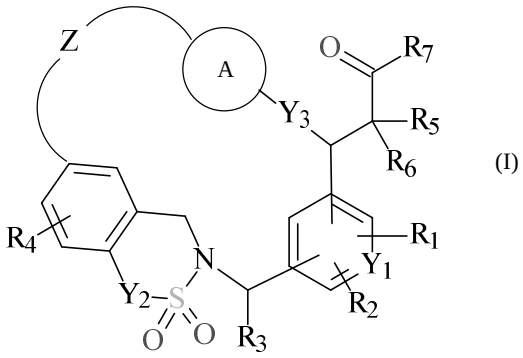
CLAIMS

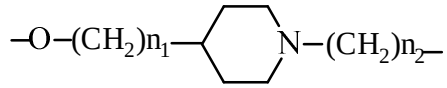
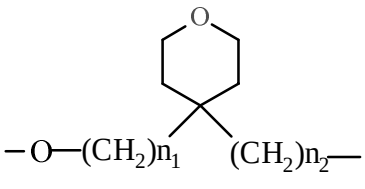
1. A compound of formula (I) :



(I)

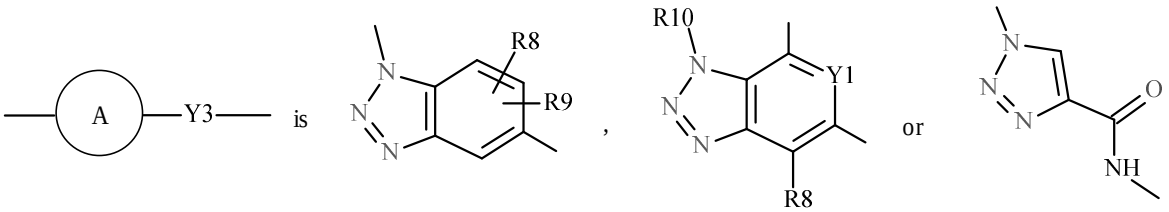
wherein

Z is -O-$(CH_2)n_1$-, -O-$(CH_2)n_1$-O-$(CH_2)n_2$, -O-$(CH_2)n_1$-S-$(CH_2)n_2$, O-$(CH_2)n_1$-S(O)-$(CH_2)n_2$, O-$(CH_2)n_1$-$S(O_2)$-$(CH_2)n_2$, -O-$(CH_2)n_1$-NR-$(CH_2)n_2$, -O-$(CH_2)n_1$-CHR'-$(CH_2)n_2$, -NR-$(CH_2)n_1$-, -NR-(CO)-$(CH_2)n_1$-, -O-$(CH_2)n_1$-Ar-$(CH_2)n_2$, -O-$(CH_2)n_1$-Ar-O-$(CH_2)n_2$, -O-$(CH_2)n_1$-Ar-S-$(CH_2)n_2$, -O-$(CH_2)n_1$-Ar-S(O)-$(CH_2)n_2$, -O-$(CH_2)n_1$-Ar-$S(O_2)$-$(CH_2)n_2$, -O-$(CH_2)n_1$-Ar-CHR'-$(CH_2)n_2$, -O-$(CH_2)n_1$-Ar-CH=CH-, O-Ar-NR-$(CH_2)n_1$, -$(CH_2)n_1$-NR-(CO)-$(CH_2)n_2$-

or Z is  or 

Y_1 is C or N,

Y_2 is O or NR',



Ar is an optionally substituted aryl or heteroaryl group,

R is a hydrogen atom, a linear or branched C_1-C_3 alkyl group or an optionally substituted aryl group,

R' is a hydrogen atom or a group selected from hydroxyl, optionally substituted aryl and linear or branched C_1-C_3 alkyl optionally substituted by alkoxy or by one to three halogen atoms,

n_1, n_2 is an integer from 1 to 6,

R_1, R_2, R_4, R_8, R_9, R_{10}, identical or different, are each a hydrogen atom or a group selected from halo, cyano, linear or branched C_1-C_3 alkyl optionally substituted by one to three halogen atoms, linear or branched C_1-C_3 alkoxy or optionally substituted aryl,

