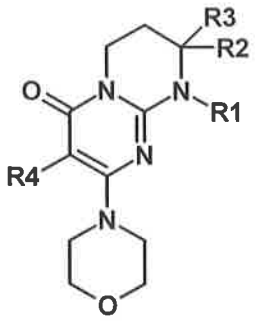
CLAIMS

1) A product of formula (I):



in which:

R1 represents an -L-aryl or -L-heteroaryl radical, such that L represents:

either a single bond,

or a linear or branched alkyl radical containing from 1 to 6 carbon atoms and optionally substituted with a hydroxyl radical,

or a CO or -CO-Alkyl- group,

or an L'-X group where L' represents a linear or branched alkyl radical containing from 1 to 6 carbon atoms, and X an oxygen or sulphur atom;

the aryl and heteroaryl radicals being optionally substituted with one or more radicals, which may be identical or different, chosen from halogen atoms and hydroxyl, CN, nitro, -COOH, -COOalkyl, -NRxRy, -CONRxRy, -NRxCORy, -NRxCO_2Rz, -CORy, alkoxy, phenoxy, alkylthio, alkyl, cycloalkyl and heterocycloalkyl radicals;

the alkoxy, phenoxy, alkylthio, alkyl and heterocycloalkyl radicals substituted on the aryl and heteroaryl radicals being themselves optionally substituted with one or more radicals, which may be identical or different, chosen from halogen atoms and NRvRw;

it being possible for the heterocycloalkyl and heteroaryl radicals to additionally contain an oxo radical;

R2 represents a hydrogen atom or an alkyl radical;

R3 represents a hydrogen atom or an alkyl radical optionally substituted with one or more halogen atoms;

R4 represents a hydrogen atom or a halogen atom;

NRxRy being such that Rx represents a hydrogen atom or an alkyl radical and Ry represents a hydrogen atom or a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, NRvRw and heterocycloalkyl radicals; or Rx and Ry form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 ring members and optionally one or more other heteroatoms chosen from O, S, NH and N-alkyl, this cyclic radical being optionally substituted;

NRvRw being such that Rv represents a hydrogen atom or an alkyl radical and Rw represents a hydrogen atom or a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy and heterocycloalkyl radicals; or Rv and Rw form, with the nitrogen atom to which they are attached, a cyclic radical

containing from 3 to 10 ring members and optionally one or more other heteroatoms chosen from O, S, NH and N-alkyl, this cyclic radical being optionally substituted;

the cyclic radicals that Rx and Ry or Rv and Rw, respectively, can form with the nitrogen atoms to which they are attached, being optionally substituted with one or more radicals, which may be identical or different, chosen from halogen atoms, and alkyl, hydroxyl, oxo, alkoxy, NH_2, NHalkyl and $N(alkyl)_2$ radicals;

Rz represents the values of Ry except for hydrogen;

Rx, Ry and Rz, in the -NRxCORy, -CORy and $NRxCO_2Rz$ radicals, being chosen from the meanings indicated above for Rx, Ry and Rz;

all the above alkyl, alkoxy and alkylthio radicals being linear or branched and containing from 1 to 6 carbon atoms, or

racemic, enantiomeric or diastereoisomeric isomers thereof, or pharmaceutically acceptable salts of said product or racemic, enantiomeric or diastereoisomeric isomers.

2) The product of Claim 1, in which:

R1 represents an -L-phenyl or -L-heteroaryl radical, such that L represents:
either a single bond,

or a linear or branched alkyl radical containing from 1 to 6 carbon atoms and optionally substituted with a hydroxyl radical,
or a CO or -CO-Alkyl- group,

or an L'-X group where L' represents a linear or branched alkyl radical containing from 1 to 6 carbon atoms, and X an oxygen or sulphur atom;

the phenyl and heteroaryl radicals being optionally substituted with one or more radicals, which may be identical or different, chosen from halogen atoms and -NRxRy, alkoxy and alkyl radicals;

the alkoxy and alkyl radicals being themselves optionally substituted with one or more radicals chosen from halogen atoms;

R2 represents an alkyl radical;

