unsubstituted alkyl (hereinafter referred to as e-3).

X is =CH- or =N- (hereinafter referred to as e-4).

X is =CH- (hereinafter referred to as e-5).

X is =N- (hereinafter referred to as e-6).

[0048]

Y is $=CR^Y-$ or =N-, wherein R^Y is a hydrogen atom, cyano, halogen, substituted or unsubstituted alkyl or substituted or unsubstituted carbamoyl (hereinafter referred to as f-1).

Y is $=CR^Y-$ or =N-, wherein R^Y is a hydrogen atom or halogen (hereinafter referred to as f-2).

Y is =CH- or =N- (hereinafter referred to as f-3).

Y is =CH- (hereinafter referred to as f-4).

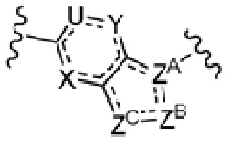
Y is =N- (hereinafter referred to as f-5).

[0049]

U is $-CR^U=$ or -N=, wherein R^U is a hydrogen atom, substituted or unsubstituted alkyloxy, substituted or unsubstituted non-aromatic heterocyclyloxy, substituted or unsubstituted non-aromatic carbocyclyloxy, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted amino, hydroxy, halogen, substituted or unsubstituted aromatic carbocyclyl, substituted or unsubstituted aromatic heterocyclyl, substituted or unsubstituted non-aromatic heterocyclyl or substituted or unsubstituted non-aromatic carbocyclyl (hereinafter referred to as g-1).

U is $-CR^U=$ or -N=, wherein R^U is a hydrogen atom, halogen, substituted or unsubstituted non-aromatic carbocyclyloxy, substituted or unsubstituted non-aromatic heterocyclyloxy or substituted or unsubstituted alkyloxy (hereinafter referred to as g-2).

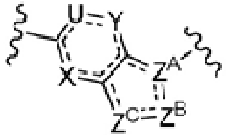
U is $-CR^U=$ or -N=, wherein R^U is a hydrogen atom, halogen, non-aromatic carbocyclyloxy substituted with pyrazolyl or unsubstituted non-aromatic carbocyclyloxy, non-aromatic heterocyclyloxy substituted with oxetanyl or unsubstituted non-aromatic heterocyclyloxy, or unsubstituted alkyloxy (hereinafter



is one represented by the formula (I-a) or (I-b).

[0061]

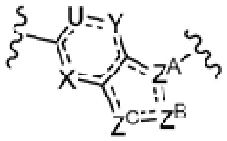
The group of the formula:



is one represented by the formula (I-a).

[0062]

The group of the formula:



is one represented by the formula (I-b).

[0063]

R^X is a hydrogen atom, cyano, halogen, substituted or unsubstituted alkyl or substituted or unsubstituted carbamoyl (hereinafter referred to as ee-1).

R^X is a hydrogen atom, halogen or substituted or unsubstituted alkyl (hereinafter referred to as ee-2).

R^X is a hydrogen atom, halogen or unsubstituted alkyl (hereinafter referred to as ee-3)

R^X is a hydrogen atom (hereinafter referred to as ee-4).

[0064]

R^Y is a hydrogen atom, cyano, halogen, substituted or unsubstituted alkyl or substituted or unsubstituted carbamoyl (hereinafter referred to as ff-1).

R^Y is a hydrogen atom or halogen (hereinafter referred to as ff-2).

R^Y is a hydrogen atom (hereinafter referred to as ff-

3).

[0065]

R^U is a hydrogen atom, substituted or unsubstituted alkyloxy, substituted or unsubstituted non-aromatic heterocyclyloxy, substituted or unsubstituted non-aromatic carbocyclyloxy, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted amino, hydroxy, halogen, substituted or unsubstituted aromatic carbocyclyl, substituted or unsubstituted aromatic heterocyclyl, substituted or unsubstituted non-aromatic heterocyclyl or substituted or unsubstituted non-aromatic carbocyclyl (hereinafter referred to as gg-1).

