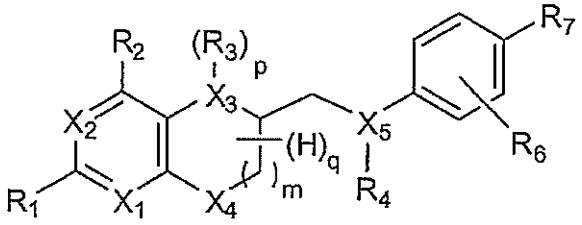
Claims

1. A compound having formula II



II

wherein

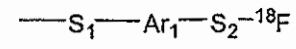
X_1 to X_5 are independently of each other C or N,

R_1 and R_2 are independently of each other H, Hal, -OR', -NHR', C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, C2-C12 alkenyl, C2-C12 alkynyl, (C1-C12 alkoxy)carbonyl, and (C1-C12 alkylamino)carbonyl, wherein R' is H or C1-C6 alkyl,

R_3, R_4 are independently of each other H, formyl, iminomethyl, nitroso, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, halosubstituted C1-C12 alkanoyl,

R_5 is H, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, and (C_1-C_{12} alkylamino)carbonyl,

R_6, R_7 are independently of each other straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a group of the formula III



III

wherein S_1 and S_2 are independently of each other a single bond or a spacer unit, such as straight-chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -N=, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-,-CH=CH-, -C≡C-, -S-, $-SO_3R'-$, -PR'- , or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof, and

Ar_1 is a triazole or a tetrazole,

with the proviso that one of R_6 and R_7 is a group of formula III,

m is 0 or 1,

p is 0, 1 or 2, and

q has a value of 1 to 7.

2. A compound according to claim 1, wherein R_6 is straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and R_7 is a group of formula III.

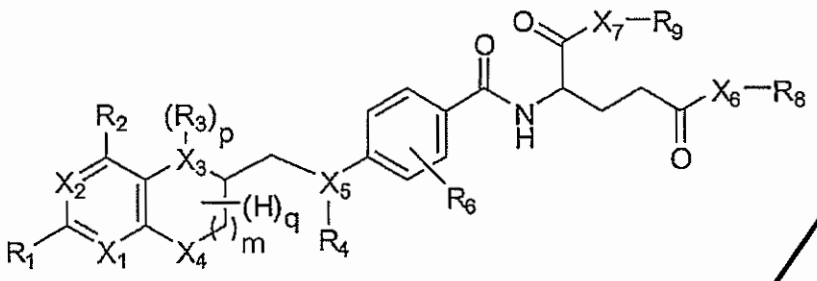
3. A compound according to claims 1 or 2, wherein R_7 is

straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and R_6 is a group of formula III.

4. A compound according to any preceding claim wherein S_1 is a single bond or a spacer unit, such as straight-chain or branched C_1-C_{18} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -NR'-, -NR'-CO-, -CO-NR'-, -CH=CH-, -C≡C-, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof.

5. A compound according to any preceding claim wherein S_2 is a single bond or a straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof, more preferably a single bond or a straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2.

6. A compound according to claim 1 having formula IV

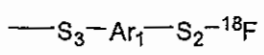


IV

wherein

X_6, X_7 are independently of each other C, N or O

R_8, R_9 are independently of each other H or straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, or a group of the formula V



V

wherein S_2, S_3 are independently of each other a single bond or a spacer unit, such as straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -N=, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-, -CH=CH-, -C≡C-, -S-, $-SO_3R'$-, -PR'- , or a five- or six-membered aromatic

ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof,

Ar_1 is a triazole or a tetrazole,

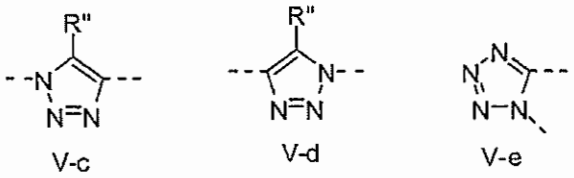
and

X_1 to X_5, R_1 to R_6, p and q, are as defined in claim 3,

with the proviso that either R_6 is a group of formula III or at least one of R_8 and R_9 is a group of formula V.

7. A compound according to claim 6, wherein S_2 and S_3 are independently of each other a single bond or a straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof, more preferably straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2.

8. A compound according to any preceding claim wherein Ar_1 is selected from formulae V-c, V-d and V-e



V-c V-d V-e

wherein the dotted lines represent linking sites to the

spacer groups and R'' is H, Hal, NH-COR', NH-SO_2R', CO_2R', COR', wherein R' represents H or C1-C6 alkyl, or straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, SO_3H, SH, CO_2H, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof.

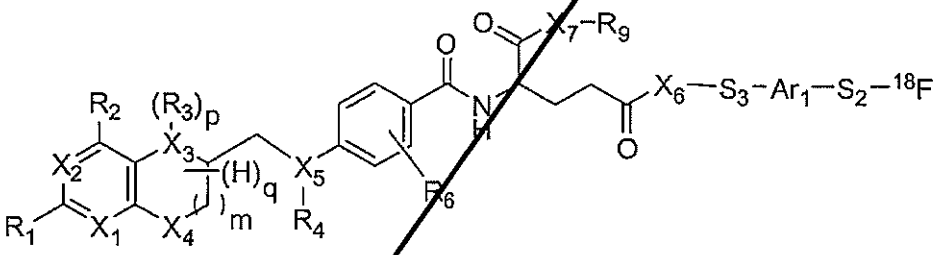
9. A compound according to claim 6, wherein R_6 is CN, Hal, NO_2, or a group R_5 and at least one of R_8 and R_9 is a group of formula V.

10. A compound according to claim 6, wherein R_6 is CN, Hal, NO_2, or a group R_5, R_9 is H or straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal or NO_2, wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, and R_9 is a group of formula V.

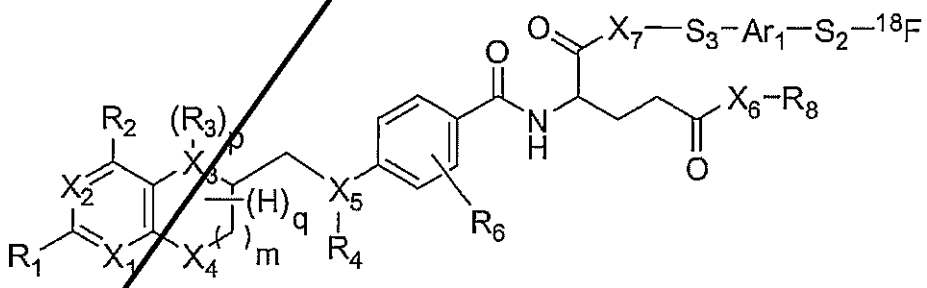
11. A compound according to claim 6, wherein R_6 is CN, Hal, NO_2, or a group R_5, R_9 is H or straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal or NO_2, wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, and R_8 is a group of formula V.

12. A compound according to claim 6, wherein R_8 and R_9 are independently of each other H or straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal or NO_2, wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, and R_6 is a group of formula V.

