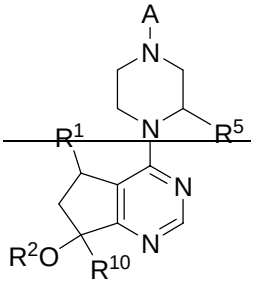
~~CLAIMS:~~

~~1. A compound of Formula **I**:~~



I

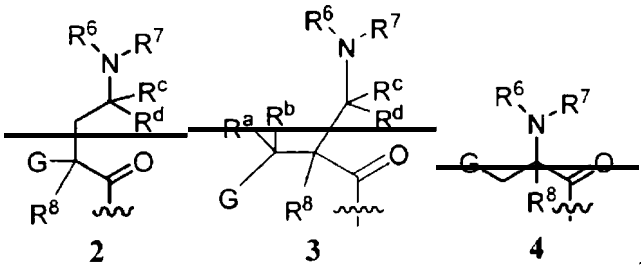
~~and tautomers, resolved enantiomers, resolved diastereomers, solvates, metabolites, and salts thereof, wherein:~~

~~R^1 is H, Me, Et, vinyl, CF_3, CHF_2 or CH_2F;~~

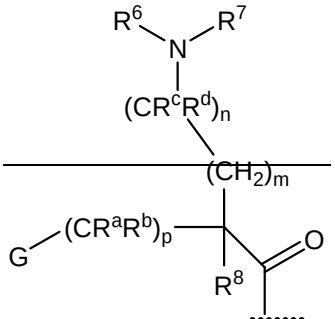
~~R^2 is H or Me;~~

~~R^5 is H, Me, Et, or CF_3;~~

~~A is selected from formulae 2, 3 and 4~~



2 **3** **4**

~~or A is~~  ~~wherein m, n and p are either all 0 or all 1;~~

~~G is phenyl optionally substituted by one to four R^9 groups or a 5-6 membered heteroaryl optionally substituted by a halogen;~~

~~R^6 and R^7 are independently H, OCH_3, (C_3-C_6 cycloalkyl)-(CH_2)-, (C_3-C_6 cycloalkyl)-(CH_2CH_2)-, V-$(CH_2)_{0-1}$- wherein V is a 5-6 membered heteroaryl, W-$(CH_2)_{1-2}$- wherein W is phenyl optionally substituted with F, Cl, Br, I, OMe, CF_3 or Me, C_3-C_6 cycloalkyl optionally substituted with C_1-C_3 alkyl or O(C_1-C_3 alkyl), hydroxy (C_3-C_6 cycloalkyl), fluoro (C_3-C_6 cycloalkyl), $CH(CH_3)CH(OH)$phenyl, 4-6 membered heterocycle optionally substituted with F, OH, C_1-C_3~~

alkyl, cyclopropylmethyl or C(=O)(C_1-C_3 alkyl), or C_1-C_6 alkyl optionally substituted with one or more groups independently selected from OH, oxo, O(C_1-C_6 alkyl), CN, F, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, cyclopropyl, phenyl, imidazolyl, piperidinyl, pyrrolidinyl, morpholinyl, tetrahydrofuranyl, oxetanyl or tetrahydropyranyl,

or R^6 and R^7 together with the nitrogen to which they are attached form a 4-7 membered heterocyclic ring optionally substituted with one or more groups independently selected from OH, halogen, oxo, CF_3, CH_2CF_3, CH_2CH_2OH, O(C_1-C_3 alkyl), C(=O)CH_3, NH_2, NHMe, N(Me)$_2$, S(O)$_2$$CH_3$, cyclopropylmethyl and C_1-C_3 alkyl;

R^a and R^b are H,

or R^a is H, and R^b and R^6 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having one or two ring nitrogen atoms;

R^c and R^d are H or Me,

or R^c and R^d together with the atom to which they are attached from a cyclopropyl ring;

R^8 is H, Me, F or OH,

or R^8 and R^6 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having one or two ring nitrogen atoms;

each R^9 is independently halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, O-(C_1-C_6-alkyl), CF_3, OCF_3, S(C_1-C_6-alkyl), CN, OCH_2-phenyl, CH_2O-phenyl, NH_2, NH-(C_1-C_6-alkyl), N-(C_1-C_6-alkyl)$_2$, piperidine, pyrrolidine, CH_2F, CHF_2, OCH_2F, $OCHF_2$, OH, SO_2(C_1-C_6-alkyl), C(O)NH_2, C(O)NH(C_1-C_6-alkyl), and C(O)N(C_1-C_6-alkyl)$_2$;

R^{10} is H or Me.

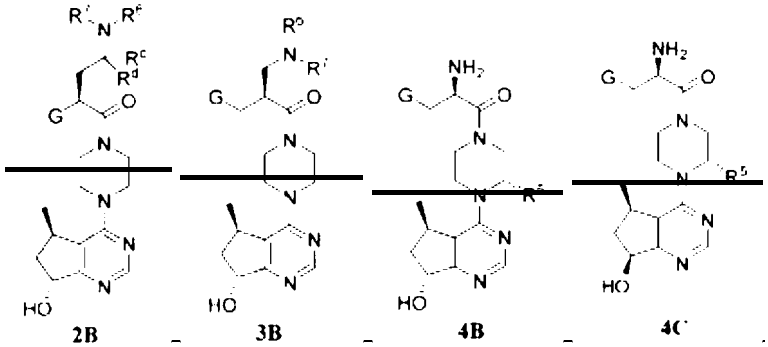
2. A compound of Claim 1, wherein OR^2 is in the (S) or (R) configuration.