R^U is a hydrogen atom, halogen, substituted or unsubstituted non-aromatic carbocyclyloxy, substituted or unsubstituted non-aromatic heterocyclyloxy or substituted or unsubstituted alkyloxy (hereinafter referred to as gg-2).

R^U is a hydrogen atom, halogen, non-aromatic carbocyclyloxy substituted with pyrazolyl or unsubstituted non-aromatic carbocyclyloxy, non-aromatic heterocyclyloxy substituted with oxetanyl or unsubstituted non-aromatic heterocyclyloxy, or unsubstituted alkyloxy (hereinafter referred to as gg-3).

R^U is a hydrogen atom (hereinafter referred to as gg-4).

[0066]

R^5 and R^6 are each independently a hydrogen atom, substituted or unsubstituted non-aromatic heterocyclyl, hydroxy or substituted or unsubstituted alkyl, or R^5 and R^6 are taken together to form oxo (hereinafter referred to as kk-1).

R^5 is a hydrogen atom, substituted or unsubstituted non-aromatic heterocyclyl, hydroxy or substituted or unsubstituted alkyl (hereinafter referred to as kk-5).

R^5 and R^6 are each independently a hydrogen atom, substituted or unsubstituted non-aromatic heterocyclyl, or R^5 and R^6 are taken together to form oxo (hereinafter referred to as kk-6).

(m-14), (m-15), (m-16), (m-17), (m-18), (m-19) or (m-20).

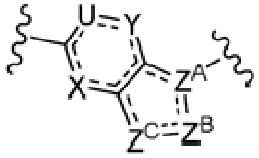
[0075]

(1-A)

In one embodiment, a compound of the formula (I) is a compound,

wherein

the group of the formula:



is as defined in (I-a),

R^X is as defined in (ee-4),

R^Y is as defined in (ff-3),

R^U is as defined in (gg-4),

R^5 and R^6 are as defined in (kk-9),

R^7 and R^8 are as defined in (ll-14),

R^1 is as defined in (a-3),

L is as defined in (b-14),

R^2 is as defined in (c-3),

R^3 is as defined in (d-5),

V is as defined in (h-6),

W is as defined in (i-4), and

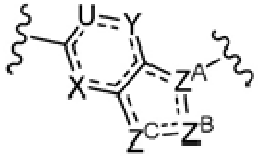
R^4 is as defined in (m-17).

[0076]

(1-B)

In one embodiment, a compound of formula (I) is a compound, wherein

the group of the formula:

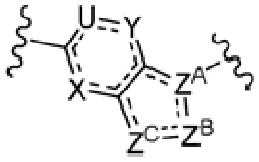


is as defined in (I-b),

R^X is as defined in (ee-4),

R^Y is as defined in (ff-3),
R^U is as defined in (gg-4),
R^7 is as defined in (ll-15),
R^1 is as defined in (a-3),
L is as defined in (b-14),
R^2 is as defined in (c-3),
R^3 is as defined in (d-5),
V is as defined in (h-6),
W is as defined in (i-3), and
R^4 is as defined in (m-17).

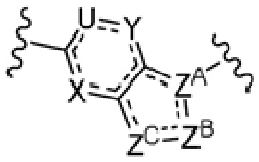
[0077]
(1-C)
In one embodiment, a compound of formula (I) is a compound, wherein
the group of the formula:



is as defined in (I-b),
R^X is as defined in (ee-4),
R^Y is as defined in (ff-3),
R^U is as defined in (gg-4),
R^7 is as defined in (ll-15),
R^1 is as defined in (a-3),
L is as defined in (b-14),
R^2 is as defined in (c-3),
R^3 is as defined in (d-5),
V is as defined in (h-6),
W is as defined in (i-4), and
R^4 is as defined in (m-16).

