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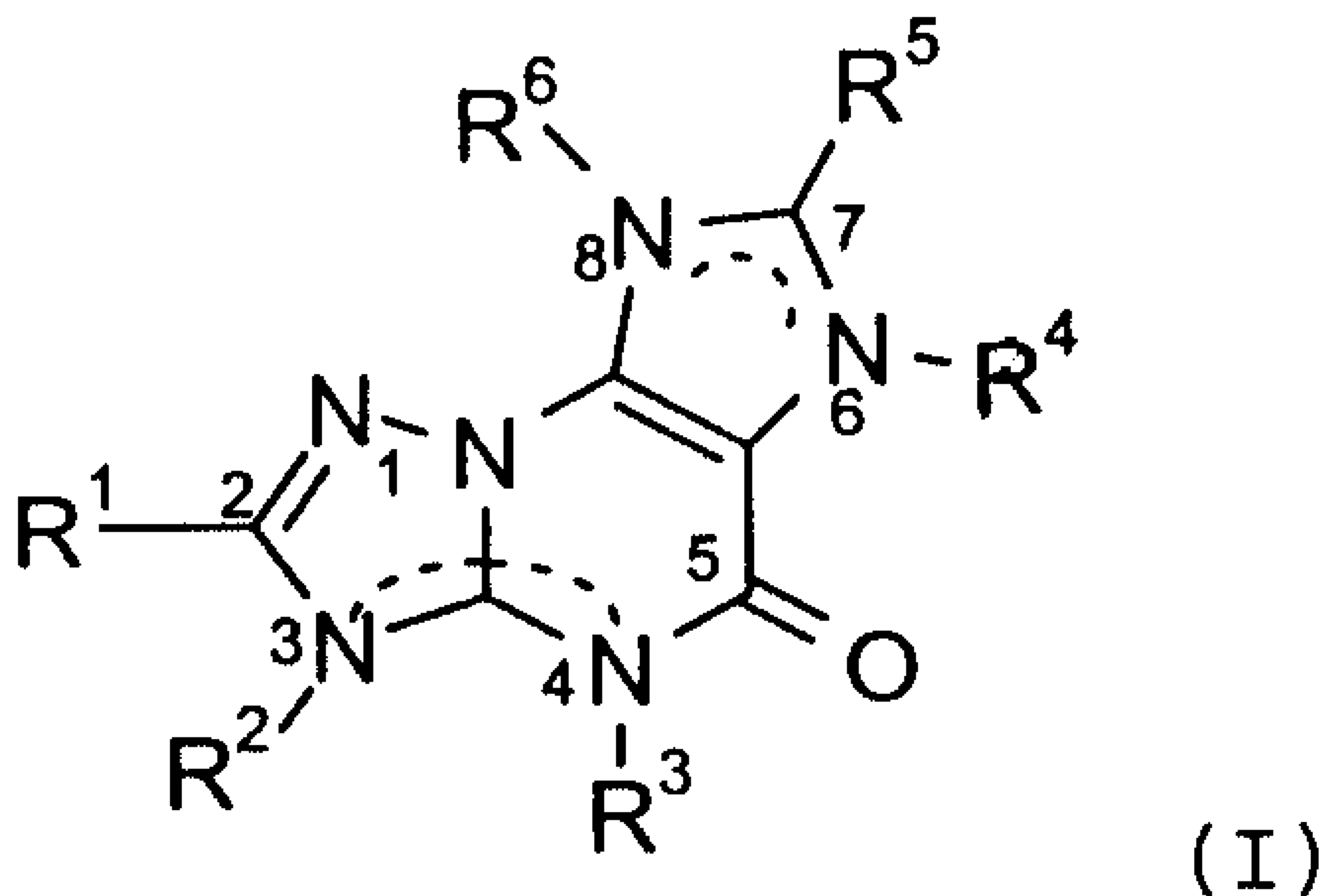
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(54) Titre : NOUVEAUX IMIDAZOTRIAZOLOPYRIMIDINES, PROCEDE POUR LES PREPARER ET LEUR UTILISATION  
EN TANT QUE COMPOSITIONS PHARMACEUTIQUES

(54) Title: NEW IMIDAZOTRIAZOLOPYRIMIDINES, PROCESSES FOR PREPARING THEM AND THEIR USE AS  
PHARMACEUTICAL COMPOSITIONS



(57) Abrégé/Abstract:

The invention relates to new imidazotriazolopyrimidine derivatives of general formula (I), processes for preparing them and their use as pharmaceutical compositions (see formula I) wherein the dotted lines between the nitrogen atoms indicate the existence of a double bond in one of two possible positions, so that the groups R<sup>4</sup> and R<sup>6</sup> and R<sup>3</sup> and R<sup>2</sup> need not be present simultaneously and wherein the groups R<sup>1</sup> to R<sup>6</sup> may have the meanings given in the specification and claims.

