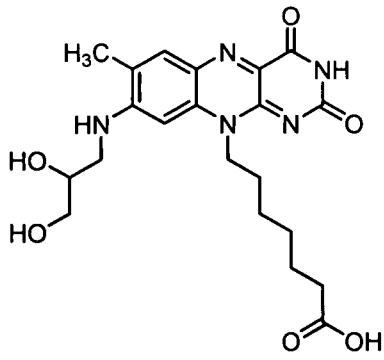
[0292] *tert*-Butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate is prepared using the procedure of Example 24 and the appropriately substituted starting materials. LC-MS m/z 446.9, 448.9 (3:1) [M+H], retention time 3.84 min.

Step 2 Preparation of *tert*-Butyl 7-(8-(2,3-dihydroxypropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



[0293] To a suspension of *tert*-butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (50 mg, 0.11 mmol) in DMSO (3 mL) at room temperature is added 2,3-dihydroxypropylamine (100 mg, 1.1 mmol). The reaction vessel is sealed and the solution is heated to 90 °C with stirring for 16 h. The reaction mixture is then purified by preparative HPLC (Method 1). *tert*-Butyl 7-(8-(2,3-dihydroxypropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate is isolated following lyophilization of the appropriate fractions (36 mg, Yield: 65 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.38 (s, 9 H), 1.50 (m, 2 H), 1.70 (m, 2 H), 2.18 (t, 2H), 2.33 (s, 3 H), 3.45 (m, 5 H), 3.58 (s, 2 H), 3.78 (d, 2 H), 4.51 (s, 2 H), 4.89 (s, 1 H), 5.07 (s, 1 H), 6.66 (s, 1 H), 7.15 (s, 1 H), 7.66 (s, 1 H), 10.96 (s, 1 H). LC-MS m/z 502.0 [M+H], retention time 2.77 min.

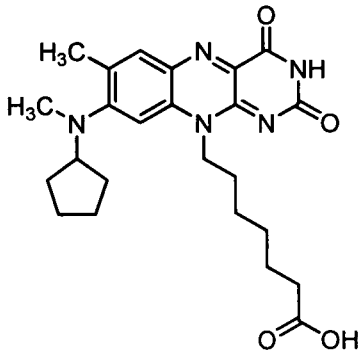
Step 3: Preparation of 7-(8-(2,3-Dihydroxypropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



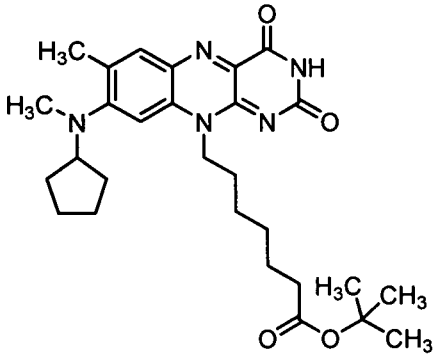
[0294] *tert*-Butyl 7-(8-(2,3-dihydroxypropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (19 mg, 0.038 mmol) is suspended in 4 M aqueous HCl (4 mL). The reaction vessel is sealed and the solution is heated to 50 °C with stirring for 4 h. The reaction mixture is lyophilized to give 7-(8-(2,3-dihydroxypropylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-

yl)heptanoic acid (12 mg, Yield: 72 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.58 (m, 6 H), 1.70 (m, 2 H), 2.25 (m, 5 H), 3.45 (m, 3 H), 3.62 (m, 3 H), 3.78 (s, 1 H), 4.51 (s, 2 H), 6.68 (s, 1 H), 7.22 (s, 1 H), 7.67 (s, 1 H), 11.00 (s, 1 H). LC-MS m/z 446.2 [M+H], retention time 2.01 min.

Example 80
7-(8-(Cyclopentyl(methyl)amino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



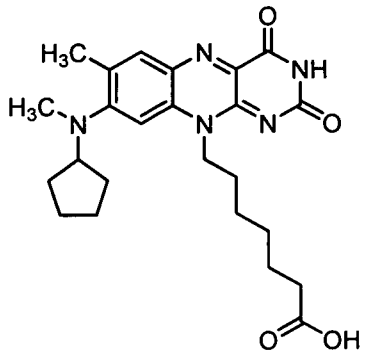
Step 1 Preparation of *tert*-Butyl 7-(8-(cyclopentyl(methyl)amino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



[0295] Prepared by a procedure similar to that of Example 79, Step 1, using *tert*-butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (Example 79, Step 1) (50 mg) and N-methylcyclopentanamine (109 mg, 10 equivalents) in DMSO (3 ml). Purified by preparative HPLC (Method 1). *tert*-Butyl 7-(8-(cyclopentyl(methyl)amino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate is isolated following lyophilization of the appropriate fractions (11 mg, Yield: 20 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.38 (s, 9 H), 1.51 (m, 7 H), 1.70 (m, 6 H), 1.85 (m, 2 H), 2.18 (t, 2 H), 2.41 (s, 3 H), 2.87 (s, 3 H), 4.07 (m, 2 H), 4.58 (s, 2 H),

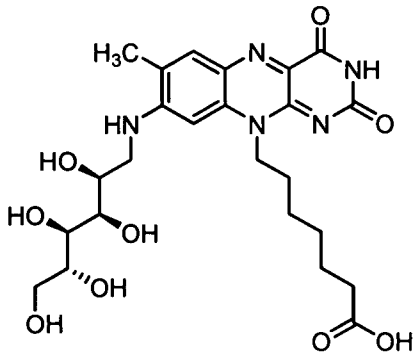
6.99 (s, 1 H), 7.83 (s, 1 H), 11.14 (s, 1 H). LC-MS m/z 510.2 [M+H], retention time 4.28 min.

Step 2 Preparation of 7-(8-(Cyclopentyl(methyl)amino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid

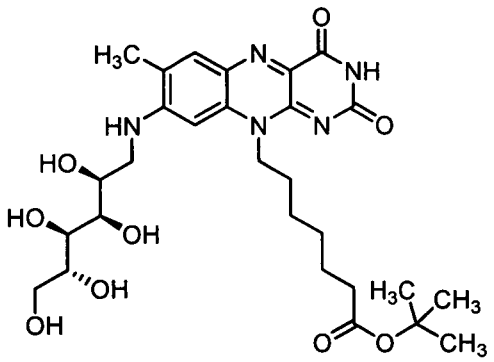


[0296] Prepared by a procedure similar to that of Example 79 using *tert*-butyl 7-(8-(cyclopentyl(methyl)amino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (8 mg, 0.016 mmol). 7-(8-(cyclopentyl(methyl)amino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (4 mg, Yield : 57 %) is obtained after lyophilization. ^{1}H NMR (400 MHz, DMSO-d6) δ 1.48 (m, 8 H), 1.70 (m, 6 H), 1.86 (m, 2 H), 2.20 (t, 2 H), 2.42 (s, 3 H), 2.88 (s, 3 H), 4.06 (m, 1 H), 4.58 (s, 2 H), 6.99 (s, 1 H), 7.83 (s, 1 H), 11.14 (s, 1 H), 12.00 (s, 1 H). LC-MS m/z 454.3 [M+H], retention time 3.26 min.

Example 81
7-(7-Methyl-2,4-dioxo-8-((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexylamino)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid

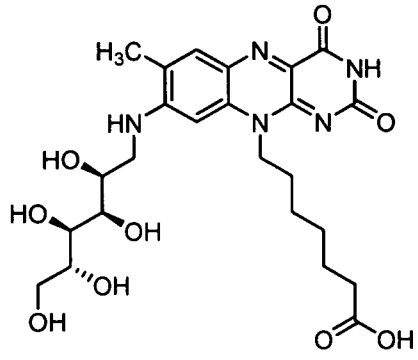


Step 1 Preparation of *tert*-Butyl 7-(7-methyl-2,4-dioxo-8-((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexylamino)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



[0297] Prepared by nucleophilic aromatic substitution by a procedure similar to that of Example 79, using *tert*-butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (Example 79, Step 1)(50 mg) and (2R,3R,4R,5S)-6-aminohexane-1,2,3,4,5-pentanol (199 mg, 10 equivalents) in DMSO (3 ml), and purified by preparative HPLC (Method 1). *tert*-Butyl 7-(7-methyl-2,4-dioxo-8-((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexylamino)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (37 mg, Yield: 57 %) is isolated following lyophilization of the appropriate fractions. ^{1}H NMR (400 MHz, DMSO-d6) δ 1.43 (m, 15 H), 1.71 (m, 2 H), 2.18 (t, 2 H), 2.27 (s, 3 H), 2.33 (m, 1 H), 2.67 (m, 1 H), 3.64 (m, 8 H), 3.91 (m, 2 H), 4.55 (m, 3 H), 6.67 (s, 1 H), 7.21 (m, 1 H), 7.66 (s, 1 H), 10.95 (s, 1 H). LC-MS m/z 592.1 [M+H], retention time 2.56 min.

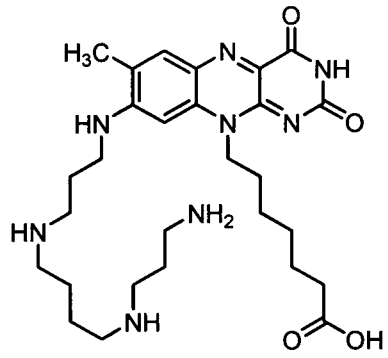
Step 2 Preparation of 7-(7-Methyl-2,4-dioxo-8-((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexylamino)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



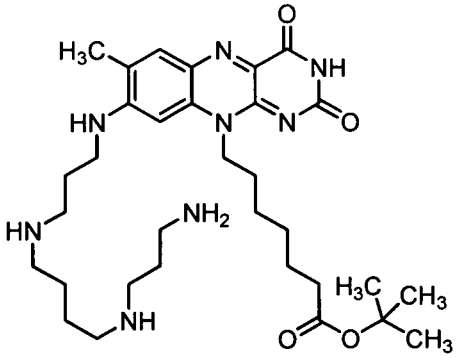
[0298] Prepared from *tert*-butyl 7-(7-methyl-2,4-dioxo-8-((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexylamino)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (33 mg, 0.056 mmol) by suspending starting material in 4 N HCl in dioxane (5 ml) with stirring at room temperature for 1 h. The product is precipitated using Et_2O then centrifuged and the supernatant is decanted, this process is then repeated three times, with

the final pellet being dried under reduced pressure to give 7-(7-methyl-2,4-dioxo-8-((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexylamino)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (23 mg, Yield: 75 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.35 (m, 2 H), 1.51 (m, 4 H), 1.60 (s, 3 H), 1.72 (m, 2 H), 2.22 (t, 2 H), 2.34 (s, 3 H), 3.42 (m, 1 H), 3.61 (t, 1 H), 3.75 (m, 2 H), 3.94 (m, 1 H), 4.57 (d, 2 H), 5.11 (br s, 5 H), 6.83 (s, 1 H), 7.78 (s, 1 H), 7.85 (s, 1 H), 11.67 (s, 1 H). LC-MS m/z 536.2 [M+H], retention time 3.27 min.

Example 82
7-(8-(3-(4-(3-Aminopropylamino)butylamino)propylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



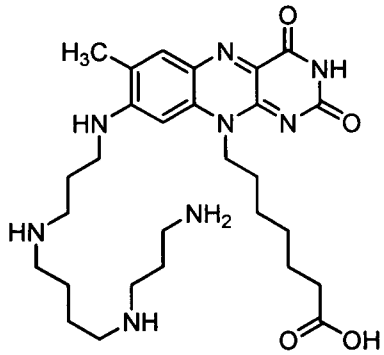
Step 1: Preparation of *tert*-Butyl 7-(8-(3-(4-(3-aminopropylamino)butylamino)propylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate



[0299] N,N′-Bis(3-aminopropyl)-1,4-butanediamine tetrahydrochloride (383 mg, 1.1 mmol) is suspended in dry DMSO (2 ml) at room temperature. NaH (52 mg, 2.2 mmol, pre-washed 3x with hexanes) is added carefully and the mixture is allowed to stir at room temperature for 20 minutes. *tert*-Butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (Example 79, Step 1) (50 mg, 0.11 mmol) is then added to the reaction vessel and dry DMSO (1 ml) is used to wash down all

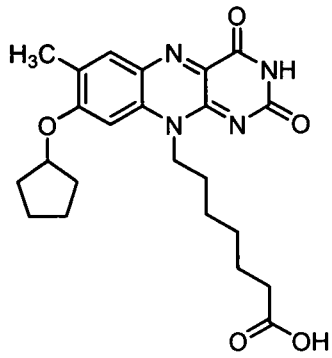
reagents from the sides of the flask. The reaction mixture is then stirred at 90 °C for 16 h. After cooling, the reaction mixture is purified by preparative HPLC (Method 1) to give *tert*-Butyl 7-(8-(3-(4-(3-aminopropylamino)butylamino)propylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate after lyophilization of the appropriate fractions (45 mg,Yield: 57 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.38 (s, 9 H), 1.42 (m, 2 H), 1.51 (quint., 2 H), 1.61 (br s, 3 H), 1.72 (m, 2 H), 1.86 (m, 2 H), 1.99 (m, 2 H), 2.08 (s, 1 H), 2.19 (t, 2 H), 2.28 (s, 3 H), 2.94 (m, 9 H), 3.54 (d, 3 H), 4.58 (m, 2 H), 6.50 (s, 1 H), 7.16 (m, 1 H), 7.70 (s, 1 H), 7.85 (m, 1 H), 8.67 (m, 3 H), 10.99 (s, 1 H). LC-MS m/z 613.3 [M+H], retention time 2.26 min.

Step 2 Preparation of 7-(8-(3-(4-(3-Aminopropylamino)butylamino)propylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



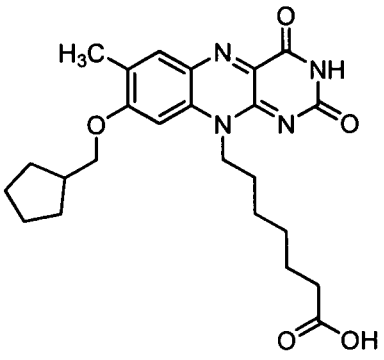
[0300] Prepared using *tert*-butyl 7-(8-(3-(4-(3-aminopropylamino)butylamino)propylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (33 mg, 0.054 mmol) in the same manner as in Example 81 to give 7-(8-(3-(4-(3-aminopropylamino)butylamino)propylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (27 mg, Yield: 90 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.38 (m, 2H), 1.50 (m, 3H), 1.60 (s, 1H), 1.74 (br s, 5H), 2.00 (m, 3H) 2.23 (t, 2H), 2.33 (br s, 2H), 2.95 (m, 7H), 3.43 (m, 1H), 3.66 (s, 2H), 4.20 (br s, 5H), 4.63 (s, 2H), 6.59 (s, 1H), 7.60 (s, 1H), 7.74 (s, 1H), 8.10 (s, 2H), 9.23 (d, 3H), 11.26 (s, 1H). LC-MS m/z 557.3 [M+H], retention time 3.27 min.

Example 83
7-(8-(Cyclopentyloxy)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



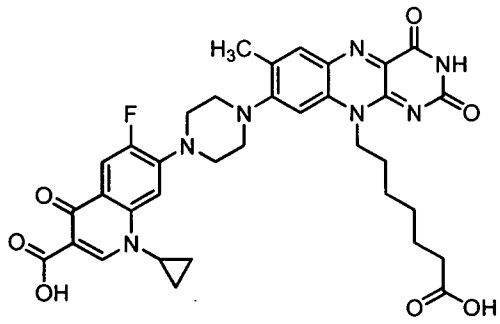
[0301] NaH (26 mg, 1.1 mmol) is added to a flask containing cyclopentanol (4 ml), and the resulting mixture is allowed to stir at room temperature for 20 minutes. *tert*-Butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (Example 79, Step 1) (50 mg, 0.11 mmol) is then added to the reaction vessel and the reaction mixture is stirred at 100 °C for 16 h. After cooling, the reaction mixture is quenched with acetic acid and the mixture is evaporated under reduced pressure to give a dark solid. The residue is purified by preparative HPLC (using an aqueous phase containing USP water with no TFA, acetonitrile as the organic phase, and a gradient from 100% aqueous to 98% organic over 29 minutes). After lyophilization of the appropriate fractions, 7-(8-(cyclopentyloxy)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid is obtained (5 mg, Yield: 10 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.36 (m, 2H), 1.49 (m, 4H), 1.72 (m, 6H), 1.83 (m, 2H), 2.03 (m, 2H), 2.18 (t, 2H), 2.26 (s, 3H), 4.64 (m, 2H), 5.30 (m, 1H), 7.10 (s, 1H), 7.90 (s, 1H), 11.22 (s, 1H). LC-MS m/z 441.1 [M+H], retention time 5.31 min.

Example 84
7-(8-(Cyclopentylmethoxy)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid

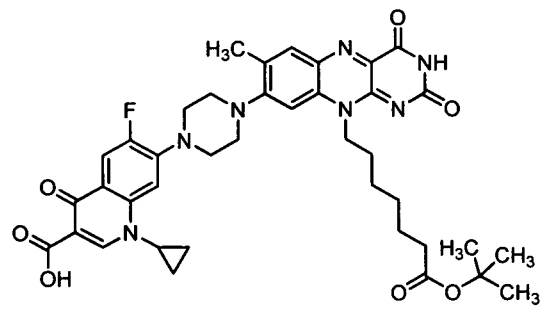


[0302] NaH (26 mg, 1.1 mmol) is added to a flask containing cyclopentylmethanol (110 mg, 1.1 mmol) in dry DMSO (1 ml), and the resulting mixture is allowed to stir at room temperature for 20 minutes. *tert*-Butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (Example 79, Step 1) (50 mg, 0.11 mmol) is then added to the reaction vessel with dry DMSO (1 ml) and the reaction mixture is stirred at 90 °C for 3 h. After cooling, the reaction mixture is quenched with acetic acid and the volatiles are removed by evaporation under reduced pressure. The resulting oily mixture is purified first by preparative TLC using a mobile phase consisting of 10 % MeOH in DCM. A mixture is obtained containing the product and various impurities, which is then repurified by preparative TLC using a mobile phase consisting of 5 % MeOH in DCM, and preparative HPLC (using an aqueous phase containing USP water with no TFA, acetonitrile as the organic phase, and a gradient from 100% aqueous to 98% organic over 29 minutes) was used for the final purification. After lyophilization of the appropriate fractions, 7-(8-(cyclopentylmethoxy)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid is obtained (4.2 mg, Yield: 9 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.38 (t, 2H), 1.45 (m, 4H), 1.51 (m, 2H), 1.59 (m, 2H), 1.64 (m, 2H), 1.73 (m, 2H), 1.84 (m, 2H), 2.21 (t, 2H), 2.30 (s, 3H), 2.43 (quin., 1H), 4.21 (d, 2H), 4.65 (t, 2H), 7.15 (s, 1H), 7.92 (s, 1H), 11.22 (s, 1H), 12.00 (br.s, 1H). LC-MS m/z 455.2 [M+H], retention time 5.67 min.

Example 85
7-(4-(10-(6-Carboxyhexyl)-7-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid

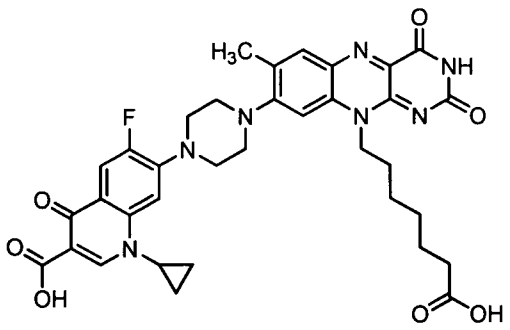


Step 1 Preparation of 7-(4-(10-(7-*tert*-Butoxy-7-oxoheptyl)-7-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid



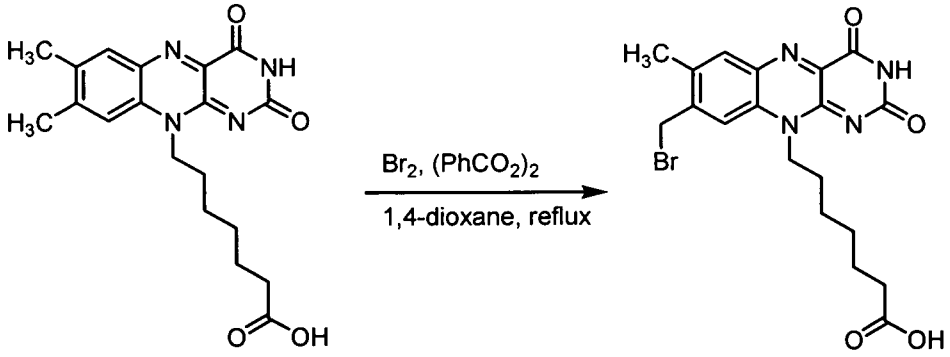
[0303] 1-Cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid (33 mg, 1.0 mmol) is suspended in dry DMSO (1 ml), and NaH (5 mg, 0.2 mmol) is added carefully with stirring at room temperature. After 20 minutes, *tert*-butyl 7-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate (Example 79, Step 1) (50 mg, 0.11 mmol) and diisopropylethylamine (0.019 ml, 0.2 mmol) are added in DMSO (2 ml), and the reaction mixture is heated to 90 °C for 40 h, then 115 °C for 4 h. The mixture is cooled and acidified with conc. AcOH (0.5 ml) and then with conc. HCl, added dropwise, to pH 4.5, and extracted with DCM (10 ml) four times. The combined organic fractions are washed successively with water acidified to pH 4.5 (10 mL) and brine, and then evaporated. The resulting mixture is purified by preparative HPLC (Method 1), and the product is precipitated from the mobile phase upon standing overnight. The product is collected by filtration, washed with water, then collected by dissolving the product cake with DCM, and then removing the solvent under reduced pressure to give 7-(4-(10-(7-*tert*-butoxy-7-oxoheptyl)-7-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (13 mg, Yield: 18 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.00 (m, 1H), 1.23 (m, 2H), 1.31 (m, 2H), 1.36 (s, 9H), 1.37 (q, 2H), 1.48 (m, 4H), 1.76 (m, 2H), 2.19 (t, 2H), 3.44 - 3.86 (m, 6H), 4.63 (s, 2H), 6.76 (s, 1H), 7.20 (s, 1H), 7.69 (d, 1H), 7.96 (m, 2H), 8.70 (s, 1H), 11.24 (s, 1H). LC-MS m/z 742.1 [M+H], retention time 5.65 min.

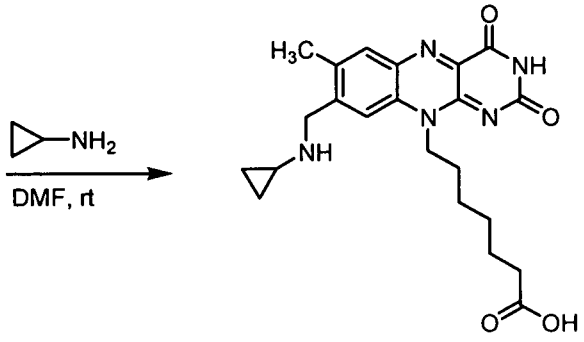
Step 2 Preparation of 7-(4-(10-(6-Carboxyhexyl)-7-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid



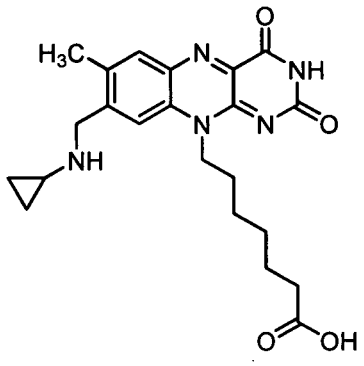
[0304] 7-(4-(10-(7-tert-Butoxy-7-oxoheptyl)-7-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (6.5 mg, 0.0088 mmol) is suspended in TFA (1 ml) and DCM (1 ml), and is stirred overnight at room temperature. After evaporating the solvent, the resulting solid is dissolved in a minimum amount of hot DMF, precipitated with USP water and collected by filtration, then loaded onto a preparative TLC plate and eluted with 10 % MeOH in DCM with 0.1 % AcOH to give 7-(4-(10-(6-carboxyhexyl)-7-methyl-2,4-dioxo-2,3,4,10-tetrahydrobenzo[g]pteridin-8-yl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (4.1 mg, Yield: 68 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 0.85 (m, 2H), 1.07 (m, 1H), 1.23 (m, 5H), 1.45 (m, 4H), 1.72 (s, 3H), 2.01 (m, 2H), 2.73 (s, 1H), 2.89 (s, 1H), 4.63 (m, 2H), 7.22 (m, 1H), 7.50 (m, 1H), 7.68 (m, 1H), 8.00 (m, 2H), 8.60 (m, 1H), 11.20 (m, 1H). LC-MS m/z 686.1 [M+H], retention time 5.72 min.

Scheme 24:

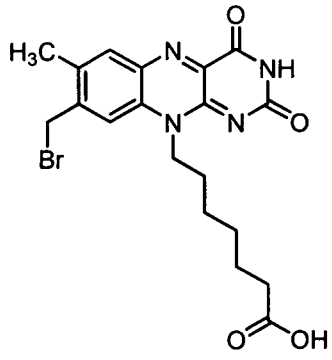




Example 86
7-(8-((Cyclopropylamino)methyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



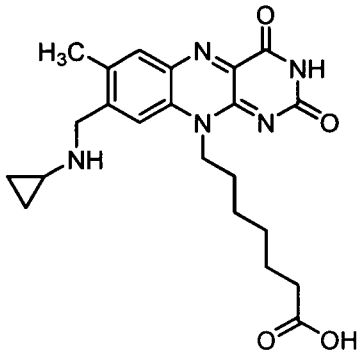
Step 1 Preparation of 7-(8-(Bromomethyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



[0305] A suspension of 7-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (Example 25, Step 3) (370 mg, 1 mmol) in 1,4-dioxane (10 mL) is heated to reflux. Two solutions are prepared: Br_2 (351 mg, 2.2 mmol) in 1,4-dioxane (4 ml); and benzoyl peroxide (121 mg, 0.5 mmol) in 1,4-dioxane (1 ml). A portion of the benzoyl peroxide solution (0.5 ml) is added in one portion to the refluxing mixture, followed by a portion-wise addition of the entirety of the bromine mixture over 15 minutes. At 15 minutes, an additional portion of the benzoyl peroxide solution (0.25 ml) is

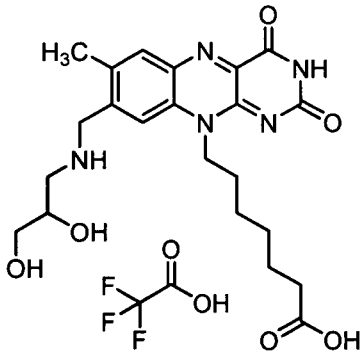
added, and the remainder (0.25 ml) is added after a further 30 minutes. The reaction is removed from the heat 70 minutes after the initial addition, cooled to room temperature and the solvent is removed under reduced pressure. Upon the addition of $CHCl_3$ (40 ml) a brown solid precipitates from solution, which is filtered and washed with $CHCl_3$ (3 x 10 ml) and dried under reduced pressure to obtain 7-(8-(bromomethyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (201 mg, Yield: 45 %) as a brown powdery solid which is used without further purification. LC-MS m/z 448.9 / 450.9 (1:1) [M+H], retention time 4.18 min.