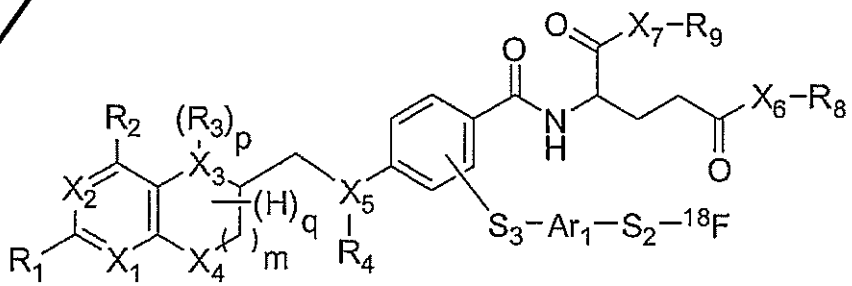
13. A compound according to claim 1 having formulae VI, VIa or VIb,



VI



VIa



VIb

wherein

X_1 to X_5 are independently of each other C or N,

X_6, X_7 are independently of each other C, N or O,

R_1 and R_2 are independently of each other H, Hal, -OR', -NHR', C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, C2-C12 alkenyl, C2-C12 alkynyl, (C1-C12 alkoxy)carbonyl, and (C1-C12 alkylamino)carbonyl, wherein R' is H or C1-C6 alkyl,

R_3, R_4 are independently of each other H, formyl, iminomethyl, nitroso, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, halosubstituted C1-C12 alkanoyl

R_6 is H, CN, Hal, NO_2, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, or (C_1-C_{12} alkylamino)carbonyl,

R_8, R_9 are independently of each other H or straight chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO2, and wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-,,

S_2, S_3 are independently of each other a single bond or a spacer unit, such as straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -N=, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-,-CH=CH-, -C≡C-, -S-, -SO_3R'-, -PR'- , or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or

COOR′, wherein R′ represents H or C_1-C_6 alkyl, or a combination thereof,

Ar_1 is a triazole or a tetrazole,

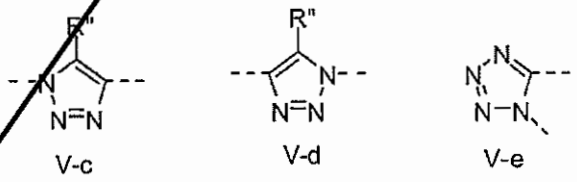
m is 0 or 1,

p is 0, 1 or 2, and

q has a value of 1 to 7.

14. A compound according to claim 13 wherein S_2 and S_3 are independently of each other a single bond or a straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR′, or COOR′, wherein R′ represents H or C_1-C_6 alkyl.

15. A compound according to claims 13 or 14, wherein Ar_1 is selected from formulae V-c, V-d and V-e

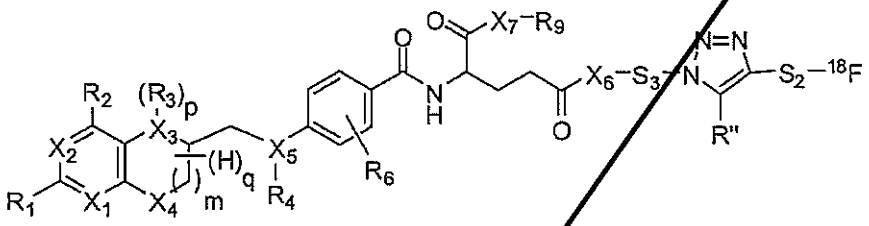


V-c V-d V-e

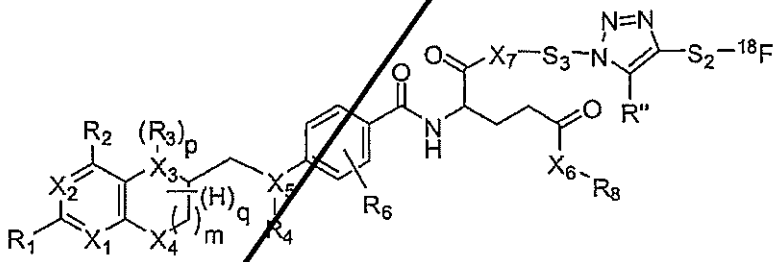
wherein the dotted lines represent linking sites to the spacer groups and R′′ is H, Hal, NH-COR′, NH-SO_2R′, CO_2R′, COR′, wherein R′ represents H or C1-C6 alkyl, or straight-chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, SO_3H, SH, CO_2H, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with

CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof.

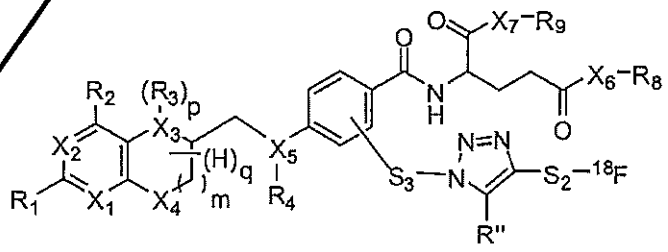
16. A compound according to any preceding claim of formulae VIIa to VIIf or VIIIa to VIIIf,