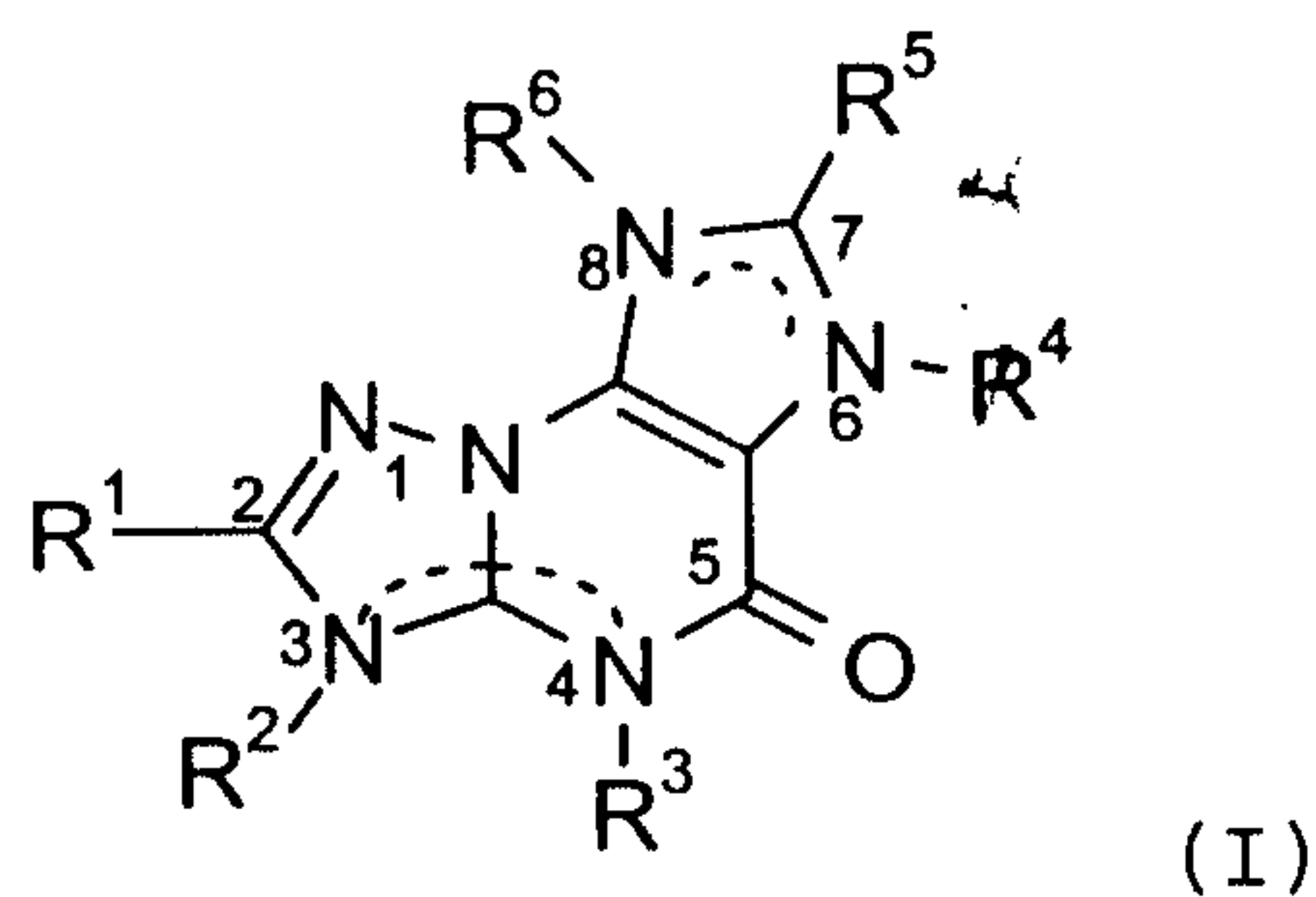




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Abstract

The invention relates to new imidazotriazolopyrimidine  
5 derivatives of general formula (I), processes for  
preparing them and their use as pharmaceutical  
compositions



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wherein the dotted lines between the nitrogen atoms  
indicate the existence of a double bond in one of two  
possible positions, so that the groups R<sup>4</sup> and R<sup>6</sup> and R<sup>3</sup> and  
15 R<sup>2</sup> need not be present simultaneously and wherein the  
groups R<sup>1</sup> to R<sup>6</sup> may have the meanings given in the  
specification and claims.