R_3 is hydrogen or a linear or branched C_1-C_3 alkyl group optionally substituted by one to three halogen atoms,

or R_2 and R_3 together form a ring with the atoms bearing them,

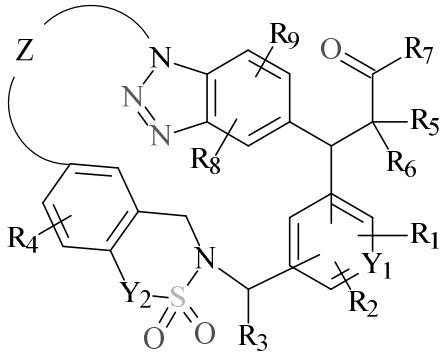
R_5, R_6, identical or different, are each a hydrogen, deuterium or halogen atom or a linear or branched C_1-C_3 alkyl group,

R_7 is a group selected from hydroxyl and NHR'$_7$,

wherein R'$_7$ is a linear or branched C_1-C_6 alkyl group or an optionally substituted aryl or heteroaryl group,

its optical isomers, and addition salts thereof with a pharmaceutically acceptable base.

2. A compound according to claim 1 of formula (IA) :

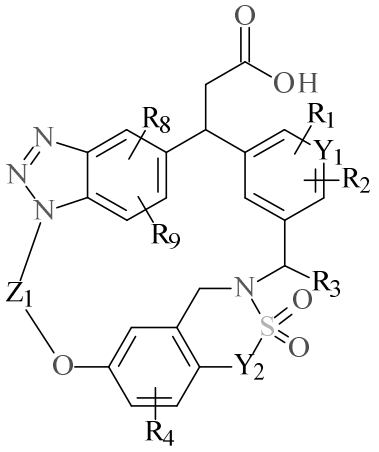


(IA)

wherein Z, Y_1, Y_2, R_1 to R_9 are as defined in claim 1,

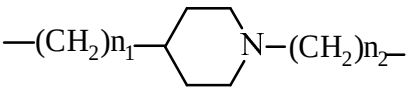
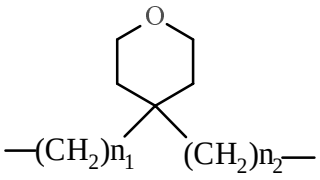
its optical isomers, and addition salts thereof with a pharmaceutically acceptable base.

3. A compound according to claim 2 of formula (IA_1) :



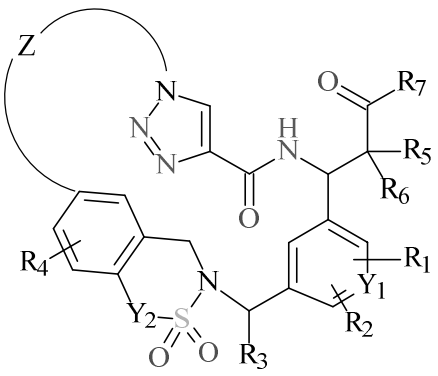
(IA_1)

wherein R_1-R_4, R_8-R_9, Y_1, Y_2 are as defined in claim 1, and Z_1 is a group selected from -$(CH_2)n_1$, -$CH_2)n_1$-O-$(CH_2)n_2$, -$CH_2)n_1$-S-$(CH_2)n_2$, -$CH_2)n_1$-NR-$(CH_2)n_2$, -$CH_2)n_1$-CHR'-$(CH_2)n_2$, -$(CH_2)n_1$-Ar_1-$(CH_2)n_2$, -$CH_2)n_1$-Ar_1-O-$(CH_2)n_2$, -$(CH_2)n_1$-Ar_1-S-$(CH_2)n_2$, -$(CH_2)n_1$-Ar_1-CHR'-$(CH_2)n_2$, -Ar_1-NR-$(CH_2)n_1$,

or Z_1 is  or 

its optical isomers, and addition salts thereof with a pharmaceutically acceptable base.