3. A compound as claimed in any one of the preceding Claims, wherein R^5 is H or methyl.

4. A compound as claimed in any one of the preceding Claims, wherein R^1 is methyl or H.

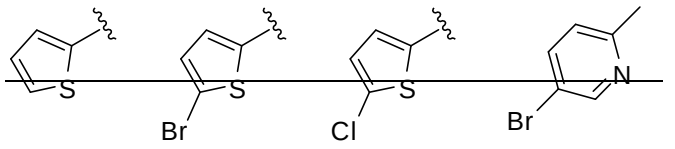
5. A compound of Claim 4, wherein R^1 is in the (R) configuration.

6. A compound according to claim 1, which has a formula selected from Formulae 2B, 3B, 4B or 4C

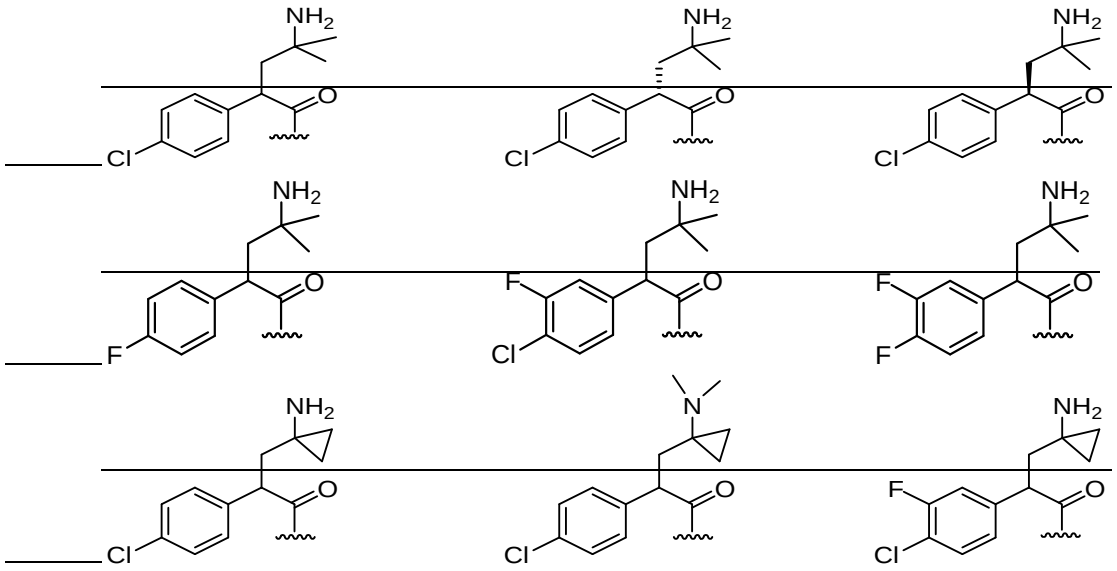


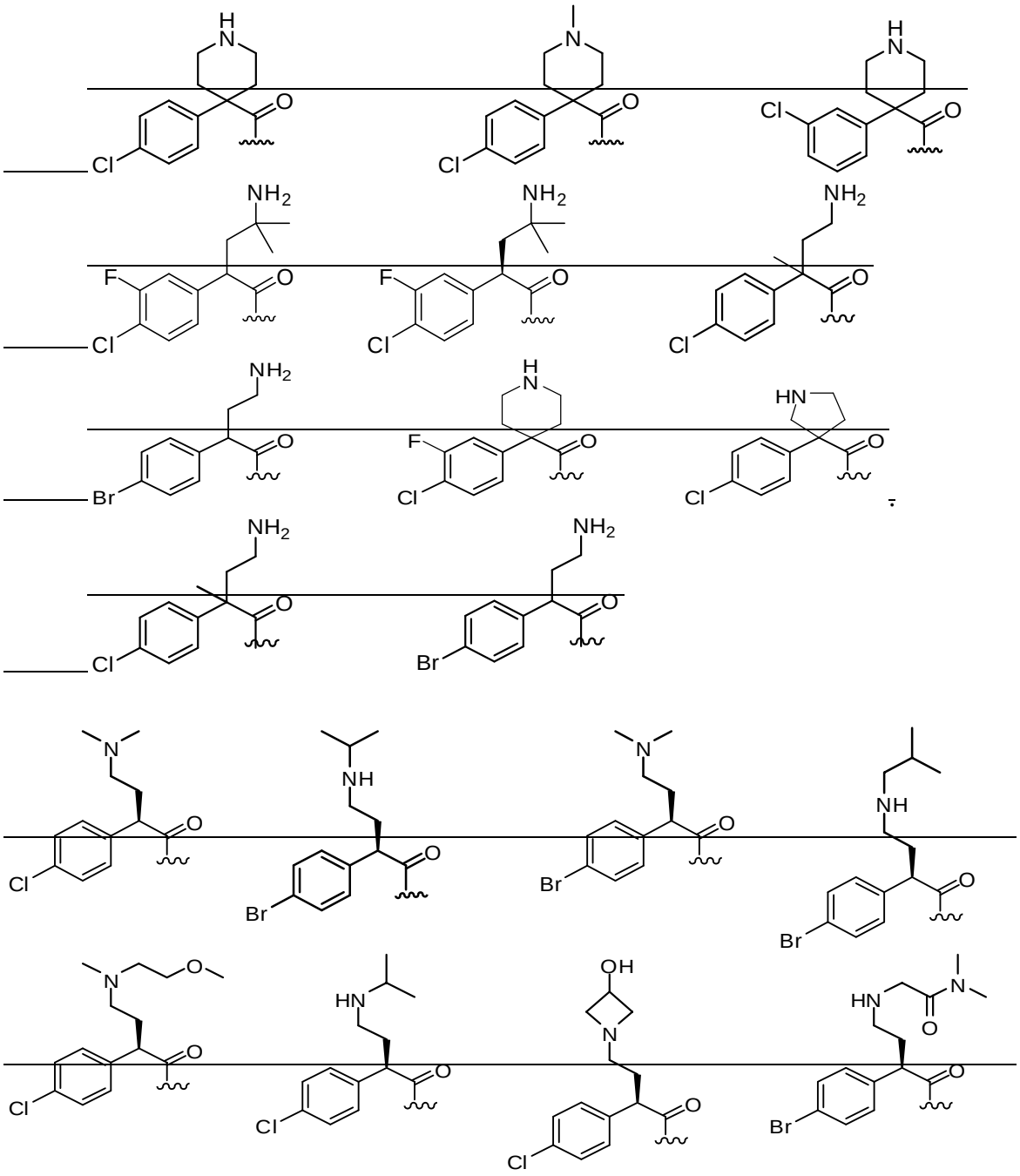
2B 3B 4B 4C

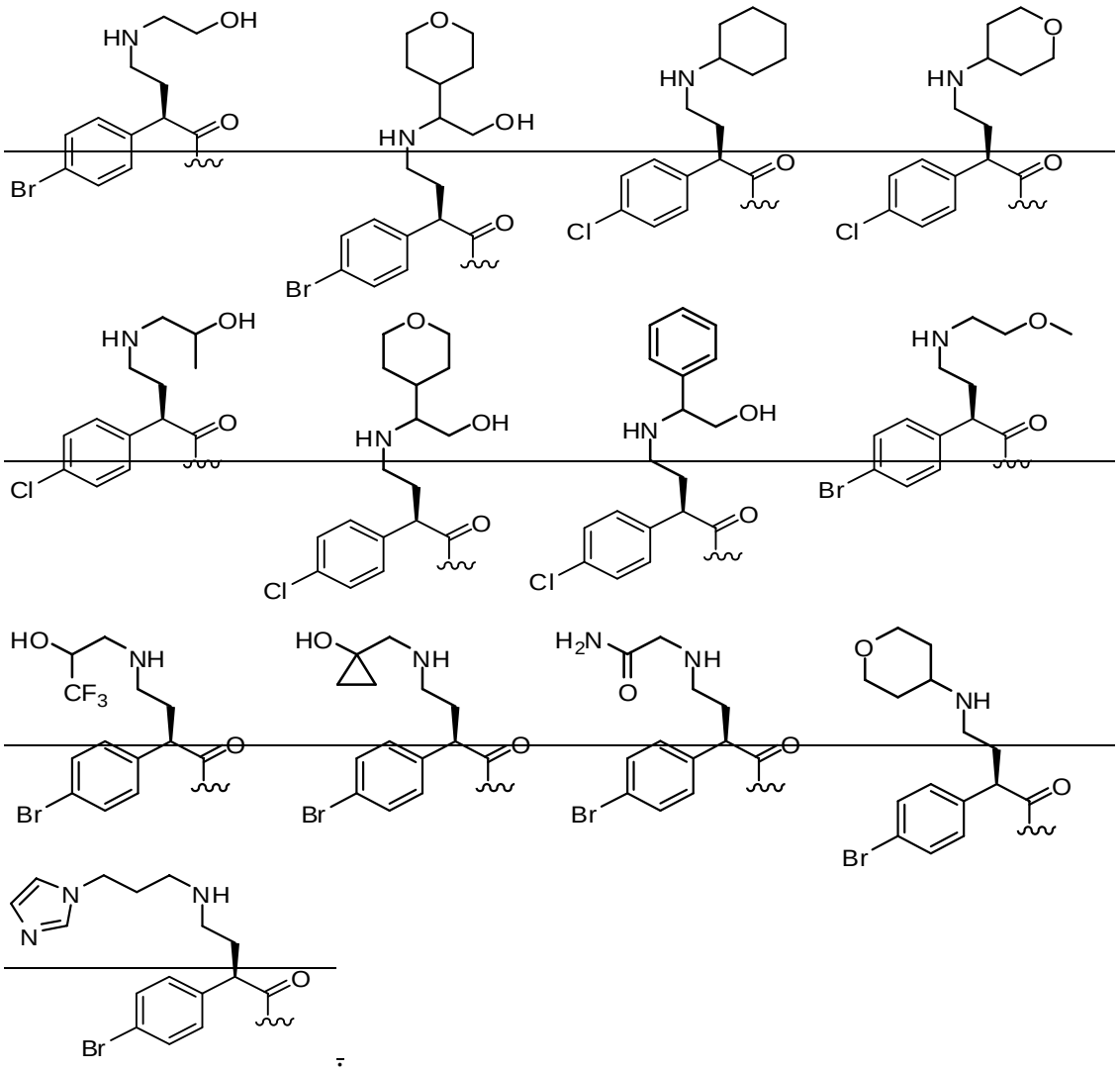
~~7. A compound as claimed in any one of the preceding Claims, wherein G is 4-chlorophenyl, 2,4-dichlorophenyl, 3-chloro-4-fluorophenyl, 3,4-difluorophenyl, 4-chloro-3-fluorophenyl, 3-fluoro-4-bromophenyl, 3,4-dichlorophenyl, 4-methoxyphenyl, 4-fluorophenyl, 4-bromophenyl, 4-cyanophenyl, 4-trifluoromethylphenyl, 4-thiomethylpyhenyl, 4-methylphenyl, 4-iodophenyl, 4-trifluoromethoxyphenyl, 3,5-difluorophenyl, 4-bromo-3-fluorophenyl, 3-fluoro-4-methoxyphenyl, 3-fluoro-4-trifluoromethylphenyl, 3-trifluoromethoxy-4-chlorophenyl, 3-fluoro-4-trifluoromethoxyphenyl, 3-trifluoromethyl-4-chlorophenyl, 3-trifluoromethoxy-4-fluorophenyl, 3,5-bis(trifluoromethyl)phenyl, 3-chloro-5-fluorophenyl, 3-bromo-4-methoxyphenyl, 2-fluoro-4-chlorophenyl, 2-fluoro-4-bromophenyl, 2-fluoro-4-trifluoromethylphenyl, or 3-trifluoromethyl-4-fluorophenyl; or wherein G is selected from the strutctures:~~



~~8. A compound as claimed in any one of the preceding Claims, wherein A is selected from:~~

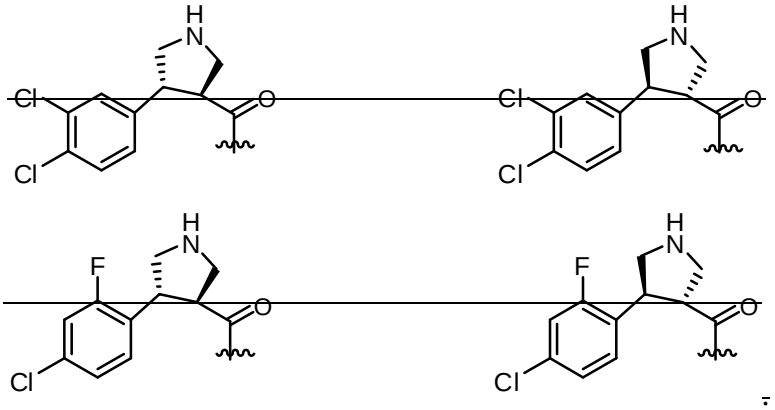




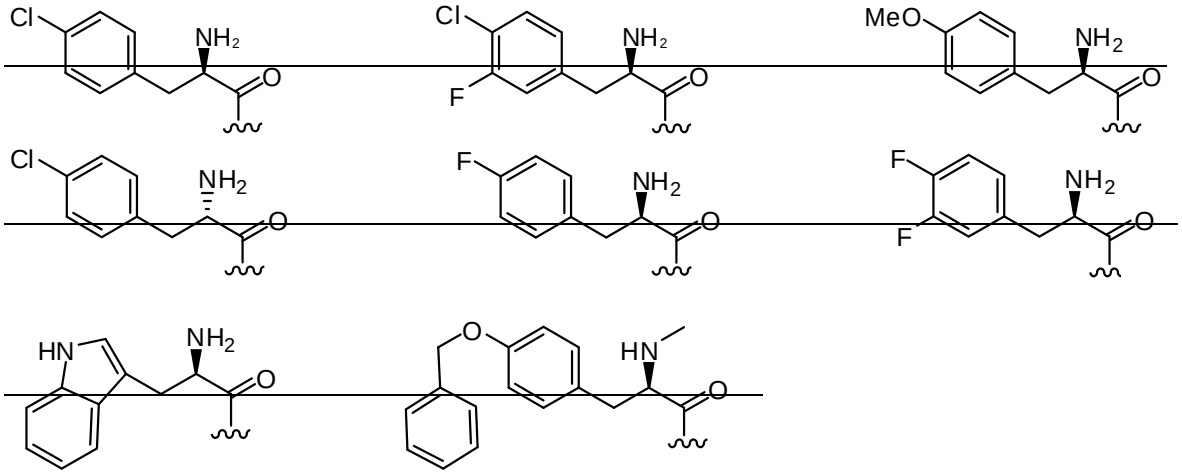


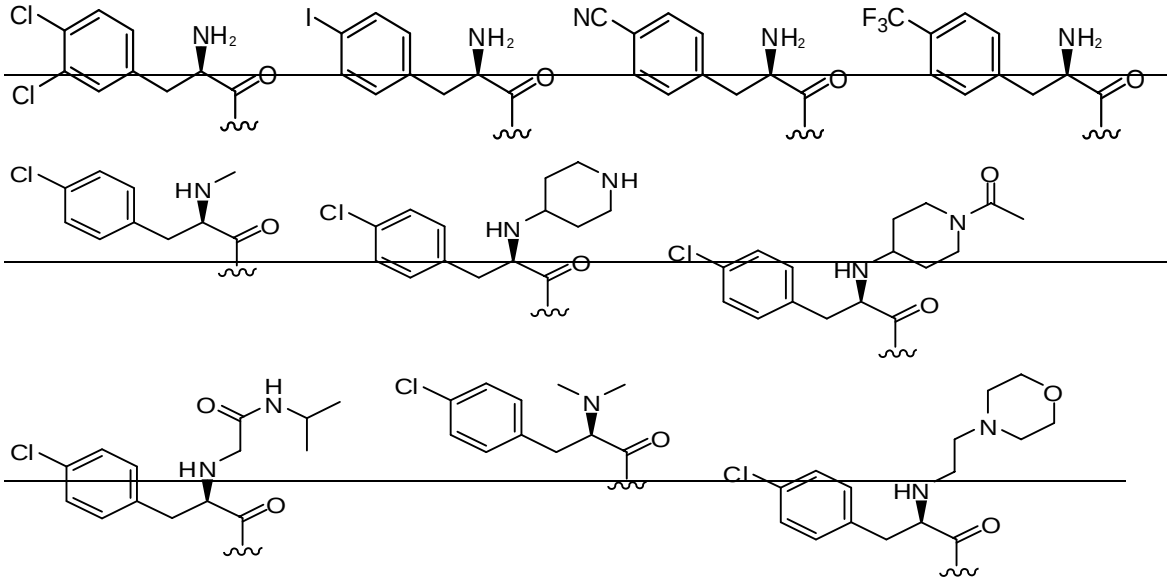
~~9. A compound as claimed in any one of Claims 1 to 7, wherein A is selected from the structures:~~