R3 represents a hydrogen atom or an alkyl radical optionally substituted with one or more halogen atoms;

R4 represents a hydrogen atom or a fluorine atom;

NRxRy being such that Rx represents a hydrogen atom or an alkyl radical and Ry represents a hydrogen atom or an alkyl radical; or Rx and Ry form, with the nitrogen atom to which they are attached, a morpholino radical;

all the above alkyl or alkoxy radicals being linear or branched and containing from 1 to 6 carbon atoms, or

racemic, enantiomeric or diastereoisomeric isomers thereof, or pharmaceutically acceptable salts of said product or racemic, enantiomeric or diastereoisomeric isomers .

3) The product of Claim 1, corresponding to the following formulae:

- (8S)-9-[2-(4-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- 9-[2-(4-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-(2-phenylethyl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-benzyl-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(2S)-2-hydroxy-2-phenylethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(2R)-2-hydroxy-2-phenylethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(2S)-2-hydroxy-2-(4-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-[(1R)-1-phenylethyl]-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[1-(4-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1S)-1-(4-bromophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1R)-1-(4-bromophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-phenyl-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(4-fluorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(3-fluorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(2-fluorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1R)-1-(3-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(4-fluorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-(phenylcarbonyl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-(pyridin-3-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-(pyridin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(4-methylphenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(2-chlorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(3-fluorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[2-(2-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[2-(3-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(3-methoxybenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(4-methoxyphenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[(2-fluorophenyl)carbonyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(3,5-difluorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(2,4-difluorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-2-(morpholin-4-yl)-9-(2,3,4-trifluorobenzyl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[(5-chloro-1-benzothiophen-3-yl)methyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[(1R or 1S)-1-(4-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[(1R or 1S)-1-(4-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(3-methylphenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(4-chlorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-2-(morpholin-4-yl)-8-(trifluoromethyl)-9-[4-(trifluoromethyl)phenyl]-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[(1R or 1S)-1-(2-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[(1R or 1S)-1-(2-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[2-(3-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-benzyl-3-fluoro-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-(3,5-difluorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[(2,6-difluorophenyl)carbonyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[(2,4-difluorophenyl)carbonyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-2-(morpholin-4-yl)-9-(phenylacetyl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

(8S)-9-[2-(3-chlorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-9-((R)-2-benzo[b]thiophen-2-yl-2-hydroxyethyl)-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[(S)-2-hydroxy-2-(3-hydroxyphenyl)ethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-2-dimethylamino-N-{3-[(S)-1-hydroxy-2-((S)-8-morpholin-4-yl-6-oxo-2-trifluoromethyl-3,4-dihydro-2H,6H-pyrimido[1,2-a]pyrimidin-1-yl)ethyl]phenyl}acetamide

-9-[(S)-2-hydroxy-2-(2-methoxyphenyl)ethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[(S)-2-(4-fluoro-2-methoxyphenyl)-2-hydroxyethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[(S)-2-(4-chloro-2-methoxyphenyl)-2-hydroxyethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[(S)-2-(2-chloro-4-methoxyphenyl)-2-hydroxyethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