Step 2 Preparation of 7-(8-((Cyclopropylamino)methyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



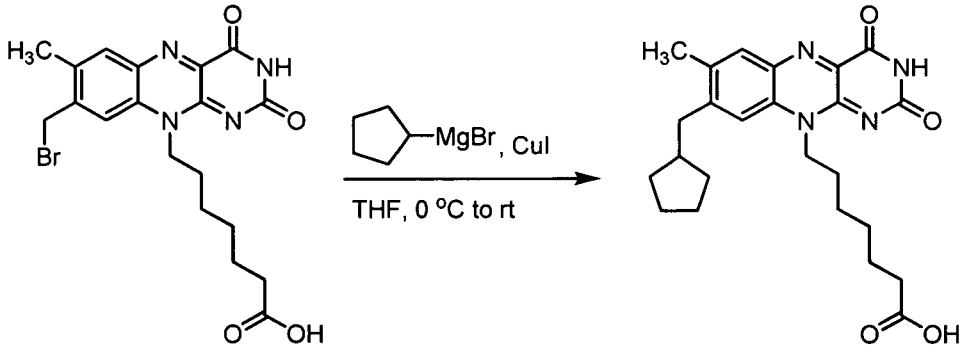
[0306] 7-(8-(Bromomethyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (35 mg, 0.08 mmol) and cyclopropylamine (9 mg, 0.16 mmol) are suspended in DMF (1 ml) and stirred at room temperature for 16 h. The reaction mixture is then purified by preparative HPLC (Method 1, using methanol in place of aceonitrile in the organic phase). 7-(8-((Cyclopropylamino)methyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid is obtained after lyophilization of the appropriate fractions (7.5 mg, Yield: 22 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 0.86 (d, 4H), 1.37 (d, 2H), 1.52 (m, 4H), 1.76 (m, 2H), 2.23 (t, 2H), 2.55 (s, 3H), 2.84 (m, 1H), 4.51 (m, 4H), 7.92 (s, 1H), 8.04 (s, 1H), 9.26 (br s, 1H), 11.40 (s, 1H). LC-MS m/z 426.0 [M+H], retention time 3.76 min.

Example 87
7-(8-((2,3-Dihydroxypropylamino)methyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid 2,2,2-trifluoroacetate

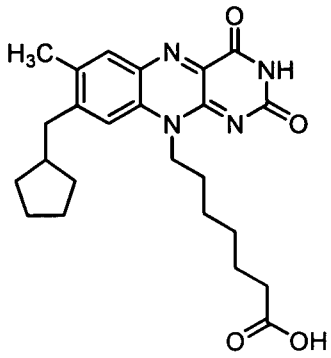


[0307] Prepared using a procedure similar to that of Example 86 using 7-(8-(bromomethyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (35 mg, 0.08 mmol) and 2,3-dihydroxypropylamine (15 mg, 0.16 mmol) in DMF (1 ml). 7-(8-((2,3-Dihydroxypropylamino)methyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid 2,2,2-trifluoroacetate is obtained after lyophilization of the appropriate fractions (5.7 mg, Yield: 17 %). ^{1}H NMR (400 MHz, DMSO-d6) δ 1.46 (m, 6H), 1.75 (m, 2H), 2.22 (t, 2H), 2.52 (s, 3H), 3.00 (t, 1H), 3.24 (m, 2H), 3.90 (m, 1H), 4.45 (s, 2H), 4.54 (s, 2H), 4.98 (br s, 1H), 5.60 (s, 1H), 7.99 (s, 1H), 8.02 (s, 1H), 9.14 (br s, 2H), 11.40 (s, 1H), 12.02 (br s, 1H). LC-MS m/z 460.3 [M+H], retention time 1.77 min.

Scheme 25:

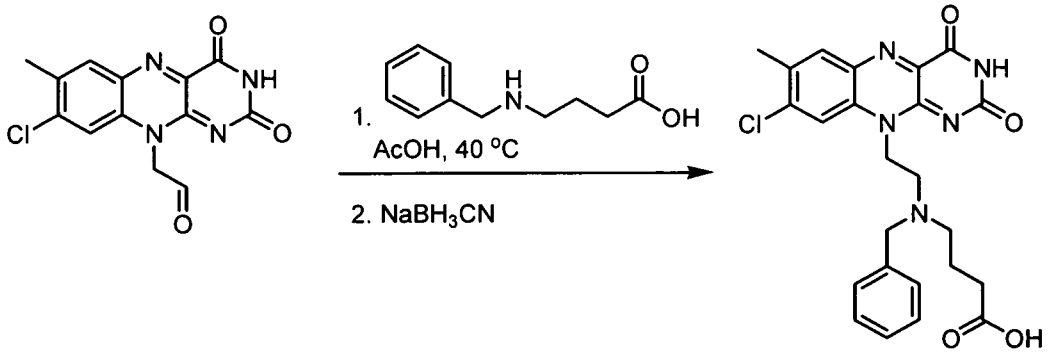


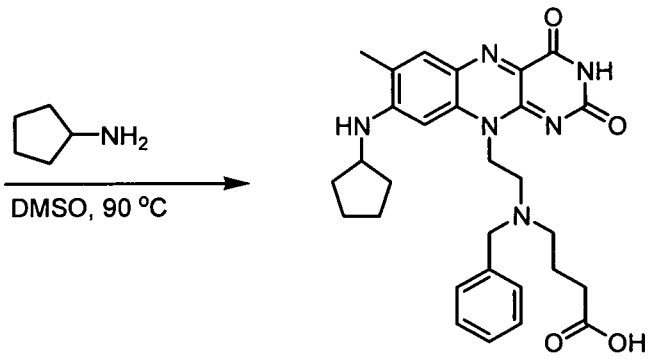
Example 88
7-(8-(Cyclopentylmethyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid



[0308] Into an oven-dried vial is added CuI (10 mg, 0.052 mmol), cyclopentyl magnesium bromide (2.0 M, 110 µl, 0.22 mmol) and anyhydrous THF (1 ml) at 0 °C under argon. 7-(8-(Bromomethyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid (Example 86, step 1)) (50 mg, 0.11 mmol) is dissolved in dry THF (4 ml), then added to the reaction vial. The reaction mixture is allowed to warm to room temperature over 16 h, and then quenched with NH_4Cl. After extracting the aqueous phase with DCM, the combined organic layers are basified and extracted with 2M NaOH (3 x 10 ml). The alkaline aqueous phase is washed with EtOAc (2 x 10 ml), then acidified with 2M HCl to pH < 3 and extracted with DCM (3 x 20 ml). The organic phase is then washed with brine (2 x 20 ml), dried with Na_2SO_4, filtered and evaporated. The residue is purified by preparative HPLC (Method 1). 7-(8-(Cyclopentylmethyl)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid is obtained after lyophilization of the appropriate fractions (1.1 mg, Yield: 2 %). ^1H NMR (400 MHz, CD_3OD) δ 0.90 (m, 2H), 1.31 (m, 4H), 1.45 (q, 2H), 1.59 (m, 5H), 1.76 (m, 2H), 1.87 (t, 2H), 2.27 (m, 2H), 2.50 (s, 3H), 2.94 (t, 2H), 4.75 (m, 2H), 7.69 (s, 1H), 7.98 (s, 1H). LC-MS m/z 439.1 [M+H], retention time 4.92 min..

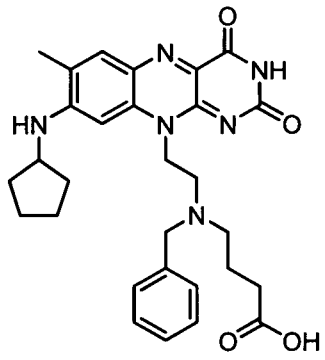
Scheme 26:



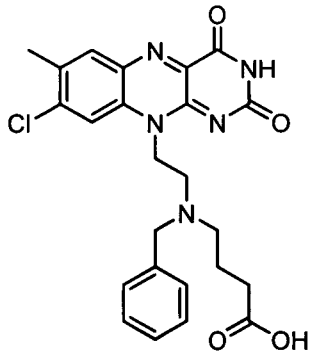


Example 89

4-(Benzyl(2-(8-(cyclopentylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)amino)butanoic acid

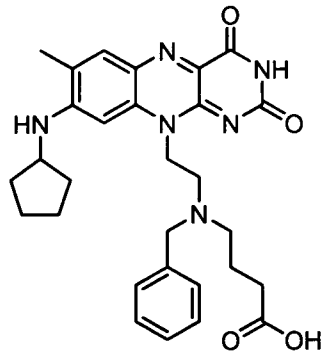


Step 1: Preparation of 4-(Benzyl(2-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)amino)butanoic acid



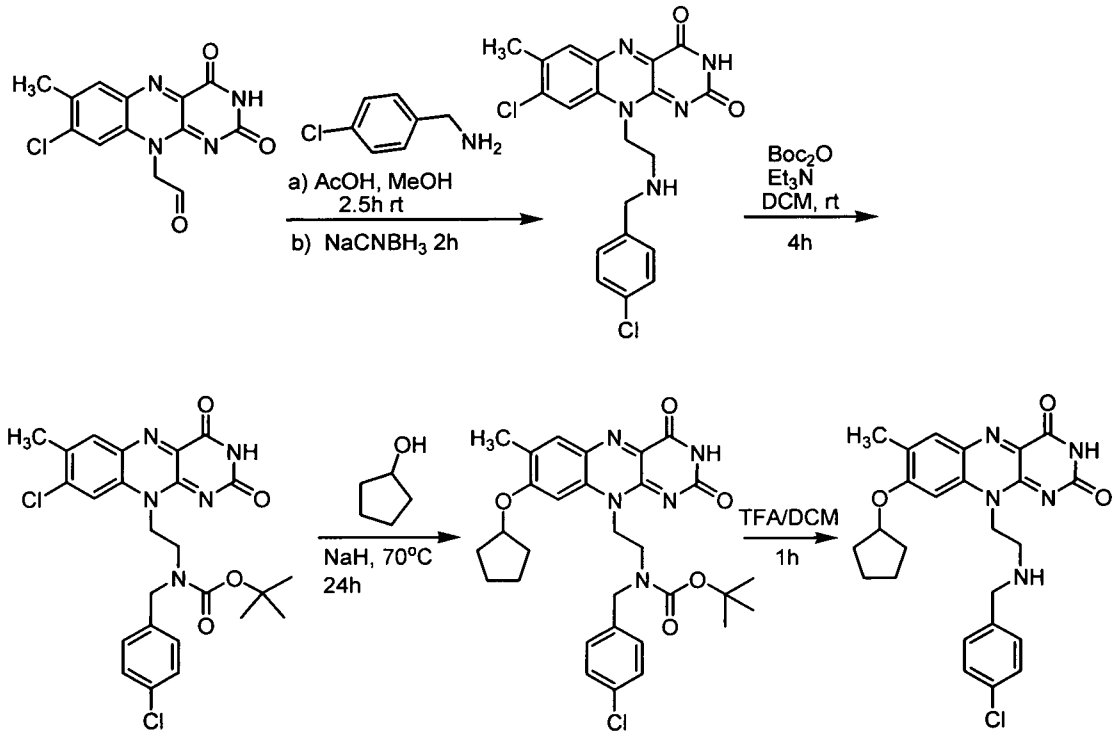
[0309] 4-(Benzyl(2-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)amino)butanoic acid is prepared in the same manner as Example 15, Step 2 starting from commercially available 4-(benzylamino)butanoic acid and (8-chloro-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-acetaldehyde (Example 73, Step 4) LC-MS m/z 481.9, 483.9 (3:1) [M+H], retention time 3.71 min.

Step 2 Preparation of 4-(Benzyl(2-(8-(cyclopentylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)amino)butanoic acid



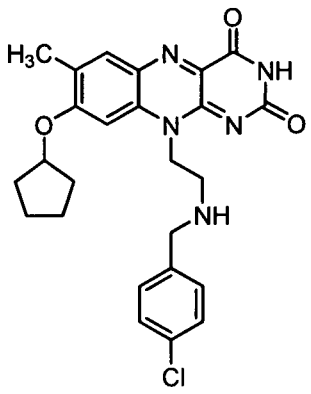
[0310] 4-(Benzyl(2-(8-(cyclopentylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)amino)butanoic acid is prepared from 4-(benzyl(2-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)amino)butanoic acid and cyclopentylamine in the same manner as Example 79, Step 2. LC-MS m/z 531.1 [M+H], retention time 4.27 min.

Scheme 27:

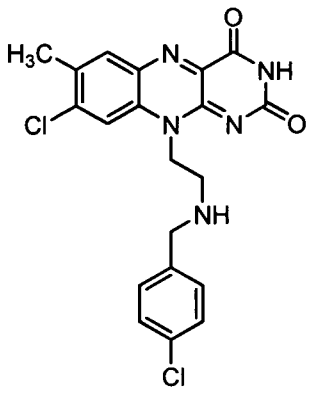


Example 90

10-[2-(4-Chloro-benzylamino)-ethyl]-8-cyclopentyloxy-7-methyl-10H-benzo[g]pteridine-2,4-dione

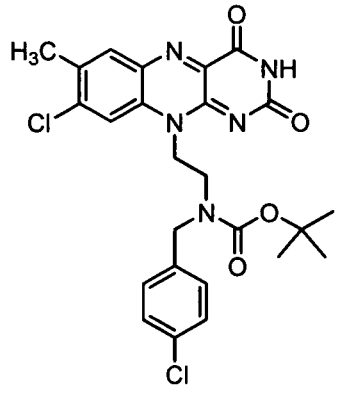


Step 1 Preparation of 8-Chloro-10-[2-(4-chloro-benzylamino)-ethyl]-7-methyl-10H-benzo[g]pteridine-2,4-dione



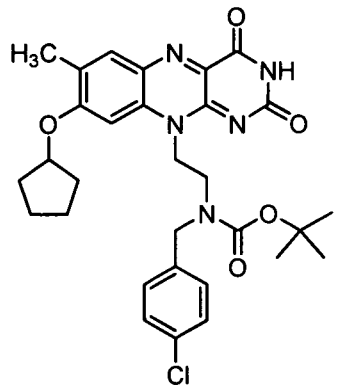
[0311] Prepared similarly to Example 73, Step 5.

Step 2 Preparation of (4-Chloro-benzyl)-[2-(8-chloro-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-carbamic acid tert-butyl ester



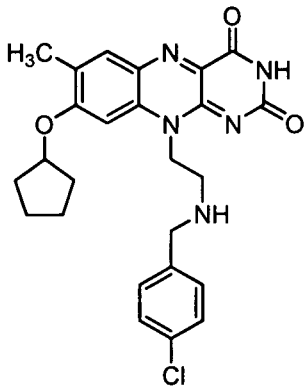
[0312] Prepared similarly to Example 74, Step 1.

Step 3 Preparation of (4-Chloro-benzyl)-[2-(8-cyclopentyloxy-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-carbamic acid tert-butyl ester



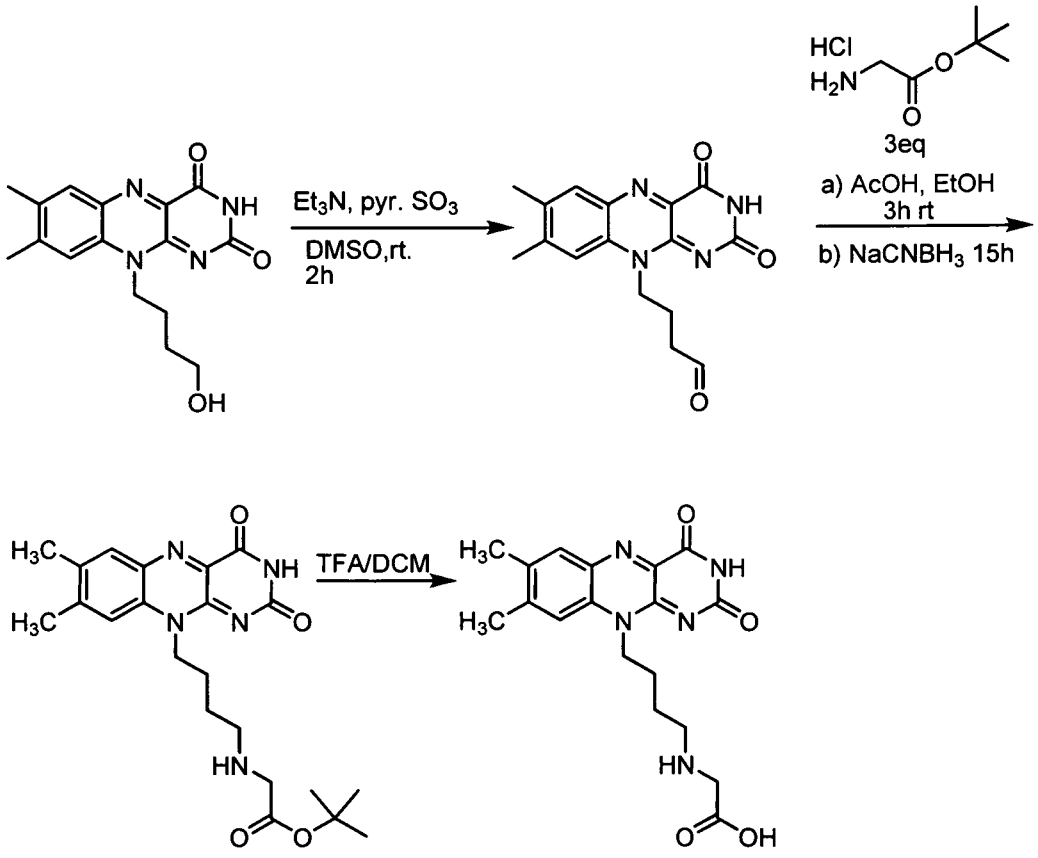
[0313] Prepared similarly to Example 74, Step 2.

Step 4 Preparation of 10-[2-(4-Chloro-benzylamino)-ethyl]-8-cyclopentyloxy-7-methyl-10H-benzo[g]pteridine-2,4-dione



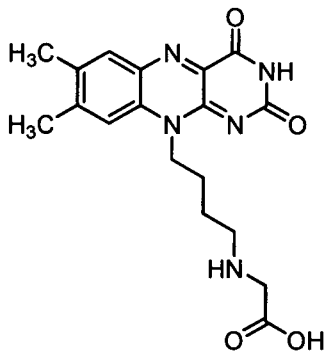
[0314] (4-Chloro-benzyl)-[2-(8-cyclopentyloxy-7-methyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-ethyl]-carbamic acid tert-butyl ester (3.98 mg, 0.00686 mmol) is dissolved in a 1:1 mixture of DCM/TFA (3 mL) and stirred at rt for 1h. The reaction mixture is concentrated and lyophilized without further purification to give 10-[2-(4-chloro-benzylamino)-ethyl]-8-cyclopentyloxy-7-methyl-10H-benzo[g]pteridine-2,4-dione (4.03 mg, Yield: 100%) as a yellow powder. ^{1}H NMR (400 MHz, CD_3OD) δ 1.80 (m, 2H), 1.95 (m, 4H), 2.12 (m, 2H), 2.34 (s, 3H), 3.69 (m, 2H), 4.40 (s, 2H), 5.14 (t, 2H), 5.30 (m, 1H), 7.01 (s, 1H), 7.48 (dd, 2H), 7.51 (dd, 2H), 7.87 (s, 1H). LC-MS m/z 480.0 $[M + H]^+$, retention time 5.03 min.

Scheme 28:

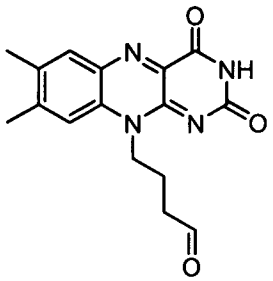


Example 91

[4-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-butylamino]-acetic acid

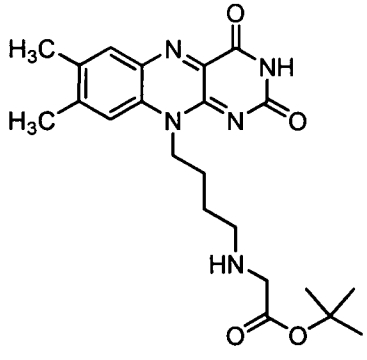


Step 1 Preparation of 4-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-butyraldehyde



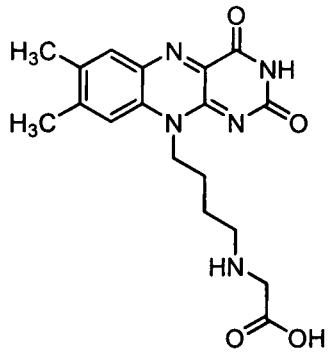
[0315] 10-(4-Hydroxy-butyl)-7,8-dimethyl-10H-benzo[g]pteridine-2,4-dione (prepared similarly to Example 77, Steps 2-4 150 mg, 0.48 mmol) is dissolved in DMSO (5mL) and then triethylamine (145 mg, 1.44 mmol) is added and stirred at rt. After 45 minutes, pyridine sulfur trioxide complex is added to the reaction mixture and the mixture is stirred at rt for an additional hour. The crude reaction mixture dissolved in DMSO is carried on to the next step.

Step 2 Preparation of [4-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-butylamino]-acetic acid tert-butyl ester



[0316] Prepared similarly to Example 73, Step 5.

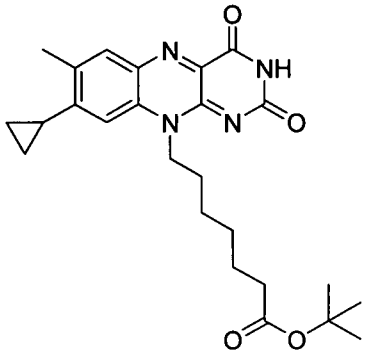
Step 3 Preparation of [4-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-butylamino]-acetic acid



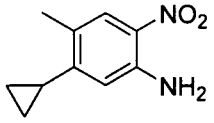
[0317] [4-(7,8-Dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-butylamino]-acetic acid tert-butyl ester (8.0 mg, 0.0187 mmol) is dissolved in a 1:1 mixture of DCM/TFA (3 mL) and stirred at rt for 1h. The reaction mixture is concentrated and lyophilized without further purification to give [4-(7,8-dimethyl-2,4-dioxo-3,4-dihydro-2H-benzo[g]pteridin-10-yl)-butylamino]-acetic acid (6.47 mg, Yield: 93%) as a yellow powder. ^{1}H NMR (400 MHz, CD_3OD) δ 1.92 (m, 2H), 2.01 (m, 2H), 2.48 (s, 3H), 2.60 (s, 3H), 3.27 (m, 2H), 3.93 (s, 2H), 4.78 (t, 2H), 7.80 (s, 1H), 7.97 (s, 1H). LC-MS m/z 372.1 $[M + H]^+$, retention time 3.41 min.

Example 92

***tert*-Butyl 7-(8-Cyclopropyl-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate**



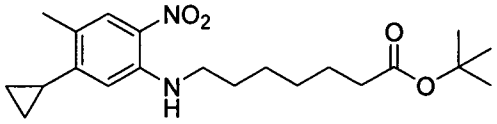
Step 1 Preparation of 4-Amino-2-cyclopropyl-5-nitrotoluene



[0318] A well-stirred slurry of 4-amino-2-chloro-5-nitrotoluene (500 mg, 2.7 mmol), cyclopropylboronic acid (460 mg, 5.4 mmol) and Cs_2CO_3 (2.60 g, 8.0 mmol) in anhydrous 1,4-dioxane (10.0 mL) is sparged with nitrogen for 10 min. [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II),complex with dichloromethane (1:1) (440 mg, 0.54 mmol) is added and sparging continued for another 10 min. The reaction is sealed under nitrogen and heated at 90 °C for 24 h. The reaction is cooled, diluted with DCM (100mL) and filtered through Celite®. The organics are washed with saturated bicarbonate solution, brine, dried with anhydrous sodium sulfate and concentrated. The residue is chromatographed on silica gel (Silicycle, 230-400 mesh, 150 g, elution with 10 % ethyl accetate/hexane) to give 290 mg of an orange solid. ^{1}H NMR

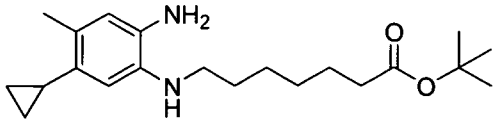
(400 MHz, $CDCl_3$) δ ppm 0.68 (2 H, m), 1.02 (2 H, m), 1.86 (1 H, m), 2.31 (3 H, s), 5.91 (2 H, br s), 6.32 (1 H, s), 7.88 (1 H, s). MS (ESI+) for $C_{10}H_{12}N_2O_2$ m/z 193.2 (M+H)+, retention time: 4.17 min (System C).

Step 2 Preparation of *tert*-Butyl 7-[(5-cyclopropyl-4-methyl-2-nitrophenyl)amino]heptanoate



[0319] A solution of 4-amino-2-cyclopropyl-5-nitrotoluene (190.0 mg, 0.9885 mmol) in dry DMF (5.0 mL) is cooled at 0 °C under nitrogen and sodium hydride (39.5 mg, 0.988 mmol) is added as a solid. Hydrogen evolution is observed and the mixture is allowed to warm to rt and stir for 30 min. *tert*-Butyl 7-bromoheptanoate (314 mg, 1.19 mmol) in DMF (2 mL) is then added dropwise via syringe and stirring is continued at rt for 18h. The reaction is concentrated *in vacuo* to remove DMF and the residue is partitioned between DCM and saturated ammonium chloride (25 mL each). The layers are separated, the aqueous is extracted with DCM (3 x 25 mL), and the organics are combined, dried with anhydrous sodium sulfate and concentrated. The residue is chromatographed on silica gel (Silicycle, 230-400 mesh, 50 g, elution with 5% EtOAc/Hexane) to give 120 mg of desired product as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 0.70 (2 H, m), 1.04 (2 H, m), 1.42 (4 H, m), 1.44 (9 H, s), 1.62 (2 H, m), 1.71 (2 H, m), 1.88 (1 H, m), 2.23 (2 H, t), 2.32 (3 H, s), 3.25 (2 H, m), 6.35 (1 H, s), 7.93 (1 H, s), 7.98 (1 H, br s.). MS (ESI+) for $C_{21}H_{32}N_2O_4$ m/z 399.2 (M+Na)+, retention time: 6.13 min (System C).

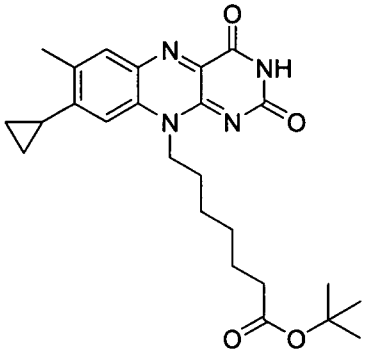
Step 3 Preparation of *tert*-Butyl 7-[(2-amino-5-cyclopropyl-4-methylphenyl)amino]heptanoate



[0320] A solution of tert-butyl 7-[(5-cyclopropyl-4-methyl-2-nitrophenyl)amino]heptanoate (120.0 mg, 0.3187 mmol) in ethanol (5.0 mL) is stirred at rt and activated (wet) Raney Nickel (20 mg, 0.3 mmol) is added. The reaction is then placed under an atmospheric pressure of hydrogen gas and evacuated and purged 4 times prior to allowing the reaction to stir at rt. After 18h, the mixture is filtered through Celite® and concentrated to give 110 mg of desired product as a clear, colorless oil that is used

immediately without further purification. MS (ESI+) for $C_{21}H_{34}N_2O_2$ m/z 347.3 (M+H)+, retention time: 3.92 min (System C).