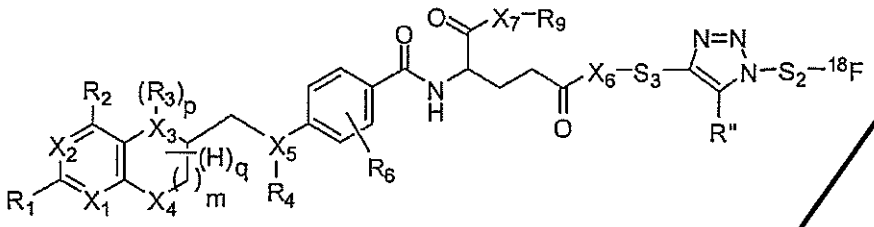
VIIa



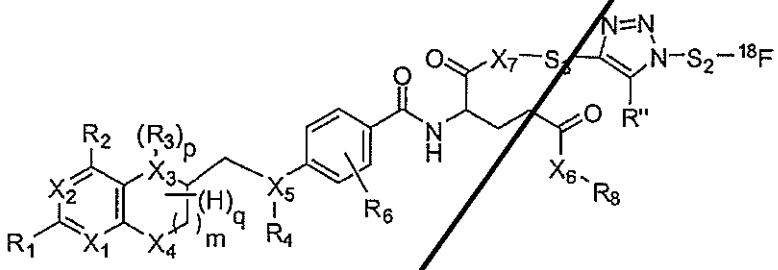
VIIb



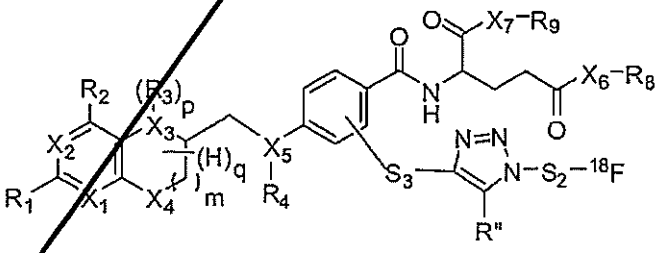
VIIc



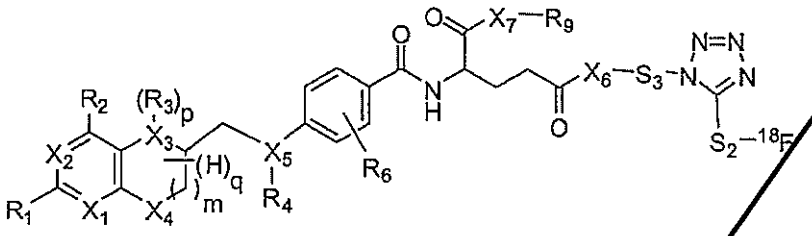
VIId



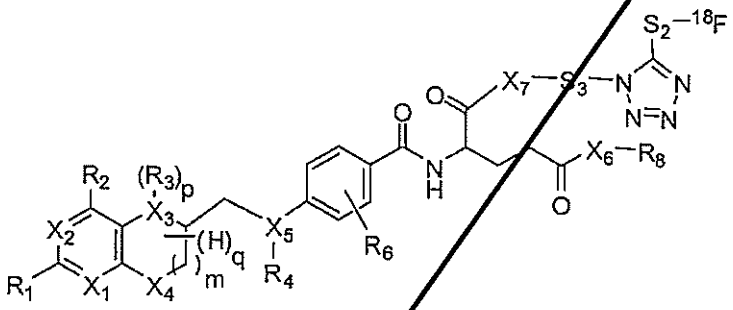
VIIe



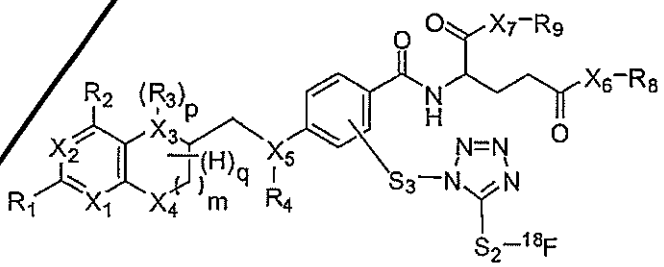
VIIf



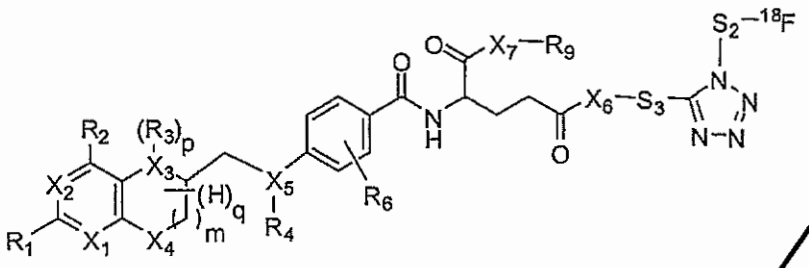
VIIIa



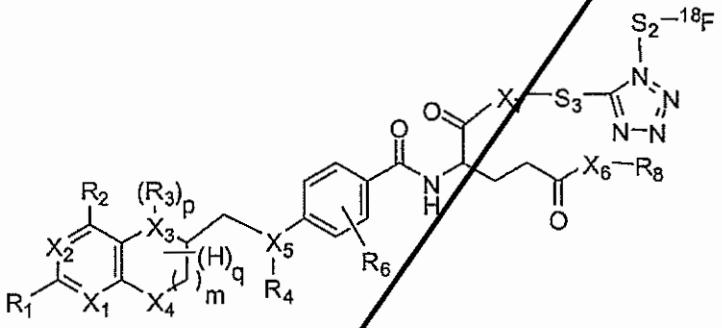
VIIIb



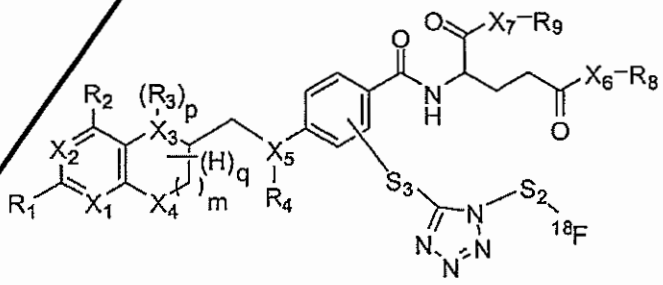
VIIIc



VIIId



VIIIe



VIIIf

wherein

X_1 to X_5 are independently of each other C or N,

X_6, X_7 are independently of each other C, N or O,

R_1, R_2 are independently of each other H, Hal, -OR', -NHR', C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, C2-C12 alkenyl, C2-C12 alkynyl, (C1-C12 alkoxy)carbonyl, and (C1-C12 alkylamino)carbonyl, wherein R' is H or C1-C6 alkyl,

R_3, R_4 are independently of each other H, formyl, iminomethyl, nitroso, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, halosubstituted C1-C12 alkanoyl,

R_6 is H, CN, Hal, NO_2, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, or (C_1-C_{12} alkylamino)carbonyl,

R_8, R_9 are independently of each other H or straight chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO2, and wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-,,

S_2, S_3 are independently of each other a single bond or a spacer unit, such as straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -N=, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-,-CH=CH-, -C≡C-, -S-, $-SO_3R'-$, -PR'- , or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof,

R'' is H, Hal, NH-COR', $NH-SO_2R'$, CO_2R', COR', or straight-chain or branched C_1-C_{12} alkyl, which is

unsubstituted or substituted by at least one CN, Hal, OH, NH_2, SO_3H, SH, CO_2H, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, and

m is 0 or 1,

p is 0, 1 or 2, and

q has a value of 1 to 7.

17. A compound according to any preceding claim, wherein R_1 and R_2 are independently of each other H, alkyl, -OR', -NHR', wherein R' represents H or C_1-C_6 alkyl.

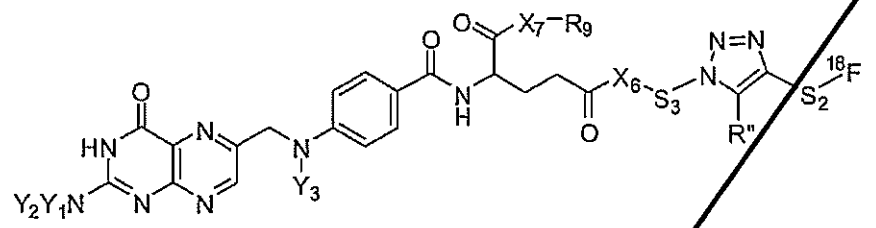
18. A compound according to any preceding claim, wherein R_3 is H, formyl, C1-C12 alkyl or C1-C12 alkanoyl.