[0078]
(1-D)
In one embodiment, a compound of formula (I) is a compound, wherein

the group of the formula:



is as defined in (I-b),

R^X is as defined in (ee-4),

R^Y is as defined in (ff-3),

R^U is as defined in (gg-4),

R^7 is as defined in (ll-13),

R^1 is as defined in (a-3),

L is as defined in (b-14),

R^2 is as defined in (c-3),

R^3 is as defined in (d-5),

V is as defined in (h-6),

W is as defined in (i-4), and

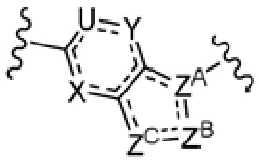
R^4 is as defined in (m-16).

[0079]

(1-E)

In one embodiment, a compound of formula (I) is a compound, wherein

the group of the formula:



is as defined in (I-i),

R^X is as defined in (ee-4),

R^Y is as defined in (ff-3),

R^5 and R^6 are as defined in (kk-9),

R^7 and R^8 are as defined in (ll-14),

R^1 is as defined in (a-3),

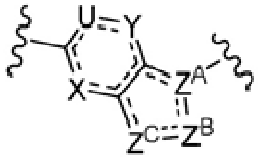
L is as defined in (b-14),

R^2 is as defined in (c-3),

R^3 is as defined in (d-5),

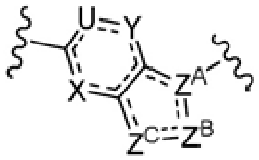
V is as defined in (h-6),
W is as defined in (i-4), and
R^4 is as defined in (m-18).

[0080]
(1-F)
In one embodiment, a compound of formula (I) is a compound, wherein
the group of the formula:



is as defined in (I-a),
R^X is as defined in (ee-4),
R^Y is as defined in (ff-3),
R^U is as defined in (gg-4),
R^5 and R^6 are as defined in (kk-9),
R^7 and R^8 are as defined in (ll-14),
R^1 is as defined in (a-3),
L is as defined in (b-14),
R^2 is as defined in (c-3),
R^3 is as defined in (d-5),
V is as defined in (h-6),
W is as defined in (i-4), and
R^4 is as defined in (m-16).

[0081]
(1-G)
In one embodiment, a compound of formula (I) is a compound, wherein
the group of the formula:



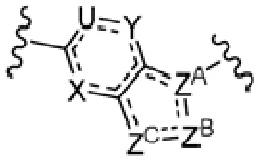
is as defined in (I-a),

R^X is as defined in (ee-4),
R^Y is as defined in (ff-3),
R^U is as defined in (gg-4),
R^5 and R^6 are as defined in (kk-9),
R^7 and R^8 are as defined in (ll-14),
R^1 is as defined in (a-3),
L is as defined in (b-14),
R^2 is as defined in (c-3),
R^3 is as defined in (d-5),
V is as defined in (h-6),
W is as defined in (i-4), and
R^4 is as defined in (m-19).

(1-H)

In one embodiment, a compound of formula (I) is a compound, wherein

the group of the formula:



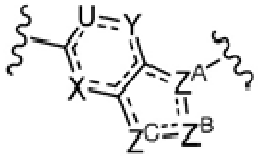
is as defined in (I-a),
R^X is as defined in (ee-4),
R^Y is as defined in (ff-3),
R^U is as defined in (gg-4),
R^5 and R^6 are as defined in (kk-9),
R^7 and R^8 are as defined in (ll-14),
R^1 is as defined in (a-3),
L is as defined in (b-14),
R^2 is as defined in (c-3),
R^3 is as defined in (d-5),
V is as defined in (h-6),
W is as defined in (i-4), and
R^4 is as defined in (m-20).

(1-I)

In one embodiment, a compound of formula (I) is a compound,

wherein

the group of the formula:



is as defined in (I-b),

R^X is as defined in (ee-4),

R^Y is as defined in (ff-3),

R^U is as defined in (gg-4),

R^7 is as defined in (ll-17),

R^1 is as defined in (a-3),

L is as defined in (b-14),

R^2 is as defined in (c-3),

R^3 is as defined in (d-5),

V is as defined in (h-6),

W is as defined in (i-4), and

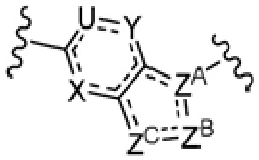
R^4 is as defined in (m-16).