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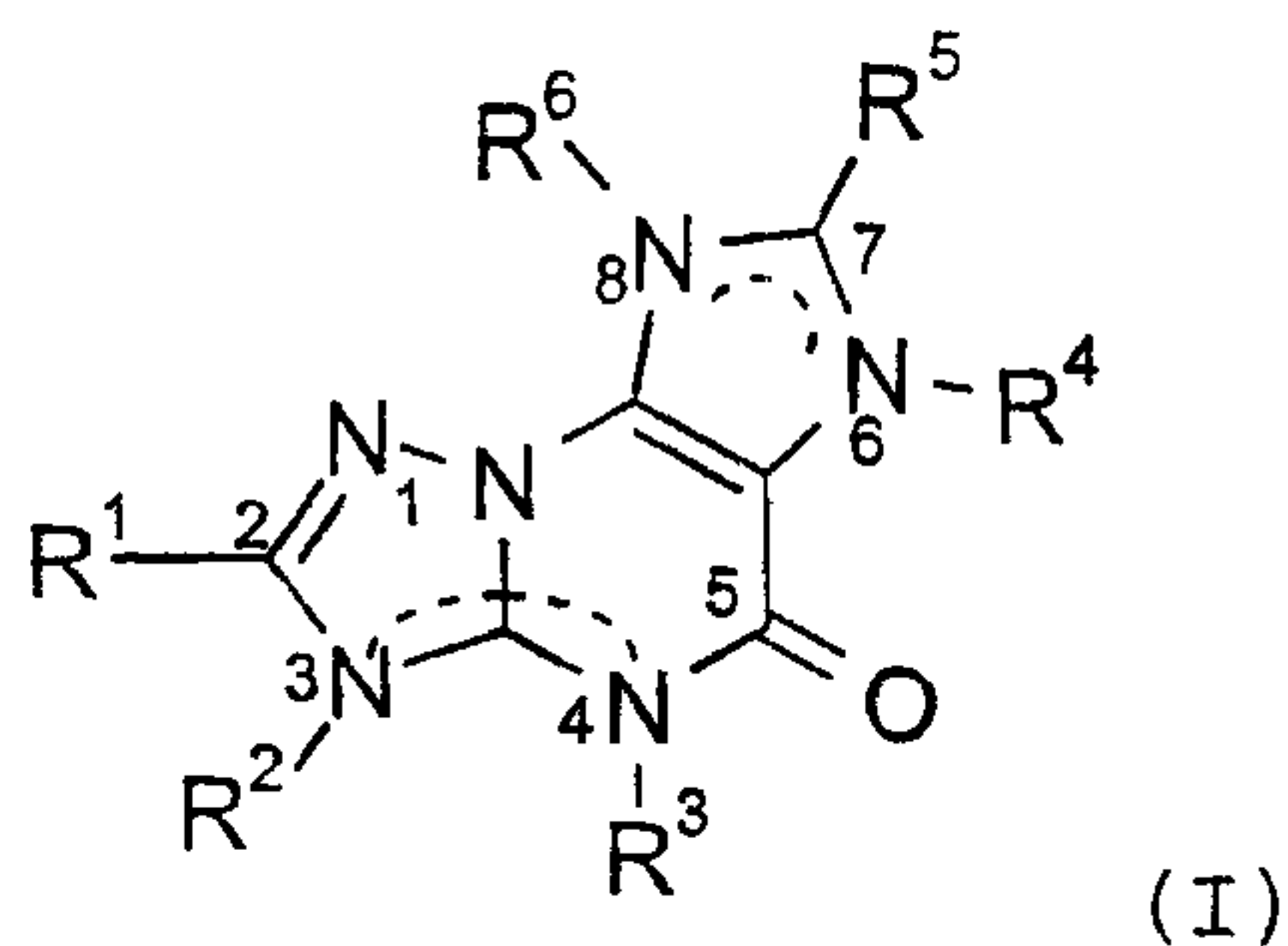
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New imidazotriazolopyrimidines, processes for preparing  
them and their use as pharmaceutical compositions

5

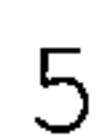
The invention relates to new imidazotriazolopyrimidines,  
processes for preparing them and their use as  
pharmaceutical compositions.

10 The new imidazotriazolopyrimidines have the structure of  
general formula (I):



15 wherein the dotted lines between the nitrogen atoms of the  
above general formula I indicate the existence of a double  
bond in one of two possible positions, so that the groups  
R<sup>4</sup> and R<sup>6</sup> and R<sup>3</sup> and R<sup>2</sup> need not be present simultaneously  
and wherein the groups R<sup>1</sup> to R<sup>6</sup> may have the meanings  
20 given in the specification which follows.





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R<sup>1</sup> denotes -CHO, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup> or NR<sup>7</sup>R<sup>8</sup>;

R<sup>1</sup> denotes C<sub>3-7</sub>-cycloalkyl which is optionally substituted by

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$R^1$  denotes phenyl which is optionally substituted by  $C_{1-4}$ -alkyl, -CN, -COOR<sup>9</sup>, NR<sup>7</sup>R<sup>8</sup>, -OR<sup>9</sup>, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>CONR<sup>7</sup>R<sup>8</sup>, -CO- $C_{1-4}$ -alkyl-NH<sub>2</sub>, -SO<sub>3</sub>H or halogen;