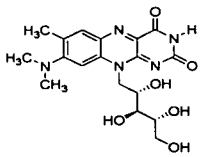
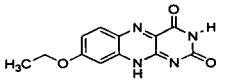
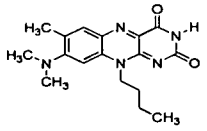
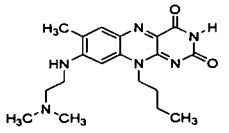
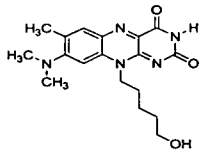
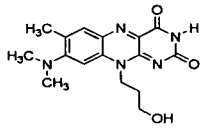
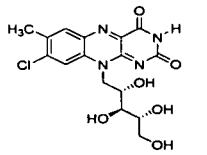
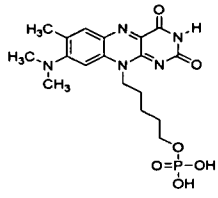
Step 4 Preparation of *tert*-Butyl 7-(8-Cyclopropyl-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate

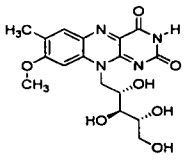
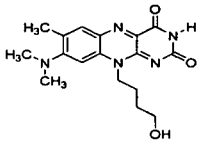
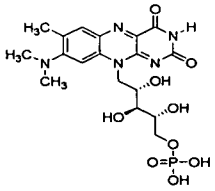
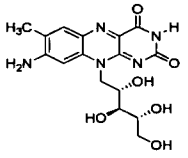
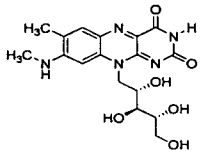
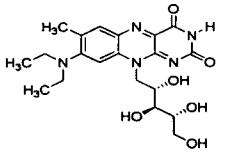
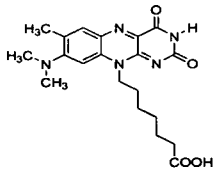
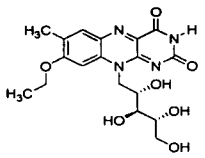


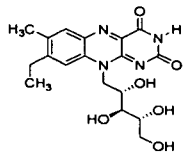
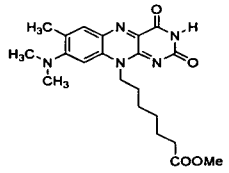
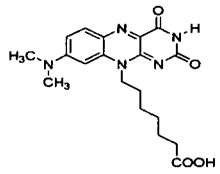
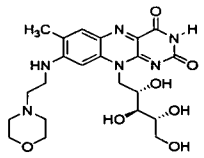
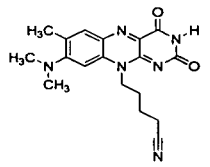
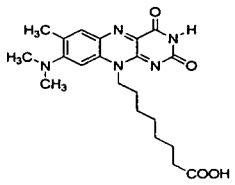
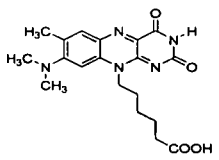
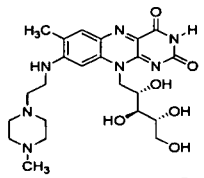
[0321] To a well-stirred mixture of *tert*-butyl 7-[(2-amino-5-cyclopropyl-4-methylphenyl)amino]heptanoate (110.0 mg, 0.32 mmol) and boron oxide (23.9 mg, 0.64 mmol) in acetic acid (1 mL) at rt under nitrogen is added alloxan (50.8 mg, 0.32 mmol) and the reaction is heated at 60 °C for 60 min. The residue is partitioned between DCM and saturated sodium bicarbonate solution (30 mL each) and the layers are separated. The aqueous layer is extracted with DCM (3 x 30 mL) and the organics are combined, dried with anhydrous sodium sulfate and concentrated. The residue is chromatographed on silica gel (Silicycle, 230-400 mesh, 50 g, elution with 2% EtOH in chloroform) to give 37 mg of desired product as an amorphous yellow solid. ^{1}H NMR (400 MHz, *DMSO-d6*) δ ppm 0.93 (2 H, m), 1.14 (2 H, m), 1.39 (9H, s), 1.41 (4 H, m), 1.51 (2 H, m), 1.66 (2 H, m), 2.19 (3 H, m), 2.55 (3 H, s), 4.61 (2 H, m), 7.22 (1 H, s), 7.91 (1 H, s), 11.29 (1 H, s). MS (ESI+) for $C_{25}H_{32}N_4O_4$ m/z 453.2 (M+H)+, retention time: 4.23 min (System C).

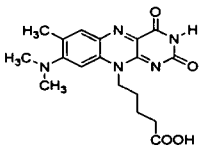
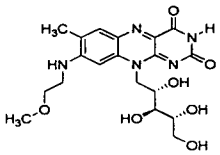
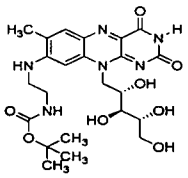
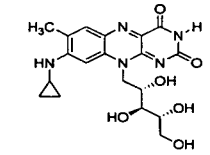
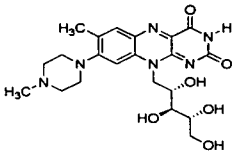
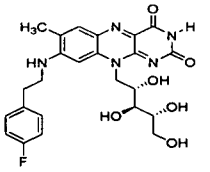
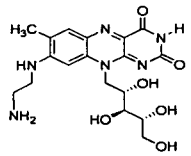
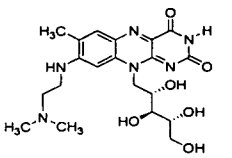
[0322] By using the methods described above and by selecting the appropriate starting materials, other compounds of the invention are prepared and characterized. These compounds, together with the Examples described above, are summarized in Table 1. The invention therefore encompasses and claims each and all compounds in Table 1 collectively and/or separately as well as compositions containing the same, methods of treatment comprising administering such compound(s) and uses of these compound(s) in the menufacture of a medicament for the prophylaxis or treatment of the disorders as hereinbefore described.

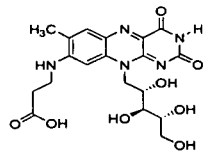
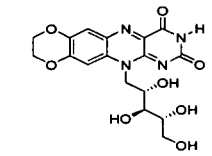
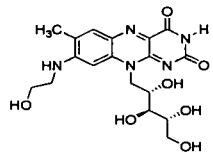
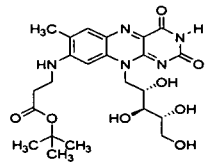
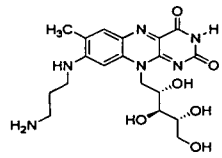
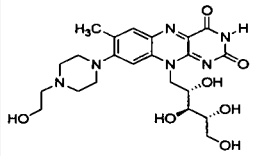
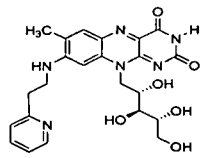
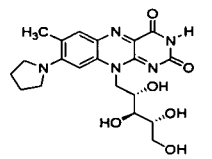
Table 1

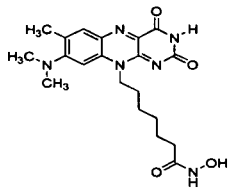
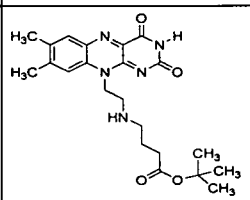
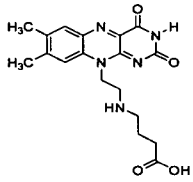
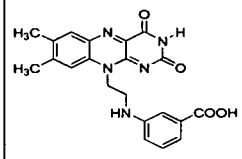
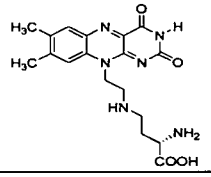
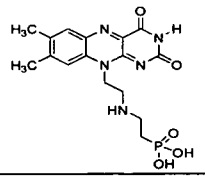
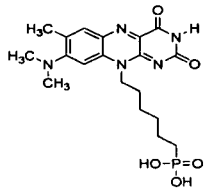
Entry	Structures	LC-MS MH+ (m/z)	LC-MS retention time (min)	LC-MS method	Preparation	Name
1						8-(dimethylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
2						8-ethoxybenzo[g]pteridine-2,4(3H,10H)-dione
3		328.3	5.9	Method A	Prepared using the synthesis of Example 10	10-butyl-8-(dimethylamino)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione
4		371.2	4.9	Method A	Prepared using the synthesis of Example 10	10-butyl-8-(2-(dimethylamino)ethylamino)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione
5		358.3	5.4	Method A	Prepared using the synthesis of Example 10	8-(dimethylamino)-10-(5-hydroxypentyl)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione
6		330.2	5.1	Method A	Prepared using the synthesis of Example 10	8-(dimethylamino)-10-(3-hydroxypropyl)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione
7		397.1	4.9	Method A	Intermediate in the synthesis of Example 4	8-chloro-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
8		436.1 (M-1)	5.3	Method A	Prepared using the synthesis of Example 3	5-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)pentyl dihydrogen phosphate

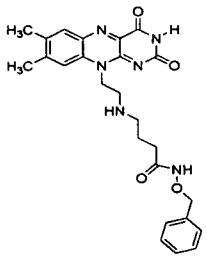
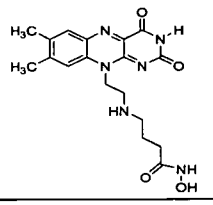
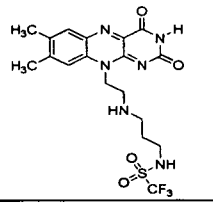
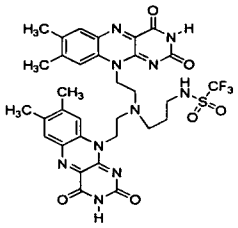
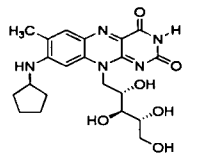
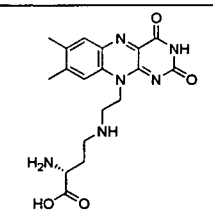
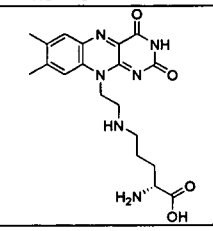
9		390.9	4.1	Method B	Prepared using the synthesis of Example 4	8-methoxy-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
10		344.3	4.8	Method B	Prepared using the synthesis of Example 10	8-(dimethylamino)-10-(4-hydroxybutyl)-7-methylbenzo[g]pteridine-2,4(3H,10H)-dione
11		484.1 (M-H)	3.7	Method B	Prepared using the synthesis of Example 2	(2R,3S,4S)-5-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-2,3,4-trihydroxypentyl dihydrogen phosphate
12		378.2	4.2	Method A	Prepared using the synthesis of Example 5	8-amino-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
13		392.1	1.9	Method B	Prepared using the synthesis of Example 4	7-methyl-8-(methylamino)-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
14		434.2	2.3	Method B	Prepared using the synthesis of Example 4	8-(diethylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
15		398.1	3.4	Method B	Prepared using the synthesis of Example 8	7-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid
16		407.2	2.1	Method C	Prepared using the synthesis of Example 4	8-ethoxy-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione

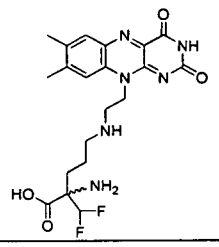
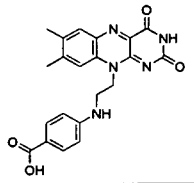
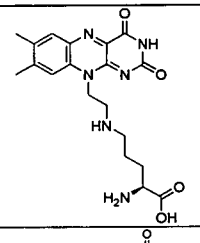
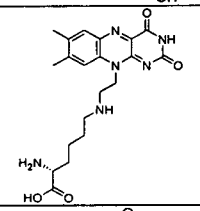
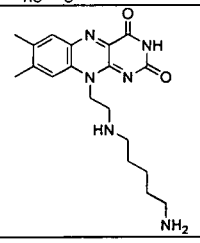
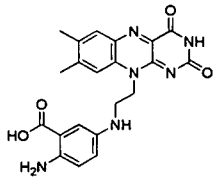
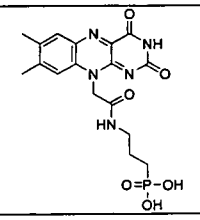
17		391.2	2.4	Method B	Prepared using the synthesis of Example 4 using 3-Ethyl-4-Methylaniline hydrochloride as starting material	8-ethyl-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
18		414.3	3.8	Method B	Prepared using the synthesis of Example 9	methyl 7-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate
19		384.1 (M-H)	3	Method B	Prepared using the synthesis of Example 7	7-(8-(dimethylamino)-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoic acid
20		491.3	1.5	Method B	Prepared using the synthesis of Example 4	7-methyl-8-(2-morpholinoethylamino)-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
21		353.3	3	Method B	Prepared using the synthesis of Example 11	5-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)pentanenitrile
22		414.3	3.6	Method B	Prepared using the synthesis of Example 8	8-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)octanoic acid
23		386.3	3.1	Method B	Prepared using the synthesis of Example 8	6-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexanoic acid
24		504.4	1.5	Method B	Prepared using the synthesis of Example 4	7-methyl-8-(2-(4-methylpiperazin-1-yl)ethylamino)-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione

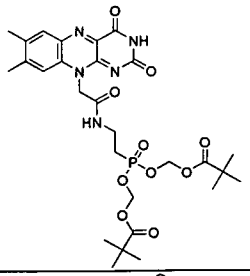
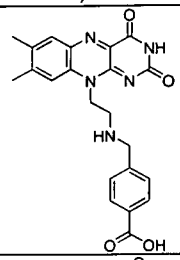
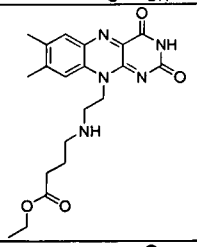
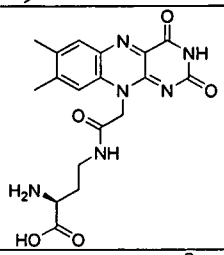
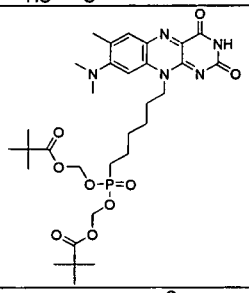
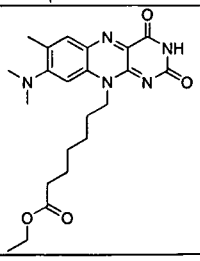
25		372.2	2.3	Method C	Prepared using the synthesis of Example 11	5-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)pentanoic acid
26		436.3	4.3	Method A	Prepared using the synthesis of Example 4	8-(2-methoxyethylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
27		521.3	5.2	Method A	Prepared using the synthesis of Example 4	tert-butyl 2-(7-methyl-2,4-dioxo-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)-2,3,4,10-tetrahydrobenzo[g]pteridin-8-ylamino)ethylcarbamate
28		418.3	4.9	Method A	Prepared using the synthesis of Example 4	8-(cyclopropylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
29		461.3	3.9	Method A	Prepared using the synthesis of Example 4	7-methyl-8-(4-methylpiperazin-1-yl)-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
30		500.3	5.5	Method A	Prepared using the synthesis of Example 4	8-(4-fluorophenethylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
31		421.3	3.7	Method A	Prepared using the synthesis of Example 4 and step 2 of Example 17	8-(2-aminoethylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
32		449.3	3.7	Method A	Prepared using the synthesis of Example 4	8-(2-(dimethylamino)ethylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione

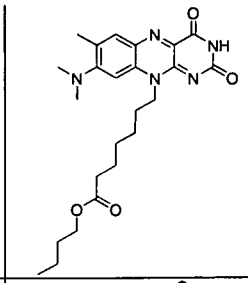
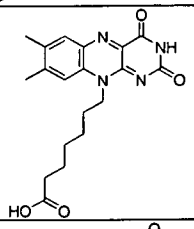
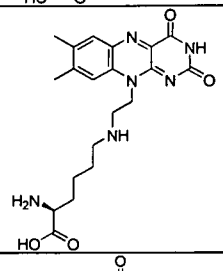
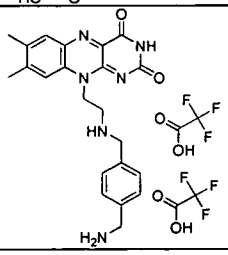
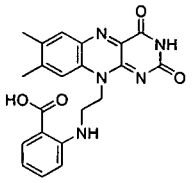
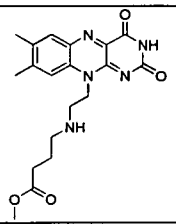
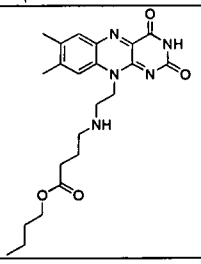
33		450.3	4.2	Method A	Prepared using the synthesis of Example 4 and step 2 of Example 17	3-(7-methyl-2,4-dioxo-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)-2,3,4,10-tetrahydrobenzo[g]pteridin-8-ylamino)propanoic acid
34		407.3	4.1	Method A	Prepared using the synthesis of Example 6	12-(2S,3S,4R,5-tetrahydroxy-pentyl)-8,9-dihydro-12H-7,10-dioxa-1,3,5,12-tetraaza-napthacene-2,4-dione
35		422.3	4	Method A	Prepared using the synthesis of Example 4	8-(2-hydroxyethylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
36		506.2	5.4	Method A	Prepared using the synthesis of Example 4	tert-butyl 3-(7-methyl-2,4-dioxo-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)-2,3,4,10-tetrahydrobenzo[g]pteridin-8-ylamino)propanoate
37		435.3	3.8	Method A	Prepared using the synthesis of Example 4	8-(3-aminopropylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
38		491.4	3.8	Method A	Prepared using the synthesis of Example 4	8-(4-(2-hydroxyethyl)piperazin-1-yl)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
39		483.3	4.1	Method A	Prepared using the synthesis of Example 4	7-methyl-8-(2-(pyridin-2-yl)ethylamino)-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
40		432.3	4.7	Method A	Prepared using the synthesis of Example 4	7-methyl-8-(pyrrolidin-1-yl)-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione

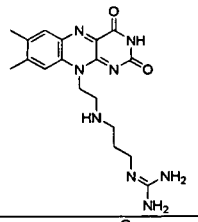
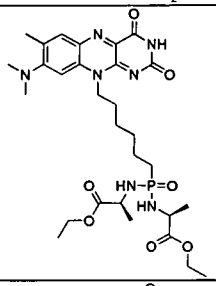
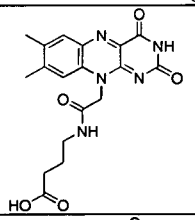
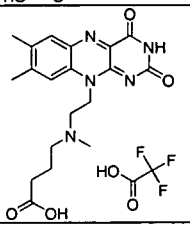
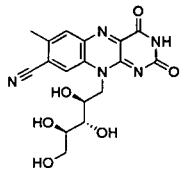
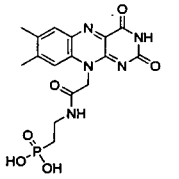
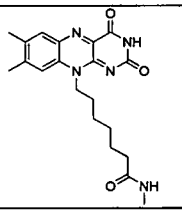
41		413.2 (M-H)	5.1	Method A	Prepared using the synthesis of Example 18	7-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)-N-hydroxyheptanamide
42		428.2	5.6	Method A	Prepared using the synthesis of Reductive Amination of Example 20	tert-butyl 4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)butanoate
43		372.2	4.4	Method A	Prepared using the synthesis of step 2, Example 15	4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)butanoic acid
44		404.1 (M-H)	6.2	Method A	Prepared using the syntheses of Example 15, step 2 and Example 17, step 2.	3-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)benzoic acid
45		385.1 (M-H)	4	Method A	Prepared using the method of Example 17	(S)-2-amino-4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)butanoic acid
46		394	3.9	Method A	Prepared using the syntheses of Example 19.	2-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)ethylphosphonic acid
47		436.3	9.2	Method D	Prepared using the synthesis of Example 13	6-(8-(dimethylamino)-7-methyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)hexylphosphonic acid

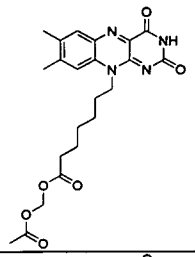
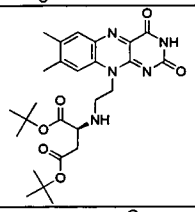
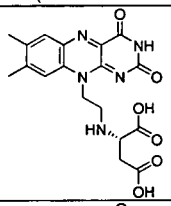
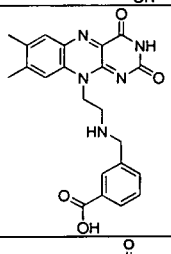
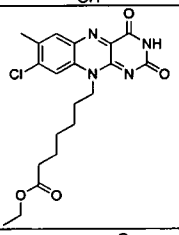
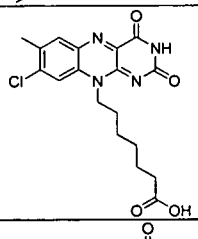
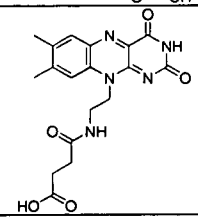
48		477	5.8	Method A	Prepared using the synthesis of Example 22	N-(benzyloxy)-4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)butanamide
49		387.1	4.4	Method A	Prepared using the synthesis of Example 23	4-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)-N-hydroxybutanamide
50		475.2	6	Method A	Prepared using the synthesis of Example 15	N-(3-(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethylamino)propyl)-1,1,1-trifluoromethanesulfonamide
51		743.3	6.7	Method A	Prepared using the synthesis of Example 16	N-(3-(bis(2-(7,8-dimethyl-2,4-dioxo-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)ethyl)amino)propyl)-1,1,1-trifluoromethanesulfonamide
52		446.3	5.08	Method A	Prepared using the synthesis of Example 4	8-(cyclopentylamino)-7-methyl-10-((2S,3S,4R)-2,3,4,5-tetrahydroxypentyl)benzo[g]pteridine-2,4(3H,10H)-dione
53		387.1	4.08	Method A	Prepared using a procedure similar to that of Example 50 except that the reaction was run at rt for 16 h.	(2R)-2-amino-4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]butanoic acid
54		401.1	4.2	Method A	Prepared using a procedure similar to that of example 50 except that the reaction was run at rt for 23 h.	(2R)-2-amino-5-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]pentanoic acid

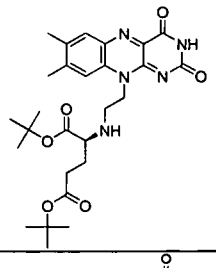
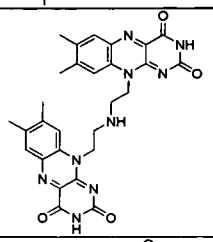
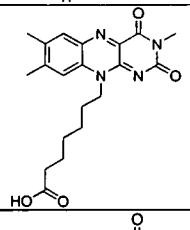
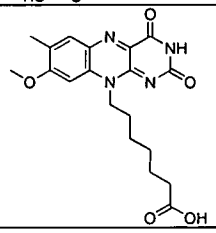
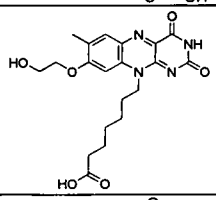
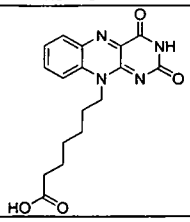
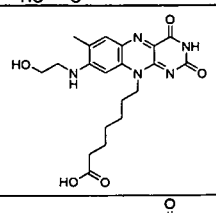
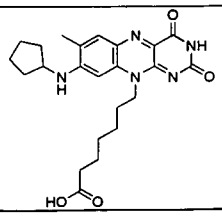
55		451.2	4.14	Method A	Prepared using the procedure of Example15, Step 2	2-amino-2-(difluoromethyl)-5-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]pentanoic acid
56		404.1 [M-H]-	2.38	Method C	Prepared using the procedure of Example 48	4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]benzoic acid
57		401.2	4.09	Method A	Prepared using the procedure of Example 50	(2S)-2-amino-5-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]pentanoic acid
58		415.3	4.21	Method A	Prepared using the procedure of Example 50	(2R)-2-amino-6-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]hexanoic acid
59		371.2	4.3	Method A	Prepared using the procedure of Example 50	10-{2-[(5-aminopentyl)amino]ethyl}-7,8-dimethyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione
60		419.1	4.62	Method A	Prepared using the procedure of Example 50	2-amino-5-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]benzoic acid
61		MH-420.4	4.343	Method A	Prepared using the procedure of Example 53	[3-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}acetamido)propyl]phosphonic acid

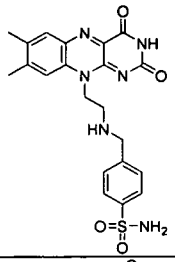
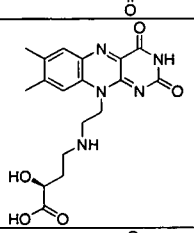
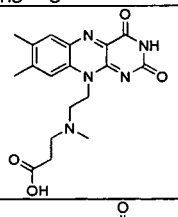
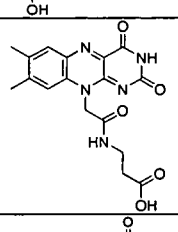
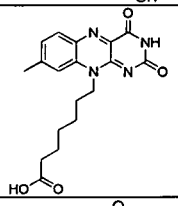
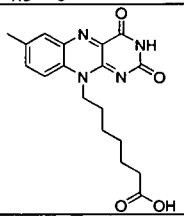
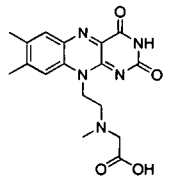
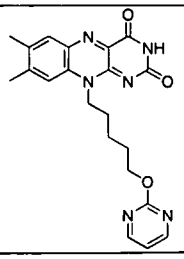
62		636.1	7.99	Method A	Prepared using the procedure of Example 26	({[2-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}acetamido)ethyl]({[(2,2-dimethylpropanoyl)oxy]methoxy})phosphoryl}oxy)methyl 2,2-dimethylpropanoate
63		418.5 {M-H]-	5.18	Method A	Prepared using the procedure of Example 59	4-{[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]methyl}benzoic acid
64		400.1	5.14	Method A	Prepared using the procedure of Example 51	ethyl 4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]butanoate
65		399.3 [M-H]-	4.34	Method A	Prepared using the procedure of Example 52	(2S)-2-amino-4-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}acetamido)butanoic acid
66		664.2	5.83	Method C	Prepared using the procedure of Example 42	[({6-[8-(dimethylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]hexyl}({[(2,2-dimethylpropanoyl)oxy]methoxy})phosphoryl)oxy]methyl 2,2-dimethylpropanoate
67		428.4	6.61	Method A	Prepared using the procedure of Example 9	ethyl 7-[8-(dimethylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoate

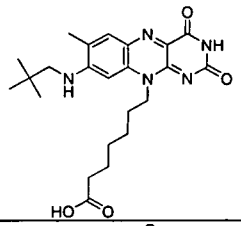
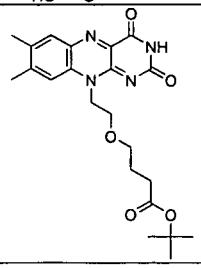
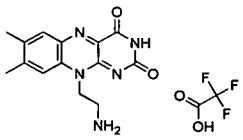
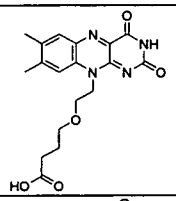
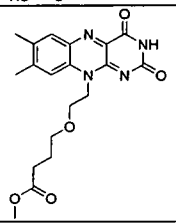
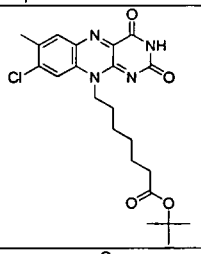
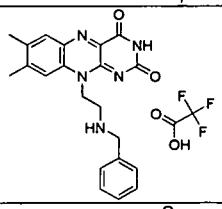
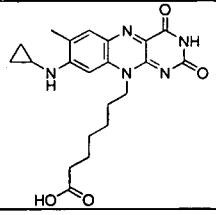
68		456.4	7.44	Method A	Prepared using the procedure of Example 9	butyl 7-[8-(dimethylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoate
69		MH-396.3	6.121	Method A	Prepared using the procedure of Example 44	7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
70		415.3	4.28	Method A	Prepared using the procedure of Example 50	(2S)-2-amino-6-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]hexanoic acid
71		405.1	4.16	Method C	Prepared using the procedure of Example 54	10-[2-({[4-(aminomethyl)phenyl]methyl}amino)ethyl]-7,8-dimethyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione; bis(2,2,2-trifluoroacetic acid)
72		404.1	6.1	Method A	Prepared using the procedure of Example 48	2-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]benzoic acid
73		386.3	5.03	Method A	Prepared using the procedure of Example 51	methyl 4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]butanoate
74		428.3	5.86	Method A	Prepared using the procedure of Example 51	butyl 4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]butanoate

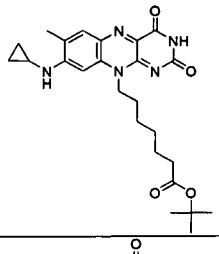
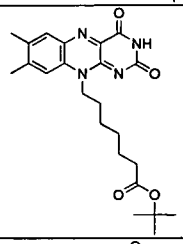
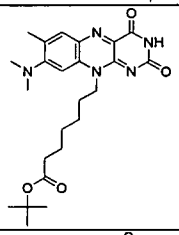
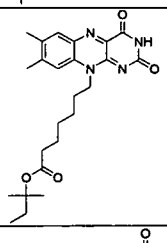
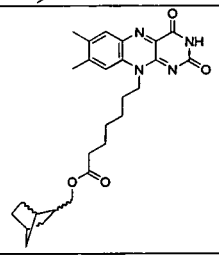
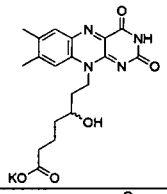
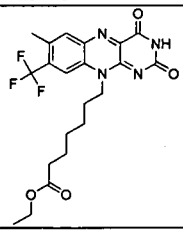
75		385.3	4.25	Method A	Prepared using the procedure of Example 58	2-{3-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]propyl}guanidine
76		634.4	3.31	Method C	Prepared using the procedure of Example 43	ethyl (2S)-2-[({6-[8-(dimethylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]hexyl}({[(2S)-1-ethoxy-1-oxopropan-2-yl]amino})phosphoryl)amino]propanoate
77		386.1	1.8	Method C	Prepared using the procedure of Example 52	4-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}acetamido)butanoic acid
78		386.3	4.43	Method A	Prepared using the procedure of Example 49	2,2,2-trifluoroacetic acid; 4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)(methyl)amino]butanoic acid
79		410.1 (M+Na)+	1.98	System D	Prepared using the procedure of Example 39	7-methyl-2,4-dioxo-10-[(2S,3S,4R)-2,3,4,5-tetrahydroxypentyl]-2H,3H,4H,10H-benzo[g]pteridine-8-carbonitrile
80		406.1 [M-H]-	3.52	Method B	Prepared using the procedure of Example 53	[2-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}acetamido)ethyl]phosphonic acid
81		384.1	2.52	Method C	Prepared using the procedure of Example 47	7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}-N-methylheptanamide

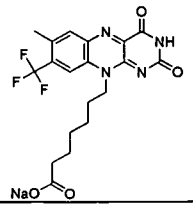
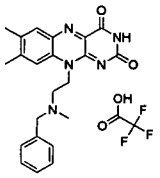
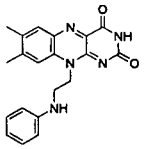
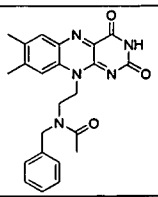
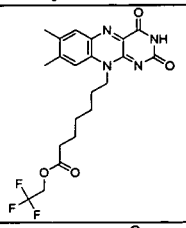
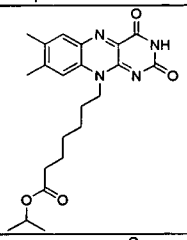
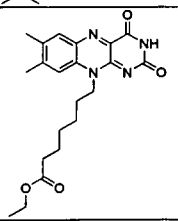
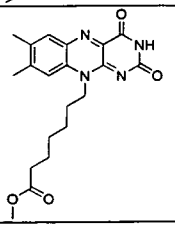
82		443.0	4.78	Method B	Prepared using the procedure of Example 46	(acetyloxy)methyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
83		514	3.02	Method C	Prepared using the procedure of Example 51	1,4-di-tert-butyl (2S)-2-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]butanedioate
84		402	1.43	Method C	Prepared using the procedure of Example 12	(2S)-2-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]butanedioic acid
85		418.2 (M-H)	5.86	Method C	Prepared using the procedure of Example 48, Step 1	3-{[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]methyl}benzoic acid
86		419.1	5.71	System B	Prepared using the procedure of Example 28	ethyl 7-{8-chloro-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
87		391.1	4.7	System B	Prepared using the procedure of Example 29	7-{8-chloro-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
88		386	2.01	Method C	Prepared using the procedure of Example 56	3-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)carbamoyl]propanoic acid

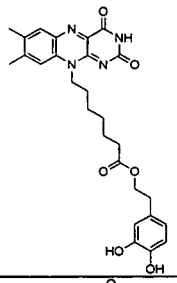
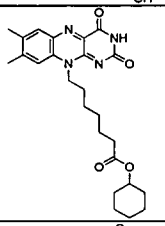
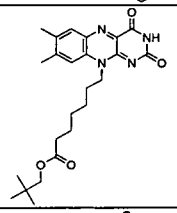
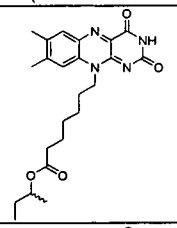
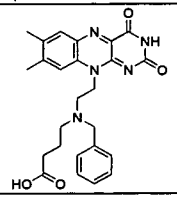
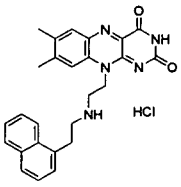
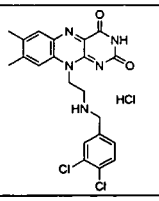
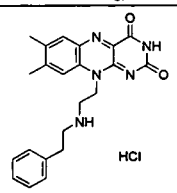
89		528.1	3	Method C	Prepared using the procedure of Example 51	1,5-di-tert-butyl (2S)-2-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]pentanedioate
90		554.1	3.79	Method B	Prepared using the procedure of Example 51	10-{2-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]ethyl}-7,8-dimethyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione
91		385.2	2.77	Method C	Prepared using the procedure of Example 41	7-{3,7,8-trimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
92		387.1	4.44	System B	Prepared using the procedure of Example 30	7-{8-methoxy-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
93		417.0	4.84	System A	Prepared using the procedure of Example 32	7-[8-(2-hydroxyethoxy)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoic acid
94		343.0	2.19	Method C	Prepared using the procedure of Example 45	7-{2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
95		416.2	4.60	System A	Prepared using the procedure of Example 31	7-{8-[(2-hydroxyethyl)amino]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
96		440.2	6.04	System A	Prepared using the procedure of Example 33	7-[8-(cyclopentylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoic acid

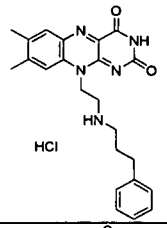
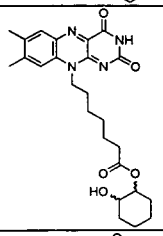
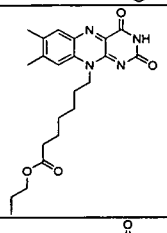
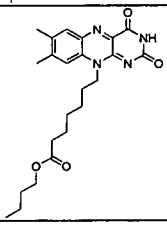
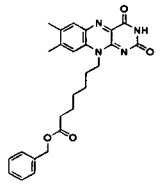
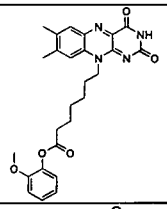
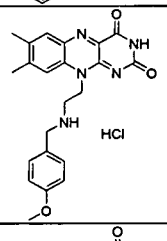
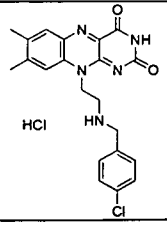
97		455.1	1.67	Method B	Prepared using the procedure of Example 48, Step 1	4-{[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]methyl}benzene-1-sulfonamide
98		388	1.47	Method C	Prepared using the procedure of Example 50	(2S)-4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]-2-hydroxybutanoic acid
99		MH-370.1	4.763	Method A	Prepared using the procedure of Example 49	3-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)(methyl)amino]propanoic acid
100		371.9	6.242	Method A	Prepared using the procedure of Example 52	3-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}acetamido)propanoic acid
101		357.13	6.272	Method A	Prepared using the procedure of Example 44	7-{8-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
102		MH-355.13	6.346	Method A	Prepared using the procedure of Example 44	7-{7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
103		358.13	5.13	Method A	Prepared using the procedure of Example 49	2-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)(methyl)amino]acetic acid
104		407.1	2.86	Method C	Prepared using the procedure of Example 57	7,8-dimethyl-10-[5-(pyrimidin-2-yloxy)pentyl]-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione

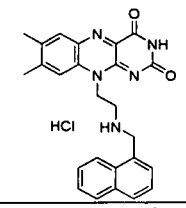
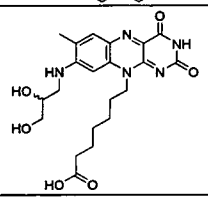
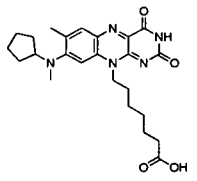
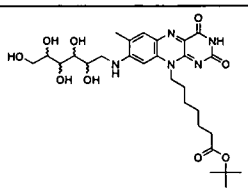
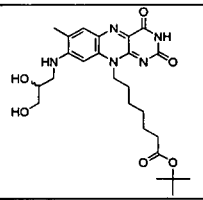
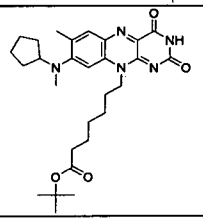
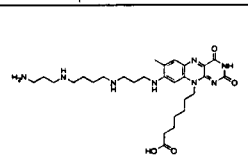
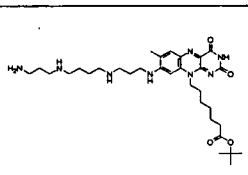
105		442.1	3.01	System C	Prepared using the procedure of Example 34	7-{8-[(2,2-dimethylpropyl)amino]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
106		429.1	3.52	System D	Prepared using the procedure of Example 37, Step 2	tert-butyl 4-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethoxy)butanoate
107		286	3.24	Method C	Prepared using the procedure of Example 40	10-(2-aminoethyl)-7,8-dimethyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione; 2,2,2-trifluoroacetic acid
108		373.0	2.38	System D	Prepared using the procedure of Example 37	4-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethoxy)butanoic acid
109		387.1	2.78	System D	Prepared using the procedure of Example 38	methyl 4-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethoxy)butanoate
110		447.0	4.2	System D	Prepared using the procedure of Example 36, Step 3	tert-butyl 7-{8-chloro-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
111		376.1	2.11	Method C	Prepared using the procedure of Example 55	10-[2-(benzylamino)ethyl]-7,8-dimethyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione; 2,2,2-trifluoroacetic acid
112		412.1	2.58	System D	Prepared using the procedure of Example 35	7-[8-(cyclopropylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoic acid

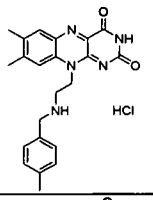
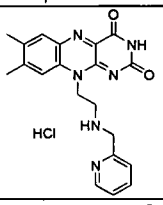
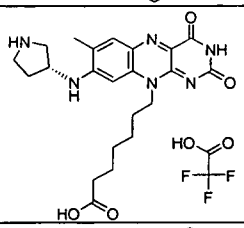
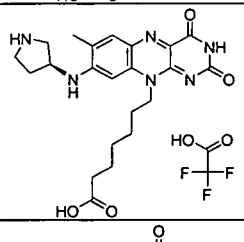
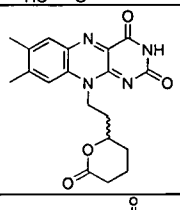
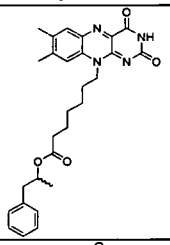
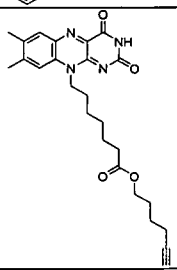
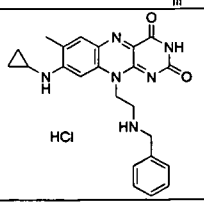
113		468.1	3.63	System C	Prepared using the procedure of Example 36	tert-butyl 7-[8-(cyclopropylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoate
114		427.1	3.64	Method B	Prepared using the procedure of Example 24	tert-butyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
115		456.1	3.74	System C	Prepared using the procedure of Example 36, step 4	tert-butyl 7-[8-(dimethylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoate
116		440.9 [M+H]+ 463.0 [M+Na]+	8.81	Method A	Prepared using the procedure of Example 66	2-methylbutan-2-yl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
117		479.2	5.65	Method C	Prepared using the procedure of Example 25	bicyclo[2.2.1]heptan-2-ylmethyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
118		424.88	3.87	System B	Prepared using the procedure of Example 64	potassium 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}-5-hydroxyheptanoate
119		451.1	5.83	System B	Prepared using the procedure of Example 63, Step 4	ethyl 7-[7-methyl-2,4-dioxo-8-(trifluoromethyl)-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoate

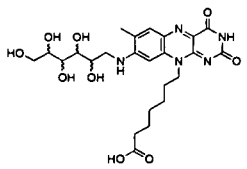
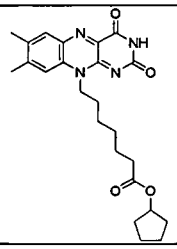
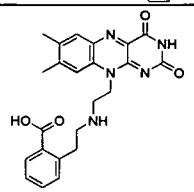
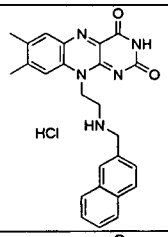
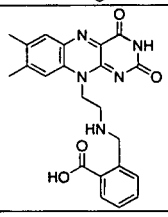
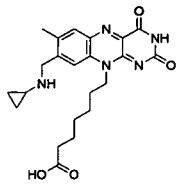
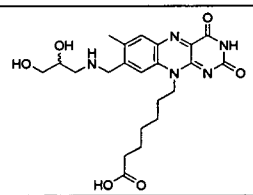
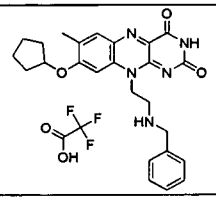
120		423.0 (M-H)-	4.92	System B	Prepared using the procedure of Example 63	sodium 7-(7-methyl-2,4-dioxo-8-(trifluoromethyl)-3,4-dihydrobenzo[g]pteridin-10(2H)-yl)heptanoate
121		389.9	3.9	Method C	Prepared using the procedure of Example 49	10-{2-[benzyl(methyl)amino]ethyl}-7,8-dimethyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione; 2,2,2-trifluoroacetic acid
122		361.9	4.82	Method C	Prepared using the procedure of Example 49	7,8-dimethyl-10-[2-(phenylamino)ethyl]-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione
123		417.9	4.56	Method C	Prepared using the procedure of Example 72	N-benzyl-N-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)acetamide
124		453.1	5.51	Method C	Prepared using the procedure of Example 25	2,2,2-trifluoroethyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
125		ESI(+) m/z = 413.1			Prepared using the procedure of Example 25	propan-2-yl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
126		399.0	5.19	Method C	Prepared using the procedure of Example 25	ethyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
127		385.0	4.94	Method C	Prepared using the procedure of Example 25	methyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate

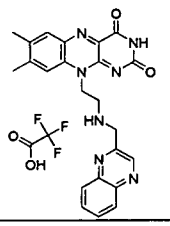
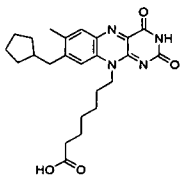
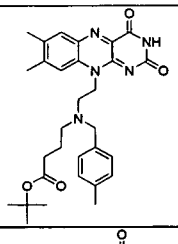
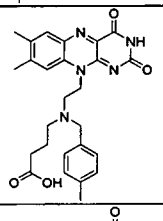
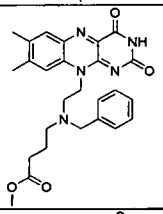
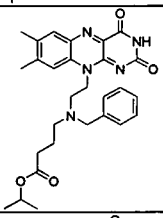
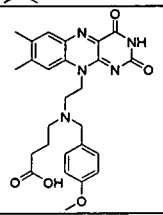
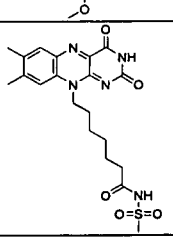
128		507.0	5.03	Method C	Prepared using the procedure of Example 25	2-(3,4-dihydroxyphenyl)ethyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
129		453.0	6.01	Method C	Prepared using the procedure of Example 25	cyclohexyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
130		441.0	5.96	Method C	Prepared using the procedure of Example 25	2,2-dimethylpropyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
131		426.9	5.69	Method C	Prepared using the procedure of Example 25	butan-2-yl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
132		461.9	3.95	Method C	Prepared using the procedure of Example 75, Step 2	4-[benzyl(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]butanoic acid
133		440.1	4.46	Method C	Prepared using the procedure of Example 70	7,8-dimethyl-10-(2-{[2-(naphthalen-1-yl)ethyl]amino}ethyl)-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride
134		443.9	4.41	Method C	Prepared using the procedure of Example 70	10-(2-{[(3,4-dichlorophenyl)methyl]amino}ethyl)-7,8-dimethyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride
135		390.1	4.04	Method C	Prepared using the procedure of Example 70	7,8-dimethyl-10-{2-[(2-phenylethyl)amino]ethyl}-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride

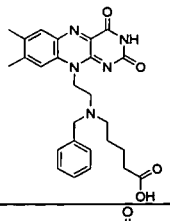
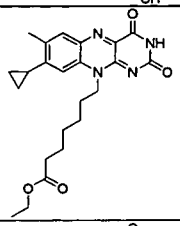
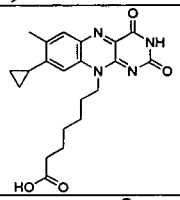
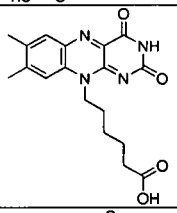
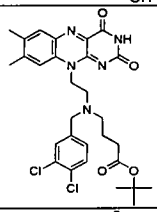
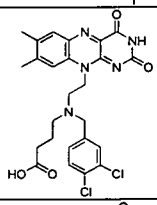
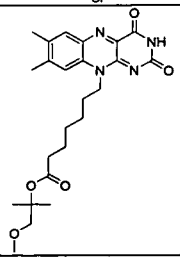
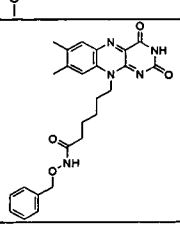
136		404.1	4.28	Method C	Prepared using the procedure of Example 70	7,8-dimethyl-10-{2-[(3-phenylpropyl)amino]ethyl}-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride
137		469.1	5.06	Method C	Prepared using the procedure of Example 25	2-hydroxycyclohexyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
138		413.2	5.46	Method C	Prepared using the procedure of Example 25	propyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
139		427.2	5.75	Method C	Prepared using the procedure of Example 25	butyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
140		461.2	5.72	Method C	Prepared using the procedure of Example 24, Step 2	benzyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
141		477.1	5.58	Method C	Prepared using the procedure of Example 24, Step 2	2-methoxyphenyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
142		406	3.93	Method C	Prepared using the procedure of Example 70	10-(2-{[(4-methoxyphenyl)methyl]amino}ethyl)-7,8-dimethyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride
143		410.1	4.17	Method C	Prepared using the procedure of Example 70	10-(2-{[(4-chlorophenyl)methyl]amino}ethyl)-7,8-dimethyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride

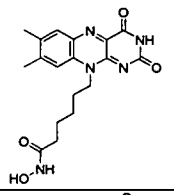
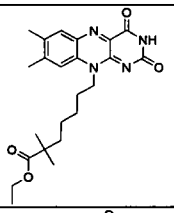
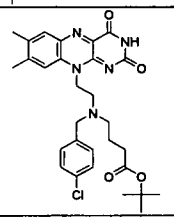
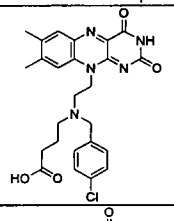
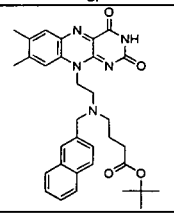
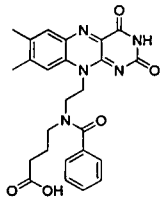
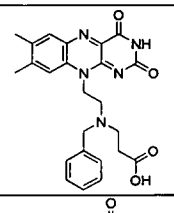
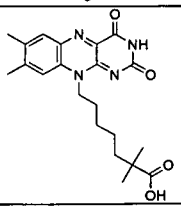
144		426	4.11	Method C	Prepared using the procedure of Example 70	7,8-dimethyl-10-{2-[(naphthalen-1-ylmethyl)amino]ethyl}-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride
145		446.2	2.01	Method C	Prepared using the procedure of Example 79	7-{8-[(2,3-dihydroxypropyl)amino]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
146		454.3	3.26	Method C	Prepared using the procedure of Example 80	7-{8-[cyclopentyl(methyl)amino]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
147		592.1	2.56	Method C	Prepared using the procedure of Example 81	tert-butyl 7-{7-methyl-2,4-dioxo-8-[(2,3,4,5,6-pentahydroxyhexyl)amino]-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
148		502	2.77	Method C	Prepared using the procedure of Example 79	tert-butyl 7-{8-[(2,3-dihydroxypropyl)amino]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
149		510.2	4.28	Method C	Prepared using the procedure of Example 80	tert-butyl 7-{8-[cyclopentyl(methyl)amino]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
150		557.3	3.27	Method C	Prepared using the procedure of Example 82	7-(8-{[3-({4-[(3-aminopropyl)amino]butyl}amino)propyl]amino}-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl)heptanoic acid
151		613.3	2.26	Method C	Prepared using the procedure of Example 82	tert-butyl 7-(8-{[3-({4-[(3-aminopropyl)amino]butyl}amino)propyl]amino}-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl)heptanoate

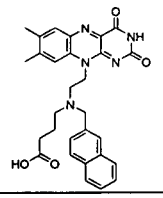
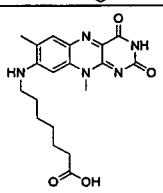
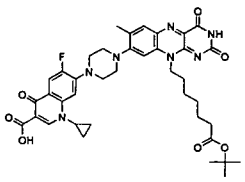
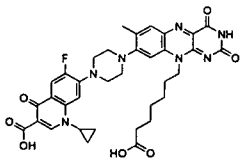
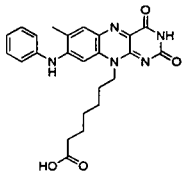
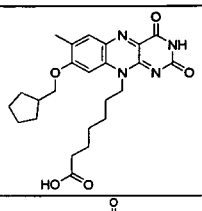
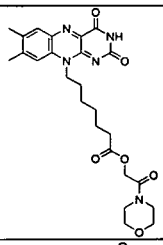
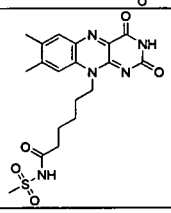
152		390.2	2.58	Method C	Prepared using the procedure of Example 70	7,8-dimethyl-10-(2-{[(4-methylphenyl)methyl]amino}ethyl)-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride
153		377.1	3.57	Method C	Prepared using the procedure of Example 70	7,8-dimethyl-10-{2-[(pyridin-2-ylmethyl)amino]ethyl}-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride
154		441.2	1.99	Method C	Prepared using the procedure of Example 61	2,2,2-trifluoroacetic acid; 7-{7-methyl-2,4-dioxo-8-[(3R)-pyrrolidin-3-ylamino]-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
155		441.2	1.99	System C	Prepared using the procedure of Example 62	2,2,2-trifluoroacetic acid; 7-{7-methyl-2,4-dioxo-8-[(3S)-pyrrolidin-3-ylamino]-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
156		367.0	4.14	System B	Prepared using the procedure of Example 64, Step 3	7,8-dimethyl-10-[2-(6-oxooxan-2-yl)ethyl]-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione
157		489.1	5.41	Method C	Prepared using the procedure of Example 25	1-phenylpropan-2-yl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
158		451.3	5.02	Method C	Prepared using the procedure of Example 25	hex-5-yn-1-yl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
159		417	3.51	Method C	Prepared using the procedure of Example 73	10-[2-(benzylamino)ethyl]-8-(cyclopropylamino)-7-methyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride

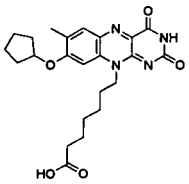
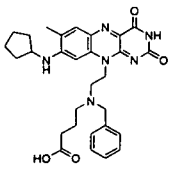
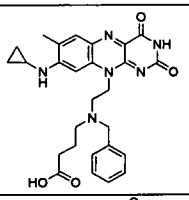
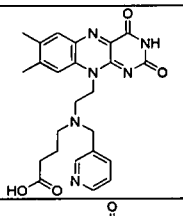
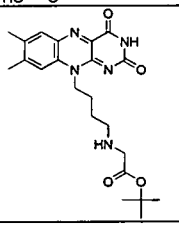
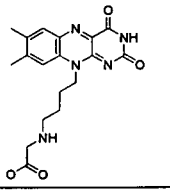
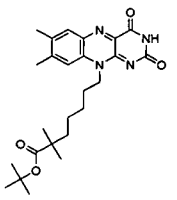
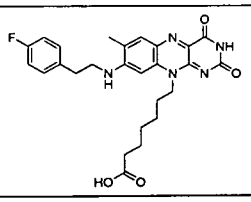
160		536.2	3.27	Method C	Prepared using the procedure of Example 81	7-{7-methyl-2,4-dioxo-8-[(2,3,4,5,6-pentahydroxyhexyl)amino]-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
161		439.1	5.09	Method C	Prepared using the procedure of Example 25	cyclopentyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
162		434	3.5	Method C	Prepared using the procedure of Example 70	2-{2-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]ethyl}benzoic acid
163		426	3.87	Method C	Prepared using the procedure of Example 71	7,8-dimethyl-10-{2-[(naphthalen-2-ylmethyl)amino]ethyl}-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione hydrochloride
164		420	3.36	Method C	Prepared using the procedure of Example 71	2-{[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]methyl}benzoic acid
165		426	3.17	Method C	Prepared using the procedure of Example 86	7-{8-[(cyclopropylamino)methyl]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
166		460.3	1.77	Method C	Prepared using the procedure of Example 81	7-(8-{[(2,3-dihydroxypropyl)amino]methyl}-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl)heptanoic acid
167		446.1	4.35	Method C	Prepared using the procedure of Example 74	10-[2-(benzylamino)ethyl]-8-(cyclopentyloxy)-7-methyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione; 2,2,2-trifluoroacetic acid

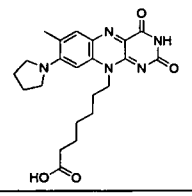
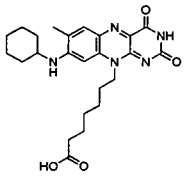
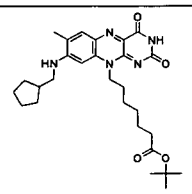
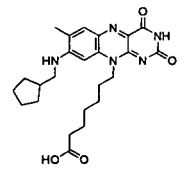
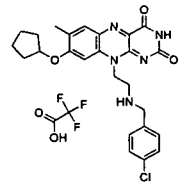
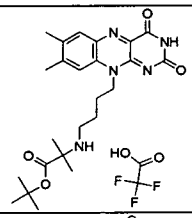
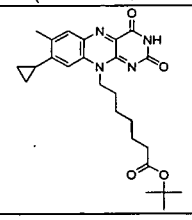
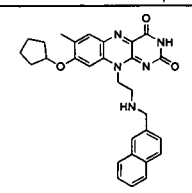
168		428.1	3.55	Method C	Prepared using the procedure of Example 71	2,2,2-trifluoroacetic acid; 7,8-dimethyl-10-{2-[(quinoxalin-2-ylmethyl)amino]ethyl}-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione
169		439.1	4.92	Method C	Prepared using the procedure of Example 88	7-[8-(cyclopentylmethyl)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoic acid
170		532.1	4.45	Method C	Prepared using the procedure of Example 75	tert-butyl 4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)[(4-methylphenyl)methyl]amino]butanoate
171		476.1	3.74	Method C	Prepared using the procedure of Example 75	4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)[(4-methylphenyl)methyl]amino]butanoic acid
172		476.0	3.81	Method C	Prepared using the procedure of Example 25	methyl 4-[benzyl(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]butanoate
173		504.1	4.14	Method C	Prepared using the procedure of Example 25	propan-2-yl 4-[benzyl(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]butanoate
174		491.9	3.61	Method C	Prepared using the procedure of Example 75	4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)[(4-methoxyphenyl)methyl]amino]butanoic acid
175		447.9	4.02	Method C	Prepared using the procedure of Example 69	7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}-N-methanesulfonylheptanamide

176		476	3.66	Method C	Prepared using the procedure of Example 75	5-[benzyl(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]pentanoic acid
177		425.2	3.7	System D	Prepared using the procedure of Example 65, Step 3	ethyl 7-{8-cyclopropyl-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
178		397.1	3.1	System D	Prepared using the procedure of Example 65	7-{8-cyclopropyl-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
179		357	2.75	Method C	Prepared using the procedure of Example 44	6-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}hexanoic acid
180		586	4.82	Method C	Prepared using the procedure of Example 75	tert-butyl 4-{[(3,4-dichlorophenyl)methyl](2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino}butanoate
181		529.9	8.85	Method B	Prepared using the procedure of Example 75	4-{[(3,4-dichlorophenyl)methyl](2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino}butanoic acid
182		456.9 [M+H]+ 479.1 [M+Na]+	4.84	Method C	Prepared using a procedure similar to that of Example 24, Step 2 (stirred at 70 °C)	1-methoxy-2-methylpropan-2-yl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
183		462.1	4.33	Method C	Prepared using the procedure of Example 66	N-(benzyloxy)-6-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}hexanamide

184		372	3.56	Method C	Prepared using the procedure of Example 67	6-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}-N-hydroxyhexanamide
185		427.1	5.05	Method C	Prepared using the procedure of Example 77	ethyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}-2,2-dimethylheptanoate
186		552	4.59	Method C	Prepared using the procedure of Example 75	tert-butyl 4-{[(4-chlorophenyl)methyl](2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino}butanoate
187		495.9	3.88	Method C	Prepared using the procedure of Example 75	4-{[(4-chlorophenyl)methyl](2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino}butanoic acid
188		568.1	4.57	Method C	Prepared using the procedure of Example 75	tert-butyl 4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)(naphthalen-2-ylmethyl)amino]butanoate
189		475.9	3.81	Method C	Prepared using the procedure of Example 52, Step 1-2 using the product of Example 20 as starting material	4-[N-(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)-1-phenylformamido]butanoic acid
190		448	3.58	Method C	Prepared using the procedure of Example 75	3-[benzyl(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)amino]propanoic acid
191		399.1	3.07	Method C	Prepared using the procedure of Example 78	7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}-2,2-dimethylheptanoic acid

192		512.1	4.28	Method C	Prepared using the procedure of Example 75	4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)(naphthalen-2-ylmethyl)amino]butanoic acid
193		386.3	2.55	Method C	Prepared using the procedure of Example 76	7-({7,10-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-8-yl}amino)heptanoic acid
194		742.1	5.65	Method C	Prepared using the procedure of Example 85	7-(4-{10-[7-(tert-butoxy)-7-oxoheptyl]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-8-yl}piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid
195		686.3	5.72	Method C	Prepared using the procedure of Example 85	7-{4-[10-(6-carboxyhexyl)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-8-yl]piperazin-1-yl}-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid
196		448.2	4.54	Method C	Prepared using the procedure of Example 4, Step 7	7-[7-methyl-2,4-dioxo-8-(phenylamino)-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoic acid
197		455.2	5.67	Method C	Prepared using the procedure of Example 84	7-[8-(cyclopentylmethoxy)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoic acid
198		498.1	4.58	Method C	Prepared using the procedure similar to that of Example 69 (stirred at 65 °C)	2-(morpholin-4-yl)-2-oxoethyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
199		434.1	2.48	Method C	Prepared using the procedure of Example 68	6-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}-N-methanesulfonylhexanamide

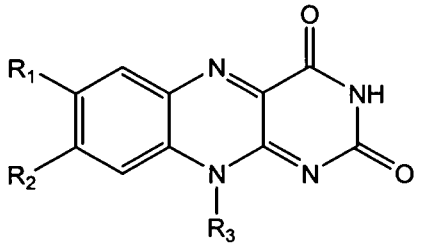
200		441.1	5.31	Method C	Prepared using the procedure of Example 83	7-[8-(cyclopentyloxy)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoic acid
201		531.1	4.27	Method C	Prepared using the procedure of Example 89	4-[benzyl({2-[8-(cyclopentylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]ethyl})amino]butanoic acid
202		503.1	3.82	Method C	Prepared using the procedure of Example 89	4-[benzyl({2-[8-(cyclopropylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]ethyl})amino]butanoic acid
203		463	3.54	Method C	Prepared using the procedure of Example 75	4-[(2-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}ethyl)(pyridin-3-ylmethyl)amino]butanoic acid
204		428.1	4.07	Method C	Prepared using the procedure of Example 91, Steps 1-2	tert-butyl 2-[(4-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}butyl)amino]acetate
205		372.1	3.48	Method C	Prepared using the procedure of Example 91	2-[(4-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}butyl)amino]acetic acid
206		455	6.24	Method C	Prepared using a procedure similar to that of Example 24, Step 2 [reaction conducted at 60 °C]	tert-butyl 7-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}-2,2-dimethylheptanoate
207		494.3	3.15	Method C	Prepared using the procedure of Example 79, Step 1-3	7-(8-{[2-(4-fluorophenyl)ethyl]amino}-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl)heptanoic acid

208		426.3	2.84	Method C	Prepared using the procedure of Example 79, Step 1-3	7-[7-methyl-2,4-dioxo-8-(pyrrolidin-1-yl)-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoic acid
209		454.1	4.96	Method C	Prepared using the procedure of Example 79, Step 1-3	7-[8-(cyclohexylamino)-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl]heptanoic acid
210		510	6.67	Method B	Prepared using the procedure of Example 79, Step 1-3	tert-butyl 7-{8-[(cyclopentylmethyl)amino]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
211		454.2	5	Method C	Prepared using the procedure of Example 79, Step 1-3	7-{8-[(cyclopentylmethyl)amino]-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoic acid
212		480	5.03	Method C	Prepared using the procedure of Example 90	10-(2-{[(4-chlorophenyl)methyl]amino}ethyl)-8-(cyclopentyloxy)-7-methyl-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione; 2,2,2-trifluoroacetic acid
213		456	4.38	Method C	Prepared using the procedure of Example 91	2,2,2-trifluoroacetic acid; tert-butyl 2-[(4-{7,8-dimethyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}butyl)amino]-2-methylpropanoate
214		453.2	4.23	System C	Prepared using the procedure of Example 92	tert-butyl 7-{8-cyclopropyl-7-methyl-2,4-dioxo-2H,3H,4H,10H-benzo[g]pteridin-10-yl}heptanoate
215		496.1	7.12	Method B	Prepared using the procedure of Example 90	8-(cyclopentyloxy)-7-methyl-10-{2-[(naphthalen-2-ylmethyl)amino]ethyl}-2H,3H,4H,10H-benzo[g]pteridine-2,4-dione

CLAIMS

1. A method for the treatment or prophylaxis of a bacterial infection comprising administering to a patient in need of such treatment an effective amount of a compound selected from:

a) a Compound of formula I(i):



Formula I(i)

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl) or C_{3-7} cycloalkyl;

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -N(R_4)(R_5), C_{3-7}cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl); or

(iii) R_1 and R_2 are connected so as to form a cyclic ring structure optionally containing one or more heteroatoms selected from N, O and S (e.g., –OCH_2CH_2O-);

(iv) R_3 is H or C_{1-8} alkyl (e.g., methyl, ethyl, n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -OP(O)(OR_9)(OR_{17}), -OP(O)(OR_9)($NR_{13}R_{14}$), -OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$), -P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -CN, -C(O)OR_9, -C(O)N(H)(R_8), -OR_{10}, -C(O)N(R_6)(R_7), and -N(R_6)(R_7);

(v) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{4-7}heterocycle (e.g., piperazinyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from –OR_{11}, –

$C(O)OR_9$, $-N(R_6)(R_7)$ (e.g., amino or dimethylamino), C_{1-8}alkoxyl (e.g., methoxy), C_{6-10}aryl (e.g., phenyl), C_{5-10} heteroaryl (e.g., pyridinyl) wherein said aryl or heteroaryl are optionally substituted with halo (e.g.,4-fluorophenyl), and C_{4-7}heterocycle wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl);

(vi) R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-propyl, n-butyl), $-C_{1-8}$alkyl-OR_{11}, $-C(O)OR_9$, $-C_{1-8}$alkyl-$C(O)OR_9$, $-C_{1-8}$alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$C(O)N(H)R_8$, $-C_{1-8}$alkyl-$P(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$ $-C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl and aryl wherein said aryl and alkyl are optionally substituted with $-COOR_9$;

(vii) R_8 is H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), $-OR_{11}$ or –OBn;

(viii) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

(ix) R_{10} is H, C_{1-8}alkyl (e.g., methyl or ethyl), $-C_{1-8}$alkyl-OR_{11}, $-C_{1-8}$alkyl-$C(O)OR_9$, $-C_{1-8}$alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$C(O)N(H)R_8$, $-C_{1-8}$alkyl-$P(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$P(O)$ $(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, $-C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl, or aryl wherein said aryl and alkyl are optionally substituted with $-COOR_9$, or $-C_{1-4}$alkyl-$OC(O)R_{12}$;

(x) R_{11} is H, or $-C_{1-4}$alkyl-$OC(O)R_{12}$ (e.g., $-CH_2$-$OC(O)R_{12}$);

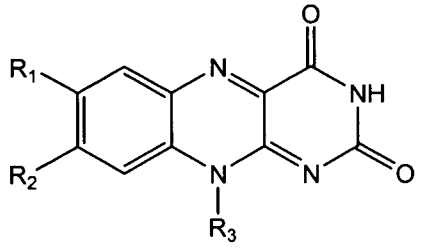
(xi) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy);

(xii) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$, -CH(isopropyl)-$COOR_{18}$, -CH(isobutyl)-$COOR_{18}$, -CH(sec-butyl)-$COOR_{18}$), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –CH(CH_2CH_2COOH)-COOH);

(xiii) R_{18} is H or C_{1-8}alkyl (e.g., ethyl);

in free, pharmaceutically accpetable salt or prodrug form;

b) a Compound of formula I:



Formula I

wherein

(i) R_1 is H, C_{1-8}alkyl (e.g., methyl) or C_{3-7}cycloalkyl;

(ii) R_2 is H, halo (e.g., chloro), C_{1-8} alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), -N(R_4)(R_5), C_{3-7}cycloalkyl or C_{4-7}heterocycle (e.g., piperazinyl or pyrrolidinyl) wherein said heterocycle is optionally substituted with C_{1-8}alkyl (e.g., 4-methyl-piperazin-1-yl) or hydroxyC_{1-8}alkyl (e.g., 4-hydroxyethyl-piperazin-1-yl);

(iii) R_3 is H or C_{1-8} alkyl (e.g., n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -OP(O)(OR_9)(OR_{17}), -OP(O)(OR_9)($NR_{13}R_{14}$), -OP(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$), -P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -CN, -C(O)OR_9, -C(O)N(H)(R_8), -OR_{10}, -C(O)N(R_6)(R_7), and -N(R_6)(R_7); or

(iv) R_1 and R_2 are connected so as to form a cyclic ring structure optionally containing one or more heteroatoms selected from N, O and S (e.g., –OCH_2CH_2O-);

(v) R_4 and R_5 are independently selected from H, C_{3-7}cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{4-7}heterocycle (e.g., piperazinyl), and C_{1-8} alkyl (e.g., methyl or ethyl) wherein said alkyl is optionally substituted with one or more groups selected from –OR_{11}, –$C(O)OR_9$, -$N(R_6)(R_7)$ (e.g., amino or dimethylamino), C_{1-8}alkoxyl (e.g., methoxy), C_{6-10} aryl (e.g., phenyl), C_{5-10}heteroaryl (e.g., pyridinyl) wherein said aryl or heteroaryl are optionally substituted with halo (e.g.,4-fluorophenyl), and C_{4-7}heterocycle wherein said heterocycle is optionally substituted with C_{1-8} alkyl (e.g., morpholin-4-yl or 4-methylpiperazin-1-yl);

(vi) R_6 and R_7 are independently selected from H, C_{1-8} alkyl (e.g., methyl or ethyl), -C_{1-8} alkyl-OR_{11}, -$C(O)OR_9$, –C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), –C_{1-8}alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$ -C_{1-8}alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-ethyl and aryl wherein said aryl is optionally substituted with –$COOR_9$;

(vii) R_8 is H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), -OR_{11} or –OBn;

(viii) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

(ix) R_{10} is H, C_{1-8} alkyl (e.g., methyl or ethyl), -C_{1-8}alkyl-OR_{11}, –C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), –C_{1-8}alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)$ $(OR_9)(NR_{13}R_{14})$, -C_{1-8}alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-}$

$_8$alkyl-N(H)-S(O)$_2$(CF$_3$), 7,8-dimethyl-isoalloxazin-10-yl-ethyl, or aryl wherein said aryl is optionally substituted with –COOR$_9$, or –C$_{1-4}$alkyl-OC(O)R$_{12}$;

(x) R$_{11}$ is H, or –C$_{1-4}$alkyl-OC(O)R$_{12}$ (e.g., –CH$_2$-OC(O)R$_{12}$);

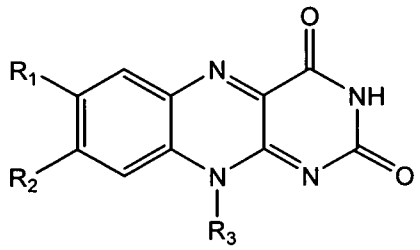
(xi) R$_{12}$ is C$_{1-8}$alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC$_{1-8}$alkyl (e.g., methoxy, ethoxy, *t*-butoxy);

(xii) R$_{13}$, R$_{14}$, R$_{15}$ and R$_{16}$ are independently selected from H, C$_{1-8}$alkyl, and -C$_{1-8}$alkyl-COOR$_{18}$ (e.g., -CH(methyl)-COOH, -CH(isopropyl)-COOH, -CH(isobutyl)-COOH, -CH(sec-butyl)-COOH), wherein the alkyl group of C$_{1-8}$alkyl-COOR$_{18}$ is optionally substituted with hydroxyC$_{1-8}$alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC$_{1-8}$alkyl (e.g., -CH(-CH$_2$COOH)-COOH or –CH(CH$_2$CH$_2$COOH)-COOH);

(xiii) R$_{18}$ is H or C$_{1-8}$alkyl;

in free, pharmaceutically acceptable salt or prodrug form;

c) a Compound of formula I(ii):



Formula I(ii)

wherein

(i) R$_1$ is H, C$_{1-8}$ alkyl (e.g., methyl);

(ii) R$_2$ is H, halo (e.g., chloro), C$_{1-8}$alkyl (e.g., methyl or ethyl), C$_{1-8}$alkoxy (e.g., methoxy or ethoxy), -N(R$_4$)(R$_5$);

(iii) R$_3$ is C$_{1-8}$ alkyl (e.g., methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -OP(O)(OR$_9$)(OR$_{17}$), -OP(O)(OR$_9$)(NR$_{13}$R$_{14}$), -OP(O)(NR$_{13}$R$_{14}$)(NR$_{15}$R$_{16}$), -P(O)(OR$_9$)(OR$_{17}$), -P(O)(OR$_9$)(NR$_{13}$R$_{14}$), -P(O)(NR$_{13}$R$_{14}$)(NR$_{15}$R$_{16}$), -CN, -C(O)OR$_9$, -C(O)N(H)(R$_8$), -OR$_{10}$, -C(O)N(R$_6$)(R$_7$), and -N(R$_6$)(R$_7$);

(iv) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from $-OR_{11}$;

(v) R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-propyl, n-butyl),$-C_{1-8}$alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$C(O)N(H)R_8$, -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$ -C_{1-8}alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl and aryl wherein said aryl and alkyl are optionally substituted with $-COOR_9$;

(vi) R_8 is H, C_{1-8}alkyl (e.g., methyl, ethyl or t-butyl);

(vii) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, phenyl and Bn wherein said phenyl and Bn are optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl);

(viii) R_{10} is $-C_{1-8}$alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(OR_{17})$, -$C_{1-8}$alkyl-$OP(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$OP(O)(NR_{13}R_{14})(NR_{15}R_{16})$, -$C_{1-8}$alkyl-$N(H)$-$S(O)_2(CF_3)$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl wherein said aryl and alkyl are optionally substituted with $-COOR_9$, or $-C_{1-4}$alkyl-$OC(O)R_{12}$;

(ix) R_{11} is H, or $-C_{1-4}$alkyl-$OC(O)R_{12}$ (e.g., $-CH_2$-$OC(O)R_{12}$);

(x) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy);

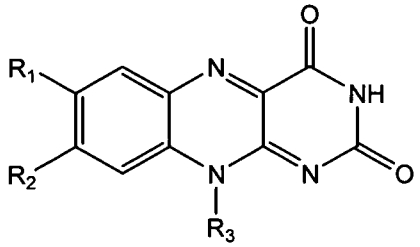
(xi) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$, -CH(isopropyl)-$COOR_{18}$, -CH(isobutyl)-$COOR_{18}$, -CH(sec-butyl)-$COOR_{18}$), wherein the alkyl group of C_{1-8}alkyl-$COOR_{18}$ is optionally substituted with

hydroxyC_{1-8}alkyl (e.g., -CH(hydroxymethyl)-COOH), carboxyC_{1-8}alkyl (e.g., -CH(-CH_2COOH)-COOH or –CH(CH_2CH_2COOH)-COOH); and

(xii) R_{18} is H or C_{1-8}alkyl (e.g., ethyl);

in free, pharmaceutically acceptable salt or prodrug form;

d) a Compound of formula I(iii):



Formula I(iii)

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy), -N(R_4)(R_5);

(iii) R_3 is C_{1-8} alkyl (e.g., methyl, ethyl, n-butyl, n-pentyl, n-propyl, n-hexyl or n-heptyl), wherein the alkyl group is optionally substituted with one or more groups selected from -P(O)(OR_9)(OR_{17}), -P(O)(OR_9)($NR_{13}R_{14}$), -P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), -C(O)OR_9, -OR_{10}, -C(O)N(R_6)(R_7), and -N(R_6)(R_7);

(iv) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from –OH;

(v) R_6 and R_7 are independently selected from H, –C_{1-8}alkyl (e.g., methyl), –C_{1-8}alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 (e.g., -CH_2CH_2CH(NH_2)COOH), -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl, wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

(vi) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$;

(vii) R_{10} is H, –C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, -C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, -$C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$;

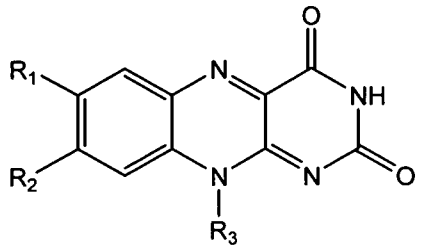
(viii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl);

(ix) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$, -CH(isopropyl)-$COOR_{18}$, -CH(isobutyl)-$COOR_{18}$, -CH(sec-butyl)-$COOR_{18}$);

(x) R_{18} is H or C_{1-8}alkyl (e.g., ethyl);

in free, pharmaceutically acceptable salt or prodrug form;

e) a Compound of formula I(iv):



Formula I(iv)

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), $-N(R_4)(R_5)$;

(iii) R_3 is C_{1-8}alkyl-$N(R_6)(R_7)$, C_{1-8}alkyl-$C(O)N(R_6)(R_7)$, C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, C_{1-8}alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, C_{1-8}alkyl-$C(O)OR_9$, C_{1-8}alkyl-OR_{10};

(iv) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from $–OR_{11}$;

(v) R_6 and R_7 are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-propyl, n-butyl),–C_{1-8}alkyl-$C(O)OR_9$, -C_{1-8}alkyl(amine)-$C(O)OR_9$ (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-

$P(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl and aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

(vi) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), –C_{1-4}alkyl-$OC(O)R_{12}$;

(vii) R_{10} is H, –C_{1-8}alkyl-$C(O)OR_9$, $-C_{1-8}$alkyl(amine)-$C(O)OR_9$ (e.g., $-CH_2CH_2CH(NH_2)COOH$), $-C_{1-8}$alkyl-$P(O)(OR_9)(OR_{17})$, $-C_{1-8}$alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, $-C_{1-8}$alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

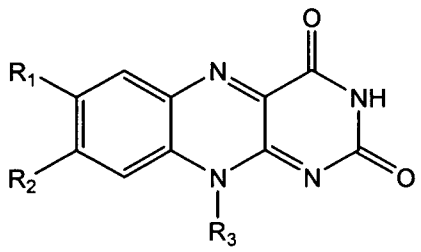
(viii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl);

(ix) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$);

(x) R_{18} is H or C_{1-8}alkyl (e.g., ethyl or t-butyl);

in free, pharmaceutically acceptable salt or prodrug form;

f) a Compound of formula I(v):



Formula I(v)

wherein

(i) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(ii) R_2 is H, halo (e.g., chloro), C_{1-8}alkyl (e.g., methyl or ethyl), C_{1-8}alkoxy (e.g., methoxy or ethoxy), $-N(R_4)(R_5)$;

(iii) R_3 is C_2alkyl-$N(R_6)(R_7)$, C_{1-2}alkyl-$C(O)N(R_6)(R_7)$, C_{1-8}alkyl-$P(O)(OR_9)(OR_{17})$, C_{1-8}alkyl-$P(O)(OR_9)(NR_{13}R_{14})$, C_{1-8}alkyl-$P(O)(NR_{13}R_{14})(NR_{15}R_{16})$, C_{1-8}alkyl-$C(O)OR_9$, C_{1-8}alkyl-OR_{10};

(iv) R_4 and R_5 are independently selected from H, C_{3-7} cycloalkyl (e.g., cyclopropyl or cyclopentyl), and C_{1-8}alkyl (e.g., methyl, ethyl or 2,2-dimethylpropyl) wherein said alkyl is optionally substituted with one or more groups selected from $-OR_{11}$;

(v) R_6 and R_7 are independently selected from $-C_{1-8}$alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl and aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

(vi) R_9 and R_{17} are independently selected from H, C_{1-8}alkyl (e.g., methyl, ethyl, n-butyl or t-butyl), $-C_{1-4}$alkyl-OC(O)R_{12};

(vii) R_{10} is H, $-C_{1-8}$alkyl-C(O)OR_9, -C_{1-8}alkyl(amine)-C(O)OR_9 (e.g., -$CH_2CH_2CH(NH_2)COOH$), -C_{1-8}alkyl-P(O)(OR_9)(OR_{17}), -C_{1-8}alkyl-P(O)(OR_9)($NR_{13}R_{14}$), -C_{1-8}alkyl-P(O)($NR_{13}R_{14}$)($NR_{15}R_{16}$), 7,8-dimethyl-isoalloxazin-10-yl-C_{1-8}alkyl, or aryl wherein said aryl and alkyl are optionally substituted with –$COOR_9$;

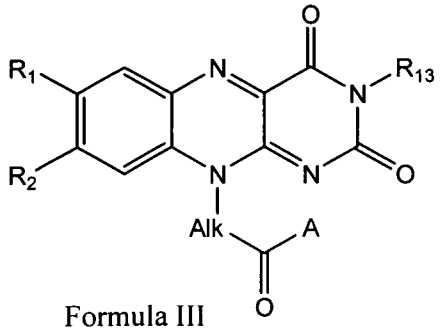
(viii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl);

(ix) R_{13}, R_{14}, R_{15} and R_{16} are independently selected from H, C_{1-8}alkyl, and -C_{1-8}alkyl-$COOR_{18}$ (e.g., -CH(methyl)-$COOR_{18}$);

(x) R_{18} is H or C_{1-8}alkyl (e.g., ethyl or t-butyl);

in free, pharmaceutically acceptable salt or prodrug form;

g) a Compound of formula III:



Formula III

wherein:

(i) Alk is C_{1-8} alkyl (e.g., n-butyl, n-pentyl, n-hexyl, 6,6-dimethylhexyl, n-heptyl);

(ii) A is $-OR_9$ or $-N(R_{14})(R_{15})$;