[0082]

(1-J)

In one embodiment, a compound of formula (I) is a compound, wherein

the group of the formula:



is as defined in (I-a),

R^X is as defined in (ee-4),

R^Y is as defined in (ff-3),

R^U is as defined in (gg-4),

R^5 and R^6 are as defined in (kk-9),

R^7 and R^8 are as defined in (ll-11),

R^1 is as defined in (a-3),
L is as defined in (b-14),
R^2 is as defined in (c-3),
R^3 is as defined in (d-5),
V is as defined in (h-6),
W is as defined in (i-4), and
R^4 is as defined in (m-16).

[0083]

Compounds of formula (I) are not limited limited to specific isomers, but include all possible isomers (e.g., keto-enol isomers, imine-enamin isomers, diastereoisomers, optical isomers, rotational isomers, etc.), racemates or mixtures thereof.

[0084]

One or more hydrogen, carbon, and/or other atom(s) of the compounds of formula (I) may be substituted by isotope(s) of hydrogen, carbon, and/or other atom(s), respectively. Examples of such isotopes include hydrogen, carbon, nitrogen, oxygen, phosphorus, sulfur, fluorine, iodine, and chlorine, as in the cases of ^{2}H, ^{3}H, ^{11}C, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, ^{123}I, and ^{36}Cl, respectively. The compounds of formula (I) also include compounds substituted with such isotopes. The compounds substituted with the isotopes are also useful as pharmaceutical products and include all radiolabeled forms of the compounds of formula (I). Furthermore, a "radiolabeling method" for producing the "radiolabeled forms" is also included in the present invention, and the "radiolabeled forms" are useful as tools for metabolic pharmacokinetics studies, studies on binding assay, and/or diagnostics.

[0085]

(brs, 1H), 7.88 (d, J = 8.4Hz, 1H), 8.11 (s, 1H), 8.14 (d, J = 8.4Hz, 1H), 8.46 (d, J = 8.8Hz, 1H).
LC/MS(ESI):m/z= 451 [M+H]+, RT=2.84 min, LC/MS Method 1

[0152]
Step 3: Synthesis of Compound 46

To Compound 45 (3.27 g, 7.26 mmol) were added tetrahydrofuran (39.2 mL), Compound 17 (1.69 g, 9.44 mmol), triphenylphosphine (2.48 g, 9.44 mmol) and DMEAD (2.21 g, 9.44 mmol). The mixture was stirred at 50°C for 1 hour, the reaction was quenched with water. The organic layer was extracted with ethyl acetate, washed with water, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane–ethyl acetate) to afford Compound 46 (4.07 g, yield 92%).
^{1}H–NMR ($CDCl_3$) δ: 1.42 (t, J = 7.2Hz, 3H), 1.72 (s, 9H), 1.90 (m, 2H), 2.06 (m, 2H), 3.76 (m, 2H), 4.19 (m, 2H), 4.44 (q, J = 7.2Hz, 2H), 4.67 (m, 1H), 6.48 (t, J = 4.4Hz, 1H), 7.06 (dd, J = 8.8, 2.0Hz, 1H), 7.83 (brs, 1H), 7.89 (d, J = 8.0Hz, 1H), 8.13-8.16 (m, 2H), 8.32 (d, J = 4.8Hz, 2H), 8.49 (d, J = 8.8Hz, 1H).
LC/MS(ESI):m/z= 612 [M+H]+, RT=3.59 min, LC/MS Method 1