$R^1$  denotes phenyl- $C_{1-6}$ -alkyl, phenyl- $C_{2-6}$ -alkenyl or  
 5 phenyl- $C_{2-6}$ -alkynyl, wherein the phenyl ring is optionally substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups selected from  $C_{1-3}$ -alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>,  
 10 -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO- $C_{1-4}$ -alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane and  
 15 1,3-dioxane;

$R^1$  denotes  $C_{3-7}$ -cycloalkyl- $C_{1-6}$ -alkyl,  $C_{3-7}$ -cycloalkyl- $C_{2-6}$ -alkenyl,  $C_{3-7}$ -cycloalkyl- $C_{2-6}$ -alkynyl, wherein the cycloalkyl group is optionally substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one  
 20 or more of the groups selected from  $C_{1-4}$ -alkyl,  $C_{1-4}$ -alkoxy, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO- $C_{1-4}$ -alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>,  
 25 -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane and 1,3-dioxane;

$R^1$  denotes a norbornane, norbornene,  $C_{3-6}$ -dicycloalkylmethyl, adamantane or noradamantane group which is optionally  
 30 substituted by  $C_{1-4}$ -alkyl; or



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$R^1$  denotes a group of formula A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenyl, A-C<sub>2-6</sub>-alkynyl or A-, where A is a C- or N-linked 5-,  
 5 6- or 7-membered heterocycle, which contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and is optionally mono- or polysubstituted by benzyl, optionally methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -COR<sup>10</sup>,  
 10 -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, =O, a ketal, ethyleneketal, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup> or halogen;

$R^2$  or  $R^3$  denotes a C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl or C<sub>2-8</sub>-alkynyl group which is optionally mono-or polysubstituted by one or more groups selected from -CN, C<sub>3-6</sub>-cycloalkyl, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>,  
 15 -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -CHO, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH=NOH, -CH=NOR<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -NHCONHPhenyl, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-  
 20 substituted 1,3-dioxolane and 1,3-dioxane;

$R^2$  or  $R^3$  denotes phenyl-C<sub>1-6</sub>-alkyl, phenyl-C<sub>2-6</sub>-alkenyl or phenyl-C<sub>2-6</sub>-alkynyl, wherein the phenyl ring is optionally substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups  
 25 selected from C<sub>1-3</sub>-alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>,  
 30 -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane and 1,3-dioxane;



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$R^2$  or  $R^3$  denotes a group of formula A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenyl, A-C<sub>2-6</sub>-alkynyl or A-, where A is a C- or N-linked 5-, 6- or 7-membered heterocycle, which contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and is optionally mono- or polysubstituted by benzyl, optionally methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -COR<sup>10</sup>, -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, =O, a ketal, ethyleneketal, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup> or halogen;

$R^4$  or  $R^6$  denotes hydrogen, C<sub>1-4</sub>-alkyl which is optionally substituted by -NR<sup>7</sup>R<sup>8</sup> or benzyl;

$R^5$  denotes hydrogen, a C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl or C<sub>2-8</sub>-alkynyl group which may optionally be mono- or polysubstituted by -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -CHO, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH=NOH, -CH=NOR<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -NHCONHPhenyl, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane or 1,3-dioxane;

$R^5$  denotes C<sub>3-7</sub>-cycloalkyl, which is optionally substituted by =O, -OR<sup>9</sup>, OCOR<sup>9</sup> or -OCOPyridyl;

$R^5$  denotes phenyl which may optionally be substituted by -OH, halogen, -OR<sup>9</sup>, C<sub>1-4</sub>-alkyl, NH<sub>2</sub>, COOH, -SO<sub>3</sub>H, -COOR<sup>9</sup>, -OCH<sub>2</sub>COOR<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -CN or -OCH<sub>2</sub>CONR<sup>7</sup>R<sup>8</sup>;

$R^5$  denotes phenyl-C<sub>1-6</sub>-alkyl, phenyl-C<sub>2-6</sub>-alkenyl or phenyl-C<sub>2-6</sub>-alkynyl, wherein the phenyl ring is optionally substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups selected from C<sub>1-3</sub>-alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>,



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-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>,  
 -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>,  
 -CO-R<sup>9</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>,  
 -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>,  
 5 -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>,  
 halogen, optionally methyl-substituted 1,3-dioxolane and  
 1,3-dioxane;

R<sup>5</sup> denotes a norbornane, norbornene, C<sub>3-6</sub>-dicycloalkylmethyl,  
 adamantane or noradamantane group which is optionally  
 10 substituted by C<sub>1-4</sub>-alkyl;

R<sup>5</sup> denotes -CHO, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup> or NR<sup>7</sup>R<sup>8</sup>;

R<sup>5</sup> denotes C<sub>3-7</sub>-cycloalkyl-C<sub>1-6</sub>-alkyl, C<sub>3-7</sub>-cycloalkyl-  
 C<sub>2-6</sub>-alkenyl, C<sub>3-7</sub>-cycloalkyl-C<sub>2-6</sub>-alkynyl, wherein the  
 cycloalkyl group is optionally substituted, either directly  
 15 or via an alkylene bridge having 1 to 4 carbon atoms, by one  
 or more of the groups C<sub>1-3</sub>-alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>,  
 -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>,  
 -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>,  
 -CO-R<sup>9</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>,  
 20 -NHCOOR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>,  
 -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>,  
 halogen, optionally methyl-substituted 1,3-dioxolane or  
 1,3-dioxane; or