(iii) R_9 is H, $-C_{1-8}$alkyl (e.g., methyl, ethyl, n-propyl, isopropyl, 1-methylpropyl, t-butyl, n-butyl, 1,1-dimethylpropyl, 2,2-dimethylpropyl, hex-5-ynyl), -haloC_{1-8}alkyl (e.g., 2,2,2-trifluoroethyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, $-C_{1-4}$alkyl-O-C_{1-4}alkyl (e.g., $-C(CH_3)(CH_3)OCH_3$ or $-C(CH_3)(CH_3)CH_2OCH_3$), $-C_{1-4}$alkyl-C(O)-(morphylin-4-yl), $-C_{3-7}$cycloalkyl (e.g., cyclopentyl, cyclohexyl), C_{3-7}cycloalkyl-C_{1-4}alkyl (e.g., norbornan-2-yl-methyl) wherein the cycloalkyl is optionally substituted with hydroxy group; aryl (e.g., phenyl) or aryl-C_{1-4}alkyl (e.g, Benzyl, 1-methyl-2-phenylethyl), wherein said aryl is optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl, 2-methoxyphenyl, 2-(3,4-dihydroxyphenyl)ethyl);

(iv) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(v) R_2 is H, halo (e.g., chloro), -O-C_{3-7}cycloalkyl (e.g., -O-cyclopentyl), -O-C_{0-7} alkylC_{3-7}cycloalkyl (e.g., -O-cyclopentyl, -O-CH_2-cyclopentyl), -$N(R_4)(R_5)$, -(CH_2)-$N(R_4)(R_5)$, -C_{0-4}alkyl-C_{3-7}cycloalkyl (e.g., cyclopropyl, cyclopentylmethyl), heteroC_{3-7}cycloalkyl (e.g., pyrrolidin-1-yl), 1-cyclopropyl-6-fluoro-7-[4-piperazin-1-yl]-4-oxo-quinoline-3-carboxylic acid), C_{1-8}alkyl (e.g., methyl or ethyl) or $-O-C_{1-8}$alkyl (e.g., methoxy), wherein the alkyl group is optionally substituted with one or more halo (e.g., fluoro) or hydroxy groups (e.g., trifluoromethyl, -O-CH_2CH_2OH);

(vi) R_4 and R_5 are independently

a. H,

b. $-C_{0-4}$alkyl-C_{3-7}cycloalkyl (e.g., cyclopropyl, cyclopentyl, cyclohexyl or cyclopentyl-methyl),

c. heteroC_{3-7}cycloalkyl (e.g., pyrrolidinyl, e.g., pyrrolidin3-yl),

d. aryl (e.g., phenyl or 2,2-dimethylpropyl),

e. aryl-C_{1-8}alkyl wherein the aryl is optionally substituted with halo (e.g., 4-fluorophenylethyl),

f. -$(CH_2)_3$-N(H)-$(CH_2)_4$-N(H)-$(CH_2)_3$-$N(H)_2$,

g. -C_{1-8}alkyl (e.g., methyl) wherein said alkyl is optionally substituted with one or more hydroxy groups (e.g., 2,3-dihydroxypropyl, 2,3,4,5,6-pentahydroxyhexyl, hydroxyethyl);

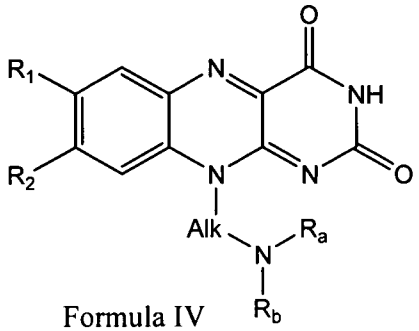
(vii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy); and

(viii) R_{13} is H or C_{1-4}alkyl (e.g., methyl);

(ix) R_{14} and R_{15} are independently H, -OH, -$S(O)_2CH_3$, -OBn or -C_{1-4}alkyl (e.g., methyl),

in free, pharmaceutically acceptable salt or prodrug form.

h) a Compound of formula IV:



Formula IV

wherein:

(i) Alk is C_{1-8} alkyl (e.g., ethyl or n-butyl);

(ii) R_a and R_b are independently H, -C_{1-4}alkyl (e.g., methyl), -$(CH_2)_3C(NH_2)(COOH)CHF_2$, -$(CH_2)_3N(H)C(=NH)NH_2$, -$(CH_2)_5NH_2$, -$(CH_2)_2C(H)(OH)COOH$, -$C(O)(CH_2)_2COOH$, -$C_{1-4}$alkyl-$C(O)OR_9$ (e.g., -$CH_2CH_2CH_2CH_2C(O)OR_9$, -$CH_2CH_2CH_2C(O)OR_9$,-$CH_2CH_2C(O)OR_9$ or -$CH_2C(O)OR_9$, -$C(CH_3)(CH_3)C(O)OR_9$), -$C(O)CH_3$, aryl (e.g., phenyl), -C(O)-aryl, aryl-C_{1-4}alkyl (e.g., benzyl, naphtha-1-ylmethyl, naphth-2-ylmethyl, phenylethyl, phenylpropyl, naphtha-1-ylethyl), heteroaryl, heteroaryl-C_{1-4}alkyl (e.g., pyrid-2-ylmethyl, pyrid-3-ylmethyl or quinoxalinyl), wherein said aryl and heteroaryl groups are optionally substituted with one or more groups selected from –$C(O)OR_9$, -NH_2, -$S(O)_2NH_2$, -CH_2NH_2, halo (e.g., chloro), C_{1-4}alkoxy (e.g., methoxy), C_{1-4}alkyl (e.g., methyl);

(iii) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(iv) R_2 is H, halo (e.g., chloro), -O-C_{3-7}cycloalkyl (e.g., -O-cyclopentyl), -N(R_4)(R_5), C_{3-7}cycloalkyl (e.g., cyclopropyl), C_{1-8}alkyl (e.g., methyl or ethyl) or –O-C_{1-8}alkyl wherein the alkyl group is optionally substituted with one or more halo or hydroxyl groups (e.g., trifluoromethyl, -O-CH_2CH_2OH);

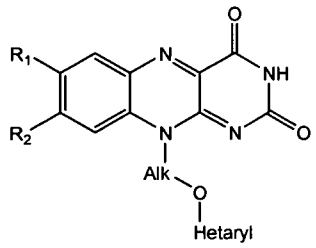
(v) R_4 and R_5 are independently H, C_{3-7}cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{1-8}alkyl (e.g., methyl) wherein said alkyl is optionally substituted with one or more hydroxy groups (e.g., 2,3-dihydroxypropyl, 2,3,4,5,6-pentahydroxyhexyl);

(vi) R_9 is H or C_{1-4}alkyl (e.g., t-butyl, isopropyl, methyl);

(vii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy),

in free, pharmaceutically acceptable salt or prodrug form;

i) a Compound of formula V:

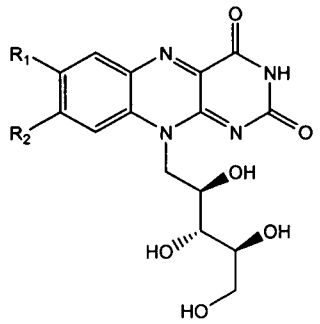


Formula V

wherein Alk is C_{1-6}alkyl and hetaryl is heteroaryl (e.g., pyrimidin-2-yl) and R_1 and R_2 are independently H, C_{1-4}alkyl (e.g., methyl), in free, pharmaceutically acceptable salt or prodrug form;

and

j) a Compound of formula VI:



Formula VI

wherein R_1 is H orC_{1-4}alkyl (e.g., methyl) and R_2 is cyano, in free, pharmaceutically acceptable salt or prodrug form,

with the proviso that: (a) when R_1 is methyl and R_2 is chloro, then R_3 is not methyl; (b) when R_1 is H and R_2 is dimethylamine, then R_3 is not H; (c) when R_3 is (2R,3S,4S)-2,3,4,5-tetrahydroxypentyl or 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl, and R_1 is methyl, then R_2 is not methyl; (d) when R_3 is (2R,3S,4S)-2,3,4,5-tetrahydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino; (e) when R_1 is methyl and R_2 is alkoxy, then R_3 is not 2,3,4,5-tetrahydroxypentyl; and (f) when the bacterial infection is an infection by chlamydophila psittacci, then R_3 is not -$(CH_2)_{2-6}$-phosphate, when R_1 and R_2 are independently selected from a group consisting of C_{1-5}alkyl, C_{1-5}alkoxy, amino, hydrogen and halogen group.

2. The method according to claim 1, wherein compound is a Compound of Formula I.

3. The method according to claim 1, wherein compound is a Compound of Formula I(i).

4. The method according to claim 1, wherein compound is a Compound of Formula I(ii).

5. The method according to claim 1, wherein compound is a Compound of Formula I(iii).

6. The method according to claim 1, wherein compound is a Compound of Formula I(iv).

7. The method according to claim 1, wherein compound is a Compound of Formula I(v).

8. The method according to claim 1, wherein compound is a Compound of Formula III.

9. The method according to claim 1, wherein compound is a Compound of Formula IV.

10. The method according to claim 1, wherein compound is a Compound of Formula V.

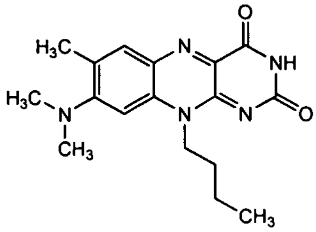
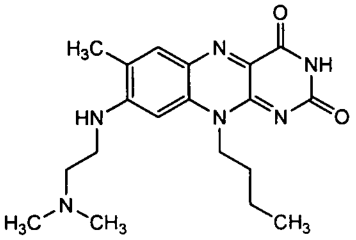
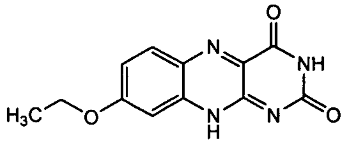
11. The method according to claim 1, wherein compound is a Compound of Formula VI.

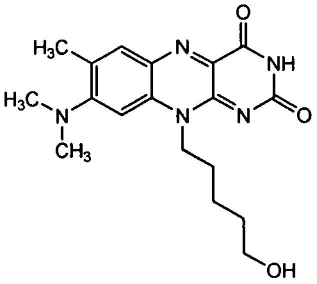
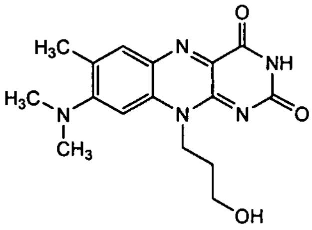
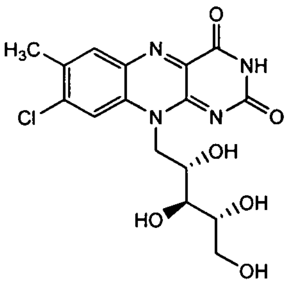
12. The method according to any of claims 1-11, wherein the infection is a Gram-positive or Gram-negative bacterial infection.

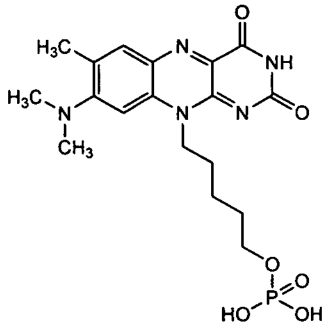
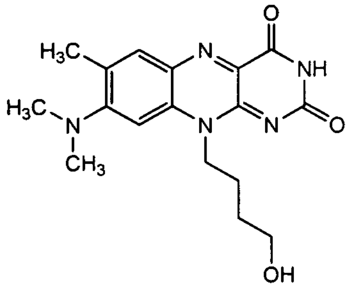
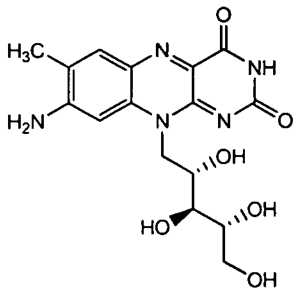
13. The method according to any of claims 1-12, wherein the bacterial infection is selected from a group consisting of *Moraxella catarrhalis, Klebsiella pneumoniae, Staphylococcus epidermidis, Streptococcus viridans, Enterococcus faecium, Staphylococcus aureus, Bacillus anthracis, Francisella tularensis, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Brucella melitensis, Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Salmonella enterica, Vibrio cholerae, Enterococcus faecalis, Yersinia pestis, Bacillus subtilis, Streptococcus pyogenes* and *Borrelia burgdorferi.*

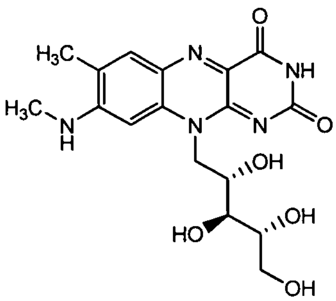
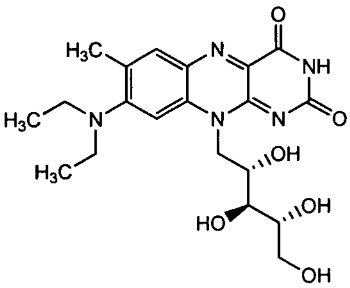
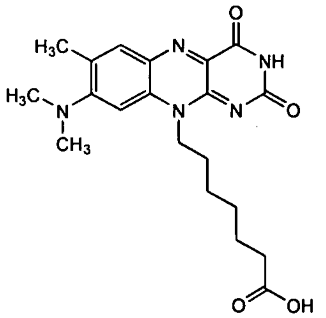
14. The method according to claim 1-13, wherein the bacterial infection is *Staphylococcus aureus* infection.

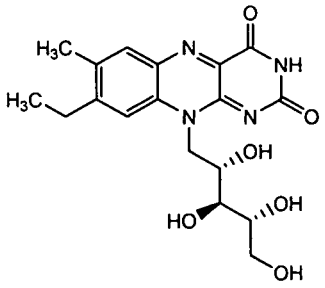
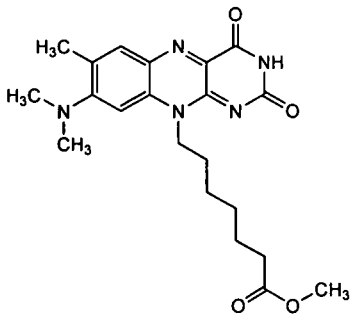
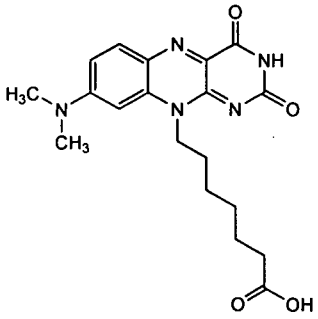
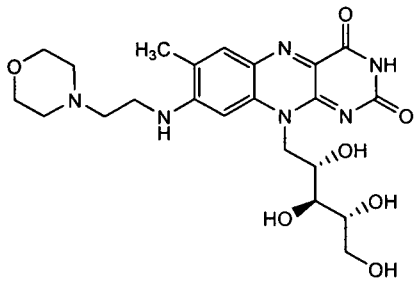
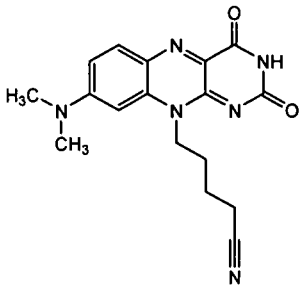
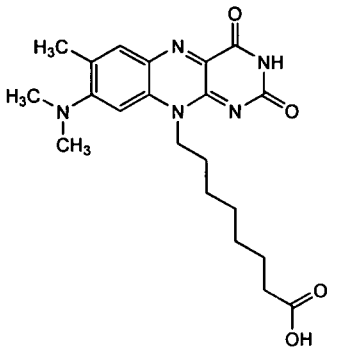
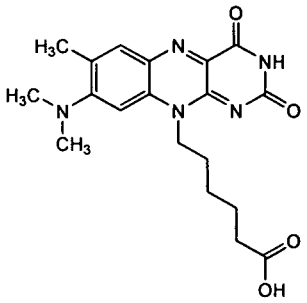
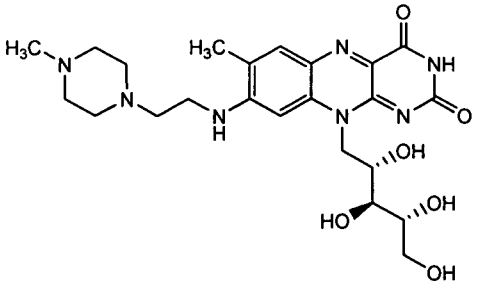
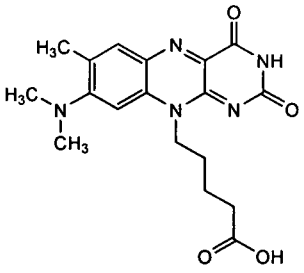
15. The method according to any of claims 1-14, wherein the compound is selected from a group consisting of

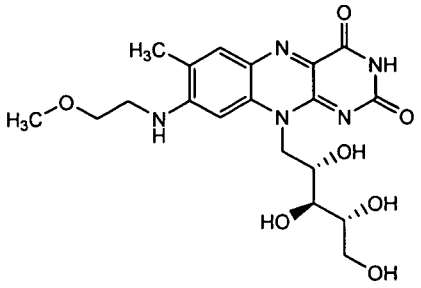
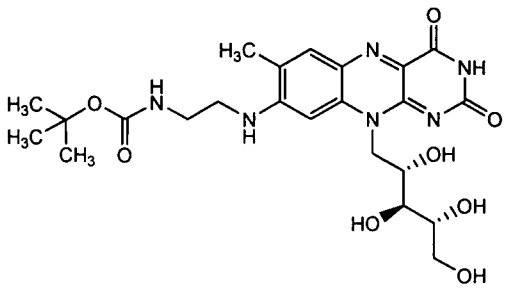
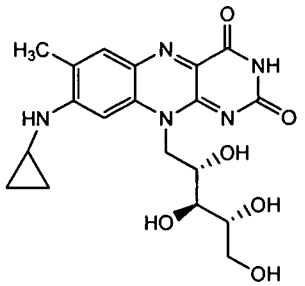
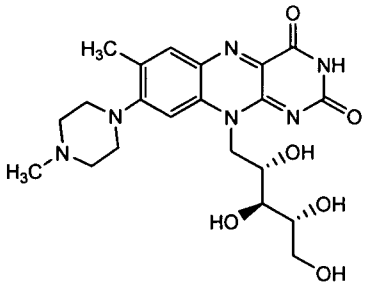
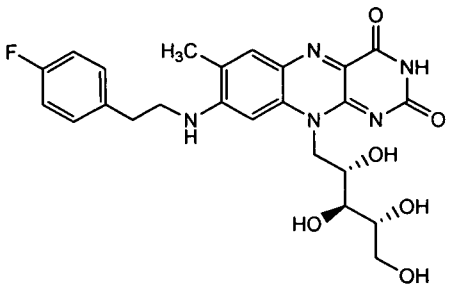
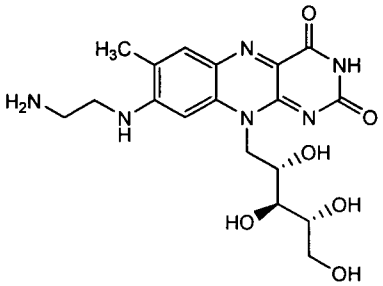
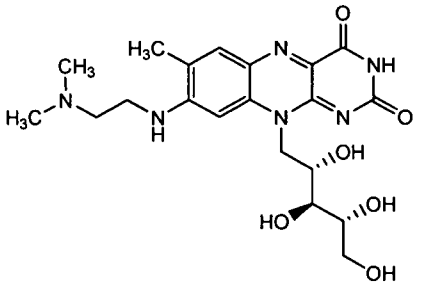
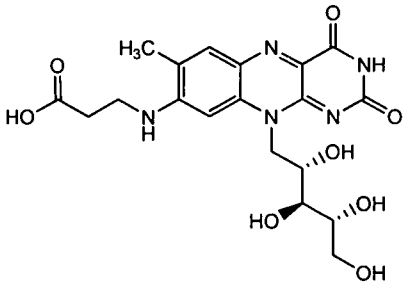
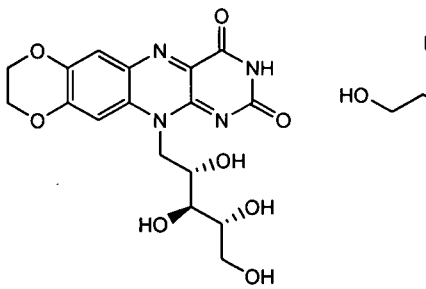
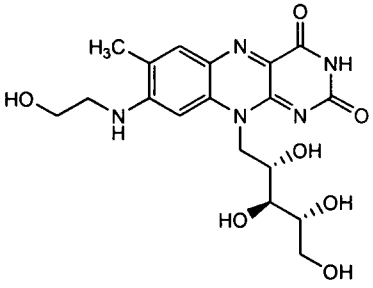

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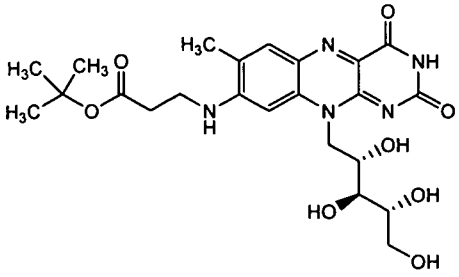
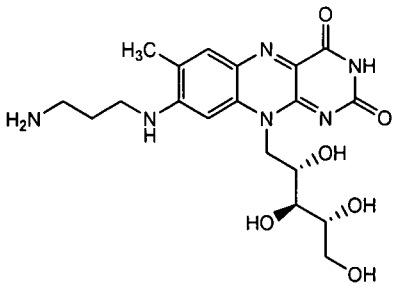
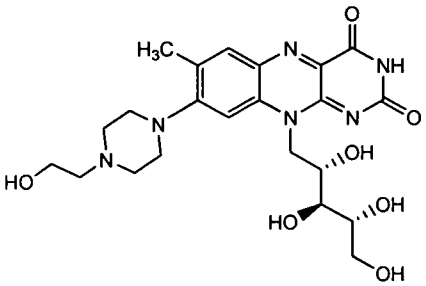
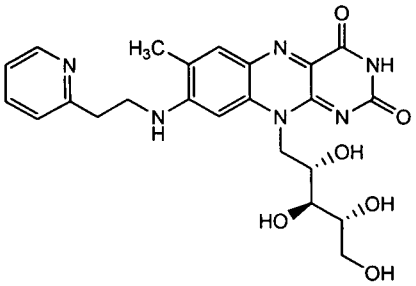
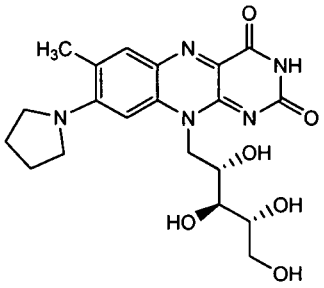
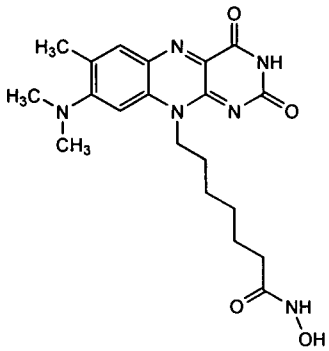
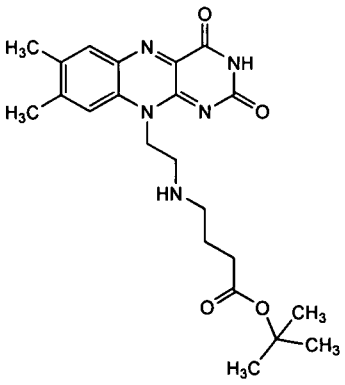
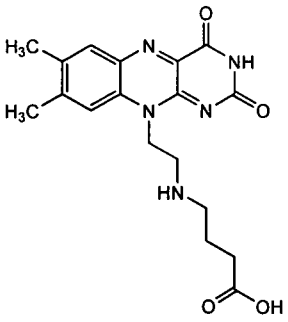
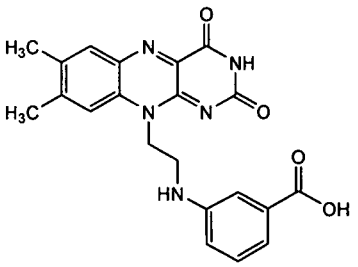

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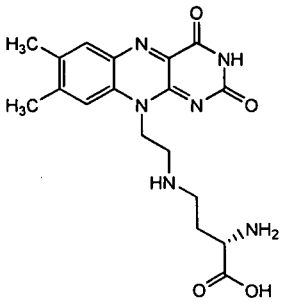
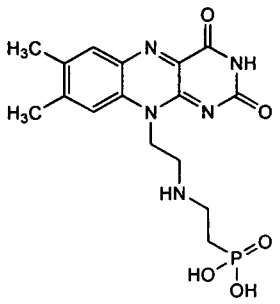
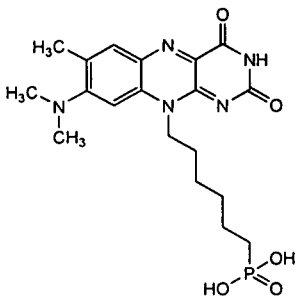
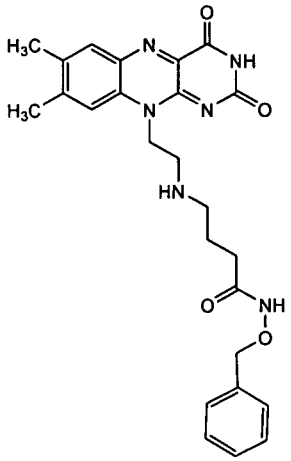
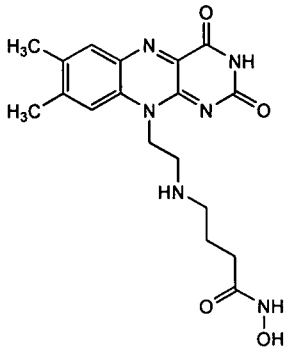
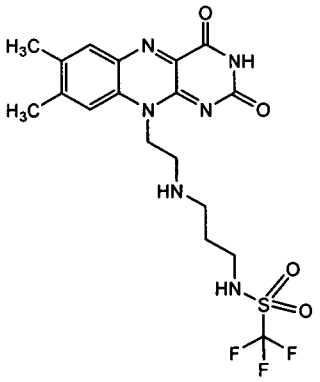
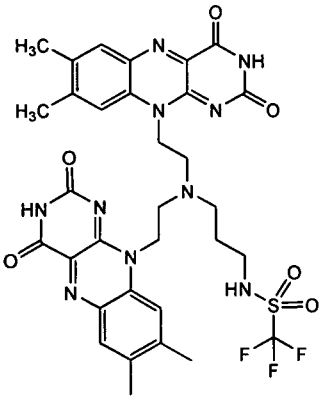
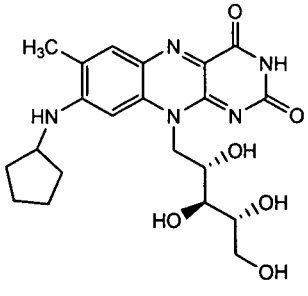

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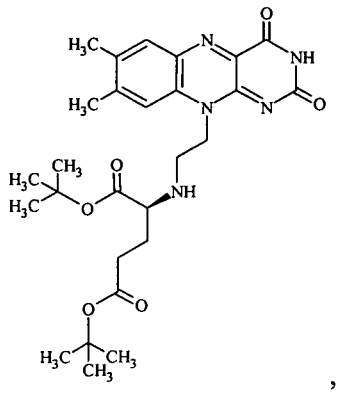
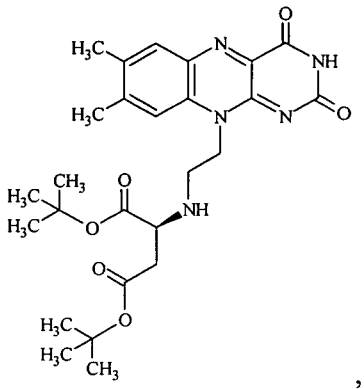
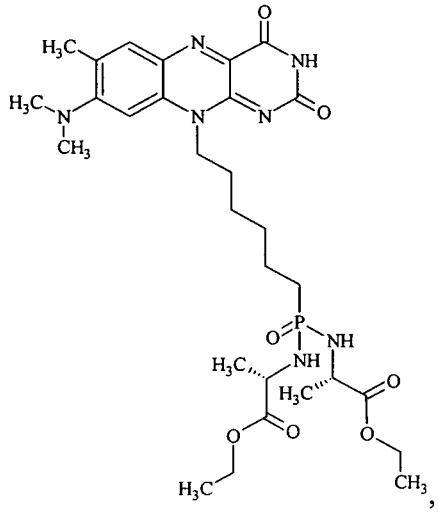
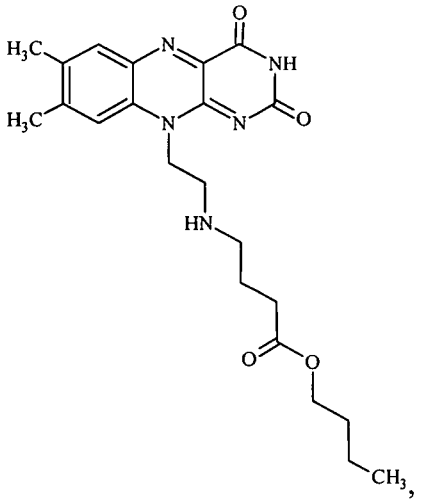
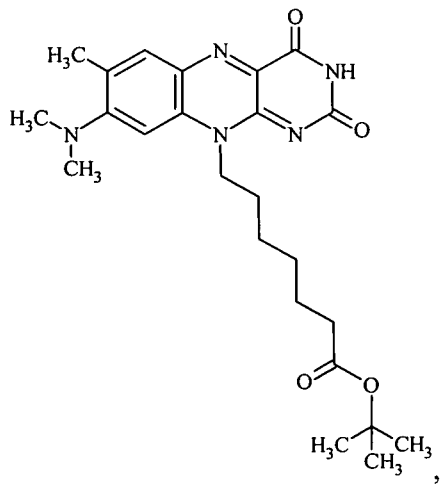
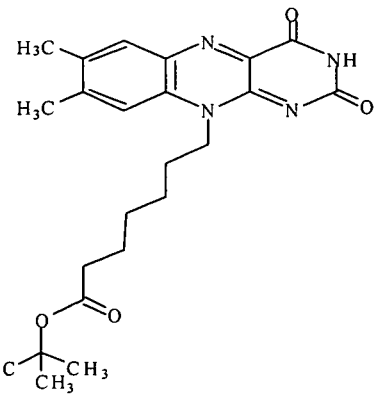

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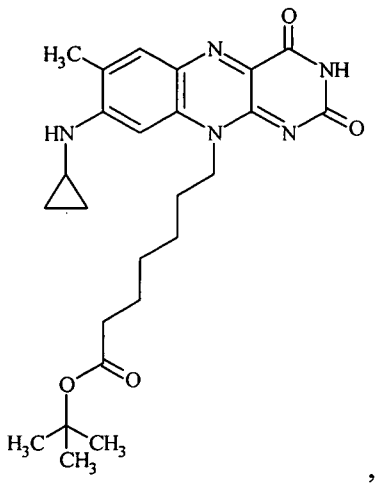
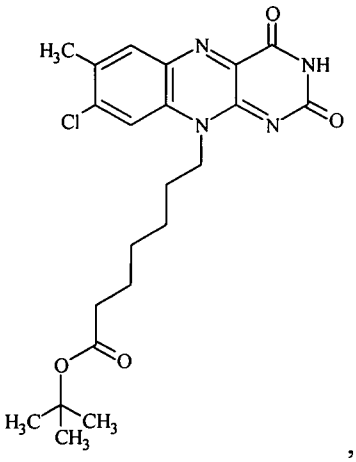
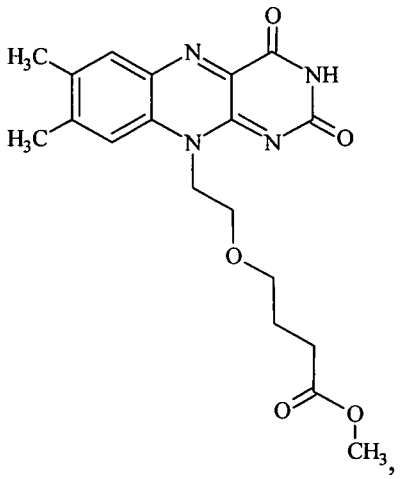
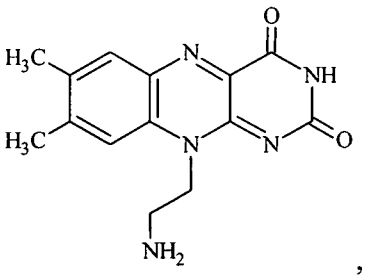
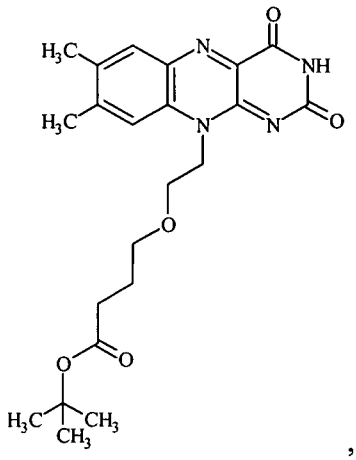
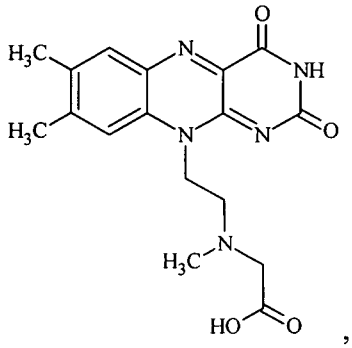

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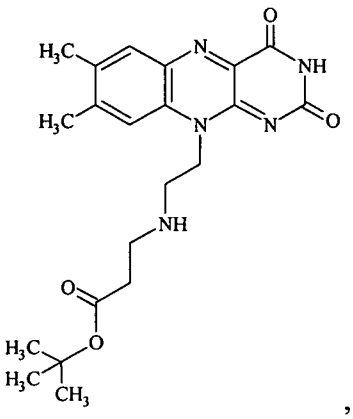
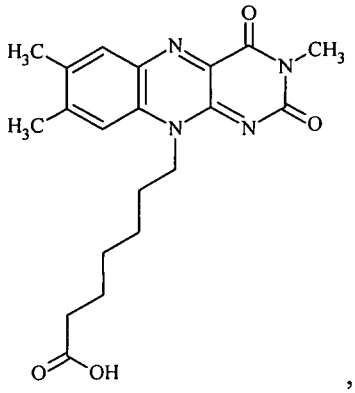
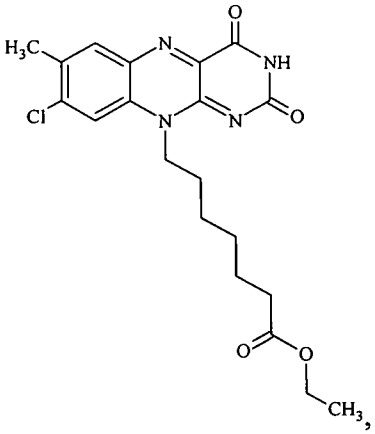
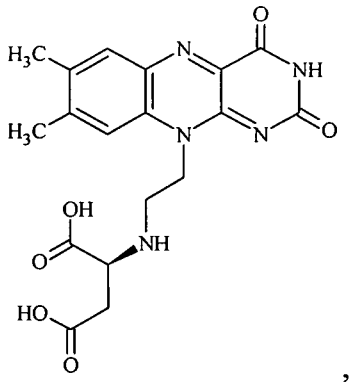
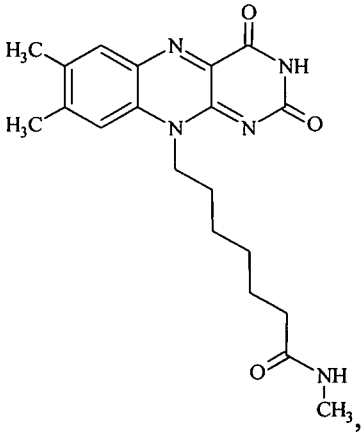
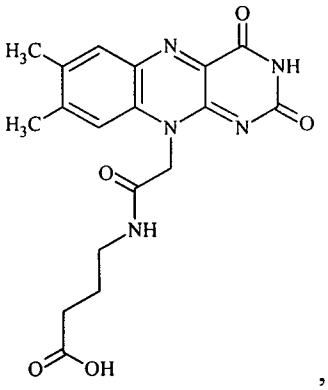

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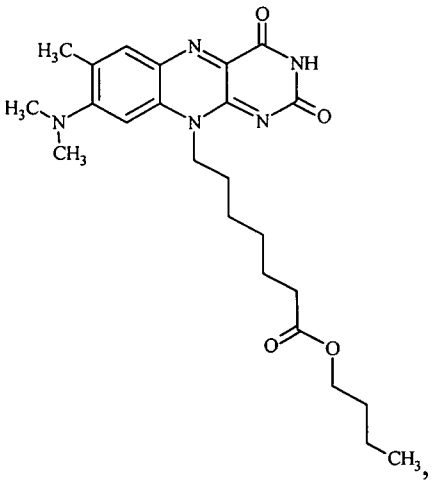
in free, pharmaceutically acceptable salt or prodrug form.

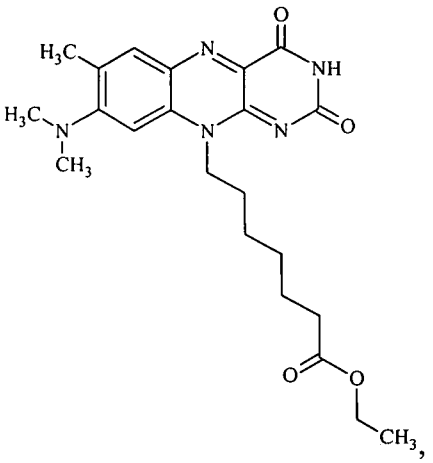
16. The method according to any of claims 1-14, wherein the compound is selected from a group consisting of

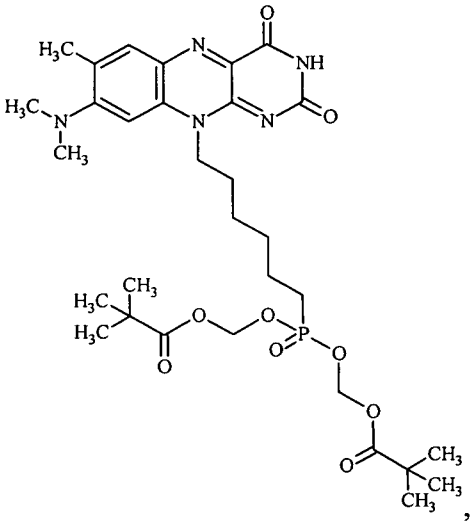

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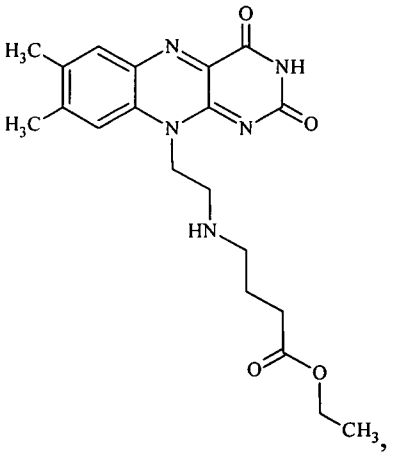

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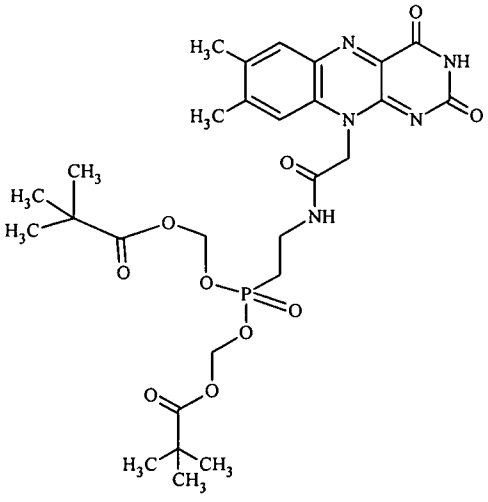

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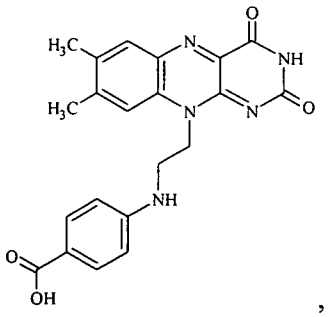


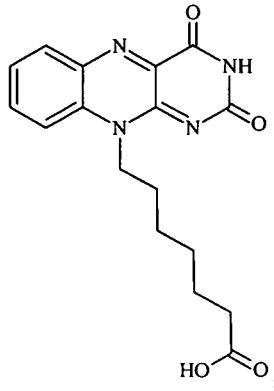




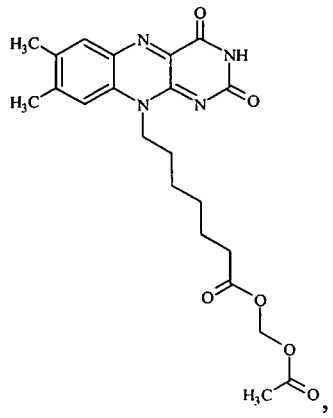




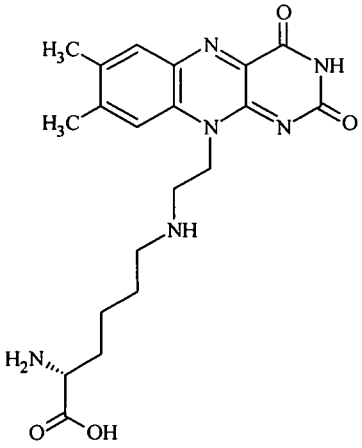




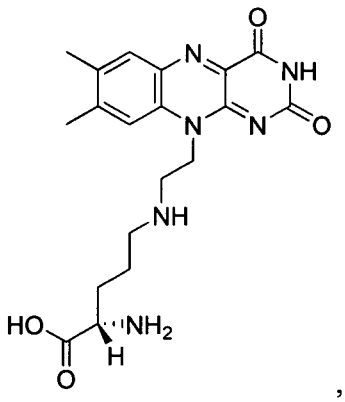
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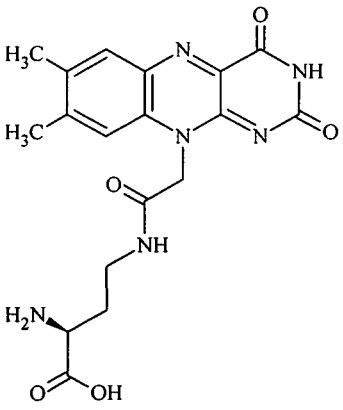
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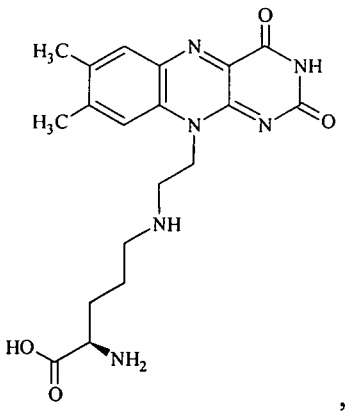
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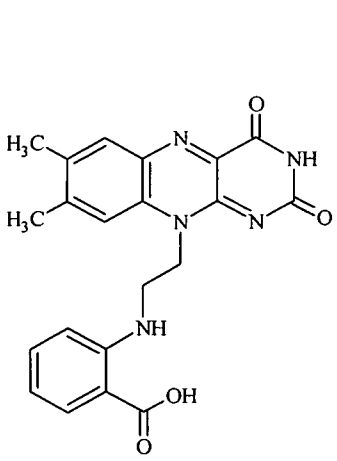
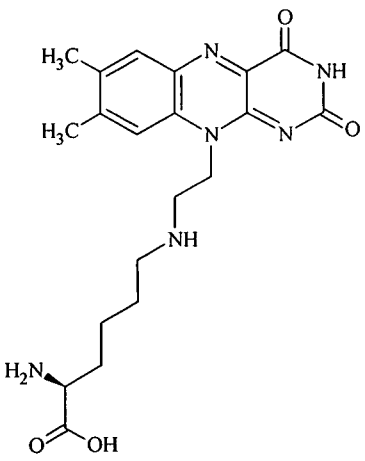
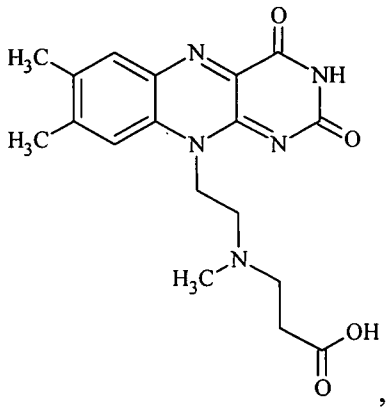
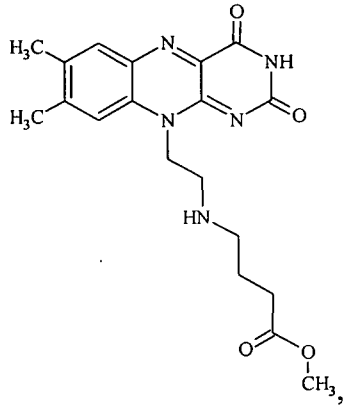
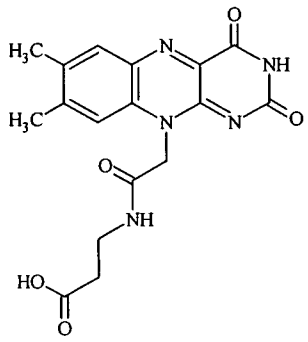
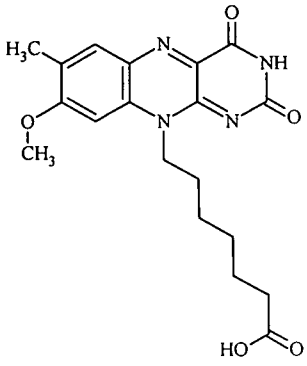
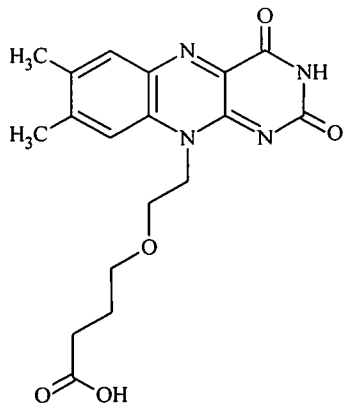
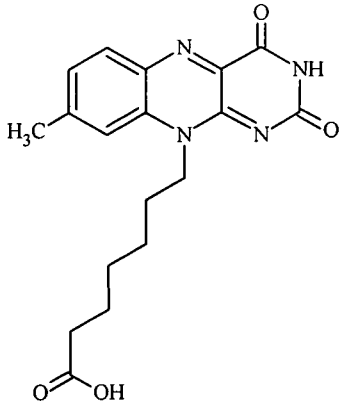
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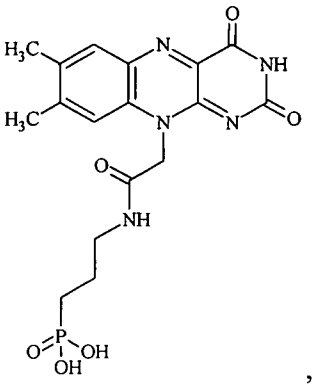
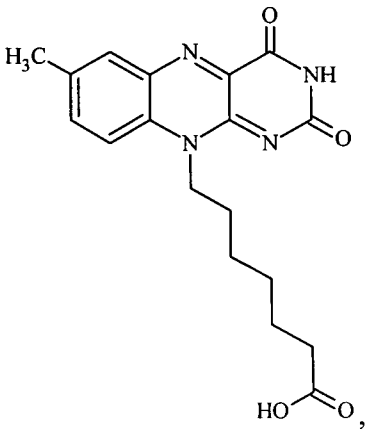
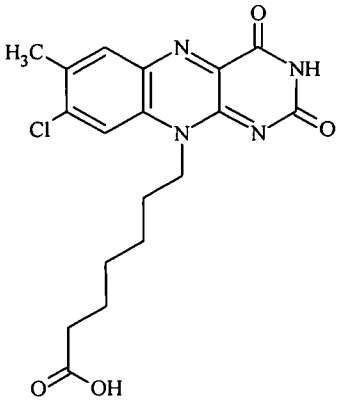
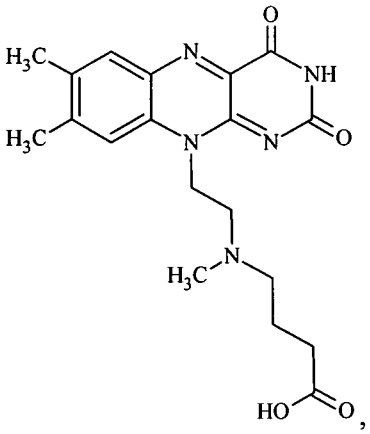
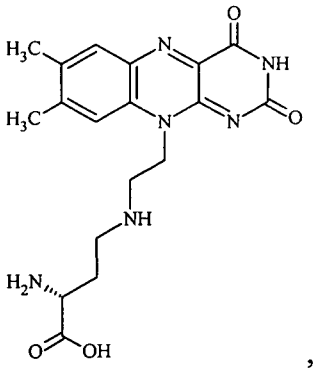
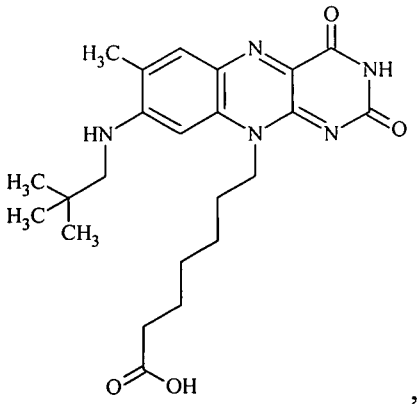


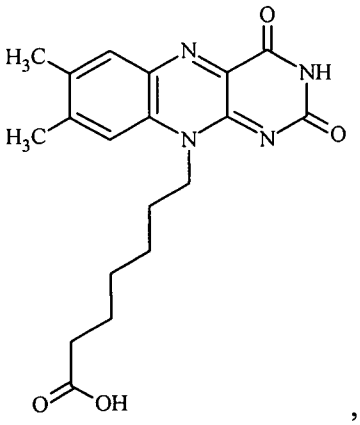
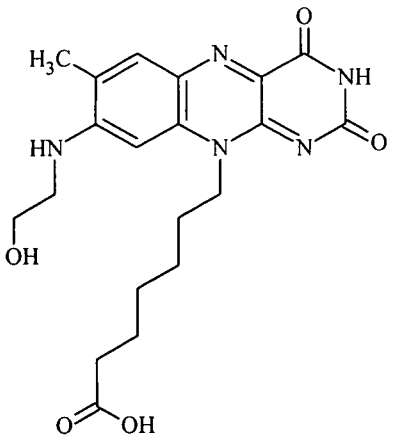
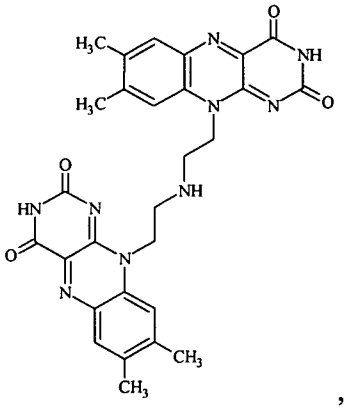
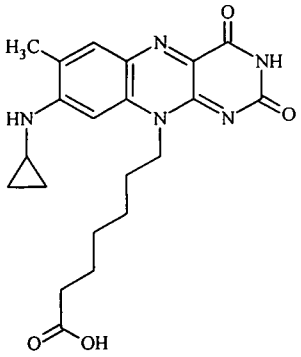
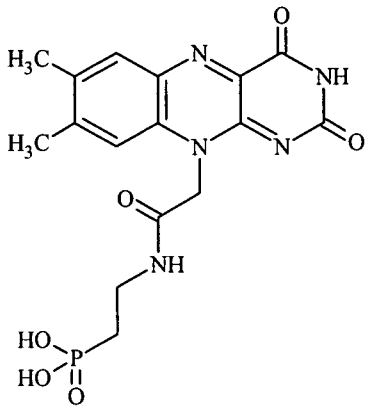
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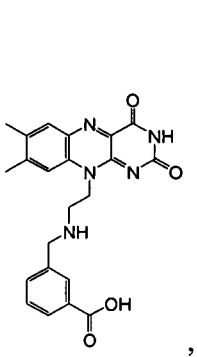
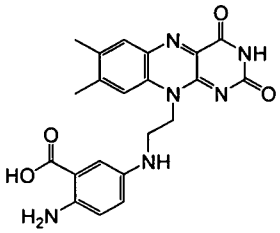
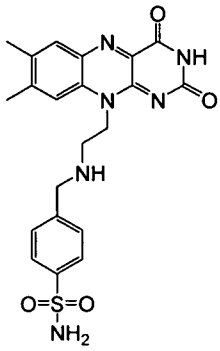
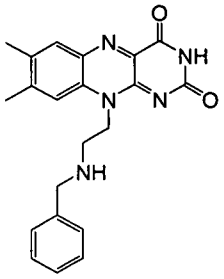
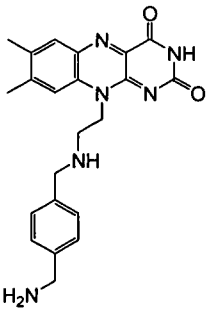
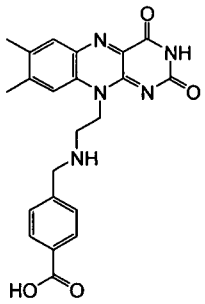
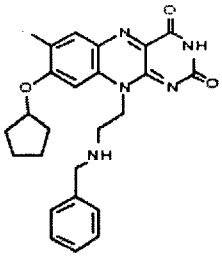
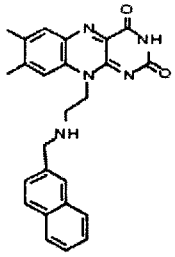
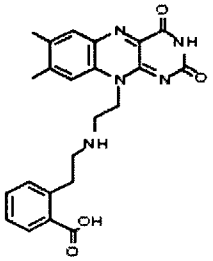
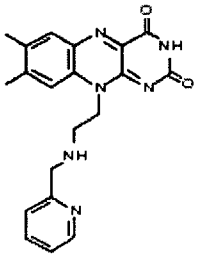
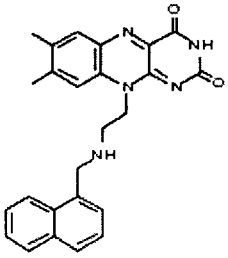
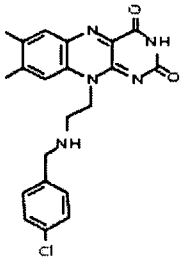
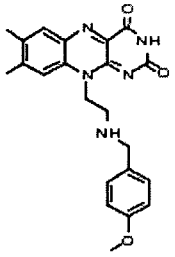
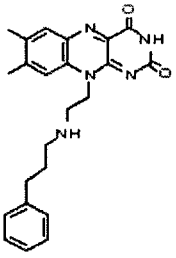
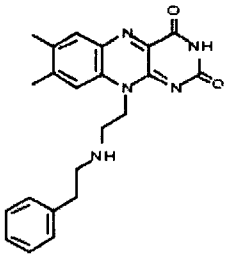
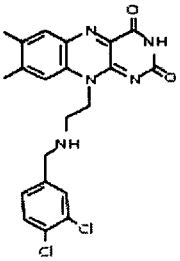
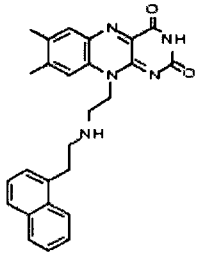

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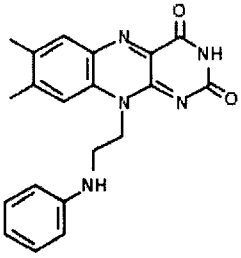
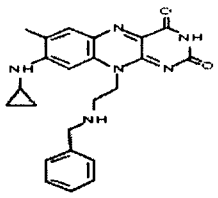
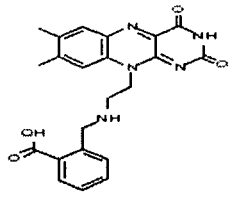
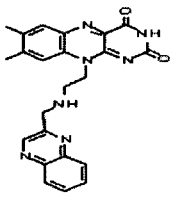
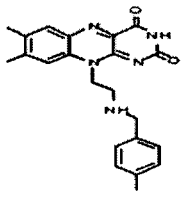
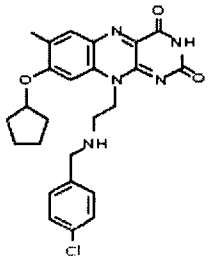
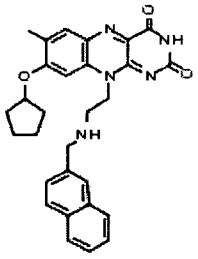

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in free, pharmaceutically acceptable salt or prodrug form.