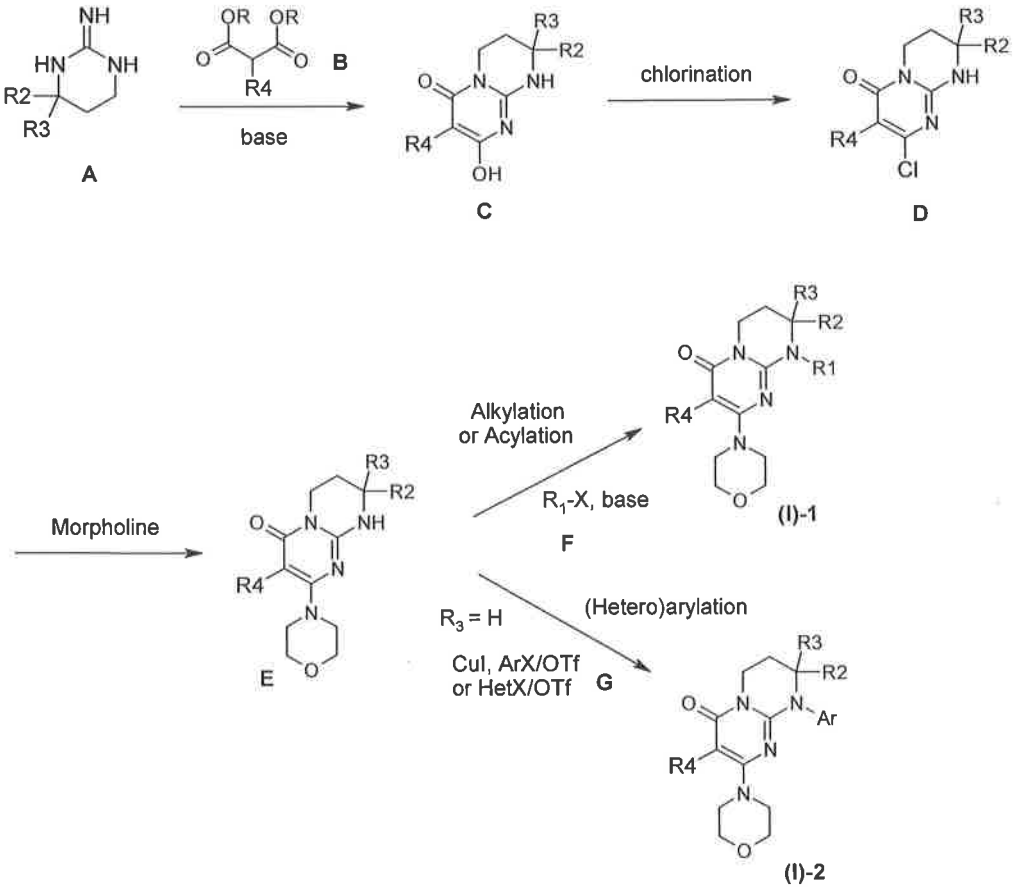
-9-(2-hydroxy-3-phenylpropyl)-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[2-(4-hydroxyphenyl)ethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

or pharmaceutically acceptable salts thereof.

4) A process for preparing the product according to Claim 1, according to scheme 1 as defined hereinafter:

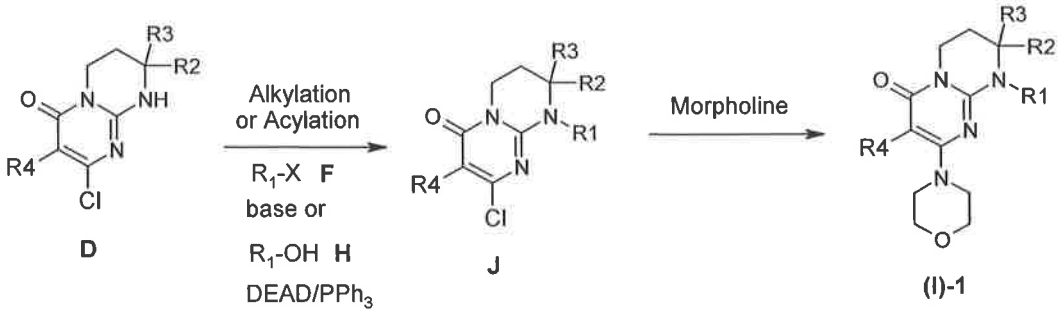
Scheme 1:



in which the substituents R1, R2, R3 and R4 have the meanings indicated in Claim 1 and in which R represents alkyl, and X represents a chlorine, bromine or iodine atom or a sulphonyloxy group such as trifluoromethylsulphonyloxy, Ar is aryl and Het is heteroaryl.

5) A process for preparing the product according to Claim 1, according to scheme 2 as defined hereinafter:

Scheme 2:



in which the substituents R1, R2, R3 and R4 have the meanings indicated in Claim 1, and X represents a chlorine, bromine or iodine atom or a sulphonyloxy group such as trifluoromethylsulphonyloxy.

6) A pharmaceutical composition comprising the product of Claim 1 or pharmaceutically acceptable salts thereof.

7) A pharmaceutical composition comprising the product of Claim 3, or pharmaceutically acceptable salts thereof.

8) A pharmaceutical composition containing, as active ingredient, at least one product according to Claim 1, or a pharmaceutically acceptable salt of said product, and a pharmaceutically acceptable carrier.

9) Use of a therapeutically effective amount of the product according to claim 1 in the manufacture of a medicament for treating cancers capable of being modulated by inhibition of P13K/AKT/mTOR pathway in a patient in need thereof.

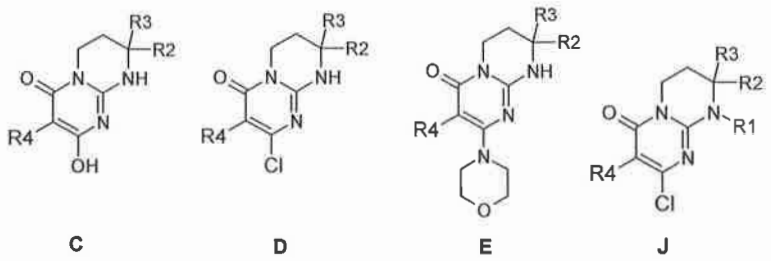
10) The use according to Claim 9, wherein solid or liquid tumours are to be treated.

11) The use according to Claim 9, wherein said cancers are resistant to cytotoxic agents.

12) The use according to Claim 9, wherein primary tumours and/or of metastases, in particular in gastric, hepatic, renal, ovarian, colon, prostate, endometrial and lung (NSCLC and SCLC) cancers, glioblastomas, thyroid, bladder and breast cancers, in melanoma, in lymphoid or myeloid haematopoietic tumours, in sarcomas, in brain, larynx and lymphatic system cancers, bone and pancreatic cancers, and in hamartomas are to be treated.

13) The product according to Claim 1, wherein said product is an inhibitor of AKT(PKB) phosphorylation.

14) A product having one of the following formulas:



C D E J

in which R1, R2, R3 and R4 have the definitions indicated in Claim 1.

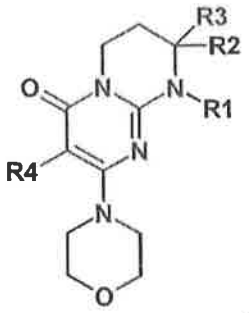
15) Use of a therapeutically effective amount of the product of Claim 1 in the manufacture of a medicament for treating glycogenosis type II or Pompe disease in a patient in need thereof.

16) Use of a therapeutically effective amount of the product of Claim 1 in the manufacture of a medicament for treating parasitic diseases selected from the group consisting of malaria, sleeping sickness, Chagas disease and leishmaniasis in a patient in need thereof.

17) The use according to claim 16 wherein the parasitic disease is malaria, Chagas disease or leishmaniasis.

CLAIMS

1) Products of formula (I):



in which:

R1 represents an -L-aryl or -L-heteroaryl radical, such that L represents:

either a single bond,

or a linear or branched alkyl radical containing from 1 to 6 carbon atoms and optionally substituted with a hydroxyl radical,

or a CO or -CO-Alk- group,

or an L'-X group where L' represents a linear or branched alkyl radical containing from 1 to 6 carbon atoms, and X an oxygen or sulphur atom;

the aryl and heteroaryl radicals being optionally substituted with one or more radicals, which may be identical or different, chosen from halogen atoms and hydroxyl, CN, nitro, -COOH, -COOalk, -NRxRy, -CONRxRy, -NRxCORy, -$NRxCO_2Rz$, -CORy, alkoxy, phenoxy, alkylthio, alkyl, cycloalkyl and heterocycloalkyl radicals;

the latter alkoxy, phenoxy, alkylthio, alkyl and heterocycloalkyl radicals being themselves optionally substituted with one or more radicals, which may be identical or different, chosen from halogen atoms and NRvRw;

it being possible for the heterocycloalkyl and heteroaryl radicals to additionally contain an oxo radical;

R2 represents a hydrogen atom or an alkyl radical;

R3 represents an alkyl radical optionally substituted with one or more halogen atoms;

R4 represents a hydrogen atom or a halogen atom;

NRxRy being such that Rx represents a hydrogen atom or an alkyl radical and Ry represents a hydrogen atom or a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy, NRvRw and heterocycloalkyl radicals; or Rx and Ry form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 ring members and optionally one or more other heteroatoms chosen from O, S, NH and N-alkyl, this cyclic radical being optionally substituted;

NRvRw being such that Rv represents a hydrogen atom or an alkyl radical and Rw represents a hydrogen atom or a cycloalkyl radical or an alkyl radical optionally substituted with one or more radicals, which may be identical or different, chosen from hydroxyl, alkoxy and heterocycloalkyl radicals; or Rv and Rw form, with the nitrogen atom to which they are attached, a cyclic radical containing from 3 to 10 ring members and optionally one or more other heteroatoms chosen from O, S, NH and N-alkyl, this cyclic radical being optionally substituted;

the cyclic radicals that Rx and Ry or Rv and Rw, respectively, can form with the nitrogen atoms to which they are attached, being optionally substituted with one or more radicals, which may be identical or different, chosen from halogen atoms, and alkyl, hydroxyl, oxo, alkoxy, NH_2, NHalk and $N(alk)_2$ radicals;

Rz represents the values of Ry except for hydrogen;

Rx, Ry and Rz, in the -NRxCORy, -CORy and $NRxCO_2Rz$ radicals, being chosen from the meanings indicated above for Rx, Ry and Rz;

all the above alkyl (alk), alkoxy and alkylthio radicals being linear or branched and containing from 1 to 6 carbon atoms,

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

2) Products of formula (I) as defined in Claim 1, in which:

R1 represents an -L-phenyl or -L-heteroaryl radical, such that L represents:

either a single bond,

or a linear or branched alkyl radical containing from 1 to 6 carbon atoms and optionally substituted with a hydroxyl radical,

or a CO or -CO-Alk- group,

or an L'-X group where L' represents a linear or branched alkyl radical containing from 1 to 6 carbon atoms, and X an oxygen or sulphur atom;

the phenyl and heteroaryl radicals being optionally substituted with one or more radicals, which may be identical or different, chosen from halogen atoms and -NRxRy, alkoxy and alkyl radicals;

the latter alkoxy and alkyl radicals being themselves optionally substituted with one or more radicals chosen from halogen atoms;

R2 represents an alkyl radical;

R3 represents an alkyl radical optionally substituted with one or more halogen atoms;

R4 represents a hydrogen atom or a fluorine atom;

NRxRy being such that Rx represents a hydrogen atom or an alkyl radical and Ry represents a hydrogen atom or an alkyl radical; or Rx and Ry form, with the nitrogen atom to which they are attached, a morpholino radical;

all the above alkyl (alk) or alkoxy radicals being linear or branched and containing from 1 to 6 carbon atoms,

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

3) Products of formula (I) as defined in either one of Claims 1 and 2, corresponding to the following formulae:

- (8S)-9-[2-(4-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- 9-[2-(4-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-(2-phenylethyl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-benzyl-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(2S)-2-hydroxy-2-phenylethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(2R)-2-hydroxy-2-phenylethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(2S)-2-hydroxy-2-(4-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-[(1R)-1-phenylethyl]-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[1-(4-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1S)-1-(4-bromophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1R)-1-(4-bromophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-

6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-phenyl-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(4-fluorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(3-fluorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(2-fluorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1R)-1-(3-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(4-fluorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-(phenylcarbonyl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-(pyridin-3-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-(pyridin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(4-methylphenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(2-chlorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(3-fluorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[2-(2-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[2-(3-methoxyphenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-

6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(3-methoxybenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(4-methoxyphenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-(8S)-9-[(2-fluorophenyl)carbonyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(3,5-difluorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(2,4-difluorobenzyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-9-(2,3,4-trifluorobenzyl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(5-chloro-1-benzothiophen-3-yl)methyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1R or 1S)-1-(4-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1R or 1S)-1-(4-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(3-methylphenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-(4-chlorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-2-(morpholin-4-yl)-8-(trifluoromethyl)-9-[4-(trifluoromethyl)phenyl]-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1R or 1S)-1-(2-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

- (8S)-9-[(1R or 1S)-1-(2-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoro-

methyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-(8S)-9-[2-(3-fluorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-(8S)-9-benzyl-3-fluoro-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-(8S)-9-(3,5-difluorophenyl)-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-(8S)-9-[(2,6-difluorophenyl)carbonyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-(8S)-9-[(2,4-difluorophenyl)carbonyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-(8S)-2-(morpholin-4-yl)-9-(phenylacetyl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-(8S)-9-[2-(3-chlorophenyl)ethyl]-2-(morpholin-4-yl)-8-(trifluoromethyl)-6,7,8,9-tetrahydro-4H-pyrimido[1,2-a]pyrimidin-4-one

-9-((R)-2-benzo[b]thiophen-2-yl-2-hydroxyethyl)-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[(S)-2-hydroxy-2-(3-hydroxyphenyl)ethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-2-dimethylamino-N-{3-[(S)-1-hydroxy-2-((S)-8-morpholin-4-yl-6-oxo-2-trifluoromethyl-3,4-dihydro-2H,6H-pyrimido[1,2-a]pyrimidin-1-yl)ethyl]phenyl}acetamide

-9-[(S)-2-hydroxy-2-(2-methoxyphenyl)ethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[(S)-2-(4-fluoro-2-methoxyphenyl)-2-hydroxyethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[(S)-2-(4-chloro-2-methoxyphenyl)-2-hydroxyethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[(S)-2-(2-chloro-4-methoxyphenyl)-2-hydroxyethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

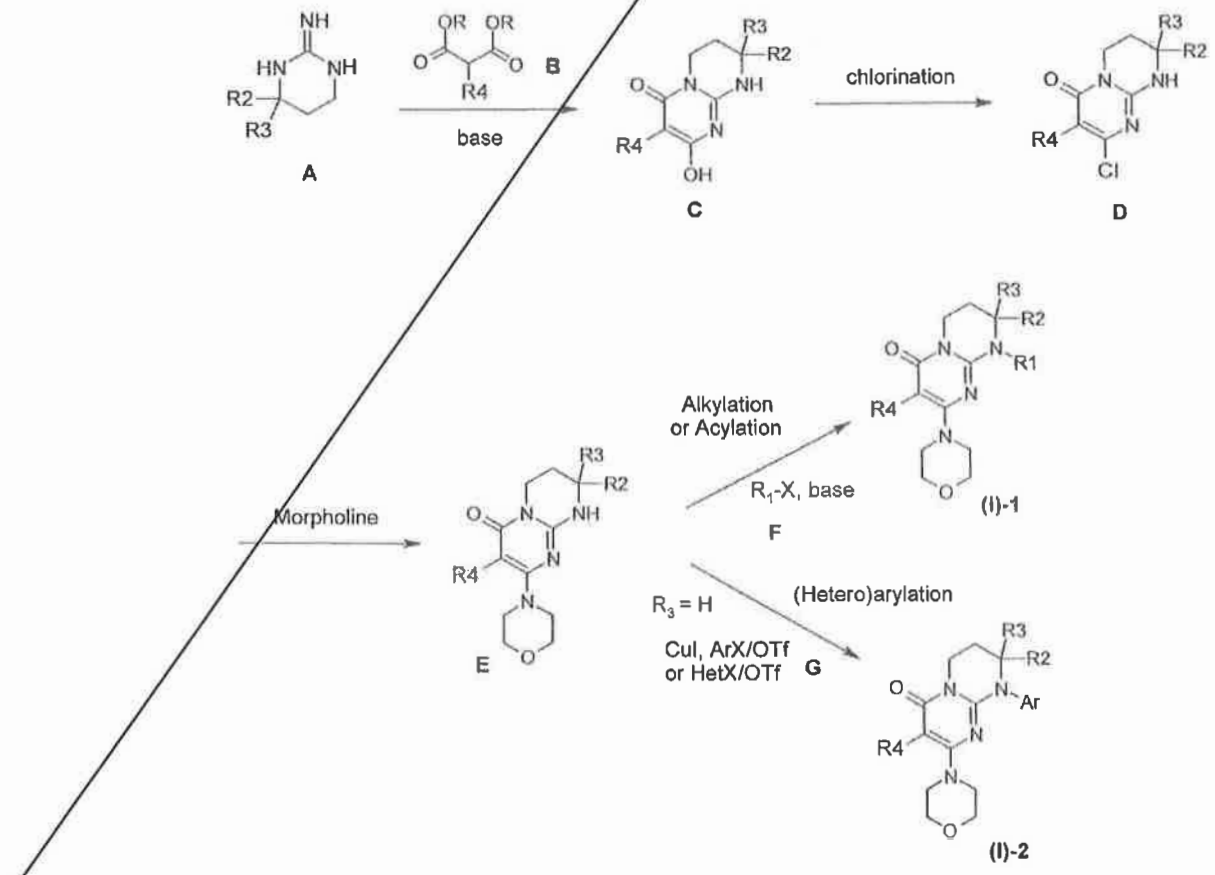
-9-(2-hydroxy-3-phenylpropyl)-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