R<sup>5</sup> denotes a group of formula A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl,  
 25 A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl,  
 A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenylene,  
 A-C<sub>2-6</sub>-alkynylene or A-, where A is a C- or N-linked 5-,  
 6- or 7-membered heterocycle, which contains one or more  
 heteroatoms selected from the group consisting of nitrogen,  
 30 oxygen and sulphur and is optionally mono- or  
 polysubstituted by benzyl, optionally methoxy-substituted  
 benzyl, C<sub>1-4</sub>-alkyl, -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -COR<sup>10</sup>,



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-NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, =O, a ketal, ethyleneketal, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup> or halogen;

R<sup>7</sup> denotes hydrogen, C<sub>1-8</sub>-alkyl which is optionally substituted by -COOR<sup>9</sup>, -COR<sup>10</sup>, -OR<sup>9</sup>, OCOR<sup>9</sup>, amino, phenyl,  
5 methoxy-substituted phenyl or amino, or a C<sub>3-6</sub>-cycloalkyl, or

R<sup>7</sup> denotes a 5-, 6- or 7-membered heterocycle C-linked directly or via a C<sub>1-4</sub>-alkyl chain, which contains one, two or three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and which is optionally mono-  
10 or polysubstituted by benzyl, methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, halogen, -OR<sup>9</sup>, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, =O, SO<sub>3</sub>H or -COOR<sup>9</sup>;

R<sup>8</sup> denotes hydrogen, C<sub>1-8</sub>-alkyl which is optionally substituted by -COOR<sup>9</sup>, -COR<sup>10</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, amino, phenyl, methoxy-substituted phenyl or amino, or a C<sub>3-6</sub>-cycloalkyl, or

15 R<sup>8</sup> denotes a 5-, 6- or 7-membered heterocycle C-linked directly or via a C<sub>1-4</sub>-alkyl chain, which contains one, two or three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and which is optionally mono- or polysubstituted by benzyl, methoxy-substituted benzyl,  
20 C<sub>1-4</sub>-alkyl, halogen, -OR<sup>9</sup>, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, =O, SO<sub>3</sub>H or -COOR<sup>9</sup>;

R<sup>7</sup> and R<sup>8</sup> together with the nitrogen atom form a saturated or unsaturated 5- or 6-membered ring which optionally comprises nitrogen, oxygen or sulphur as a further heteroatom, wherein the heterocycle is optionally substituted by a branched or  
25 unbranched alkyl group having 1 to 4 carbon atoms, -CN, -COOR<sup>9</sup>, -CONH<sub>2</sub>, -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup>, halogen or -(CH<sub>2</sub>)<sub>n</sub>-phenyl, -(CH<sub>2</sub>)<sub>n</sub>-NH<sub>2</sub>, =O, -OCH<sub>2</sub>-CH<sub>2</sub>-O, -OCH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O, -(CH<sub>2</sub>)<sub>n</sub>-NH-C<sub>1-4</sub>-alkyl, -(CH<sub>2</sub>)<sub>n</sub>-N(C<sub>1-4</sub>-alkyl)<sub>2</sub>, or -(CH<sub>2</sub>)<sub>n</sub>-NHCOOR<sup>9</sup>, wherein n=1, 2, 3 or 4;



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R<sup>9</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl, C<sub>2-4</sub>-alkynyl, a benzyl or phenyl group which is optionally mono- or polysubstituted by -OCH<sub>3</sub>;

R<sup>10</sup> denotes C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl, C<sub>2-4</sub>-alkynyl, optionally methoxy-substituted phenyl, optionally methoxy-substituted benzyl, C<sub>3-6</sub>-cycloalkyl;

R<sup>11</sup> denotes hydrogen, C<sub>1-3</sub>-alkyl, -COOR<sup>9</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -CONR<sup>7</sup>R<sup>8</sup> or optionally methoxy-substituted phenyl,

or a racemate thereof, an enantiomer thereof, a diastereomer thereof, a mixture thereof or a pharmacologically acceptable acid addition salt thereof.

#### Prior art

The first and only two representatives of the category of imidazotriazolopyrimidine derivatives according to general formula (I) have been known in the prior art since the middle of the sixties (E. Tenor and C.-F. Kroger, Chem. Ber. Vol. 97 (1964), page 1373-1382). They have a methyl



substituent at position 7 of general formula (I) and an ethyl or n-propyl group at position 2.

#### Background of the invention

- 5 Surprisingly, it has been found that imidazotriazolopyrimidines of general formula I have an affinity for adenosine receptors and thus constitute a new category of adenosine antagonists.
- 10 Adenosine antagonists may have a therapeutically useful effect in those cases where diseases or pathological situations are connected with the activation of adenosine receptors.
- 15 Adenosine is an endogenous modulator with predominantly inhibitory effects in the CNS, in the heart, in the kidneys and other organs. The effects of adenosine are mediated via at least three receptor sub-types: adenosine A<sub>1</sub>, A<sub>2</sub> and A<sub>3</sub> receptors. Adenosine A<sub>2</sub> receptors are
- 20 further subdivided into two subtypes, A<sub>2a</sub> and A<sub>2b</sub>. The two A<sub>2</sub> receptor subtypes can be differentiated, e.g. because specific adenosine antagonists such as CGS 21680 stimulate predominantly only the A<sub>2a</sub> subtype. It is presumed that the A<sub>2b</sub> subtype has a relatively low affinity for
- 25 adenosine. For this reason, relatively high concentrations of adenosine are necessary in order to stimulate this subtype. Such high concentrations would be expected, for example, in the epithelial surface fluid in the lungs of asthmatics or in ischaemic tissue damage.
- 30
- In the CNS, adenosine develops inhibitory effects mainly by activating A<sub>1</sub> receptors: presynaptically by inhibiting



the synaptic transmission (inhibiting the release of neurotransmitters such as acetylcholine, dopamine, noradrenaline, serotonin, glutamate, etc.), and postsynaptically by inhibiting neuronal activity.

5

A<sub>1</sub> antagonists cancel out the inhibitory effects of adenosine and promote neuronal transmission and neuronal activity.

10 A<sub>1</sub> antagonists are thereof of great interest for treating degenerative diseases of the central nervous system such as senile dementia of the Alzheimer's type and age-related disorders of memory and learning capacity.

15 The disease includes, in addition to forgetfulness in its mild form and total helplessness and absolute dependence on care in its severe form, a number of other accompanying symptoms such as sleep disorders, motor co-ordination disorders ranging up to Parkinson's syndrome, in addition  
20 to increased emotional instability and depressive symptoms. The disease is progressive and can lead to death. The treatments used hitherto have been unsatisfactory. At present there are no specific therapeutic agents at all. Attempts at treatment with  
25 acetylcholinesterase inhibitors show an effect in only a small proportion of the patients, but involve a high level of side effects.

The pathophysiology of Alzheimer's disease and SDAT is  
30 characterised by a severe deterioration of the cholinergic system, but other transmitter systems are also affected. As a result of the loss of presynaptic cholinergic and



other neurones and the resulting lack of preparation of neurotransmitters the neuronal transmission and neuronal activity in the areas of the brain essential for learning and memory are significantly reduced.

5

Selective adenosine A<sub>1</sub> receptor antagonists promote neuronal transmission by the increased production of neurotransmitters, increase the excitability of postsynaptic neurones and can therefore counteract the  
10 symptoms of the disease.

The high receptor affinity and selectivity of some of the compounds claimed ought to make it possible to treat Alzheimer's disease and SDAT with low doses, so that  
15 hardly any side effects need be expected which cannot be put down to the blockade of A<sub>1</sub> receptors.

Another indication for centrally-acting adenosine A<sub>1</sub> antagonists is depression. The therapeutic success of  
20 antidepressant substances appears to be linked to the regulation of A<sub>1</sub> receptors. A<sub>1</sub> antagonists may lead to the regulation of adenosine A<sub>1</sub> receptors and thus offer a new therapeutic approach to the treatment of depressive patients.

25

Other areas of use for A<sub>2</sub> selective adenosine antagonists, in particular, are neurodegenerative diseases such as Parkinson's disease and also migraine. Adenosine inhibits the release of dopamine from central synaptic endings by  
30 interacting with dopamine-D<sub>2</sub> receptors. A<sub>2</sub> antagonists increase the release and availability of dopamine and thus



offer a new therapeutic approach to the treatment of Parkinson's disease.

In migraine, the vasodilatation of cerebral blood vessels mediated by  $A_2$  receptors appears to be involved. Selective  $A_2$  antagonists inhibit the vasodilatation and can therefore be useful in treating migraine.

Adenosine antagonists may also be used for treating peripheral indications.

For example, the activation of  $A_1$ ,  $A_2$  or  $A_3$  receptors in the lung may lead to bronchoconstriction. Selective adenosine  $A_1$  antagonists relax the tracheal smooth muscle, cause bronchodilatation and can thus be useful as antiasthmatic agents.

Adenosine  $A_2$  or  $A_3$  receptors are located on mast cells. Their activation causes the release of mast cell products such as histamine, tryptase or interleukin 8. Adenosine  $A_3$  receptors are found on eosinophiles and the stimulation of these receptors can influence the activation, chemotaxis and apoptosis of eosinophiles. Therefore, antagonists of  $A_2$  or  $A_3$  receptors are very promising for the treatment of allergic diseases such as e.g. rhinitis, urticaria, pruritis, allergic dermatitis, allergic eye diseases and nasal polyps. In addition, the effect of adenosine  $A_2$  or  $A_3$  antagonists on mast cells and eosinophiles may also be helpful in the treatment of asthma. Furthermore, the anti-mast cell activity may be useful for reducing reperfusion damage after cardiac ischaemia.