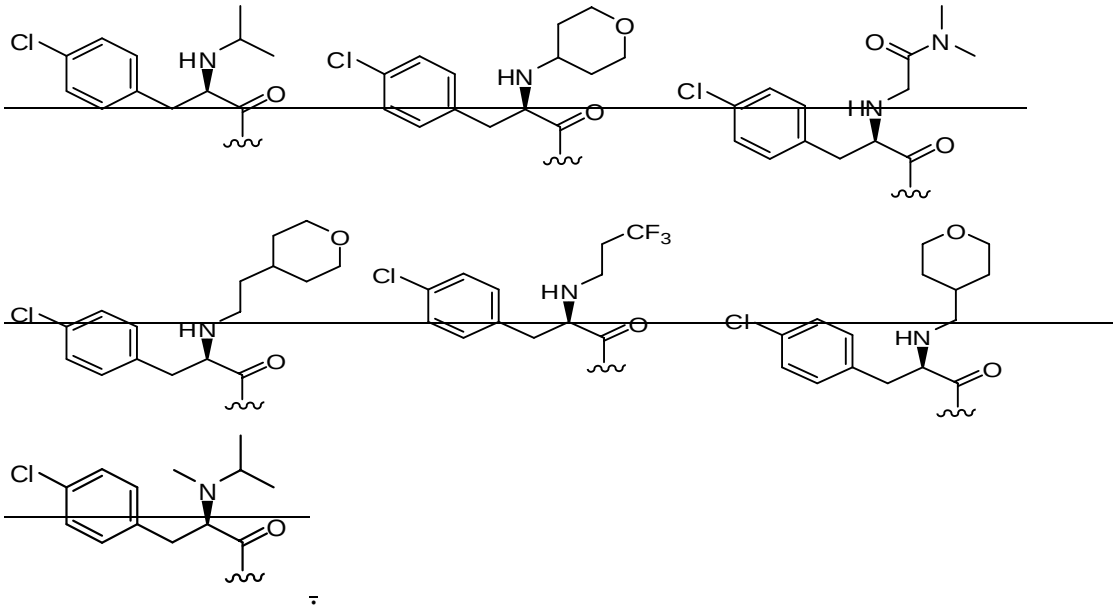




~~10. A compound as claimed in any one of Claims 1 to 7, wherein A is selected from:~~







~~11. A compound of Formula I as defined in Claim 1 and named in any one of Examples 2-4, 6-13, 22-27, 36-40, 42, 43, 50, 65-67, 75, 76, 85, 93, 94-104, 107, 111-115, 117-122, 175-183, 196-199 or 217.~~

~~12. A pharmaceutical composition comprising a compound as claimed in any one of the preceding Claims.~~

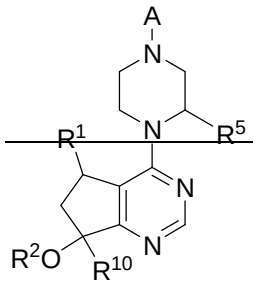
~~13. A compound as claimed in any one of Claims 1 to 10 for use in the treatment of AKT protein kinase-mediated conditions.~~

~~14. The use of a compound as claimed in any one of Claims 1 to 10 in the manufacture of a medicament for the treatment of AKT protein kinase-mediated conditions.~~

~~15. A compound of claim 13 or use of claim 14, wherein the AKT protein kinase-mediated condition is a selected from hyperproliferative disorders selected from cardiac cancer, lung cancer, gastrointestinal cancer, genitourinary tract cancer, prostate cancer (adenocarcinoma, sarcoma), liver cancer, bone cancer, cancer of the nervous system, gynecological cancer, hematological cancer, skin cancer, cancer of the adrenal gland, breast cancer, colon cancer, cancer of the oral cavity, hairy cell leukemia, head or neck cancer, metastatic disease, Kaposi's sarcoma, Bannayan-Zonana syndrome, Cowden disease and Lhermitte-Duclos disease; rheumatoid arthritis; osteoarthritis; Chron's disease; angiofibroma; ocular diseases (e.g., retinal vascularisation, diabetic retinopathy, age-related macular degeneration,~~

macular degeneration); multiple sclerosis; obesity; Alzheimer's disease; restenosis; autoimmune diseases; allergy; asthma; endometriosis; atherosclerosis; vein graft stenosis; perianastomatic prothetic graft stenosis; prostate hyperplasia; chronic obstructive pulmonary disease; psoriasis; inhibition of neurological damage due to tissue repair; scar tissue formation; multiple sclerosis; inflammatory bowel disease; infections (e.g. bacterial, viral, retroviral or parasitic infections); pulmonary disease; neoplasm; Parkinson's disease; transplant rejection; and septic shock.