-9-[2-(4-hydroxyphenyl)ethyl]-2-morpholin-4-yl-8-(S)-trifluoromethyl-6,7,8,9-tetrahydropyrimido[1,2-a]pyrimidin-4-one

and also the addition salts with inorganic and organic acids or with inorganic and organic bases, of said products of formula (I).

4) Process for preparing the products of formula (I) as defined in any one of Claims 1 to 3, according to scheme 1 as defined hereinafter.

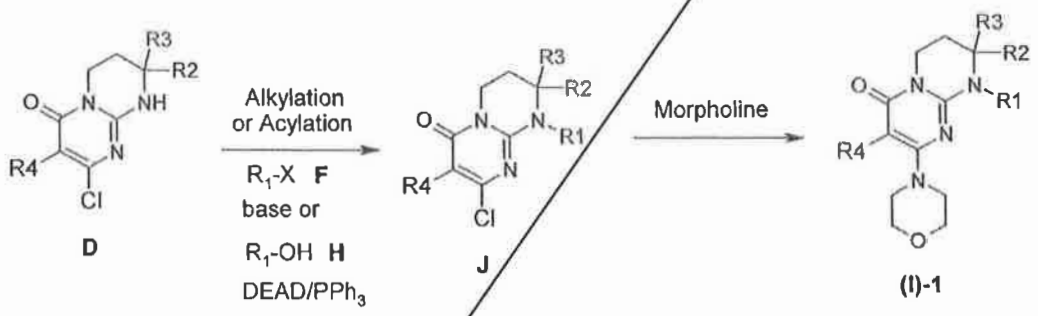
Scheme 1:



in which the substituents R1, R2, R3 and R4 have the meanings indicated in either one of Claims 1 and 2 and in which R represents alkyl, and X represents a chlorine, bromine or iodine atom or a sulphonyloxy group such as trifluoromethylsulphonyloxy.

5) Process for preparing the products of formula (I) as defined in any one of Claims 1 to 3, according to scheme 2 as defined hereinafter.

Scheme 2:



in which the substituents R1, R2, R3 and R4 have the meanings indicated in either one of Claims 1 and 2, and X represents a chlorine, bromine or iodine atom or a sulphonyloxy group such as trifluoromethylsulphonyloxy.

6) As medicaments, the products of formula (I) as defined in any one of Claims 1 to 3, and also the pharmaceutically acceptable addition salts with inorganic and organic acids or with inorganic and organic bases, of said products of formula (I).

7) As medicaments, the products of formula (I) as defined in Claim 3, and also the pharmaceutically acceptable addition salts with inorganic and organic acids or with inorganic and organic bases, of said products of formula (I).