By activating  $A_2$  receptors, adenosine may cause, *inter alia*, respiratory depression and cessation of breathing.  $A_2$  antagonists bring about respiratory stimulation. For example, adenosine antagonists (theophyllin) are used to  
5 treat respiratory distress and prevent sudden infant death in premature babies.

Adenosine stimulates the production of mucus by epithelial cells. The activation of adenosine  $A_{2b}$  receptors on  
10 bronchial epithelial cells stimulates the chloride transportation which affects the consistency of mucus. Consequently, adenosine antagonists offer new therapeutic approaches to the treatment of diseases in which the quantity or consistency of the mucus is pathological, as  
15 in bronchitis and chronic obstructive pulmonary diseases, for example.

Adenosine  $A_{2b}$  receptors are also located on the epithelial cells of the intestine. In the intestinal cells, too, the  
20 activation of these receptors can lead to increased chloride transportation. It is suspected that during inflammations of the intestines adenosine is released by neutrophiles, for example. The effect of the released adenosine on the chloride transportation influences the  
25 motility and absorption capacity of the intestinal epithelium. As a result, adenosine antagonists are possible therapeutic agents for inflammatory intestinal diseases and diarrhoea.

30 Other important therapeutic fields for adenosine antagonists are cardiovascular diseases and kidney diseases.



In the heart, adenosine inhibits electrical and contractile activity by activating  $A_1$  receptors. Combined with coronary vasodilatation mediated via  $A_2$  receptors, adenosine has a negative chronotropic, inotropic, dromotropic, bathmotropic and bradycardiac effect and reduces the volume of the heart per minute.

Adenosine  $A_1$  receptor antagonists or adenosine  $A_3$  receptor antagonists can prevent the damage caused to the heart and brain or lungs by ischaemia and subsequent reperfusion. As a result, adenosine antagonists can be used for the prevention or early treatment of damage to the heart caused by ischaemia/reperfusion e.g. after coronary bypass surgery, heart transplants, angioplasty or thrombolytic therapy of the heart and similar interventions. Moreover, adenosine antagonists can be used for the early treatment of cerebral ischaemia. The same is true of the lungs.

On the kidneys, the activation of  $A_1$  receptors causes vasoconstriction of afferent arterioles and as a result a drop in renal bloodflow and glomerular filtration.  $A_1$  antagonists act on the kidneys as powerful potassium-saving diuretics and can thus be used to protect the kidneys and to treat oedema, renal insufficiency and acute kidney failure.

On account of the adenosine antagonism on the heart and the diuretic effect,  $A_1$  antagonists can be used to therapeutic effect in various cardiovascular diseases, e.g. in cardiac insufficiency, arrhythmias (bradyarrhythmias) associated with hypoxia or ischaemia, transmission disorders, hypertension, ascites in liver



failure (hepato-renal syndrome) and as an analgesic in circulatory disorders.

Adenosine may stimulate or inhibit cell apoptosis, via the  
5 adenosine A<sub>3</sub> receptors and depending on the type of cell  
and the concentration of the receptor ligand. This effect  
can be reversed by adenosine A<sub>3</sub> receptor antagonists.  
Consequently, adenosine A<sub>3</sub> receptor antagonists are  
possible therapeutic agents for diseases in which a  
10 disruption of apoptosis is involved, such as for example  
inflammatory diseases such as arthritis, autoimmune  
diseases such as lupus erythematosus disseminatus or  
scleroderma and cancer. Types of cancer which overexpress  
the adenosine receptor would be particularly suitable for  
15 treatment with adenosine A<sub>3</sub> receptor antagonists.  
Moreover, adenosine A<sub>3</sub> receptor antagonists may be used to  
promote the immunological protective mechanisms against  
any remaining malignant cancer cells (e.g. after surgical  
removal of a colon carcinoma or other types of tumour).  
20 Cystic fibrosis - also known as mucoviscidosis - is a  
major metabolic disorder caused by a genetic defect on a  
certain chromosome. As a result of increased production  
and greater viscosity of the secretions of the mucosal  
glands in the bronchi, it may lead to severe complications  
25 in the airways. Preliminary investigations have shown  
that A<sub>1</sub> antagonists increase the efflux of chloride ions,  
e.g. in CF PAC cells. On the basis of these findings, it  
may be expected that, in patients suffering from cystic  
fibrosis (mucoviscidosis), the compounds according to the  
30 invention will regulate the disrupted electrolyte balance  
of the cells and alleviate the symptoms of the disease.