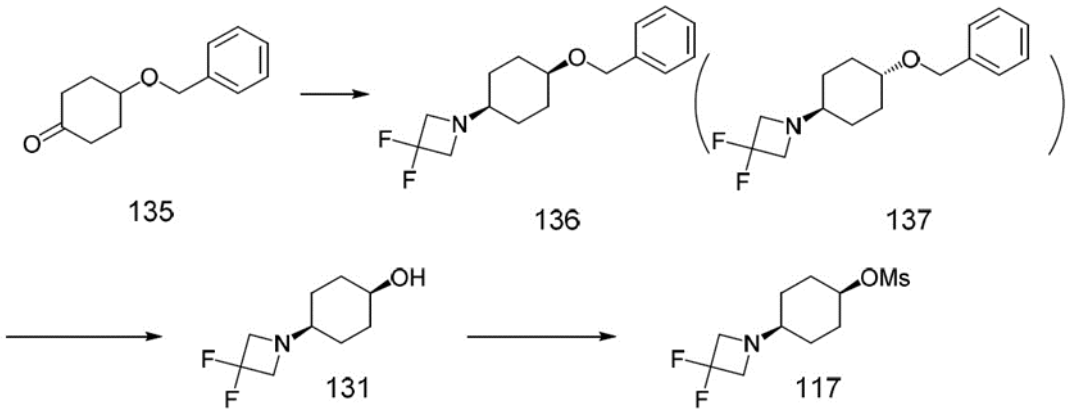
[0153]
Step 4: Synthesis of Compound 21

To Compound 46 (4.17 g, 6.82 mmol) were added dichloromethane (41.7 mL) and trifluoroacetic acid (41.7mL, 541 mmol), and the mixture was stirred at room temperature for 1 hour 30 minutes. The reaction solution was concentrated under reduced pressure and neutralized with saturated aqueous sodium bicarbonate solution. The mixture was extracted with chloroform and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and chloroform was added to the residue. The solid was filtered to obtain Compound 21 (800 mg, yield 22%). The filtrate was again concentrated under reduced pressure. Tolene was added to solidify the residure, and the solid was filtered to obtain Compound 21 (1.73 g, yield 48%). The filtrate was further concentrated under

[0227]

(Reference Example)

Synthesis of Compound 117 and Compound 131



Step 1: Synthesis of Compound 136 and Compound 137

Compound 135 (1.0 g, 4.90 mmol) was dissolved in dichloromethane (10 mL), and 3,3-Difluoroazetidine hydrochloride (1.27 g, 9.79 mmol), triethylamine (1.26 mL, 9.79 mmol), acetic acid (0.28 mL, 4.90 mmol) and sodium triacetoxyborohydride (2.08 g, 9.79 mmol) were added and stirred for 3 hours. Water was added, followed by extraction with chloroform. The organic layer was washed with water and dried over anhydrous sodium sulfate. The residue was purified by silica gel column chromatography (hexane-ethyl acetate) to afford Compound 136 (846 mg, 61% yield) and Compound 137 (454 mg, yield 33%).

Compound 136

^{1}H-NMR ($CDCl_3$) δ: 1.44-1.60 (m, 6H), 1.90-1.96 (m, 2H), 2.14-2.19 (m, 1H), 3.53 (t, J = 12.4Hz, 4H), 3.55 (m, 1H), 4.50 (s, 2H), 7.23-7.28 (m, 1H), 7.30-7.36 (m, 4H).

LC/MS(ESI):m/z= 282 [M+H]+, RT=1.24 min, LC/MS Method 1

Compound 137

^{1}H-NMR ($CDCl_3$) δ: 1.08-1.18 (m, 2H), 1.26-1.39 (m, 2H), 1.77-1.81 (m, 2H), 2.05-2.15 (m, 3H), 3.33-3.40 (m, 1H), 3.54 (t, J = 11.6Hz, 4H), 4.54 (s, 2H), 7.25-7.30 (m, 1H), 7.31-7.34 (m, 4H).

LC/MS(ESI):m/z= 282 [M+H]+, RT=1.20 min, LC/MS Method 1

[0228]