16. A process for preparing a compound of Formula I



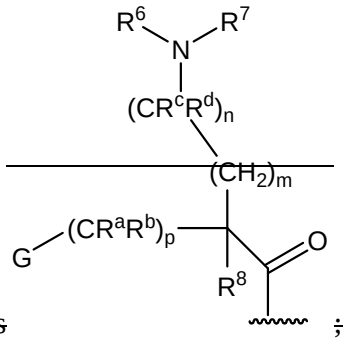
I

and tautomers, resolved enantiomers, resolved diastereomers, solvates, and salts thereof; wherein in Formula I:

R^1 is H, Me, Et, vinyl, CF_3, CHF_2 or CH_2F;

R^2 is H or Me;

R^5 is H, Me, Et, or CF_3;



A is ;

G is phenyl optionally substituted by one to four R^9 groups or a 5-6 membered heteroaryl optionally substituted by a halogen;

R^6 and R^7 are independently H, OCH_3, (C_3-C_6-cycloalkyl)-(CH_2), (C_3-C_6-cycloalkyl)-(CH_2CH_2), V-$(CH_2)_{0-1}$ wherein V is a 5-6 membered heteroaryl, W-$(CH_2)_{1-2}$ wherein W is phenyl optionally substituted with F, Cl, Br, I, OMe, CF_3 or Me, C_3-C_6-cycloalkyl optionally substituted with C_1-C_3 alkyl or O(C_1-C_3 alkyl), hydroxy-(C_3-C_6-cycloalkyl), fluoro-(C_3-C_6-cycloalkyl), $CH(CH_3)CH(OH)$phenyl, 4-6 membered heterocycle optionally substituted with F, OH, C_1-C_3 alkyl, cyclopropylmethyl or C(=O)(C_1-C_3 alkyl), or C_1-C_6-alkyl optionally substituted with one or

more groups independently selected from OH, oxo, O(C_1-C_6-alkyl), CN, F, NH_2, NH(C_1-C_6-alkyl), N(C_1-C_6-alkyl)$_2$, cyclopropyl, phenyl, imidazolyl, piperidinyl, pyrrolidinyl, morpholinyl, tetrahydrofuranyl, oxetanyl or tetrahydropyranyl,

or R^6 and R^7 together with the nitrogen to which they are attached form a 4-7 membered heterocyclic ring optionally substituted with one or more groups independently selected from OH, halogen, oxo, CF_3, CH_2CF_3, CH_2CH_2OH, O(C_1-C_3 alkyl), C(=O)CH_3, NH_2, NHMe, N(Me)$_2$, S(O)$_2CH_3$, cyclopropylmethyl and C_1-C_3 alkyl;

R^a and R^b are H,

or R^a is H, and R^b and R^6 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having one or two ring nitrogen atoms;

R^e and R^d are H or Me,

or R^e and R^d together with the atom to which they are attached from a cyclopropyl ring;

R^8 is H, Me, F or OH,

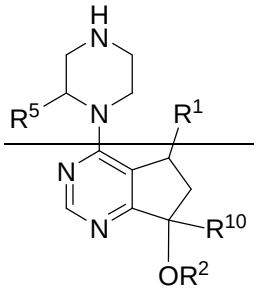
or R^8 and R^6 together with the atoms to which they are attached form a 5-6 membered heterocyclic ring having one or two ring nitrogen atoms;

each R^9 is independently halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, O (C_1-C_6-alkyl), CF_3, OCF_3, S(C_1-C_6-alkyl), CN, OCH_2-phenyl, CH_2O-phenyl, NH_2, NH-(C_1-C_6-alkyl), N-(C_1-C_6-alkyl)$_2$, piperidine, pyrrolidine, CH_2F, CHF_2, OCH_2F, $OCHF_2$, OH, SO_2(C_1-C_6-alkyl), C(O)NH_2, C(O)NH(C_1-C_6-alkyl), and C(O)N(C_1-C_6-alkyl)$_2$;

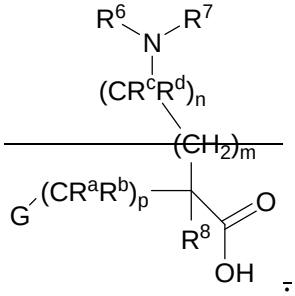
R^{10} is H or Me; and

m, n and p are independently 0 or 1;