19. A compound according to any preceding claim, wherein R_4 is H, nitroso, C1-C12 alkoxy, or C1-C12 alkanoyl.

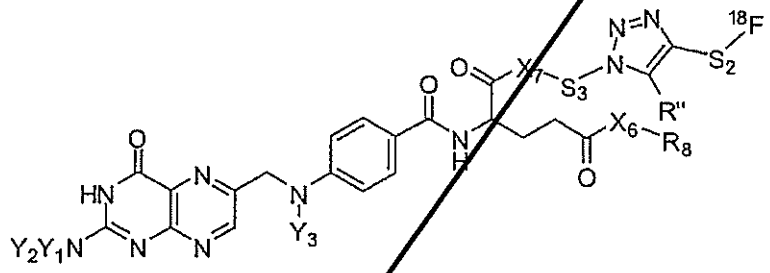
20. A compound according to any preceding claim, wherein R_5 is H, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, (C_1-C_{12} alkoxy)carbonyl, or (C_1-C_{12} alkylamino)carbonyl.

21. A compound according to any preceding claim, wherein R_6 is H, CN, Hal, NO_2, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, or (C_1-C_{12} alkoxy)carbonyl.

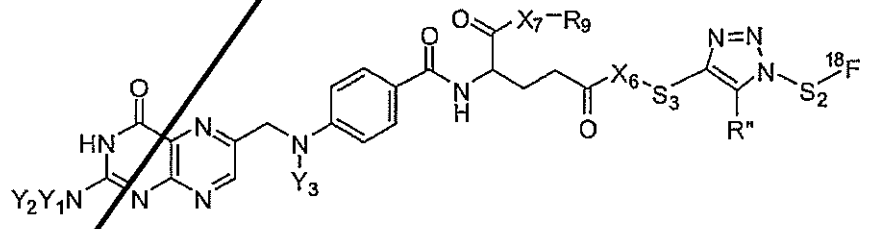
22. A compound according to any preceding claim having formulae IX, IXa, X or Xa,



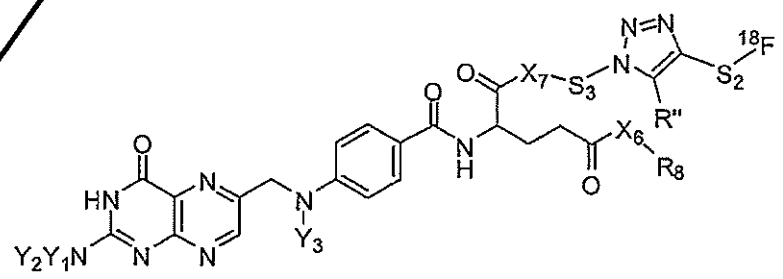
IX



IXa



X



Xa

wherein,

X_6, X_7 are independently of each other C, N or O,

Y_1, Y_2 are independently of each other selected from H, formyl, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR′-, -CH=CH-, -C≡C-,

Y_3 is selected from H, formyl, nitroso, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR′-, -CH=CH-, -C≡C-,

R_8, R_9 are independently of each other H or straight chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO2, and wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR′-, -CH=CH-, -C≡C-,,

R′′ is H, Hal, NH-COR′, NH-SO_2R′, CO_2R′, COR′, wherein R′ represents H or C1-C6 alkyl, or straight-chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, SO_3H, SH, CO_2H, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR′, or COOR′, wherein R′ represents H or C_1-C_6 alkyl, or a combination thereof and

S_2, S_3 are independently of each other a single bond or a spacer unit, such as straight-chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-, -CH=CH-, -C≡C-, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C1-C6 alkyl, or a combination thereof.

23. A compound according to claim 22, wherein S_2 and S_3 are independently of each other straight-chain or branched C1-C8 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C1-C6 alkyl.

24. A method for preparing a compound according to claim 1 comprising the steps of (a) reacting an azido-derivatized folic acid with an ^{18}F-labelled alkyne or alkyne substitute in a 1,3-cycloaddition and (b) isolating the compound.

25. Method according to claim 24, wherein the ^{18}F-labelled alkyne or alkyne substitute is prepared in a displacement reaction by reacting an alkyne or alkyne substitute provided with a leaving group with [^{18}F]fluoride to give

the ^{18}F-labelled alkyne or alkyne substitute.

26. A method for preparing a compound according to claim 1 comprising the steps of (a) reacting a folic acid derivatized with an alkyne or alkyne substitute with an ^{18}F-labelled azide in a 1,3-cycloaddition and (b) isolating the compound.

27. Method according to claim 26, wherein the ^{18}F-labelled azide is prepared in a displacement reaction by reacting an azide provided with a leaving group with [^{18}F]fluoride to give the ^{18}F-labelled azide.

28. Method according to claims 24 to 27, wherein the cycloaddition is performed either under thermal conditions or in the presence of a catalyst.

29. Method according to claim 24, comprising the steps of (a) reacting a (C2-C12)alk-1-yne or substitute thereof, provided with a suitable leaving group, with [^{18}F]fluoride, and (b) coupling the obtained product with an azido-folic acid or derivative in a Cu(I)-catalyzed 1,3-dipolar cycloaddition.

30. Method according to claim 26, comprising the steps of (a) reacting a (C1-C12)azide, provided with a suitable leaving group, with [^{18}F]fluoride, and (b) coupling the obtained product with an folic acid derivatized with an alkynyl or substitute thereof in a Cu(I)-catalyzed 1,3-dipolar cycloaddition.

31. Compound according to claims 1 to 23 for use in diagnostic imaging of a cell or population of cells expressing a folate-receptor in vitro or in vivo.

32. Compound according to claims 1 to 23 for use in convenient and effective administration to a subject in need for diagnostic imaging.

33. Compound according to claims 1 to 23 for use in a method for diagnostic imaging of a cell or population of cells expressing a folate-receptor, said method comprising the steps of administering at least one compound according to claims 1 to 23 in a diagnostic imaging amount, and obtaining a diagnostic image of said cell or population of cells.

34. Compound according to claim 33, wherein the diagnostic imaging is performed of a cell or population of cells expressing a folate-receptor in vitro or in vivo.

35. Method for in vitro detection of a cell expressing the folate receptor in a tissue sample which includes contacting said tissue sample with a compound according to claims 1 to 23 in effective amounts and for sufficient time and conditions to allow binding to occur and detecting such binding by PET imaging.

36. Compound according to claims 1 to 23 for use in a method of diagnostic imaging or monitoring a subject comprising

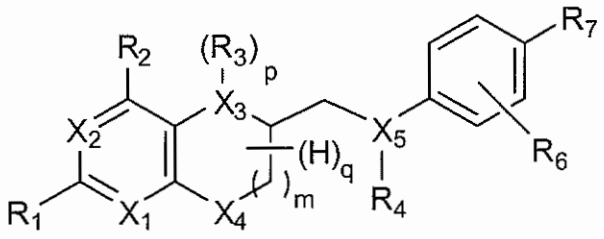
the steps of (i) administering at least one compound according to claims 1 to 23 in a diagnostic imaging amount, and (ii) performing diagnostic imaging using PET by detecting a signal from said at least one compound.