17. The method according to any of claims 1-14, wherein the compound is selected from a group consisting of

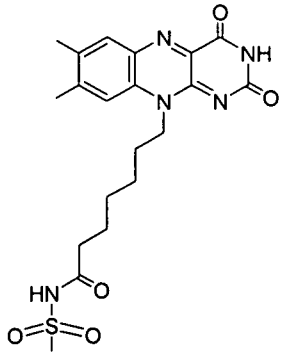
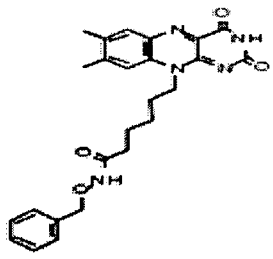
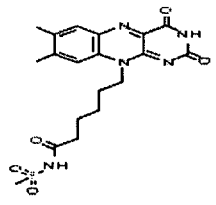

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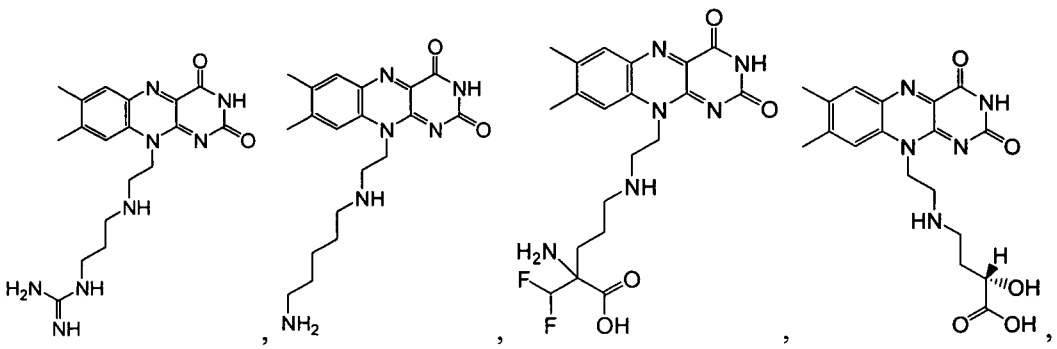
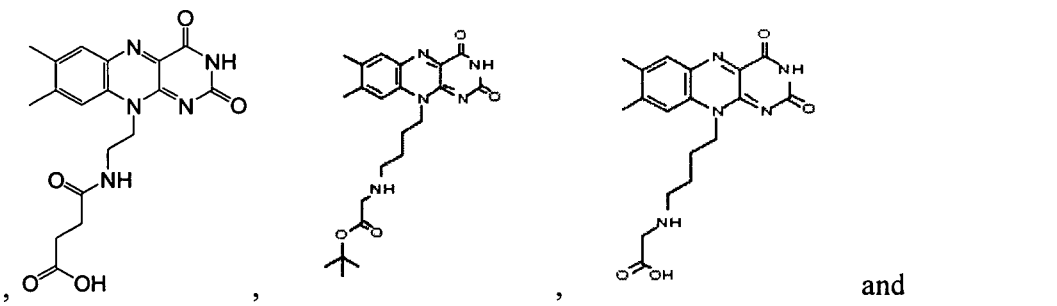
in free, pharmaceutically acceptable salt or prodrug form.

18. The method according to any of claims 1-14, wherein the compound is selected from a group consisting of:


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and

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in free, pharmaceutically acceptable salt or prodrug form.

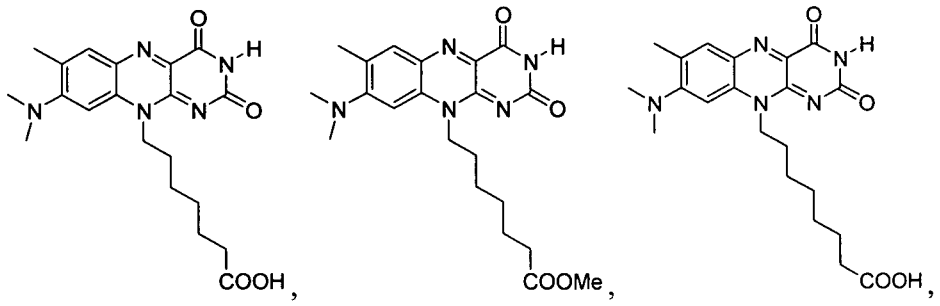
19. The method according to any of claims 1-14, wherein the compound is selected from a group consisting of:

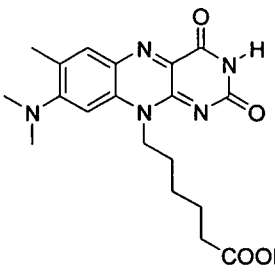
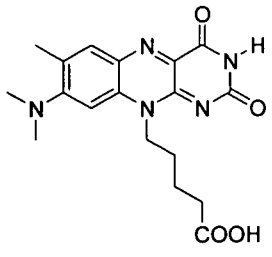




and

in free, pharmaceutically acceptable salt or prodrug form.

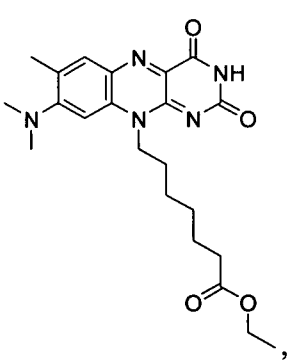
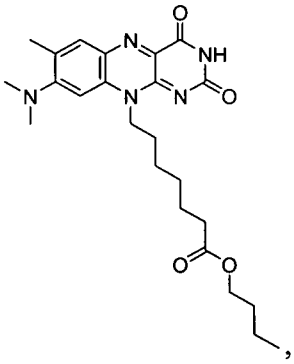
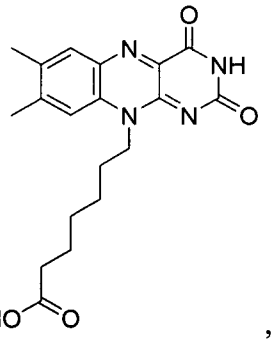
20. The method according to any of claims 1-14, wherein the compound is selected from a group consisting of:

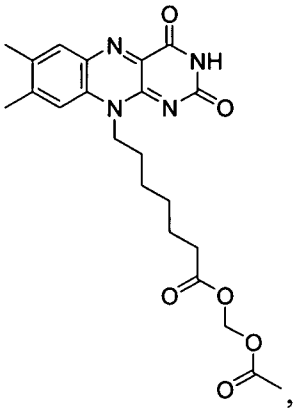
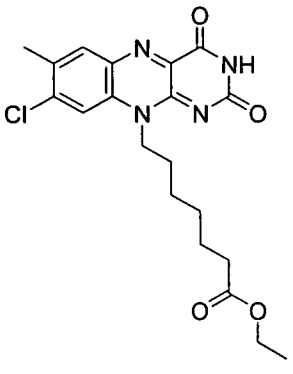
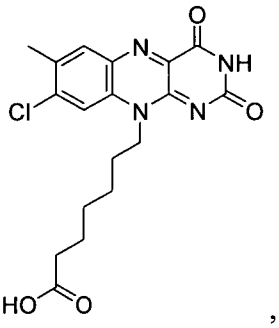


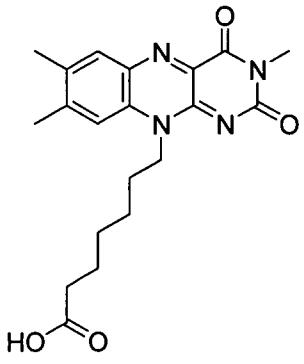
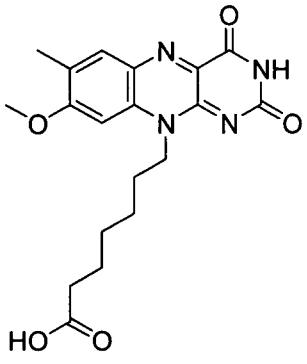
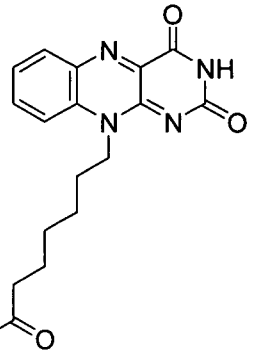


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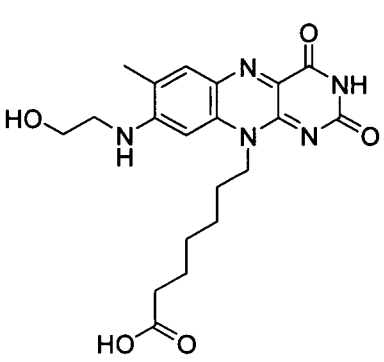
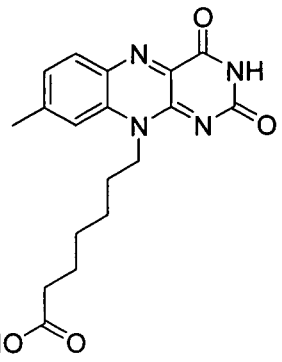
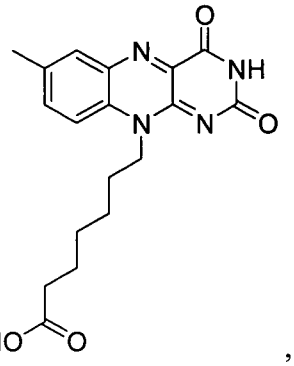
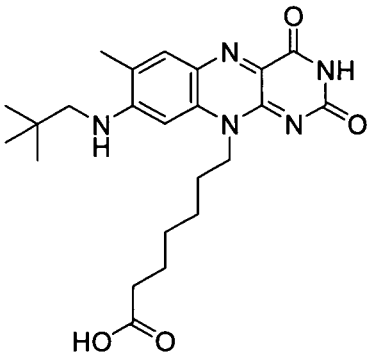
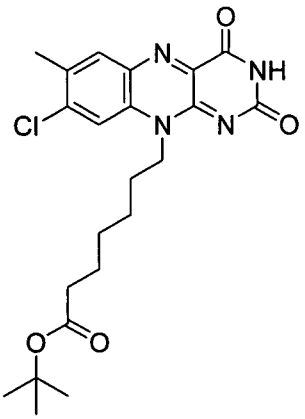
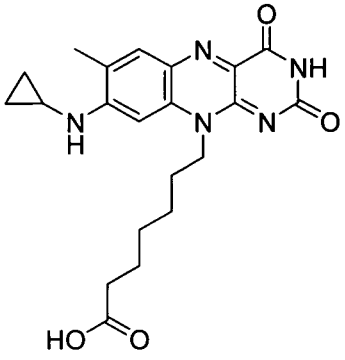
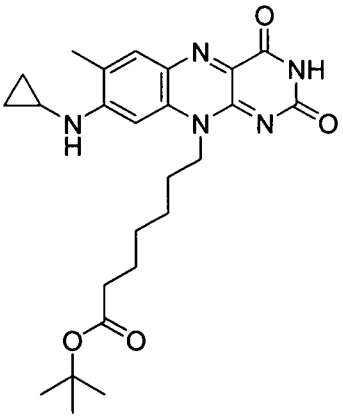
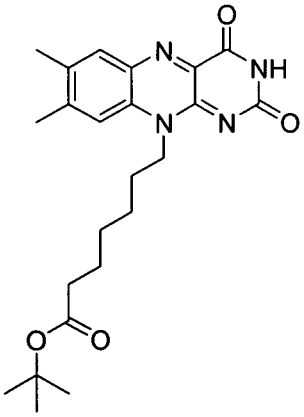
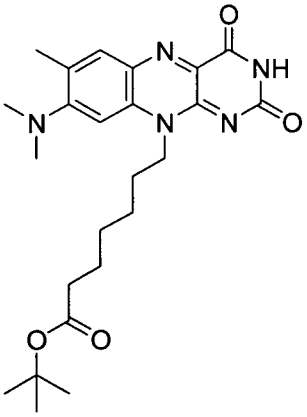
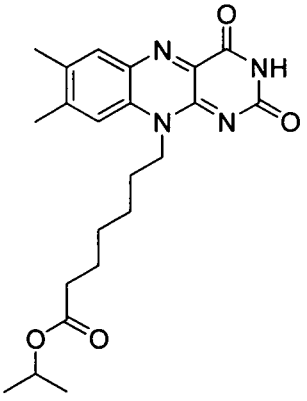
in free, pharmaceutically acceptable salt or prodrug form.

21. The method according to any of claims 1-14, wherein the compound is selected from a group consisting of:




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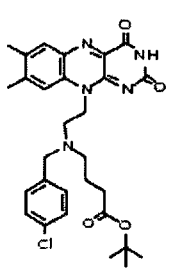
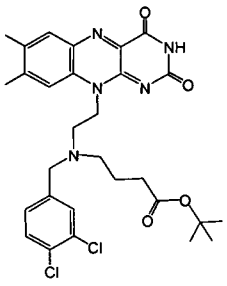
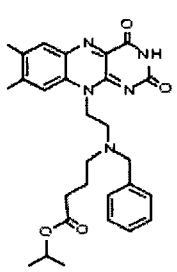



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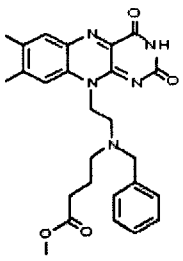
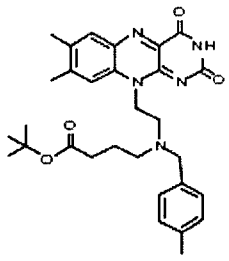
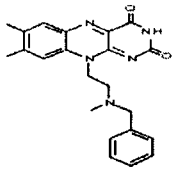



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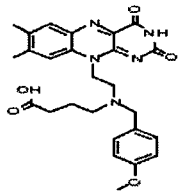
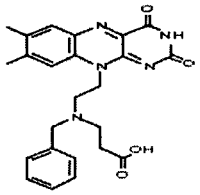
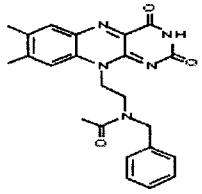

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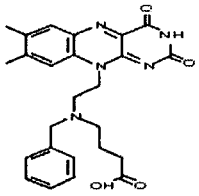
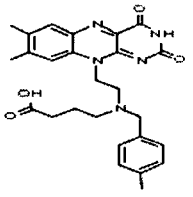
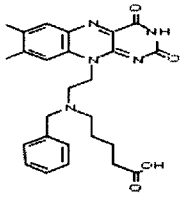
in free, pharmaceutically acceptable salt or prodrug form.

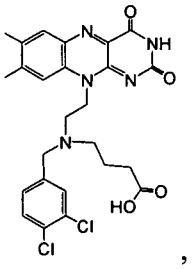
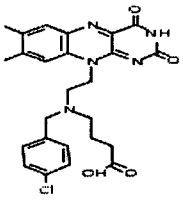
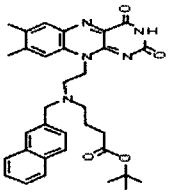
22. The method according to any of claims 1-14, wherein the compound is selected from a group consisting of:

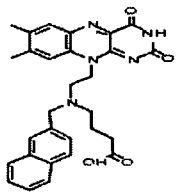

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in free, pharmaceutically acceptable salt or prodrug form.

23. The method according to any of claims 1-22, wherein the Compound of Formula I further provides a proviso that when R_3 is 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino.

24. Use of a compound as described in any of claims 1-22, in free, pharmaceutically acceptable salt or prodrug form, in the manufacture of a medicament for the treatment of a bacterial infection.

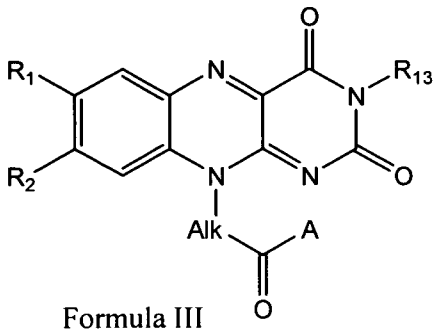
25. Use according to claim 24, wherein the infection is an infection by one or more of the following bacteria: *Moraxella catarrhalis, Klebsiella pneumoniae, Staphylococcus epidermidis, Streptococcus viridans, Enterococcus faecium, Staphylococcus aureus, Bacillus anthracis, Francisella tularensis, Streptococcus pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Brucella melitensis, Escherichia coli, Haemophilus influenzae, Listeria monocytogenes, Salmonella enterica, Vibrio cholerae, Enterococcus faecalis, Yersinia pestis, Bacillus subtilis, Streptococcus pyogenes* and *Borrelia burgdorferi.*

26. Use of a compound as described in any of claims 1-22, in the manufacture of a medicament for the treatment of a disease, condition or infection selected from a group consisting of anthrax, staphylococcal scalded skin syndrome (staph infections), pneumonia, impetigo, boils, cellulitis folliculitis, furuncles, carbuncles, scalded skin syndrome, abscesses, meningitis, osteomyelitis endocarditis, Toxic Shock Syndrome (TSS), septicemia, acute sinusitis, otitis media, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, brain abscess, tularemia, urinary tract infection, empyema, food poisoning, diarrhea and conjunctivitis.

27. Use according to any of claims 24-26, wherein the Compound of Formula I further

provides the proviso that when R_3 is 5-dihydrogen phosphate (2R,3S,4S)-trihydroxypentyl and R_1 is methyl, then R_2 is not dimethylamino.

28. A compound of Formula III,



Formula III

wherein:

(i) Alk is C_{1-8} alkyl (e.g., n-butyl, n-pentyl, n-hexyl, 6,6-dimethylhexyl, n-heptyl);

(ii) A is $-OR_9$ or $-N(R_{14})(R_{15})$;

(iii) R_9 is H, $-C_{1-8}$alkyl (e.g., methyl, ethyl, n-propyl, isopropyl, 1-methylpropyl, t-butyl, n-butyl, 1,1-dimethylpropyl, 2,2-dimethylpropyl, hex-5-ynyl), -haloC_{1-8}alkyl (e.g., 2,2,2-trifluoroethyl), $-C_{1-4}$alkyl-$OC(O)R_{12}$, $-C_{1-4}$alkyl-O-C_{1-4}alkyl (e.g., $-C(CH_3)(CH_3)OCH_3$ or $-C(CH_3)(CH_3)CH_2OCH_3$), $-C_{1-4}$alkyl-C(O)-(morphylin-4-yl), $-C_{3-7}$cycloalkyl (e.g., cyclopentyl, cyclohexyl), C_{3-7}cycloalkyl-C_{1-4}alkyl (e.g., norbornan-2-yl-methyl) wherein the cycloalkyl is optionally substituted with hydroxy group; aryl (e.g., phenyl) or aryl-C_{1-4}alkyl (e.g, Benzyl, 1-methyl-2-phenylethyl), wherein said aryl is optionally substituted with one or more halo or C_{1-4}alkoxy (e.g., 3-chloro-phenylmethyl, 3-fluoro-phenylmethyl, 4-methoxy-3-fluorophenylmethyl, 2-methoxyphenyl, 2-(3,4-dihydroxyphenyl)ethyl);

(iv) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(v) R_2 is H, halo (e.g., chloro), -O-C_{3-7}cycloalkyl (e.g., -O-cyclopentyl), -O-C_{0-7} alkylC_{3-7}cycloalkyl (e.g., -O-cyclopentyl, -O-CH_2-cyclopentyl), -$N(R_4)(R_5)$, -(CH_2)-$N(R_4)(R_5)$, -C_{0-4}alkyl-C_{3-7}cycloalkyl (e.g., cyclopropyl, cyclopentylmethyl), heteroC_{3-7}cycloalkyl (e.g., pyrrolidin-1-yl), 1-cyclopropyl-6-fluoro-7-[4-piperazin-1-yl]-4-oxo-quinoline-3-carboxylic

acid), C_{1-8}alkyl (e.g., methyl or ethyl) or –O-C_{1-8}alkyl (e.g., methoxy), wherein the alkyl group is optionally substituted with one or more halo (e.g., fluoro) or hydroxy groups (e.g., trifluoromethyl, -O-CH_2CH_2OH);

(vi) R_4 and R_5 are independently

a. H,

b. –C_{0-4}alkyl-C_{3-7}cycloalkyl (e.g., cyclopropyl, cyclopentyl, cyclohexyl or cyclopentyl-methyl),

c. heteroC_{3-7}cycloalkyl (e.g., pyrrolidinyl, e.g., pyrrolidin3-yl),

d. aryl (e.g., phenyl or 2,2-dimethylpropyl),

e. aryl-C_{1-8}alkyl wherein the aryl is optionally substituted with halo (e.g., 4-fluorophenylethyl),

f. -$(CH_2)_3$-N(H)-$(CH_2)_4$-N(H)-$(CH_2)_3$-$N(H)_2$,

g. -C_{1-8}alkyl (e.g., methyl) wherein said alkyl is optionally substituted with one or more hydroxy groups (e.g., 2,3-dihydroxypropyl, 2,3,4,5,6-pentahydroxyhexyl, hydroxyethyl);

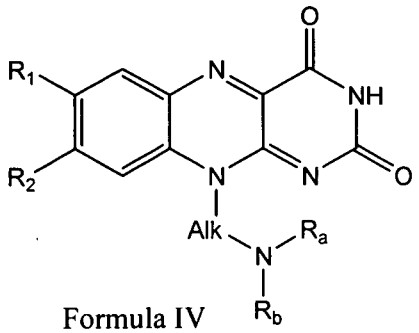
(vii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy); and

(viii) R_{13} is H or C_{1-4}alkyl (e.g., methyl);

(ix) R_{14} and R_{15} are independently H, -OH, -$S(O)_2CH_3$, -OBn or -C_{1-4}alkyl (e.g., methyl),

in free, salt or prodrug form.

29. A compound of Formula IV:



Formula IV

wherein:

(i) Alk is C_{1-8} alkyl (e.g., ethyl or n-butyl);

(ii) R_a and R_b are independently H, -C_{1-4}alkyl (e.g., methyl), -$(CH_2)_3C(NH_2)(COOH)CHF_2$, -$(CH_2)_3N(H)C(=NH)NH_2$, -$(CH_2)_5NH_2$, -$(CH_2)_2C(H)(OH)COOH$, -$C(O)(CH_2)_2COOH$, -$C_{1-4}$alkyl-$C(O)OR_9$ (e.g., -$CH_2CH_2CH_2CH_2C(O)OR_9$, -$CH_2CH_2CH_2C(O)OR_9$,-$CH_2CH_2C(O)OR_9$ or -$CH_2C(O)OR_9$, -$C(CH_3)(CH_3)C(O)OR_9$), -$C(O)CH_3$, aryl (e.g., phenyl), -C(O)-aryl, aryl-C_{1-4}alkyl (e.g., benzyl, naphtha-1-ylmethyl, naphth-2-ylmethyl, phenylethyl, phenylpropyl, naphtha-1-ylethyl), heteroaryl, heteroaryl-C_{1-4}alkyl (e.g., pyrid-2-ylmethyl, pyrid-3-ylmethyl or quinoxalinyl), wherein said aryl and heteroaryl groups are optionally substituted with one or more groups selected from –$C(O)OR_9$, -NH_2, -$S(O)_2NH_2$, -CH_2NH_2, halo (e.g., chloro), C_{1-4}alkoxy (e.g., methoxy), C_{1-4}alkyl (e.g., methyl);

(iii) R_1 is H, C_{1-8} alkyl (e.g., methyl);

(iv) R_2 is H, halo (e.g., chloro), -O-C_{3-7}cycloalkyl (e.g., -O-cyclopentyl), -$N(R_4)(R_5)$, C_{3-7}cycloalkyl (e.g., cyclopropyl), C_{1-8}alkyl (e.g., methyl or ethyl) or –O-C_{1-8}alkyl wherein the alkyl group is optionally substituted with one or more halo or hydroxyl groups (e.g., trifluoromethyl, -O-CH_2CH_2OH);

(v) R_4 and R_5 are independently H, C_{3-7}cycloalkyl (e.g., cyclopropyl or cyclopentyl), C_{1-8}alkyl (e.g., methyl) wherein said alkyl is optionally substituted with one or more hydroxy groups (e.g., 2,3-dihydroxypropyl, 2,3,4,5,6-pentahydroxyhexyl);

(vi) R_9 is H or C_{1-4}alkyl (e.g., t-butyl, isopropyl, methyl);

(vii) R_{12} is C_{1-8}alkyl (e.g., methyl, ethyl, *t*-Butyl) or -OC_{1-8}alkyl (e.g., methoxy, ethoxy, *t*-butoxy),

in free, salt or prodrug form.