4. A compound according to claim 1 of formula (IB) :

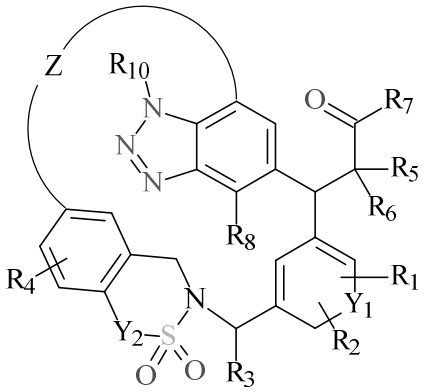


(IB)

wherein Z, Y_1, Y_2, R_1 to R_7 are as defined in claim 1,

its optical isomers, and addition salts thereof with a pharmaceutically acceptable base.

5. A compound according to claim 1 of formula (IC) :



(IC)

wherein Z, Y_1, Y_2, R_1 to R_8 and R_{10} are as defined in claim 1,

its optical isomers, and addition salts thereof with a pharmaceutically acceptable base.

6. A compound of formula (I) according to any one of claims 1, 2, 4 or 5, wherein Z is -O-$(CH_2)n_1$-, -O-$(CH_2)n_1$-O-$(CH_2)n_2$ or -O-$(CH_2)n_1$-S-$(CH_2)n_2$.

7. A compound of formula (I) according to any one of claims 1 to 6, wherein Y_1 is C.

8. A compound of formula (I) according to any one of claims 1 to 7, wherein Y_2 is O or NCH_3.

9. A compound of formula (I) according to claim 1, which is selected from :

[4,32-dimethyl-28,28-dioxo-22,27-dioxa-28λ^6-thia-1,14,15,16-tetraazahexacyclo [21.5.3.$1^{3,7}$.$1^{9,13}$.$0^{12,16}$.$0^{26,30}$]tritriaconta-3(33),4,6,9(32),10,12,14,23,25,30-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[2,4,31-trimethyl-27,27-dioxo-21,26-dioxa-27λ^6-thia-1,14,15,16-tetraazahexacyclo [20.5.3.$1^{3,7}$.$1^{9,13}$.$0^{12,16}$.$0^{25,29}$]dotriaconta-3(32),4,6,9(31),10,12,14,22,24,29-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[4,31-dimethyl-27,27-dioxo-21,26-dioxa-27λ^6-thia-1,14,15,16-tetraazahexacyclo [20.5.3.$1^{3,7}$.$1^{9,13}$.$0^{12,16}$.$0^{25,29}$]dotriaconta-3(32),4,6,9(31),10,12,14,22,24,29-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[4-chloro-31-methyl-27,27-dioxo-21,26-dioxa-27λ^6-thia-1,14,15,16-tetraazahexacyclo [20.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{25,29}]dotriaconta-3(32),4,6,9(31),10,12,14,22,24,29-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[4-methoxy-31-methyl-27,27-dioxo-21,26-dioxa-27λ^6-thia-1,14,15,16-tetraazahexacyclo [20.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{25,29}]dotriaconta-3(32),4,6,9(31),10,12,14,22,24,29-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[4,33-dimethyl-29,29-dioxo-23,28-dioxa-29λ^6-thia-1,14,15,16-tetraazahexacyclo [22.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{27,31}]tetratriaconta-3(34),4,6,9(33),10,12,14,24,26,31-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[2,4,32-trimethyl-28,28-dioxo-19,22,27-trioxa-28λ^6-thia-1,14,15,16-tetraazahexacyclo [21.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{26,30}]tritriaconta-3(33),4,6,9(32),10,12,14,23,25,30-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[2,4,33-trimethyl-29,29-dioxo-23,28-dioxa-29λ^6-thia-1,14,15,16-tetraazahexacyclo[22.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{27,31}]tetratriaconta-3(34),4,6,9(33),10,12,14,24,26,31-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[23-chloro-4,31-dimethyl-27,27-dioxo-21,26-dioxa-27λ^6-thia-1,14,15,16-tetraazahexacyclo [20.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{25,29}]dotriaconta-3(32),4,6,9(31),10,12,14,22,24,29-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[23-methoxy-4,31-dimethyl-27,27-dioxo-21,26-dioxa-27λ^6-thia-1,14,15,16-tetraazahexacyclo[20.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{25,29}]dotriaconta-3(32),4,6,9(31),10,12,14,22,24,29-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[23-fluoro-4,31-dimethyl-27,27-dioxo-21,26-dioxa-27λ^6-thia-1,14,15,16-tetraazahexacyclo [20.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{25,29}]dotriaconta-3(32),4,6,9(31),10,12,14,22,24,29-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

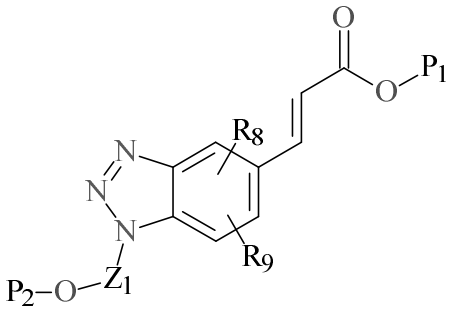
[4,26,31-trimethyl-27,27-dioxo-21-oxa-27λ^6-thia-1,14,15,16,26-pentaazahexacyclo [20.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{25,29}]dotriaconta-3(32),4,6,9(31),10,12,14,22,24,29-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[4,32-dimethyl-28,28-dioxo-22,27-dioxa-19,28λ^6-dithia-1,14,15,16-tetraazahexacyclo [21.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{26,30}]tritriaconta-3(33),4,6,9(32),10,12,14,23,25,30-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[30-chloro-4,31-dimethyl-27,27-dioxo-21,26-dioxa-27λ^6-thia-1,14,15,16-tetraazahexacyclo [20.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{25,29}]dotriaconta-3(32),4,6,9(31),10,12,14,22,24,29-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base,

[4,32-dimethyl-28,28-dioxo-19,22,27-trioxa-28λ^6-thia-1,14,15,16-tetraazahexacyclo [21.5.3.1^{3,7}.1^{9,13}.0^{12,16}.0^{26,30}]tritriaconta-3(33),4,6,9(32),10,12,14,23,25,30-decaen-8-yl]acetic acid, its optical isomers, and addition salts thereof with a pharmaceutically acceptable base.

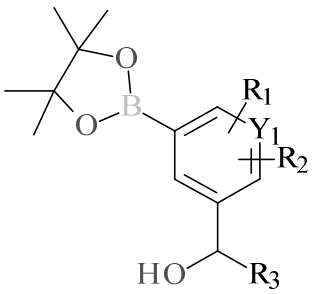
10. A process for the preparation of a compound of formula (IA$_1$) according to claim 3, starting from a compound of formula (II) :



(II)

wherein P_1 is a protecting group of the acid function, and P_2 is a protecting group of the alcohol function,

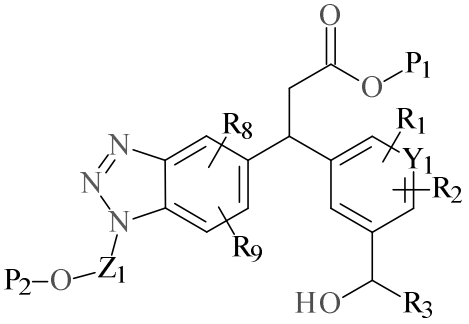
which is reacted with a compound of formula (III) :



(III)

wherein R_1-R_3 and Y_1 are as defined in claim 1,

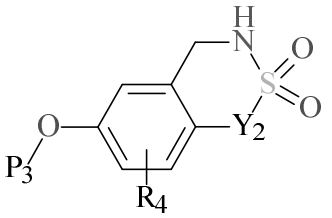
to give a compound of formula (IV) :



(IV)

wherein R_1-R_3, R_8-R_9, Y_1, Z_1 and P_1-P_2 are as defined before,

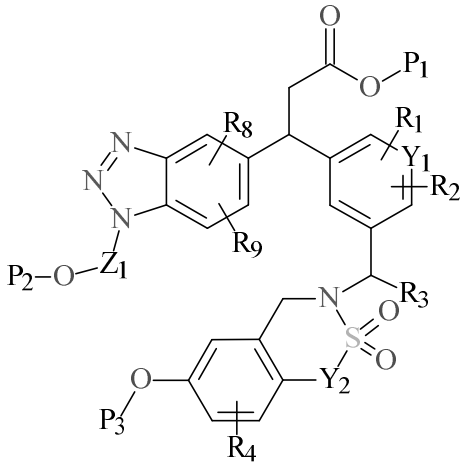
which is reacted with a compound of formula (V) :



(V)

wherein R_4 and Y_2 are as defined in claim 1, and P_3 is a protecting group of the alcohol function,

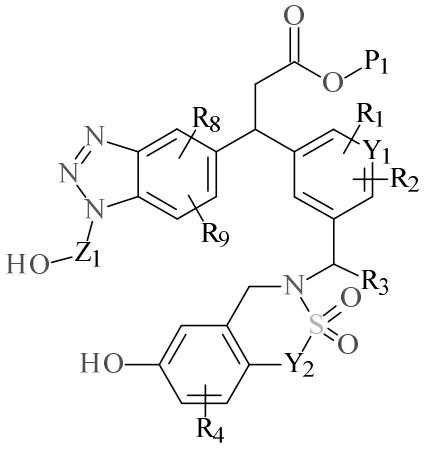
to give a compound of formula (VI) :



(VI)

wherein R_1-R_4, R_8-R_9, Y_1, Y_2, Z_1 and P_1-P_3 are as defined before,

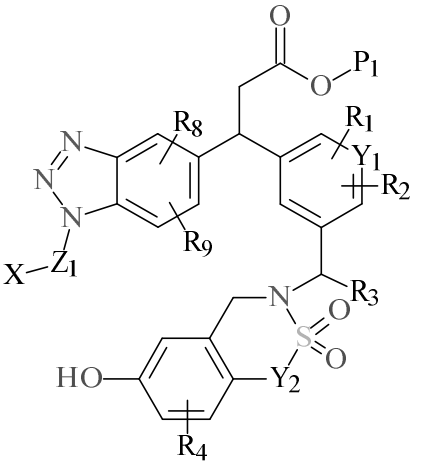
which is deprotected to give a compound of formula (VII) :



(VII)

wherein R_1-R_4, R_8-R_9, Y_1, Y_2, Z_1 and P_1 are as defined before,

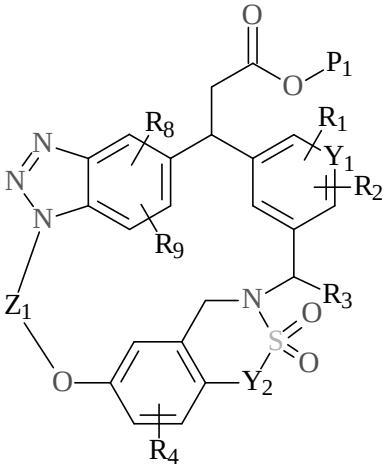
which is halogenated to give a compound of formula (VIII) :



(VIII)

wherein R_1-R_4, R_8-R_9, Y_1, Y_2, Z_1 and P_1 are as defined before, and X is a halogen atom,

which is reacted with a base to give a compound of formula (IX) :



(IX)

which is deprotected by reaction of a base to give a compound of formula (IA_1), the stereoisomers thereof are separated, if desired, using chiral separation techniques.

11. A pharmaceutical composition comprising a compound of formula (I) according to any one of claims 1 to 9, in combination with one or more inert, non-toxic, pharmaceutically acceptable excipients or carriers.

12. A pharmaceutical composition according to claim 11, characterised in that it further comprises one or more further active ingredients.

13. A compound according to any one of claims 1 to 9 for use as an Nrf2 activator.

14. A compound according to any one of claims 1 to 9 for use in the treatment of diseases that are linked to increased oxidative stress and inflammation, impaired redox potential, impaired detoxification or deregulated metabolism.

15. A compound according to any one of claims 1 to 9 for use in the treatment of type II diabetes, non alcoholic steatohepatitis, Autosomal dominant polycystic kidney disease, Acute Kidney Injury, Alport Syndrome or Alström syndrome.