37. Compound according to claims 1 to 23 for use in a method of monitoring therapy of cancer and inflammatory and autoimmune diseases in a subject comprising the steps of (i) administering to a subject in need thereof at least one compound according to claims 1 to 23 in a diagnostic imaging amount in combination with a therapeutically active, and (ii) performing diagnostic imaging using PET by detecting a signal from said at least one compound to follow the course of therapy of cancer and inflammatory and autoimmune diseases.

38. Compound of claims 36 or 37 used in combination with any other methods of diagnosis or therapy of cancer and inflammatory and autoimmune diseases.

Claims

1. A compound having formula II



II

wherein

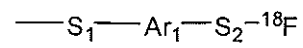
X_1 to X_5 are independently of each other C or N,

R_1 and R_2 are independently of each other H, Hal, -OR', -NHR', C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, C2-C12 alkenyl, C2-C12 alkynyl, (C1-C12 alkoxy)carbonyl, and (C1-C12 alkylamino)carbonyl, wherein R' is H or C1-C6 alkyl,

R_3, R_4 are independently of each other H, formyl, iminomethyl, nitroso, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, halosubstituted C1-C12 alkanoyl,

R_5 is H, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, and (C_1-C_{12} alkylamino)carbonyl,

R_6, R_7 are independently of each other straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a group of the formula III



III

wherein S_1 and S_2 are independently of each other a single bond or a spacer unit, such as straight-chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -N=, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-,-CH=CH-, -C≡C-, -S-, $-SO_3R'-$, -PR'- , or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof, and

Ar_1 is a triazole or a tetrazole,

with the proviso that one of R_6 and R_7 is a group of formula III,

m is 0 or 1,

p is 0, 1 or 2, and

q has a value of 1 to 7.

2. A compound according to claim 1, wherein R_6 is straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and R_7 is a group of formula III.

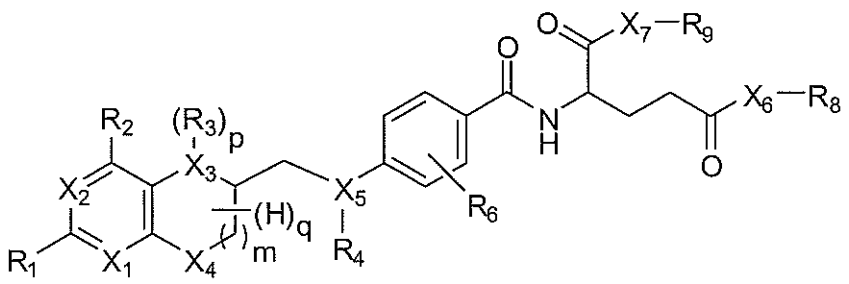
3. A compound according to claims 1 or 2, wherein R_7 is

straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and R_6 is a group of formula III.

4. A compound according to any preceding claim wherein S_1 is a single bond or a spacer unit, such as straight-chain or branched C_1-C_{18} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -NR'-, -NR'-CO-, -CO-NR'-, -CH=CH-, -C≡C-, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof.

5. A compound according to any preceding claim wherein S_2 is a single bond or a straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof, more preferably a single bond or a straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2.

6. A compound according to claim 1 having formula IV

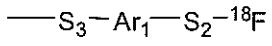


IV

wherein

X_6, X_7 are independently of each other C, N or O

R_8, R_9 are independently of each other H or straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, or a group of the formula V



V

wherein S_2, S_3 are independently of each other a single bond or a spacer unit, such as straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -N=, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-,-CH=CH-, -C≡C-, -S-, -SO_3R'-, -PR'- , or a five- or six-membered aromatic

ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof,

Ar_1 is a triazole or a tetrazole,

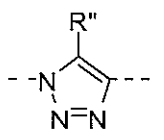
and

X_1 to X_5, R_1 to R_6, p and q, are as defined in claim 3,

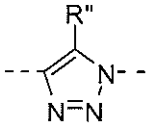
with the proviso that either R_6 is a group of formula III or at least one of R_8 and R_9 is a group of formula V.

7. A compound according to claim 6, wherein S_2 and S_3 are independently of each other a single bond or a straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof, more preferably straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2.

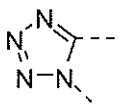
8. A compound according to any preceding claim wherein Ar_1 is selected from formulae V-c, V-d and V-e



V-c



V-d



V-e

wherein the dotted lines represent linking sites to the

spacer groups and R'' is H, Hal, NH-COR', NH-SO_2R', CO_2R', COR', wherein R' represents H or C1-C6 alkyl, or straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, SO_3H, SH, CO_2H, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof.

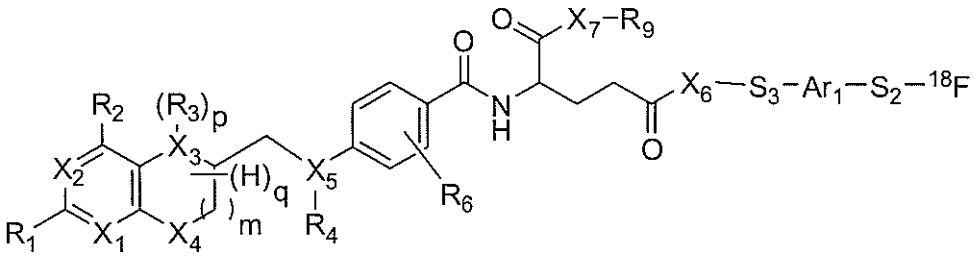
9. A compound according to claim 6, wherein R_6 is CN, Hal, NO_2, or a group R_5 and at least one of R_8 and R_9 is a group of formula V.

10. A compound according to claim 6, wherein R_6 is CN, Hal, NO_2, or a group R_5, R_8 is H or straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal or NO_2, wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, and R_9 is a group of formula V.

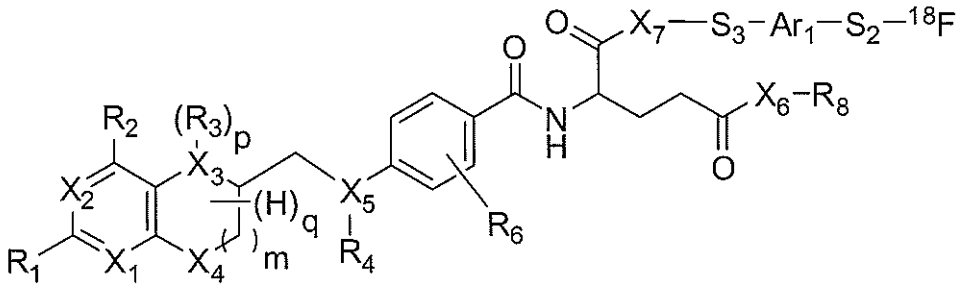
11. A compound according to claim 6, wherein R_6 is CN, Hal, NO_2, or a group R_5, R_9 is H or straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal or NO_2, wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, and R_8 is a group of formula V.

12. A compound according to claim 6, wherein R_8 and R_9 are independently of each other H or straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal or NO_2, wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-, and R_6 is a group of formula V.

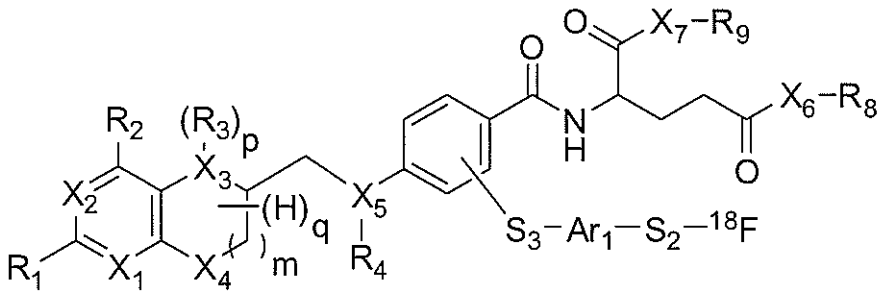
13. A compound according to claim 1 having formulae VI, VIa or VIb,



VI



VIa



VIb

wherein

X_1 to X_5 are independently of each other C or N,

X_6, X_7 are independently of each other C, N or O,

R_1 and R_2 are independently of each other H, Hal, -OR', -NHR', C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, C2-C12 alkenyl, C2-C12 alkynyl, (C1-C12 alkoxy)carbonyl, and (C1-C12 alkylamino)carbonyl, wherein R' is H or C1-C6 alkyl,

R_3, R_4 are independently of each other H, formyl, iminomethyl, nitroso, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, halosubstituted C1-C12 alkanoyl,

R_6 is H, CN, Hal, NO_2, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, or (C_1-C_{12} alkylamino)carbonyl,

R_8, R_9 are independently of each other H or straight chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO2, and wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-,,

S_2, S_3 are independently of each other a single bond or a spacer unit, such as straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -N=, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-,-CH=CH-, -C≡C-, -S-, -SO_3R'-, -PR'- , or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or

COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof,

Ar_1 is a triazole or a tetrazole,

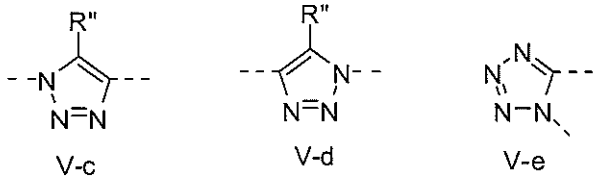
m is 0 or 1,

p is 0, 1 or 2, and

q has a value of 1 to 7.

14. A compound according to claim 13 wherein S_2 and S_3 are independently of each other a single bond or a straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl.

15. A compound according to claims 13 or 14, wherein Ar_1 is selected from formulae V-c, V-d and V-e

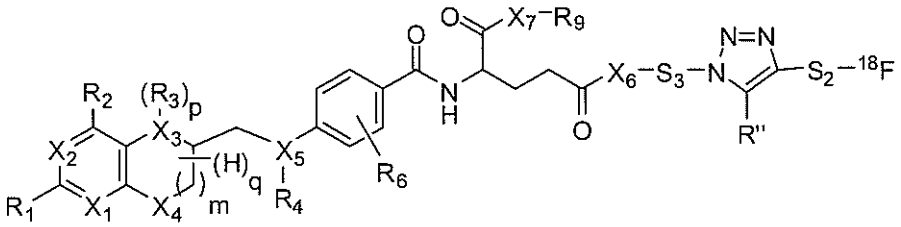


V-c V-d V-e

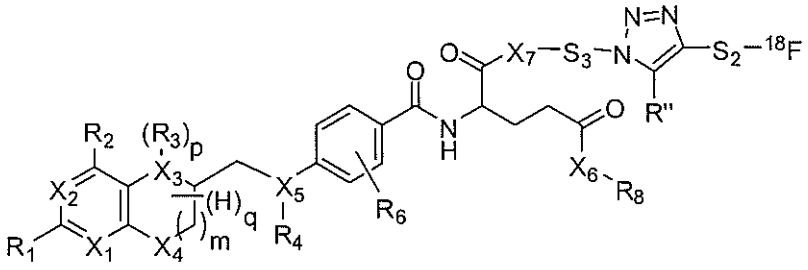
wherein the dotted lines represent linking sites to the spacer groups and R'' is H, Hal, NH-COR', NH-SO_2R', CO_2R', COR', wherein R' represents H or C1-C6 alkyl, or straight-chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, SO_3H, SH, CO_2H, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with

CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof.

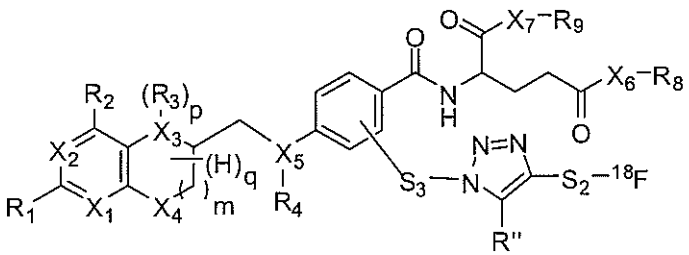
16. A compound according to any preceding claim of formulae VIIa to VIIf or VIIIa to VIIIf,



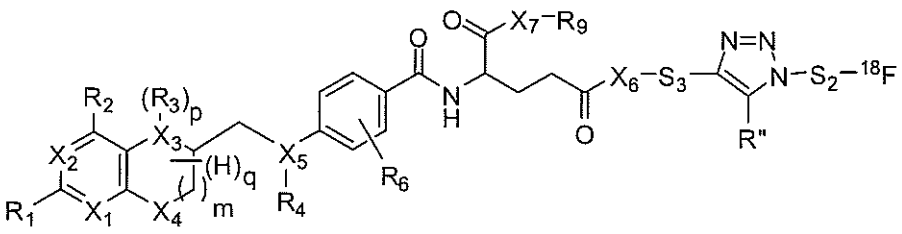
VIIa



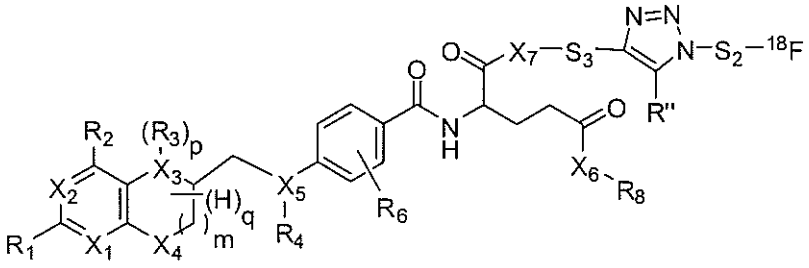
VIIb



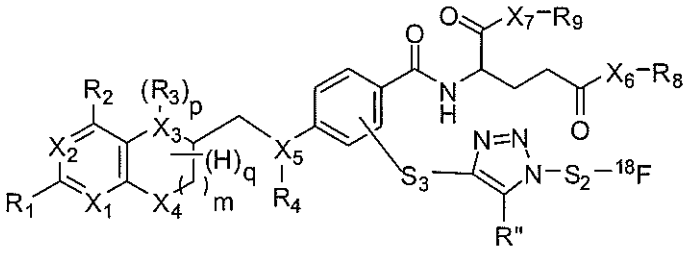
VIIc



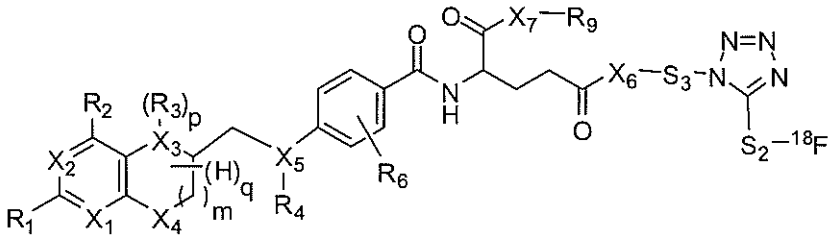
VIId



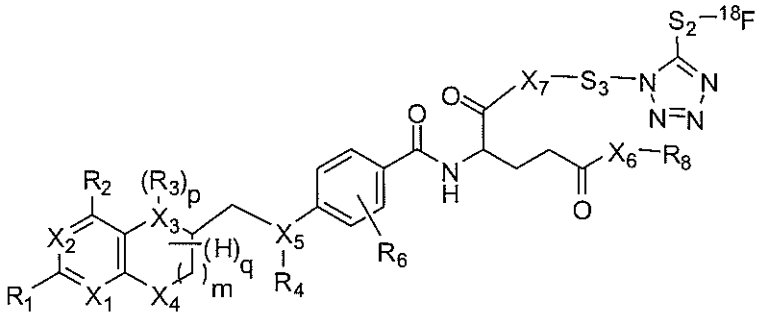
VIIe



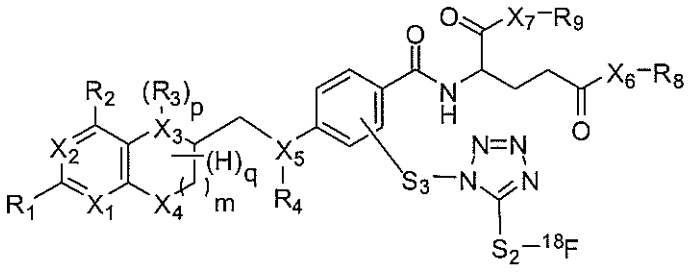
VIIf



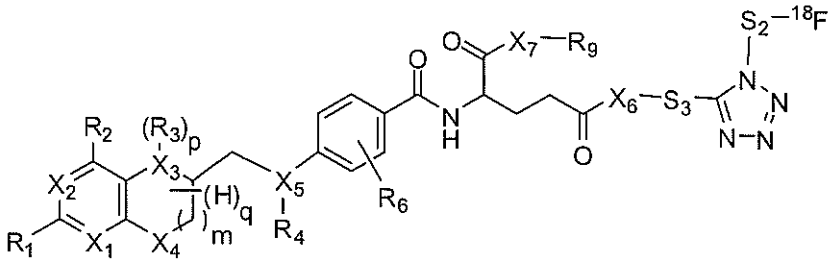
VIIIa



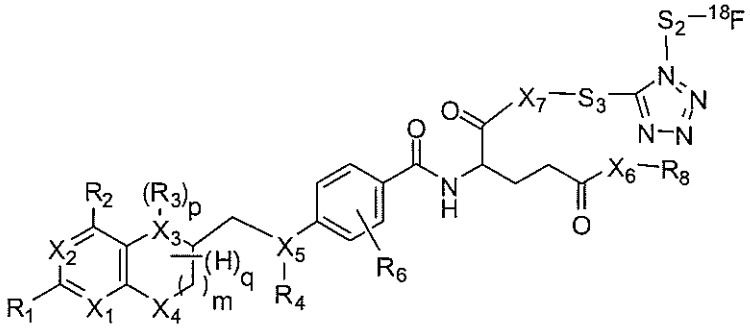
VIIIb



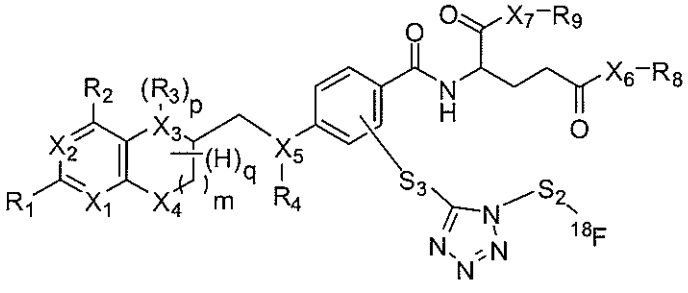
VIIIc



VIIId



VIIIe



VIIIf

wherein

X_1 to X_5 are independently of each other C or N,

X_6, X_7 are independently of each other C, N or O,

R_1, R_2 are independently of each other H, Hal, -OR', -NHR', C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, C2-C12 alkenyl, C2-C12 alkynyl, (C1-C12 alkoxy)carbonyl, and (C1-C12 alkylamino)carbonyl, wherein R' is H or C1-C6 alkyl,

R_3, R_4 are independently of each other H, formyl, iminomethyl, nitroso, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, halosubstituted C1-C12 alkanoyl,

R_6 is H, CN, Hal, NO_2, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, (C_1-C_{12} alkoxy)carbonyl, or (C_1-C_{12} alkylamino)carbonyl,

R_8, R_9 are independently of each other H or straight chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO2, and wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-,,

S_2, S_3 are independently of each other a single bond or a spacer unit, such as straight-chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -N=, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-,-CH=CH-, -C≡C-, -S-, -SO_3R'-, -PR'- , or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof,

R'' is H, Hal, NH-COR', NH-SO_2R', CO_2R', COR', or straight-chain or branched C_1-C_{12} alkyl, which is

unsubstituted or substituted by at least one CN, Hal, OH, NH_2, SO_3H, SH, CO_2H, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, and

m is 0 or 1,

p is 0, 1 or 2, and

q has a value of 1 to 7.

17. A compound according to any preceding claim, wherein R_1 and R_2 are independently of each other H, alkyl, -OR', -NHR', wherein R' represents H or C_1-C_6 alkyl.

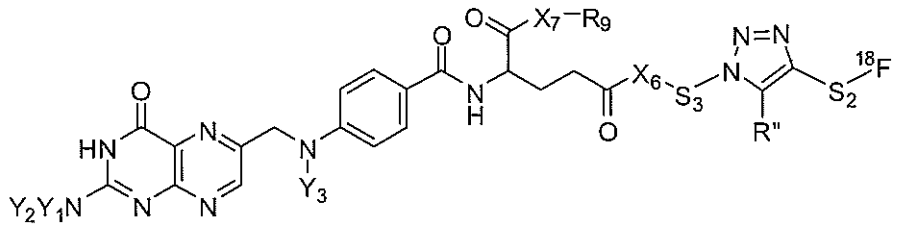
18. A compound according to any preceding claim, wherein R_3 is H, formyl, C1-C12 alkyl or C1-C12 alkanoyl.