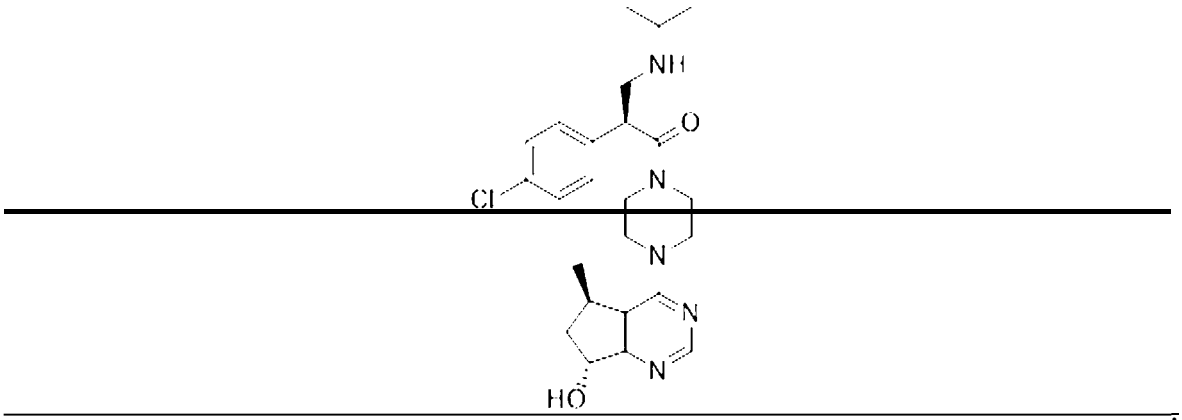
comprising reacting a compound having the formula:



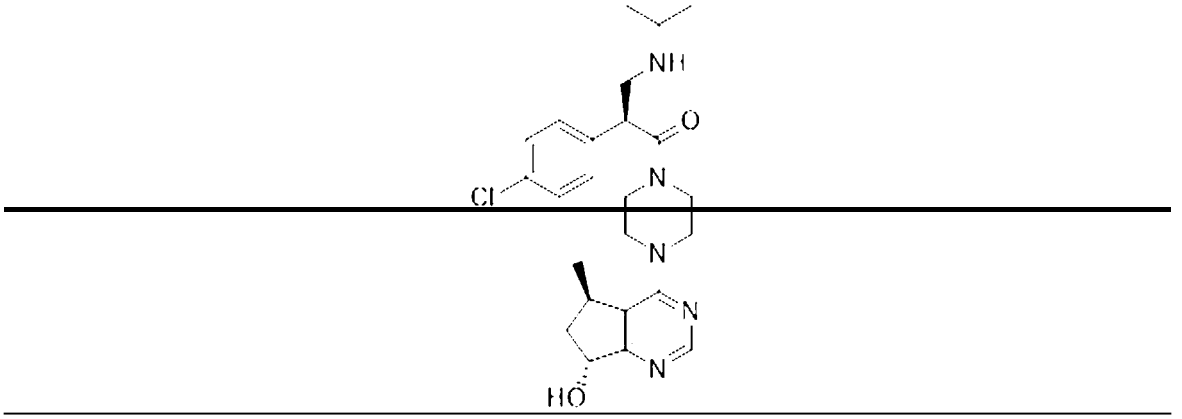
with a compound having the formula:



17. A pharmaceutical composition comprising a compound having the formula:

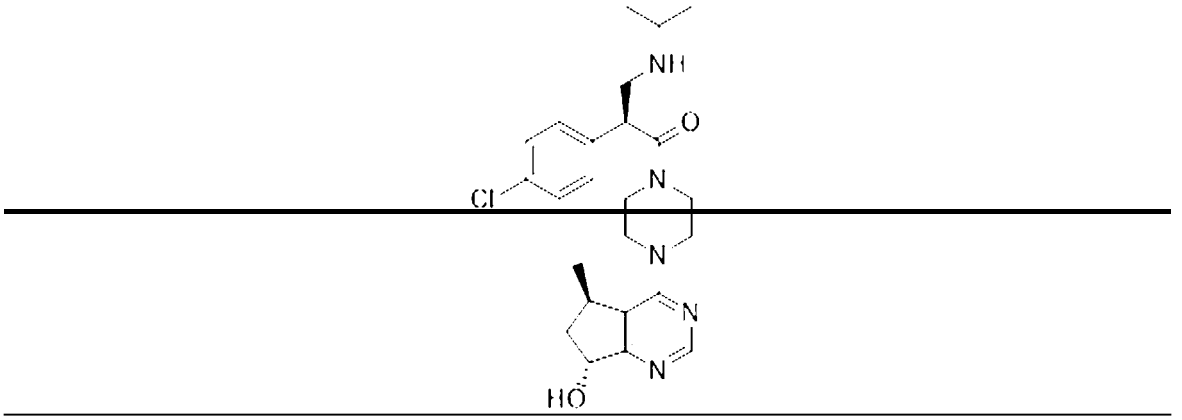


18. A pharmaceutical composition comprising a compound having the formula:



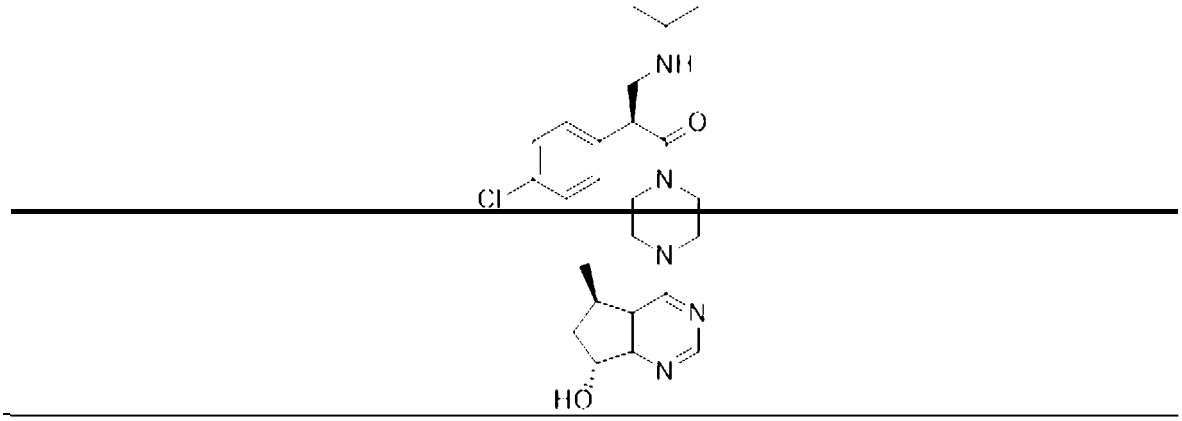
for use in the treatment of an AKT protein kinase-mediated condition.

