(2) amidating and silylating (2S,3S,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-hydroxy-4-methoxytetrahydrofuran-2-carboxylic acid to obtain (2S,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-N,4-dimethoxy-N-methyltetrahydrofuran-2-carboxamide;

(3) adding an organometallic moiety to (2S,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-N,4-dimethoxy-N-methyltetrahydrofuran-2-carboxamide to obtain 1-((2R,3R,4S,5S)-5-acetyl-4-((tert-butyldimethylsilyl)oxy)-3-methoxytetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione;

(4) oxidizing 1-((2R,3R,4S,5S)-5-acetyl-4-((tert-butyldimethylsilyl)oxy)-3-methoxytetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione to obtain (2R,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-2-yl acetate;

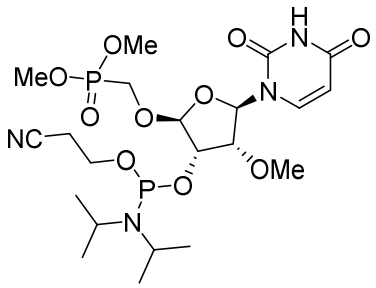
(5) desilylating and benzoylating (2R,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-2-yl acetate to obtain (2R,3S,4R,5R)-2-acetoxy-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-3-yl benzoate;

(6) hydrolyzing and alkylating (2R,3S,4R,5R)-2-acetoxy-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-3-yl benzoate to obtain [(2R,3S,4R,5R)-2-(dimethoxyphosphorylmethoxy)-5-(2,4-dioxopyrimidin-1-yl)-4-methoxy-tetrahydrofuran-3-yl] benzoate;

(7) debenzoylating [(2R,3S,4R,5R)-2-(dimethoxyphosphorylmethoxy)-5-(2,4-dioxopyrimidin-1-yl)-4-methoxy-tetrahydrofuran-3-yl] benzoate to obtain dimethyl ((((2R,3S,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-hydroxy-4-methoxytetrahydrofuran-2-yl)oxy)methyl)phosphonate; and

(8) phosphorylating dimethyl ((((2R,3S,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-hydroxy-4-methoxytetrahydrofuran-2-yl)oxy)methyl)phosphonate to obtain 2-cyanoethyl ((2R,3S,4R,5R)-2-((dimethoxyphosphoryl)methoxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-3-yl) diisopropylphosphoramidite (MeMOP).

[0005a] In an aspect, there is provided a method of making a compound represented by a structure of:



(MeMOP),

the method comprising the steps of:

oxidizing 1-((2R,3R,4R,5R)-4-hydroxy-5-(hydroxymethyl)-3-methoxytetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione to obtain (2S,3S,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-hydroxy-4-methoxytetrahydrofuran-2-carboxylic acid;

amidating and silylating (2S,3S,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-hydroxy-4-methoxytetrahydrofuran-2-carboxylic acid to obtain (2S,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-N,4-dimethoxy-N-methyltetrahydrofuran-2-carboxamide;

adding an organometallic moiety to (2S,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-N,4-dimethoxy-N-methyltetrahydrofuran-2-carboxamide to obtain 1-((2R,3R,4S,5S)-5-acetyl-4-((tert-butyldimethylsilyl)oxy)-3-methoxytetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione;

oxidizing 1-((2R,3R,4S,5S)-5-acetyl-4-((tert-butyldimethylsilyl)oxy)-3-methoxytetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione to obtain (2R,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-2-yl acetate;

desilylating and benzoylating (2R,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-2-yl acetate to obtain (2R,3S,4R,5R)-2-acetoxy-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-3-yl benzoate;

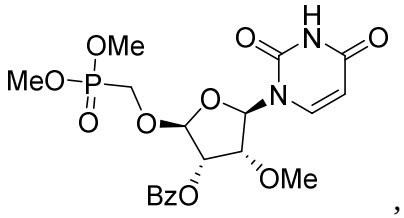
hydrolyzing and alkylating (2R,3S,4R,5R)-2-acetoxy-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-3-yl benzoate to obtain

[(2R,3S,4R,5R)-2-(dimethoxyphosphorylmethoxy)-5-(2,4-dioxopyrimidin-1-yl)-4-methoxy-tetrahydrofuran-3-yl] benzoate;

debenzoylating [(2R,3S,4R,5R)-2-(dimethoxyphosphorylmethoxy)-5-(2,4-dioxopyrimidin-1-yl)-4-methoxy-tetrahydrofuran-3-yl] benzoate to obtain dimethyl ((((2R,3S,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-hydroxy-4-methoxytetrahydrofuran-2-yl)oxy)methyl)phosphonate; and

phosphorylating dimethyl ((((2R,3S,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-hydroxy-4-methoxytetrahydrofuran-2-yl)oxy)methyl)phosphonate to obtain 2-cyanoethyl ((2R,3S,4R,5R)-2-((dimethoxyphosphoryl)methoxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-3-yl) diisopropylphosphoramidite (MeMOP).

[0005b] In another aspect, there is provided a method of making a compound represented by a structure of:



,

the method comprising the steps of:

oxidizing 1-((2R,3R,4R,5R)-4-hydroxy-5-(hydroxymethyl)-3-methoxytetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione to obtain (2S,3S,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-hydroxy-4-methoxytetrahydrofuran-2-carboxylic acid;

amidating and silylating (2S,3S,4R,5R)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-3-hydroxy-4-methoxytetrahydrofuran-2-carboxylic acid to obtain (2S,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-N,4-dimethoxy-N-methyltetrahydrofuran-2-carboxamide;

adding an organometallic moiety to (2S,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-N,4-dimethoxy-N-methyltetrahydrofuran-2-carboxamide to obtain 1-((2R,3R,4S,5S)-5-acetyl-4-((tert-butyldimethylsilyl)oxy)-3-methoxytetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione;

oxidizing 1-((2R,3R,4S,5S)-5-acetyl-4-((tert-butyldimethylsilyl)oxy)-3-methoxytetrahydrofuran-2-yl)pyrimidine-2,4(1H,3H)-dione to obtain (2R,3S,4R,5R)-3-((tert-

butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-2-yl acetate;

desilylating and benzoylating (2R,3S,4R,5R)-3-((tert-butyldimethylsilyl)oxy)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-2-yl acetate to obtain (2R,3S,4R,5R)-2-acetoxy-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-3-yl benzoate; and

hydrolyzing and alkylating (2R,3S,4R,5R)-2-acetoxy-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-4-methoxytetrahydrofuran-3-yl benzoate to obtain [(2R,3S,4R,5R)-2-(dimethoxyphosphorylmethoxy)-5-(2,4-dioxopyrimidin-1-yl)-4-methoxy-tetrahydrofuran-3-yl] benzoate.

[0006] In some instances, a compound represented by a structure of: