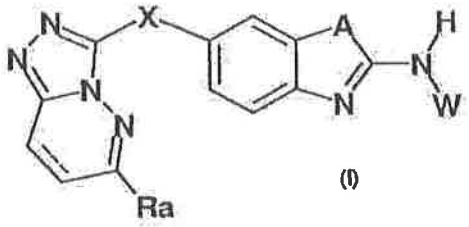
CLAIMS

1 – Products of formula (I):



(I)

in which

---- represents a single or double bond;

Ra represents a hydrogen atom; a halogen atom; an alkoxy radical optionally substituted with a chlorine atom, a hydroxyl radical or a heterocycloalkyl radical, itself optionally substituted; an O-cycloalkyl radical; an optionally substituted heteroaryl radical; an optionally substituted phenyl radical; an NHCOalk or NHCOcycloalk radical; or an NR1R2 radical as defined hereinafter;

X represents S, SO or SO_2;

A represents NH or S;

W represents a hydrogen atom; an alkyl radical optionally substituted with alkoxy, heterocycloalkyl or NR3R4; or the COR radical in which R represents:

- a cycloalkyl radical or an alkyl radical optionally substituted with an NR3R4, alkoxy, hydroxyl, phenyl, heteroaryl or heterocycloalkyl radical, themselves optionally substituted;
- an alkoxy radical optionally substituted with NR3R4, alkoxy, hydroxyl or with heterocycloalkyl; an O-phenyl radical or an O-$(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 4;

- or the NR1R2 radical in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents a hydrogen atom, a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, heteroaryl, heterocycloalkyl, NR3R4 and optionally substituted phenyl radicals, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with R3 and R4, which may be identical or different, representing a hydrogen atom or an alkyl radical, a cycloalkyl radical, a heteroaryl radical or a phenyl radical that is optionally substituted, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

all the heterocycloalkyl, heteroaryl and phenyl radicals defined above and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, oxo, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, cycloalkyl, heterocycloalkyl, CH_2-heterocycloalkyl, phenyl, CH_2-phenyl, heteroaryl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, oxo, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$,

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral

and organic acids or with mineral and organic bases of said products of formula (I).

2 – Products of formula (I) as defined in claim 1, in which ---- , X and A have the meanings indicated in claim 1,

Ra represents an alkoxy radical optionally substituted with a chlorine atom, a hydroxyl radical or a heterocycloalkyl radical, itself optionally substituted; an O-cycloalkyl radical; an NHCOalk radical; or an NR1aR2a radical; such that R1a and R2a represent a hydrogen atom, a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, heteroaryl, heterocycloalkyl, NR3R4 and optionally substituted phenyl radicals;

and W represents a hydrogen atom; an alkyl radical optionally substituted with alkoxy, heterocycloalkyl or NR3R4; or the COR radical in which R represents:

- a cycloalkyl radical or an alkyl radical optionally substituted with an NR3R4, alkoxy, hydroxyl, phenyl, heteroaryl or heterocycloalkyl radical, themselves optionally substituted;
- an alkoxy radical optionally substituted with NR3R4, alkoxy, hydroxyl or with heterocycloalkyl; an O-phenyl radical or an O-$(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 4;
- or the NR1R2 radical in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents a hydrogen atom, a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, heteroaryl, heterocycloalkyl, NR3R4 and optionally substituted phenyl radicals, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and

optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with R3 and R4, which may be identical or different, representing a hydrogen atom or an alkyl radical, a cycloalkyl radical, a heteroaryl radical or a phenyl radical that is optionally substituted, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

all the heterocycloalkyl, heteroaryl and phenyl radicals defined above and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, oxo, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, cycloalkyl, heterocycloalkyl, CH_2-heterocycloalkyl, phenyl, CH_2-phenyl, heteroaryl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, oxo, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$,

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

3 – Products of formula (I) as defined in any one of the preceding claims, in which ---- , Ra and X have the values defined in any one of the preceding claims and:

A represents NH or S;

W represents a hydrogen atom; an alkyl radical optionally substituted with

alkoxy or heterocycloalkyl; or the COR radical in which R represents:

- a cycloalkyl radical or an alkyl radical optionally substituted with an NR3R4, alkoxy, hydroxyl, phenyl, heteroaryl or heterocycloalkyl radical, themselves optionally substituted;

- an alkoxy radical optionally substituted with NR3R4, alkoxy, hydroxyl or with heterocycloalkyl; an O-phenyl radical or an O-$(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 4;

- or the NR1R2 radical, in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents a hydrogen atom, a cycloalkyl radical or an alkyl radical optionally substituted with NR3R4 or with alkoxy, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with NR3R4 such that R3 and R4, which may be identical or different, represent a hydrogen atom or an alkyl radical, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

the heterocycloalkyl, heteroaryl and phenyl radicals and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, defined above, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, heterocycloalkyl, CH_2-heterocycloalkyl, phenyl, CH_2-phenyl, heteroaryl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from

halogen atoms and the radicals: hydroxyl, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$;

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

4 – Products of formula (I) as defined in any one of the preceding claims, in which:

---- represents a single or double bond;

Ra represents a hydrogen atom or a halogen atom or an optionally substituted phenyl radical;

X represents S, SO or SO_2;

A represents NH or S;

W represents a hydrogen atom or the COR radical in which R represents:

- a cycloalkyl radical or an alkyl radical optionally substituted with a phenyl, heteroaryl, NR3R4 or heterocycloalkyl radical, themselves optionally substituted;
- an alkoxy radical optionally substituted with NR3R4, i.e. an $O-(CH_2)_n-NR3R4$ radical, an O-phenyl radical or an $O-(CH_2)_n$-phenyl radical, with phenyl optionally substituted and n representing an integer from 1 to 4;
- or the NR1R2 radical in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, heteroaryl, heterocycloalkyl, NR3R4 and optionally substituted phenyl radicals, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical

optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with R3 and R4, which may be identical or different, representing a hydrogen atom or an alkyl radical, a cycloalkyl radical, a heteroaryl radical or an optionally substituted phenyl radical, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

all the heterocycloalkyl, heteroaryl and phenyl radicals defined above and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, oxo, alkoxy, NH_2, NHalk, $N(alk)_2$ radicals and alkyl, cycloalkyl, CH_2-heterocycloalkyl, CH_2-phenyl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, oxo, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$;

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

5 – Products of formula (I) as defined in any one of the preceding claims, in which  , Ra and X have the values defined in any one of the preceding claims and:

A represents NH or S;

W represents a hydrogen atom or an alkyl radical or the COR radical in which R represents:

-an alkyl radical optionally substituted with OCH_3 or NR3R4;

-a cycloalkyl radical;

-an alkoxy radical optionally substituted with OCH_3 or NR3R4, i.e. an $O-(CH_2)_n-OCH_3$ radical or an $O-(CH_2)_n-NR3R4$ radical, an O-phenyl radical or an $O-(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 2;

- or the NR1R2 radical, in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom, a cycloalkyl radical or an alkyl radical and the other of R1 and R2 represents an alkyl radical optionally substituted with NR3R4, or else R1 and R2 form with the nitrogen atom to which they are attached, a cyclic (*morpholinyl*) radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with NR3R4 such that R3 and R4, which may be identical or different, represent a hydrogen atom or an alkyl radical, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

the phenyl radicals and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, defined above, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, CH_2-heterocycloalkyl, CH_2-phenyl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$;

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral

and organic acids or with mineral and organic bases of said products of formula (I).

6 – Products of formula (I) as defined in any one of the preceding claims, in which ---- , Ra and X have the values defined in any one of the preceding claims and:

A represents NH or S;

W represents a hydrogen atom or the COR radical in which R represents:

- an alkyl radical optionally substuituted with NR3R4;

- an alkoxy radical optionally substituted with NR3R4, i.e. an O-$(CH_2)_n$-NR3R4 radical, an O-phenyl radical or an O-$(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 2;

- or the NR1R2 radical, in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents an alkyl radical optionally substituted with NR3R4, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

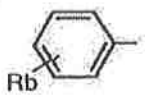
with NR3R4 such that R3 and R4, which may be identical or different, represent a hydrogen atom or an alkyl radical, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

the phenyl radicals and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, defined above, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, CH_2-heterocycloalkyl, CH_2-phenyl, CO-phenyl and S-heteroaryl radicals, such that,

in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$;

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

7 – Products of formula (I) as defined in any one of the preceding claims, in which ---- , X, A and W have the meanings indicated in any one of the preceding claims, Ra represents a hydrogen atom or a chlorine atom or the radical:



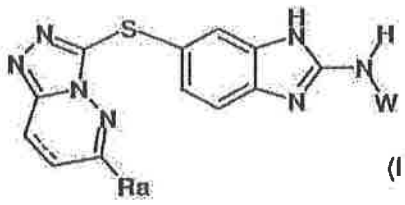
with Rb representing a halogen atom or an S-heteroaryl radical optionally substituted with a radical chosen from halogen atoms and the radicals: hydroxyl, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$,

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

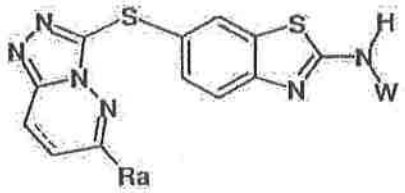
8 – Products of formula (I) as defined in any one of the preceding claims, in which A represents NH, and in which ---- , Ra, X and W have the meanings indicated in any one of the preceding claims, said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

9 – Products of formula (I) as defined in any one of the preceding claims, in which A represents S, and in which ---- , Ra, X and W have the meanings indicated in any one of the preceding claims, said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

10 – Products of formula (I) as defined in any one of the preceding claims, corresponding to formula (Ia) or (Ib):



(Ia)



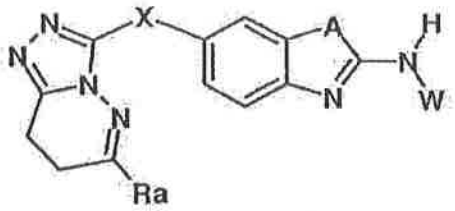
(Ib)

In which ---- , Ra and W are chosen from the meanings indicated in any one of the other claims,

said products of formula (Ia) and (Ib) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (Ia) and (Ib).

11–Products of formula (I) as defined in any one of the preceding claims, in which ---- represents a single bond, corresponding to the products of

formula (I'):

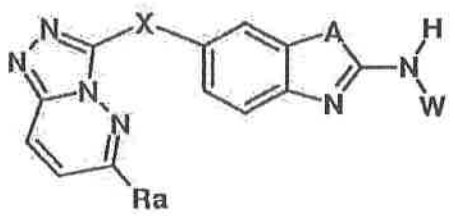


(I')

the substituents Ra, X, A and W having the meanings indicated in any one of the preceding claims,

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

12 – Products of formula (I) as defined in any one of the preceding claims, in which ---- represents a double bond, corresponding to the products of formula (I''):



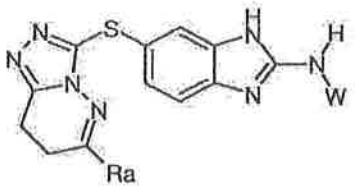
(I'')

in which the substituents Ra, X, A and W have the meanings indicated in any one of the preceding claims,

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of

formula (I).

13 – Products of formula (Ia) as defined in any one of the preceding claims, in which ---- represents a single bond, corresponding to the products of formula (I'a):

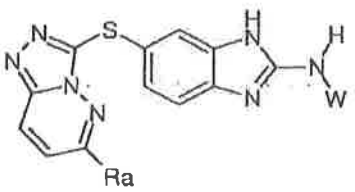


(I'a)

in which Ra and W are chosen from the meanings indicated in any one of the preceding claims,

said products of formula (I'a) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I'a).

14 – Products of formula (Ia) as defined in any one of the preceding claims, in which ---- represents a double bond, corresponding to the products of formula (I"a):

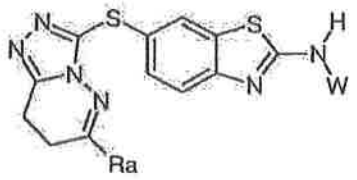


(I"a)

in which Ra and W are chosen from the meanings indicated in any one of the preceding claims,

said products of formula (I"a) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I"a).

15 – Products of formula (Ib) as defined in any one of the preceding claims, in which ---- represents a single bond, corresponding to the products of formula (I'b):

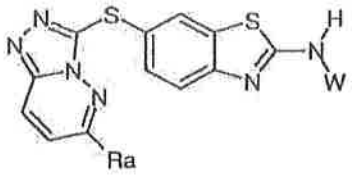


(I'b)

in which Ra and W are chosen from the meanings indicated in any one of the preceding claims,

said products of formula (I'b) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I'b).

16 – Products of formula (Ib) as defined in any one of the preceding claims, in which ---- represents a double bond, corresponding to the products of formula (I"b):



(I"b)

in which Ra and W are chosen from the meanings indicated in any one of the preceding claims,

said products of formula (I"b) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I"b).

17 – Products of formula (I) as defined in any one of the preceding claims, corresponding to the following formulae:

- methyl (6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)carbamate

- 6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-amine

- methyl (6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1H-benzimidazol-2-yl)carbamate

- 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1H-benzimidazol-2-yl)-3-(2-morpholin-4-ylethyl)urea

- 6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1H-benzimidazol-2-amine

- 1-(2-morpholin-4-ylethyl)-3-[6-([1,2,4]triazolo[4,3-b]pyridazin-3-ylsulphanyl)-1,3-benzothiazol-2-yl]urea

- 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea

- 1-{2-[(2R,6S)-2,6-dimethylmorpholin-4-yl]ethyl}-3-(6-{[6-(4-fluorophenyl)-[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)urea

- (6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)carbamate of 2-morpholin-4-ylethyl

- 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-[2-(4-methylpiperazin-1-yl)ethyl]urea

- N-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-4-morpholin-4-ylbutanamide

- 1-[2-(diethylamino)ethyl]-3-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)urea

- 1-{6-[(6-methoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}-3-[2-(morpholin-4-yl)ethyl]urea

- N-[6-({6-[(2-methoxyethyl)amino][1,2,4]triazolo[4,3-b]pyridazin-3-yl}sulphanyl)-1,3-benzothiazol-2-yl]acetamide

- 6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-N-[2-(morpholin-4-yl)ethyl]-1,3-benzothiazol-2-amine

- phenyl 6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)carbamate

- 1-{6-[(6-ethoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}-3-[2-(morpholin-4-yl)ethyl]urea

- 1-{6-[(6-ethoxy-7,8-dihydro[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}-3-[2-(morpholin-4-yl)ethyl]urea

- N-[6-({6-[(2-methoxyethyl)amino][1,2,4]triazolo[4,3-b]pyridazin-3-yl}sulphanyl)-1,3-benzothiazol-2-yl]cyclopropanecarboxamide

- 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-[2-(4-oxidomorpholin-4-yl)ethyl]urea

- 6-{[6-(1-methyl-1H-pyrazol-4-yl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-amine

- 1-(6-{[6-(4-fluorophenyl)-7,8-dihydro[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-[2-(morpholin-4-yl)ethyl]urea

- oxetan-2-ylmethyl (6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)carbamate

- N-{6-[(6-methoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}cyclopropanecarboxamide

- N-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)acetamide

- 1-{6-[(6-methoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}-3-[2-(pyrrolidin-1-yl)ethyl]urea

- 6-[(6-ethoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-amine

- 6-{[6-(3-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-amine

- 1-cyclopropyl-3-{6-[(6-ethoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}urea

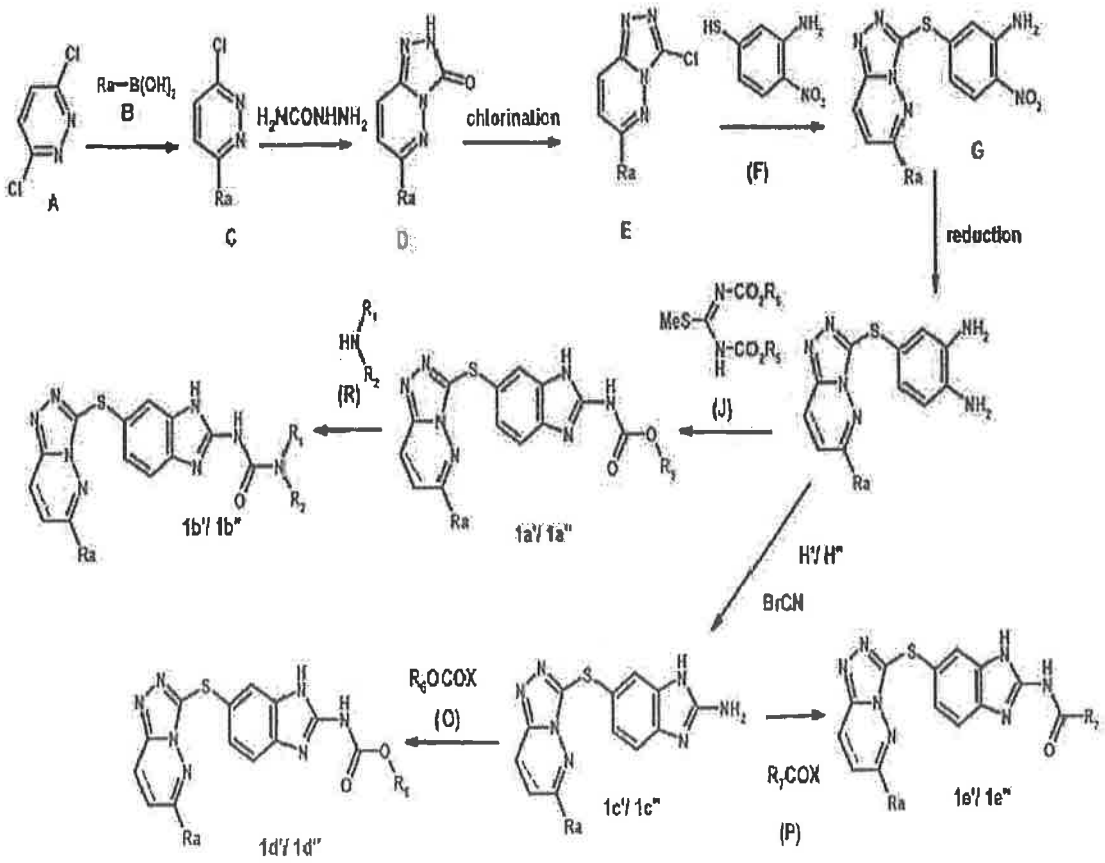
- N-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)cyclopropanecarboxamide

- N-(6-{[6-(4-fluorophenyl)-7,8-dihydro[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)cyclopropanecarboxamide

- 1-(6-{[6-(3-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-[2-(morpholin-4-yl)ethyl]urea

and also the addition salts with pharmaceutically acceptable mineral and organic acids or with pharmaceutically acceptable mineral and organic bases of said products of formula (I).

18 – Process for preparing the products of formula (I) as defined in claim 1 in which A represents NH, characterized by the following scheme:



in which:

the substituents Ra, R1 and R2 have the meanings indicated in claim 1, the substituent R5 represents an alkyl radical and the substituent R6 represents an alkyl radical optionally substituted with NR3R4 (a $-(CH_2)_n$ -NR3R4 radical),

alkoxy, hydroxyl, heterocycloalkyl, phenyl or $-(CH_2)_n$-phenyl, with phenyl being optionally substituted, the substituent R7 represents a cycloalkyl or alkyl radical optionally substituted with an NR3R4, alkoxy, hydroxyl, phenyl, heteroaryl or heterocycloalkyl radical, each of which is optionally substituted with R3 and R4 having the meanings indicating in claim 1 and n represents an integer from 1 to 4;

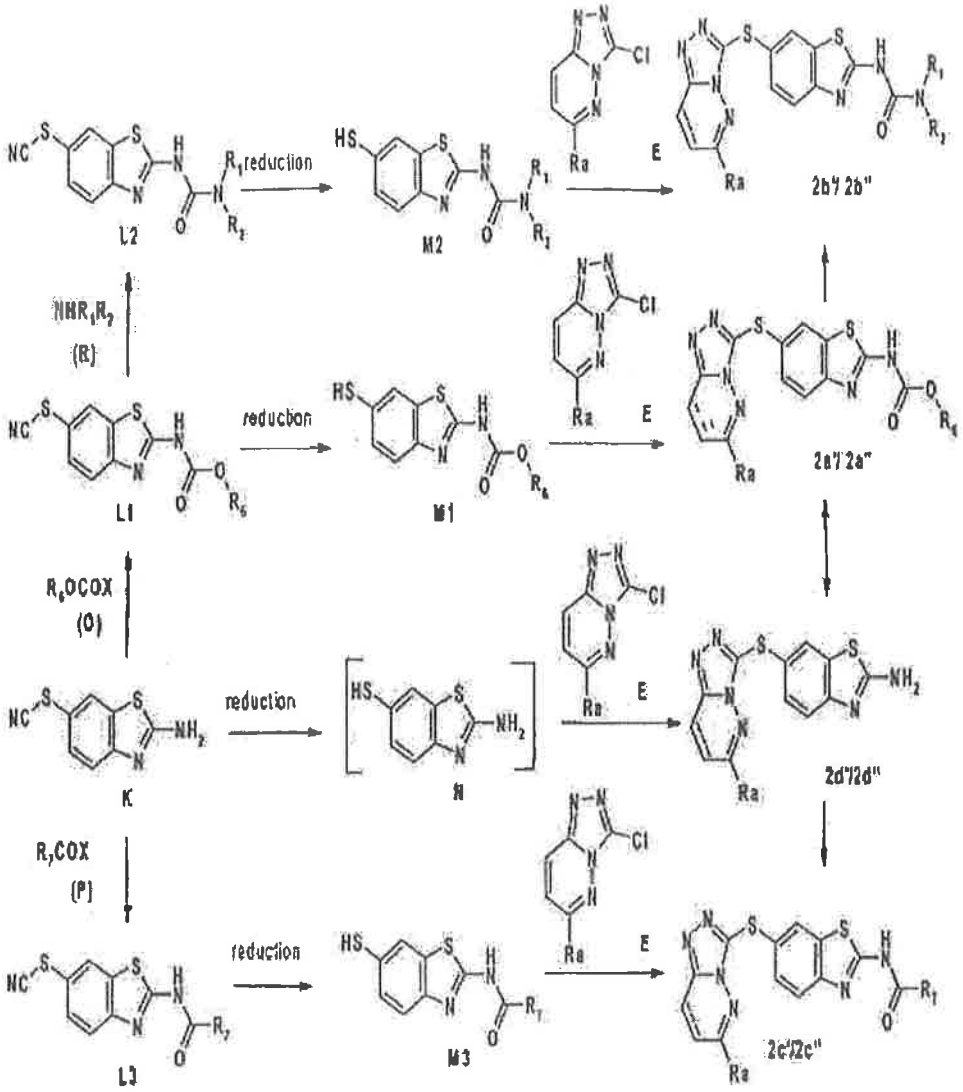
in the compounds of formulae H', Ia', Ib', Ic', Id' and Ie', ⁻⁻⁻⁻ represents a single bond and in the compounds of formulae H", Ia", Ib", Ic", Id" and Ie", ⁼⁼⁼⁼ represents a double bond;

the compound (E) is obtained by reaction of phosphoric trichloride (phosphorus oxychloride) with the compound of formula (D),

the compound (H") such that ⁼⁼⁼⁼ represents a double bond is obtained by reduction with iron (0) of the compound of formula (G) in a solvent in the presence of acetic acid at a temperature in the region of 70°C; and the compound (H') such that ⁻⁻⁻⁻ represents a single bond is obtained by reduction with zinc (0) of the compound of formula (G) in the presence of acetic acid at a temperature in the region of 20°C;

said products of formula (I) thus obtained being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms.

19 – Process for preparing the products of formula (I) as defined inclaim 1 in which A represents S, characterized by the following scheme:



in which the substituents Ra, R1 and R2 have the meanings indicated in claim 1, the substituent R6 represents an alkyl radical optionally substituted with an NR3R4 (a $-(CH_2)_n$-NR3R4 radical), alkoxy, hydroxyl, heterocycloalkyl, phenyl or $-(CH_2)_n$-phenyl group, with phenyl being optionally substituted, the substituent R7 represents a cylcoalkyl or alkyl radical optionally substituted with an NR3R4, alkoxy or hydroxyl radical or a phenyl, heteroaryl or heterocycloalkyl radical, each of which is optionally substituted, in which R3 and R4 have the meanings indicated in claim 1 and n represents an integer from 1 to 4;

in the compounds of formulae 2a', 2b', 2c' and 2d', ---- represents a single bond and in the compounds of formulae 2a", 2b", 2c" and 2d", ---- represents a double bond,

compounds of formulae (M1), (M2) and (M3) are obtained by reduction of compounds (L1), (L2), (L3), with DL-dithiothreitol in the presence of sodium dihydrogen carbonate in a solvent and at a temperature in the region of 80°C,

the compound of formula (N) is obtained by reduction of the compound (K) with sodium borohydride in a solvent such as N, N-dimethylformamide, in the presence of a base, and at a temperature in the region of 95°C or between 20°C and 95°C;

said products of formula (I) thus obtained being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms.

20 –Medicament comprising the products of formula (I) as defined in any one of Claims 1 to **17**, and also the addition salts with pharmaceutically acceptable mineral and organic acids or with pharmaceutically acceptable mineral and organic bases of said products of formula (I).

21–medicament comprising the products of formula (I) as defined in Claim **17**, and also the addition salts with pharmaceutically acceptable mineral and organic acids or with pharmaceutically acceptable mineral and organic bases of said products of formula (I).

22– Pharmaceutical compositions containing, as active ingredient, at least one of the products of formula (I) as defined in any one of Claims 1 to **17**, or a pharmaceutically acceptable salt of this product, and a pharmaceutically acceptable carrier.

23 – Use of the products of formula (I) as defined in any one of Claims 1 to **17**, or of pharmaceutically acceptable salts of these products, for the preparation of a medicament for use in inhibiting the activity of the MET protein kinase and mutant forms thereof.

24 – Use as defined in Claim **23**, in which the protein kinase is in a cell culture.

25– Use as defined in Claim **23** or **24**, in which the protein kinase is in a mammal.

26 – Use of a product of formula (I) as defined in any one of Claims 1 to **17**, for the preparation of a medicament for use in the treatment or prevention of a disease chosen from the following group: blood vessel proliferation disorders, fibrotic disorders, 'mesangial' cell proliferation disorders, metabolic disorders, allergies, asthma, thrombosis, nervous system diseases, retinopathy, psoriasis, rheumatoid arthritis, diabetes, muscle degeneration and cancers.

27 – Use of a product of formula (I) as defined in any one of Claims 1 to **17**, for the preparation of a medicament for use in the treatment of cancers.

28 – Use according to Claim **27**, wherein the medicament is for use in the treatment of solid or liquid tumours.

29 – Use according to Claim **27** or **28**, wherein the medicament is for use in the treatment of cancers resistant to cytotoxic agents.

30 – Use according to one or more of Claims **27** to **29**, wherein the medicament is for use in the treatment of primary tumours and/or metastases, in particular in gastric, hepatic, renal, ovarian, colon, prostate and lung (NSCLC and SCLC) cancers, glioblastomas, thyroid, bladder or breast cancers, in melanomas, in lympyhoic or myeloid hematopoietic tumours, in sarcomas, in brain, larynx or lymphatic system cancers, bone cancers and pancreatic cancers.