19. Use of a pharmaceutical composition comprising a compound having the formula:



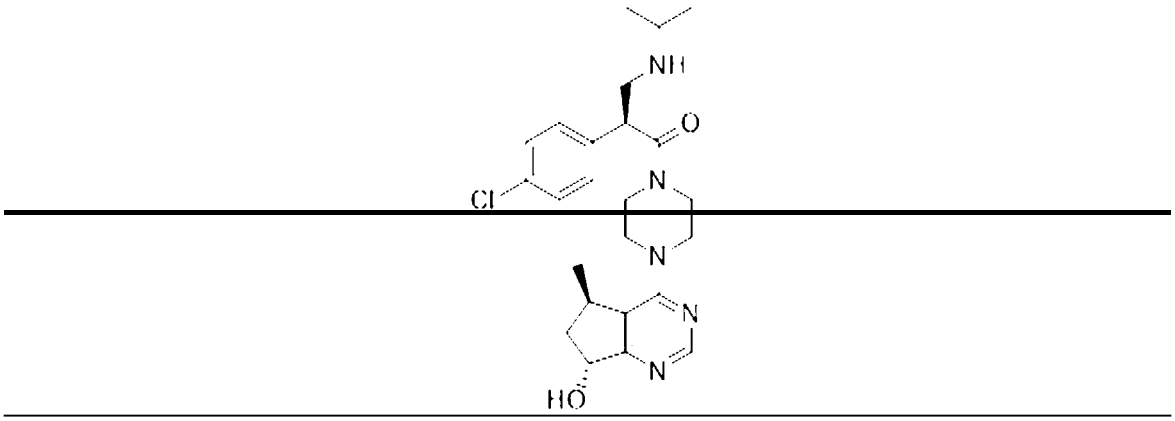
~~in the manufacture of a medicament for the treatment of an AKT protein kinase-mediated condition, wherein the AKT protein kinase-mediated condition is a selected from hyperproliferative disorders selected from cardiac cancer, lung cancer, gastrointestinal cancer, genitourinary tract cancer, prostate cancer (adenocarcinoma, sarcoma), liver cancer, bone cancer, cancer of the nervous system, gynecological cancer, hematological cancer, skin cancer, cancer of the adrenal gland, breast cancer, colon cancer, cancer of the oral cavity, hairy cell leukemia, head or neck cancer, metastatic disease, Kaposi's sarcoma, Bannayan-Zonana syndrome, Cowden disease and Lhermitte-Duclos disease; rheumatoid arthritis; osteoarthritis; Chron's disease; angiofibroma; ocular diseases (e.g., retinal vascularisation, diabetic retinopathy, age-related macular degeneration, macular degeneration); multiple sclerosis; obesity; Alzheimer's disease; restenosis; autoimmune diseases; allergy; asthma; endometriosis; atherosclerosis; vein graft stenosis; perianastomatic prothetic graft stenosis; prostate hyperplasia; chronic obstructive pulmonary disease; psoriasis; inhibition of neurological damage due to tissue repair; scar tissue formation; multiple sclerosis; inflammatory bowel disease; infections (e.g. bacterial, viral, retroviral or parasitic infections); pulmonary disease; neoplasm; Parkinson's disease; transplant rejection; and septic shock.~~

~~20. A compound of formula:~~



~~for use in the treatment of an AKT protein kinase-mediated condition.~~

~~21. Use of a compound of formula:~~



~~in the manufacture of a medicament for the treatment of an AKT protein kinase-mediated condition, wherein the AKT protein kinase-mediated condition is a selected from hyperproliferative disorders selected from cardiac cancer, lung cancer, gastrointestinal cancer, genitourinary tract cancer, prostate cancer (adenocarcinoma, sarcoma), liver cancer, bone cancer, cancer of the nervous system, gynecological cancer, hematological cancer, skin cancer, cancer of the adrenal gland, breast cancer, colon cancer, cancer of the oral cavity, hairy cell leukemia, head or neck cancer, metastatic disease, Kaposi's sarcoma, Bannayan-Zonana syndrome, Cowden disease and Lhermitte-Duclos disease; rheumatoid arthritis; osteoarthritis; Chron's disease; angiofibroma; ocular diseases (e.g., retinal vascularisation, diabetic retinopathy, age-related macular degeneration, macular degeneration); multiple sclerosis; obesity; Alzheimer's disease; restenosis; autoimmune diseases; allergy; asthma; endometriosis; atherosclerosis; vein graft stenosis; perianastomatic prothetic graft stenosis; prostate hyperplasia; chronic obstructive pulmonary disease; psoriasis; inhibition of neurological damage due to tissue repair; scar tissue formation; multiple sclerosis; inflammatory bowel disease; infections (e.g. bacterial, viral, retroviral or parasitic infections); pulmonary disease; neoplasm; Parkinson's disease; transplant rejection; and septic shock.~~

Claims

1. An invention not claimed in any divisional application.