8) Pharmaceutical compositions containing, as active ingredient, at least one

of the products of formula (I) as defined in any one of Claims 1 to 3, or a pharmaceutically acceptable salt of this product or a prodrug of this product, and a pharmaceutically acceptable carrier.

9) Use of a product of formula (I) as defined in any one of Claims 1 to 3, for the preparation of a medicament for use in the treatment of cancers.

10) Use according to Claim 9, for the treatment of solid or liquid tumours.

11) Use according to Claim 9 and 10, for the treatment of cancers resistant to cytotoxic agents.

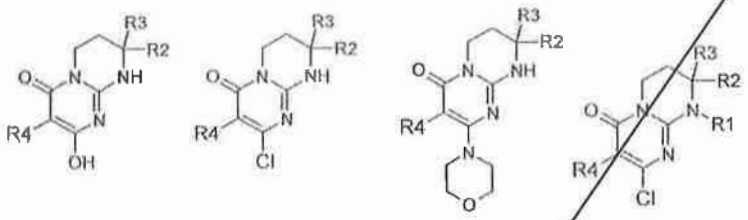
12) Use according to one or more of Claims 9 to 11, for the treatment of primary tumours and/or of metastases, in particular in gastric, hepatic, renal, ovarian, colon, prostate, endometrial and lung (NSCLC and SCLC) cancers, glioblastomas, thyroid, bladder and breast cancers, in melanoma, in lymphoid or myeloid haematopoietic tumours, in sarcomas, in brain, larynx and lymphatic system cancers, bone and pancreatic cancers, and in hamartomas.

13) Use of the products of formula (I) as defined in Claims 1 to 3, for the preparation of medicaments for use in cancer chemotherapy.

14) Use of the products of formula (I) as defined in Claims 1 to 3, for the preparation of medicaments for use in cancer chemotherapy alone or in combination.

15) Products of formula (I) as defined in any one of Claims 1 to 3, as inhibitors of AKT(PKB) phosphorylation.

16) As novel industrial products, the synthesis intermediates of formulae C, D, E and J as defined in Claims 4 and 5 above and recalled below:



C D E J

in which R1, R2, R3 and R4 have the definitions indicated in either one of Claims 1 and 2.

17) Products of formula (I) as defined in any one of Claims 1 to 3, for the use thereof in the treatment of cancers.

18) Products of formula (I) as defined in any one of Claims 1 to 3, for the use thereof in the treatment of solid or liquid tumours.

19) Products of formula (I) as defined in any one of Claims 1 to 3, for the use thereof in the treatment of cancers resistant to cytotoxic agents.

20) Products of formula (I) as defined in any one of Claims 1 to 3, for the use thereof in the treatment of primary tumours and/or metastases, in particular in gastric, hepatic, renal, ovarian, colon, prostate, endometrial and lung (NSCLC and SCLC) cancers, glioblastomas, thyroid, bladder and breast cancers, in melanoma, in lymphoid or myeloid haematopoietic tumours, in sarcomas, in brain, larynx and lymphatic system cancers, bone and pancreatic cancers, and in hamartomas.

21) Products of formula (I) as defined in any one of Claims 1 to 3, for the use thereof in cancer chemotherapy.

22) Products of formula (I) as defined in any one of Claims 1 to 3, for the use thereof in cancer chemotherapy, alone or in combination.

23) Products of formula (I) as defined in any one of Claims 1 to 3, for the prevention or treatment of lysosomal diseases such as glycogenosis type II or Pompe disease.

24) Use of the products of formula (I) as defined in any one of Claims 1 to 3, for the preparation of a medicament for use in the prevention or treatment of lysosomal diseases such as glycogenosis type II or Pompe disease.

25) Use as defined in Claim 23 or 24, in which said products of formula (I) are alone or in combination.

26) Products of formula (I) as defined in any one of Claims 1 to 3, for the treatment of parasitic diseases such as malaria, sleeping sickness, Chagas disease or leishmaniasis.

27) Use of the products of formula (I) as defined in any one of Claims 1 to 3 for the preparation of a medicament for the treatment of parasitic diseases such as malaria, sleeping sickness, Chagas disease or leishmaniasis.