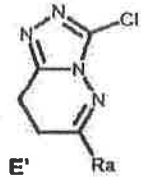
31 – Use of the products of formula (I) as defined in Claims 1 to **17**, for the preparation of medicaments for use in cancer chemotherapy.

32 – Use of the products of formula (I) as defined in Claims 1 to **17**, for the preparation of medicaments for use in cancer chemotherapy alone or in combination.

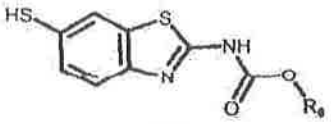
33 – Products of formula (I) as defined in any one of Claims 1 to **17**, as kinase inhibitors.

34 – Products of formula (I) as defined in any one of Claims 1 to **17**, as MET inhibitors.

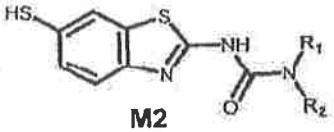
35 –The synthesis intermediates of formulae E', M1, M2 and M3.



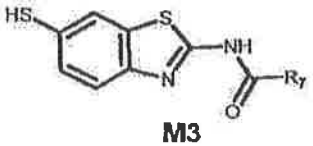
E'



M1



M2



M3

in which R6 represents an alkyl radical optionally substituted with an NR3R4 (a $-(CH_2)_n$-NR3R4 radical), alkoxy, hydroxyl, heterocycloalkyl, phenyl or $-(CH_2)_n$-phenyl group, with phenyl optionally substituted and n representing an integer from 1 to 4, such that OR6 represents the corresponding values of R as defined above; R7 represents a cycloalkyl or alkyl radical optionally substituted with an NR3R4, alkoxy or hydroxyl radical or a phenyl, heteroaryl or heterocycloalkyl radical, themselves optionally substituted as indicated in Claim 1; and Ra, R1, R2, R3 and R4 have the meanings indicated in Claim 1.

36 – A method of inhibiting the activity of the MET protein kinase and mutant forms thereof, the method comprising administering to a subject a therapeutically effective amount of a product of formula (I) as defined in any one of Claims 1 to 17, or a pharmaceutically acceptable salt thereof.

37 – The method of Claim 36, in which the subject is a mammal.

38 – A method for the treatment or prevention of a disease chosen from the following group: blood vessel proliferation disorders, fibrotic disorders, 'mesangial' cell proliferation disorders, metabolic disorders, allergies, asthma, thrombosis, nervous system diseases, retinopathy, psoriasis, rheumatoid

arthritis, diabetes, muscle degeneration and cancers; the method comprising administering to a subject, a therapeutically effective amount of a product of formula (I) as defined in any one of Claims 1 to **17**, or pharmaceutically acceptable salt thereof.

39 – A method for the treatment of cancers, the method comprising administering to a subject, a therapeutically effective amount of a product of formula (I) as defined in any one of Claims 1 to **17**, or pharmaceutically acceptable salt thereof.

40 – A method according to Claim 39, wherein the cancers comprise solid or liquid tumours.

41 – A method according to Claim 39 or 40, wherein the cancers are resistant to cytotoxic agents.

42 – A method for the treatment of primary tumours and/or metastases, the method comprising administering to a subject, a therapeutically effective amount of a product of formula (I) as defined in any one of Claims 1 to **17**, or pharmaceutically acceptable salt thereof.

43 – A method according to Claim 42 wherein the primary tumors and/or metastasese are in gastric, hepatic, renal, ovarian, colon, prostate and lung (NSCLC and SCLC) cancers, glioblastomas, thyroid, bladder or breast cancers, in melanomas, in lympyhoic or myeloid hematopoietic tumours, in sarcomas, in brain, larynx or lymphatic system cancers, bone cancers and pancreatic cancers.

44 – A method of cancer chemotherapy comprising administering to a subject in need thereof a therapeutically effective amount of a product of formulas (I) as defined in Claims 1 to 17, or a pharmaceutically acceptable salt thereof.

45 – A method according to claim 44, wherein the product of formula (I) or pharmaceutically acceptable salt thereof, is administered alone or in combination with other cancer chemotherapy.

46 – A product according to claim 1, substantially as herein described with reference to any example thereof.

47 – A process according to claim 19, substantially as herein described with reference to any example thereof.

48 – A medicament according to claim 20 or 21, substantially as herein described with reference to any example thereof.

49 – A pharmaceutical composition according to claim 22, substantially as herein described with reference to any example thereof.

50 – A use according to any one of claims 23, 26, 27, 31, 32, substantially as herein described with reference to any example thereof.

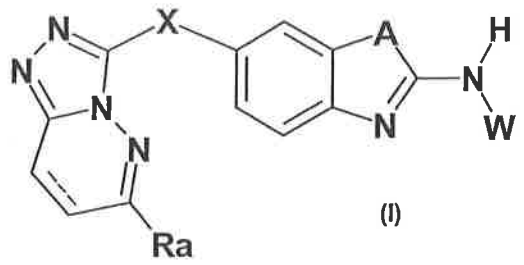
51 – A synthesis intermediate according to claim 35, substantially as herein

described with reference to any example thereof.

52 – A method according to any one of claims 36, 38, 39, 42 or 44, substantially as herein described with reference to any example thereof.

CLAIMS

1 – Products of formula (I):



(I)

in which

---- represents a single or double bond;

Ra represents a hydrogen atom; a halogen atom; an alkoxy radical optionally substituted with a chlorine atom, a hydroxyl radical or a heterocycloalkyl radical, itself optionally substituted; an O-cycloalkyl radical; an optionally substituted heteroaryl radical; an optionally substituted phenyl radical; an NHCOalk or NHCOcycloalk radical; or an NR1R2 radical as defined hereinafter;

X represents S, SO or SO_2;

A represents NH or S;

W represents a hydrogen atom; an alkyl radical optionally substituted with alkoxy, heterocycloalkyl or NR3R4; or the COR radical in which R represents:

- a cycloalkyl radical or an alkyl radical optionally substituted with an NR3R4, alkoxy, hydroxyl, phenyl, heteroaryl or heterocycloalkyl radical, themselves optionally substituted;
- an alkoxy radical optionally substituted with NR3R4, alkoxy, hydroxyl or with heterocycloalkyl; an O-phenyl radical or an O-$(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 4;

- or the NR1R2 radical in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents a hydrogen atom, a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, heteroaryl, heterocycloalkyl, NR3R4 and optionally substituted phenyl radicals, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with R3 and R4, which may be identical or different, representing a hydrogen atom or an alkyl radical, a cycloalkyl radical, a heteroaryl radical or a phenyl radical that is optionally substituted, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

all the heterocycloalkyl, heteroaryl and phenyl radicals defined above and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, oxo, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, cycloalkyl, heterocycloalkyl, CH_2-heterocycloalkyl, phenyl, CH_2-phenyl, heteroaryl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, oxo, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$,

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral

and organic acids or with mineral and organic bases of said products of formula (I).

2 – Products of formula (I) as defined in any one of the other claims, in which ---- , X and A have the meanings indicated in any one of the other claims,

Ra represents an alkoxy radical optionally substituted with a chlorine atom, a hydroxyl radical or a heterocycloalkyl radical, itself optionally substituted; an O-cycloalkyl radical; an NHCOalk radical; or an NR1aR2a radical; such that R1a and R2a represent a hydrogen atom, a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, heteroaryl, heterocycloalkyl, NR3R4 and optionally substituted phenyl radicals;

and W represents a hydrogen atom; an alkyl radical optionally substituted with alkoxy, heterocycloalkyl or NR3R4; or the COR radical in which R represents:

- a cycloalkyl radical or an alkyl radical optionally substituted with an NR3R4, alkoxy, hydroxyl, phenyl, heteroaryl or heterocycloalkyl radical, themselves optionally substituted;
- an alkoxy radical optionally substituted with NR3R4, alkoxy, hydroxyl or with heterocycloalkyl; an O-phenyl radical or an O-$(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 4;
- or the NR1R2 radical in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents a hydrogen atom, a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, heteroaryl, heterocycloalkyl, NR3R4 and optionally substituted phenyl radicals, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and

optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with R3 and R4, which may be identical or different, representing a hydrogen atom or an alkyl radical, a cycloalkyl radical, a heteroaryl radical or a phenyl radical that is optionally substituted, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

all the heterocycloalkyl, heteroaryl and phenyl radicals defined above and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, oxo, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, cycloalkyl, heterocycloalkyl, CH_2-heterocycloalkyl, phenyl, CH_2-phenyl, heteroaryl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, oxo, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$,

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

3 – Products of formula (I) as defined in any one of the other claims, in which ---- , Ra and X have the values defined in any one of the other claims and:

A represents NH or S;

W represents a hydrogen atom; an alkyl radical optionally substituted with alkoxy or heterocycloalkyl; or the COR radical in which R represents:

- a cycloalkyl radical or an alkyl radical optionally substituted with an NR3R4, alkoxy, hydroxyl, phenyl, heteroaryl or heterocycloalkyl radical, themselves optionally substituted;

- an alkoxy radical optionally substituted with NR3R4, alkoxy, hydroxyl or with heterocycloalkyl; an O-phenyl radical or an O-$(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 4;

- or the NR1R2 radical, in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents a hydrogen atom, a cycloalkyl radical or an alkyl radical optionally substituted with NR3R4 or with alkoxy, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with NR3R4 such that R3 and R4, which may be identical or different, represent a hydrogen atom or an alkyl radical, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 members and optionally one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

the heterocycloalkyl, heteroaryl and phenyl radicals and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, defined above, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, heterocycloalkyl, CH_2-heterocycloalkyl, phenyl, CH_2-phenyl, heteroaryl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$;

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

4 – Products of formula (I) as defined in any one of the other claims, in which:

---- represents a single or double bond;

Ra represents a hydrogen atom or else a halogen atom or else an optionally substituted phenyl radical;

X represents S, SO or SO_2;

A represents NH or S;

W represents a hydrogen atom or the COR radical in which R represents:

- a cycloalkyl radical or an alkyl radical optionally substituted with a phenyl, heteroaryl, NR3R4 or heterocycloalkyl radical, themselves optionally substituted;
- an alkoxy radical optionally substituted with NR3R4, i.e. an O-$(CH_2)_n$-NR3R4 radical, an O-phenyl radical or an O-$(CH_2)_n$-phenyl radical, with phenyl optionally substituted and n representing an integer from 1 to 4;
- or the NR1R2 radical in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, heteroaryl, heterocycloalkyl, NR3R4 and optionally substituted phenyl radicals, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with R3 and R4, which may be identical or different, representing a hydrogen atom or an alkyl radical, a cycloalkyl radical, a heteroaryl radical or an optionally substituted phenyl radical, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

all the heterocycloalkyl, heteroaryl and phenyl radicals defined above and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, oxo, alkoxy, NH_2, NHalk, $N(alk)_2$ radicals and alkyl, cycloalkyl, CH_2-heterocycloalkyl, CH_2-phenyl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, oxo, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$;

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

5 – Products of formula (I) as defined in any one of the other claims, in which ---- , Ra and X have the values defined in any one of the other claims and:

A represents NH or S;

W represents a hydrogen atom or an alkyl radical or the COR radical in which R represents:

-an alkyl radical optionally substituted with OCH_3 or NR3R4;

-a cycloalkyl radical;

-an alkoxy radical optionally substituted with OCH_3 or NR3R4, i.e. an

$O\text{-}(CH_2)_n\text{-}OCH_3$ radical or an $O\text{-}(CH_2)_n\text{-}NR3R4$ radical, an O-phenyl radical or an $O\text{-}(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 2;

- or the NR1R2 radical, in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom, a cycloalkyl radical or an alkyl radical and the other of R1 and R2 represents an alkyl radical optionally substituted with NR3R4, or else R1 and R2 form with the nitrogen atom to which they are attached, a cyclic (*morpholinyl*) radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with NR3R4 such that R3 and R4, which may be identical or different, represent a hydrogen atom or an alkyl radical, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

the phenyl radicals and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, defined above, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, CH_2-heterocycloalkyl, CH_2-phenyl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$;

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

6 – Products of formula (I) as defined in any one of the other claims, in which

---- , Ra and X have the values defined in any one of the other claims and:

A represents NH or S;

W represents a hydrogen atom or the COR radical in which R represents:

- an alkyl radical optionally substuituted with NR3R4;

- an alkoxy radical optionally substituted with NR3R4, i.e. an O-$(CH_2)_n$-NR3R4 radical, an O-phenyl radical or an O-$(CH_2)_n$-phenyl radical, with phenyl being optionally substituted and n representing an integer from 1 to 2;

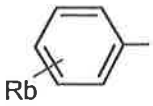
- or the NR1R2 radical, in which R1 and R2 are such that one of R1 and R2 represents a hydrogen atom or an alkyl radical and the other of R1 and R2 represents an alkyl radical optionally substituted with NR3R4, or else R1 and R2 form, with the nitrogen atom to which they are attached, a cyclic radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

with NR3R4 such that R3 and R4, which may be identical or different, represent a hydrogen atom or an alkyl radical, or else R3 and R4 form, with the nitrogen atom to which they are attached, a cyclic radical optionally containing one or more other heteroatoms chosen from O, S, N and NH, this radical, including the possible NH that it contains, being optionally substituted;

the phenyl radicals and also the cyclic radicals that R1 and R2 or R3 and R4 can form with the nitrogen atom to which they are attached, defined above, being optionally substituted with one or more radicals chosen from halogen atoms, hydroxyl, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals and alkyl, CH_2-heterocycloalkyl, CH_2-phenyl, CO-phenyl and S-heteroaryl radicals, such that, in the latter radicals, the alkyl, heterocycloalkyl, phenyl and heteroaryl radicals are themselves optionally substituted with one or more radicals chosen from halogen atoms and the radicals: hydroxyl, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$;

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

7 – Products of formula (I) as defined in any one of the other claims, in which ---- , X, A and W have the meanings indicated in any one of the other claims, Ra represents a hydrogen atom or else a chlorine atom or else the radical:



with Rb representing a halogen atom or an S-heteroaryl radical optionally substituted with a radical chosen from halogen atoms and the radicals: hydroxyl, alkyl and alkoxy containing from 1 to 4 carbon atoms, NH_2, NHalk and $N(alk)_2$,

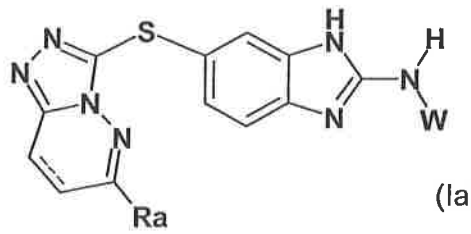
said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

8 – Products of formula (I) as defined in any one of the other claims, in which A represents NH, the substituents ---- , Ra, X and W being chosen from all the values defined for these radicals in any one of the other claims, said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

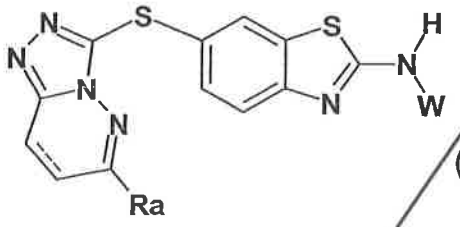
9 – Products of formula (I) as defined in any one of the other claims, in which A represents S, the substituents ---- , Ra, X and W being chosen from all the values defined for these radicals in any one of the other claims, said

products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

10 – Products of formula (I) as defined in any one of the other claims, corresponding to formula (Ia) or (Ib):



(Ia)

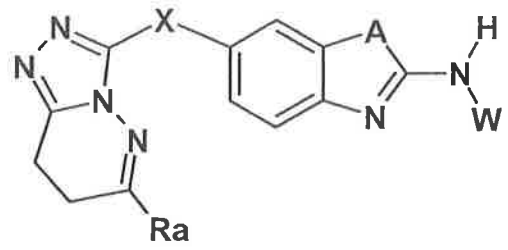


(Ib)

in which ---- , Ra and W are chosen from the meanings indicated in any one of the other claims,

said products of formula (Ia) and (Ib) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (Ia) and (Ib).

11-Products of formula (I) as defined in any one of the other claims, in which ---- represents a single bond, corresponding to the products of formula (I'):

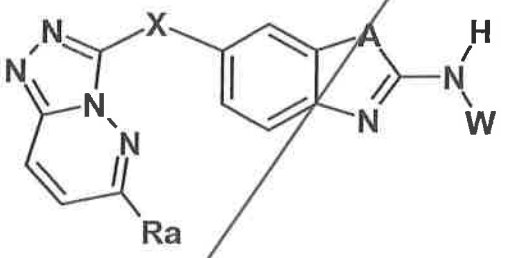


(I')

the substituents Ra, X, A and W having the meanings indicated in any one of the other claims,

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

12 – Products of formula (I) as defined in any one of the other claims, in which ---- represents a double bond, corresponding to the products of formula (I''):

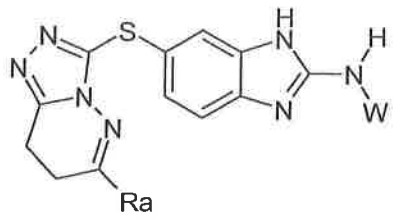


(I'')

in which the substituents Ra, X, A and W have the meanings indicated in any one of the other claims,

said products of formula (I) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I).

13 – Products of formula (Ia) as defined in any one of the other claims, in which ---- represents a single bond, corresponding to the products of formula (I'a):

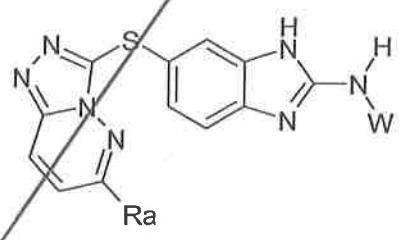


(I'a)

in which Ra and W are chosen from the meanings indicated in any one of the other claims,

said products of formula (I'a) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I'a).

14 – Products of formula (Ia) as defined in any one of the other claims, in which ---- represents a double bond, corresponding to the products of formula (I''a):

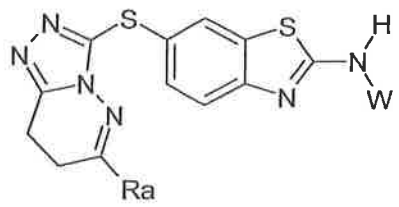


(I''a)

in which Ra and W are chosen from the meanings indicated in any one of the other claims,

said products of formula (I"a) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I"a).

15 – Products of formula (Ib) as defined in any one of the other claims, in which ---- represents a single bond, corresponding to the products of formula (I'b):

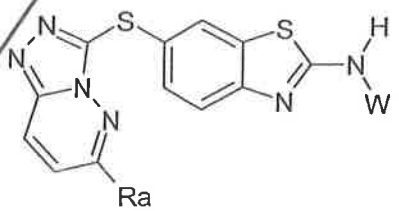


(I'b)

in which Ra and W are chosen from the meanings indicated in any one of the other claims,

said products of formula (I'b) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I'b).

16 – Products of formula (Ib) as defined in any one of the other claims, in which ---- represents a double bond, corresponding to the products of formula (I"b):



(I"b)

in which Ra and W are chosen from the meanings indicated in any one of the other claims,

said products of formula (I"b) being in any of the possible racemic, enantiomeric and diastereoisomeric isomer forms, and also the addition salts with mineral and organic acids or with mineral and organic bases of said products of formula (I"b).

17 – Produits of formula (I) as defined in any one of the other claims, corresponding to the following formulae:

- methyl (6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)carbamate

- 6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-amine

- methyl (6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1H-benzimidazol-2-yl)carbamate

- 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1H-benzimidazol-2-yl)-3-(2-morpholin-4-ylethyl)urea

- 6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1H-benzimidazol-2-amine

- 1-(2-morpholin-4-ylethyl)-3-[6-([1,2,4]triazolo[4,3-b]pyridazin-3-ylsulphanyl)-1,3-benzothiazol-2-yl]urea

- 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-(2-morpholin-4-ylethyl)urea

- 1-{2-[(2R,6S)-2,6-dimethylmorpholin-4-yl]ethyl}-3-(6-{[6-(4-fluorophenyl)-[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)urea

- (6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)carbamate of 2-morpholin-4-ylethyl

- 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-[2-(4-methylpiperazin-1-yl)ethyl]urea

- N-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-4-morpholin-4-ylbutanamide

- 1-[2-(diethylamino)ethyl]-3-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)urea

- 1-{6-[(6-methoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}-3-[2-(morpholin-4-yl)ethyl]urea

- N-[6-({6-[(2-methoxyethyl)amino][1,2,4]triazolo[4,3-b]pyridazin-3-yl}sulphanyl)-1,3-benzothiazol-2-yl]acetamide

- 6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-N-[2-(morpholin-4-yl)ethyl]-1,3-benzothiazol-2-amine

- phenyl 6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)carbamate

- 1-{6-[(6-ethoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}-3-[2-(morpholin-4-yl)ethyl]urea

- 1-{6-[(6-ethoxy-7,8-dihydro[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}-3-[2-(morpholin-4-yl)ethyl]urea

- N-[6-({6-[(2-methoxyethyl)amino][1,2,4]triazolo[4,3-b]pyridazin-3-yl}sulphanyl)-1,3-benzothiazol-2-yl]cyclopropanecarboxamide

- 1-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-[2-(4-oxidomorpholin-4-yl)ethyl]urea

- 6-{[6-(1-methyl-1H-pyrazol-4-yl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-amine

- 1-(6-{[6-(4-fluorophenyl)-7,8-dihydro[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-[2-(morpholin-4-yl)ethyl]urea

- oxetan-2-ylmethyl (6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)carbamate

- N-{6-[(6-methoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}cyclopropanecarboxamide

- N-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)acetamide

- 1-{6-[(6-methoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}-3-[2-(pyrrolidin-1-yl)ethyl]urea

- 6-[(6-ethoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-amine

- 6-{[6-(3-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-amine

- 1-cyclopropyl-3-{6-[(6-ethoxy[1,2,4]triazolo[4,3-b]pyridazin-3-yl)sulphanyl]-1,3-benzothiazol-2-yl}urea

- N-(6-{[6-(4-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)cyclopropanecarboxamide

- N-(6-{[6-(4-fluorophenyl)-7,8-dihydro[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)cyclopropanecarboxamide

- 1-(6-{[6-(3-fluorophenyl)[1,2,4]triazolo[4,3-b]pyridazin-3-yl]sulphanyl}-1,3-benzothiazol-2-yl)-3-[2-(morpholin-4-yl)ethyl]urea

and also the addition salts with pharmaceutically acceptable mineral and organic acids or with pharmaceutically acceptable mineral and organic bases of said products of formula (I).

18 – Process for preparing the products of formula (I) as defined in any one of the other claims.

19 – Process for preparing the products of formula (I) as defined in any one of the other claims in which A represents NH.

20 – Process for preparing the products of formula (I) as defined in any one of the other claims in which A represents S.

21 – As medicaments, the products of formula (I) as defined in any one of Claims 1 to **17**, and also the addition salts with pharmaceutically acceptable mineral and organic acids or with pharmaceutically acceptable mineral and organic bases of said products of formula (I).

22 – As medicaments, the products of formula (I) as defined in Claim **17**, and also the addition salts with pharmaceutically acceptable mineral and organic acids or with pharmaceutically acceptable mineral and organic bases of said products of formula (I).

23 – Pharmaceutical compositions containing, as active ingredient, at least one of the products of formula (I) as defined in any one of Claims 1 to **17**, or a pharmaceutically acceptable salt of this product or a prodrug of this product, and a pharmaceutically acceptable carrier.

24 – Use of the products of formula (I) such as defined in any one of Claims 1 to **17**, or of pharmaceutically acceptable salts of these products, for the

preparation of a medicament for use in inhibiting the activity of the MET protein kinase and mutant forms thereof.

25 – Use as defined in Claim **24**, in which the protein kinase is in a cell culture.

26 – Use as defined in Claim **24** or **25**, in which the protein kinase is in a mammal.

27 – Use of a product of formula (I) as defined in any one of Claims 1 to **17**, for the preparation of a medicament for use in the treatment or prevention of a disease chosen from the following group: blood vessel proliferation disorders, fibrotic disorders, 'mesangial' cell proliferation disorders, metabolic disorders, allergies, asthma, thrombosis, nervous system diseases, retinopathy, psoriasis, rheumatoid arthritis, diabetes, muscle degeneration and cancers.

28 – Use of a product of formula (I) as defined in any one of Claims 1 to **17**, for the preparation of a medicament for use in the treatment of cancers.

29 – Use according to Claim **28**, for the treatment of solid or liquid tumours.

30 – Use according to Claim **28** or **29**, for the treatment of cancers resistant to cytotoxic agents.

31 – Use according to one or more of Claims **28** to **30**, for the treatment of primary tumours and/or metastases, in particular in gastric, hepatic, renal,

ovarian, colon, prostate and lung (NSCLC and SCLC) cancers, glioblastomas, thyroid, bladder or breast cancers, in melanomas, in lympyhoic or myeloid hematopoietic tumours, in sarcomas, in brain, larynx or lymphatic system cancers, bone cancers and pancreatic cancers.

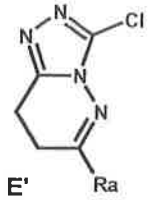
32 – Use of the products of formula (I) as defined in Claims 1 to **17**, for the preparation of medicaments for use in cancer chemotherapy.

33 – Use of the products of formula (I) as defined in Claims 1 to **17**, for the preparation of medicaments for use in cancer chemotherapy alone or in combination.

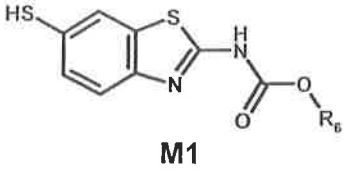
34 – Products of formula (I) as defined in any one of Claims 1 to **17**, as kinase inhibitors.

35 – Products of formula (I) as defined in any one of Claims 1 to **17**, as MET inhibitors.

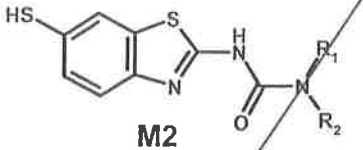
36 – As new industrial products, the synthesis intermediates of formulae E', M1, M2, M3 and N:



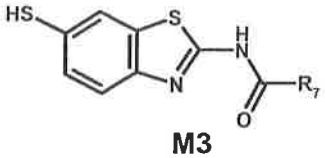
E'



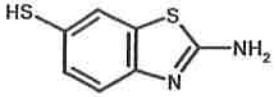
M1



M2



M3



N

in which R6 represents an alkyl radical optionally substituted with an NR3R4 (a $-(CH_2)_n$-NR3R4 radical), alkoxy, hydroxyl, heterocycloalkyl, phenyl or $-(CH_2)_n$-phenyl group, with phenyl optionally substituted and n representing an integer from 1 to 4, such that OR6 represents the corresponding values of R as defined above; R7 represents a cycloalkyl or alkyl radical optionally substituted with an NR3R4, alkoxy or hydroxyl radical or a phenyl, heteroaryl or heterocycloalkyl radical, themselves optionally substituted as indicated in Claim 1; and Ra, R1, R2, R3 and R4 have the meanings indicated in Claim 1.