19. A compound according to any preceding claim, wherein R_4 is H, nitroso, C1-C12 alkoxy, or C1-C12 alkanoyl.

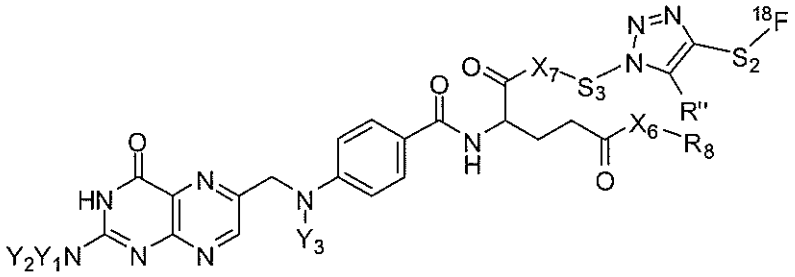
20. A compound according to any preceding claim, wherein R_5 is H, C1-C12 alkyl, C1-C12 alkoxy, C1-C12 alkanoyl, (C_1-C_{12} alkoxy)carbonyl, or (C_1-C_{12} alkylamino)carbonyl.

21. A compound according to any preceding claim, wherein R_6 is H, CN, Hal, NO_2, C_1-C_{12} alkyl, C_1-C_{12} alkoxy, C_1-C_{12} alkanoyl, or (C_1-C_{12} alkoxy)carbonyl.

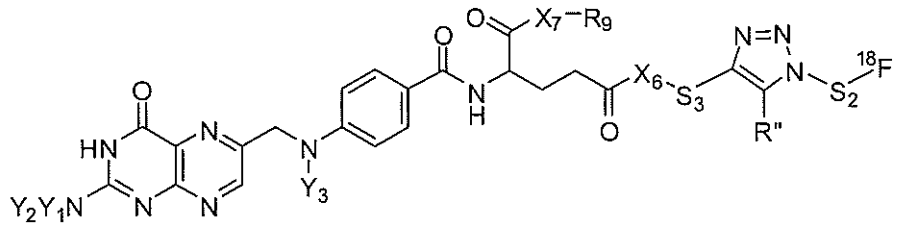
22. A compound according to any preceding claim having formulae IX, IXa, X or Xa,



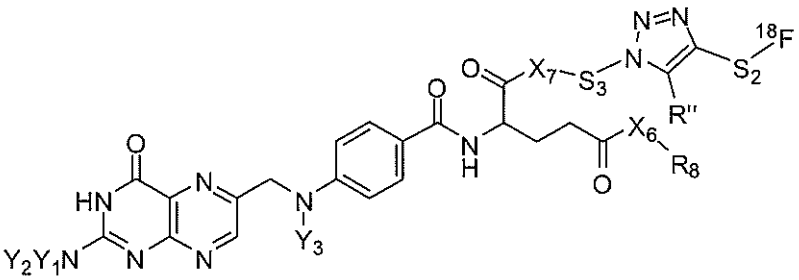
IX



IXa



X



Xa

wherein,

X_6, X_7 are independently of each other C, N or O,

Y_1, Y_2 are independently of each other selected from H, formyl, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-,

Y_3 is selected from H, formyl, nitroso, straight chain or branched C_1-C_{12} alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of embedded, non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-,

R_8, R_9 are independently of each other H or straight chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO2, and wherein one or more of embedded, non-adjacent CH2 groups may independently be replaced by -O-, -CO-, -CO-O-, -CO-NR'-, -CH=CH-, -C≡C-,,

R'' is H, Hal, NH-COR', NH-SO_2R', CO_2R', COR', wherein R' represents H or C1-C6 alkyl, or straight-chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, OH, NH_2, SO_3H, SH, CO_2H, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C_1-C_6 alkyl, or a combination thereof and

S_2, S_3 are independently of each other a single bond or a spacer unit, such as straight-chain or branched C1-C12 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, and wherein one or more of the non-adjacent CH_2 groups may independently be replaced by -O-, -CO-, -CO-O-, -O-CO-, -NR'-, -NR'-CO-, -CO-NR'-, -NR'-CO-O-, -O-CO-NR'-, -NR'-CO-NR'-, -CH=CH-, -C≡C-, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C1-C6 alkyl, or a combination thereof.

23. A compound according to claim 22, wherein S_2 and S_3 are independently of each other straight-chain or branched C1-C8 alkyl, which is unsubstituted or substituted by at least one CN, Hal, or NO_2, or a five- or six-membered aromatic ring, which is unsubstituted or substituted with CN, Hal, NO_2, COR', or COOR', wherein R' represents H or C1-C6 alkyl.

24. A method for preparing a compound according to claim 1 comprising the steps of (a) reacting an azido-derivatized folic acid with an ^{18}F-labelled alkyne or alkyne substitute in a 1,3-cycloaddition and (b) isolating the compound.

25. Method according to claim 24, wherein the ^{18}F-labelled alkyne or alkyne substitute is prepared in a displacement reaction by reacting an alkyne or alkyne substitute provided with a leaving group with [^{18}F]fluoride to give

the ^{18}F-labelled alkyne or alkyne substitute.

26. A method for preparing a compound according to claim 1 comprising the steps of (a) reacting a folic acid derivatized with an alkyne or alkyne substitute with an ^{18}F-labelled azide in a 1,3-cycloaddition and (b) isolating the compound.

27. Method according to claim 26, wherein the ^{18}F-labelled azide is prepared in a displacement reaction by reacting an azide provided with a leaving group with [^{18}F]fluoride to give the ^{18}F-labelled azide.

28. Method according to claims 24 to 27, wherein the cycloaddition is performed either under thermal conditions or in the presence of a catalyst.

29. Method according to claim 24, comprising the steps of (a) reacting a (C2-C12)alk-1-yne or substitute thereof, provided with a suitable leaving group, with [^{18}F]fluoride, and (b) coupling the obtained product with an azido-folic acid or derivative in a Cu(I)-catalyzed 1,3-dipolar cycloaddition.

30. Method according to claim 26, comprising the steps of (a) reacting a (C1-C12)azide, provided with a suitable leaving group, with [^{18}F]fluoride, and (b) coupling the obtained product with an folic acid derivatized with an alkynyl or substitute thereof in a Cu(I)-catalyzed 1,3-dipolar cycloaddition.

31. Compound according to claims 1 to 23 for use in diagnostic imaging of a cell or population of cells expressing a folate-receptor in vitro or in vivo.

32. Compound according to claims 1 to 23 for use in convenient and effective administration to a subject in need for diagnostic imaging.

33. Method for in vitro detection of a cell expressing the folate receptor in a tissue sample which includes contacting said tissue sample with a compound according to claims 1 to 23 in effective amounts and for sufficient time and conditions to allow binding to occur and detecting such binding by PET imaging.