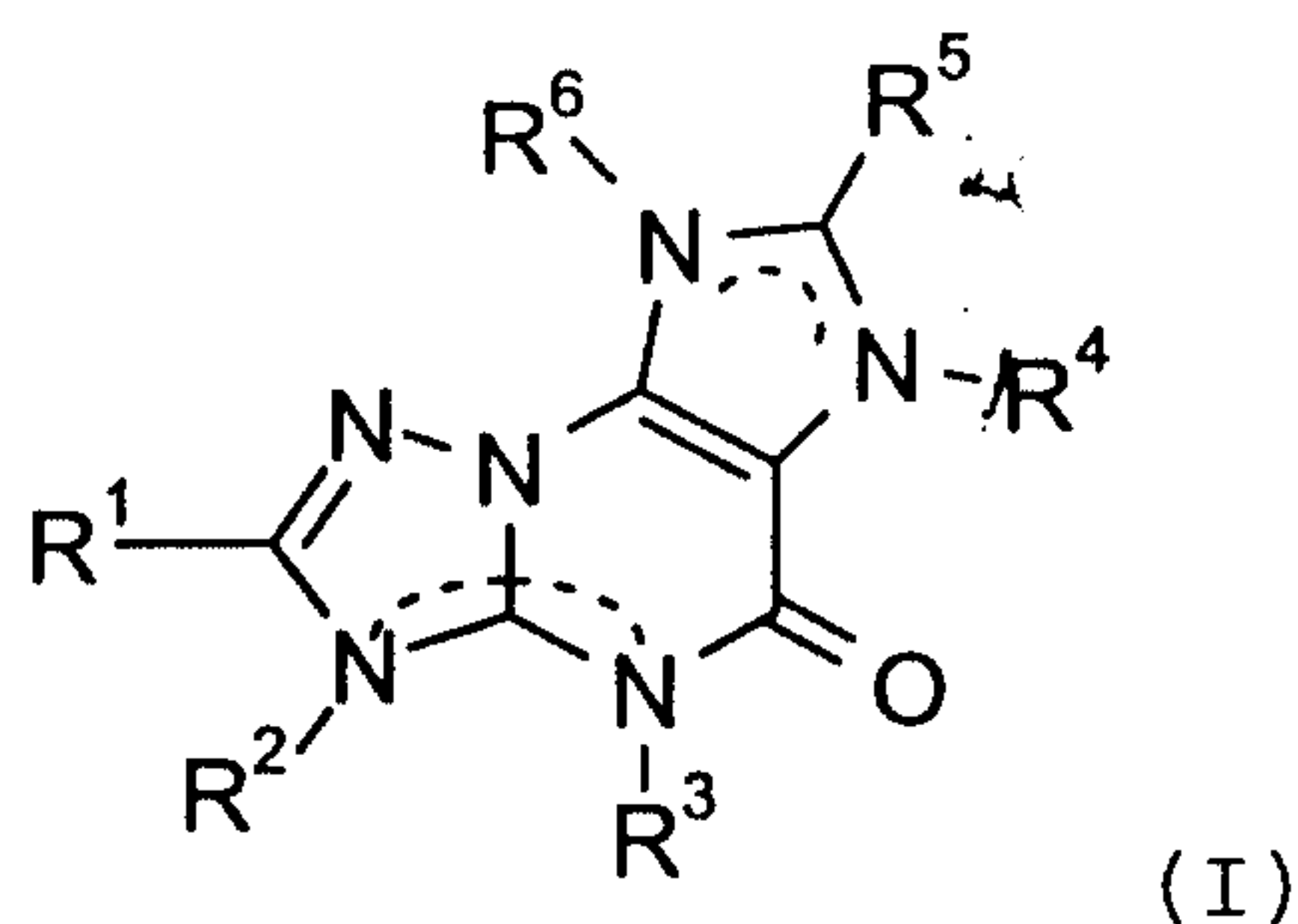


### Detailed description of the invention

The invention relates to new imidazotriazolopyrimidine derivatives, processes for preparing them and their use as pharmaceutical compositions.

5

The new imidazotriazolopyrimidine derivatives have the structure of general formula (I):



10

wherein the dotted lines between the nitrogen atoms of the above general formula I indicate the existence of a double bond in one of two possible positions, so that the groups R<sup>4</sup> and R<sup>6</sup> and R<sup>3</sup> and R<sup>2</sup> need not be present simultaneously

15 and wherein

R<sup>1</sup> denotes hydrogen, a C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl or C<sub>2-8</sub>-alkynyl group which may optionally be mono- or polysubstituted by -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -CHO, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH=NOH, -CH=NOR<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -NHCONHPhenyl, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl- substituted 1,3-dioxolane or 1,3-dioxane, or

25

R<sup>1</sup> denotes -CHO, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup> or NR<sup>7</sup>R<sup>8</sup>, or



$R^1$  denotes  $C_{3-7}$ -cycloalkyl, preferably cyclopentyl or cyclohexyl, which may optionally be substituted by =O, -OR<sup>9</sup>, OCOR<sup>9</sup> or -OCOPyridyl, or

- 5  $R^1$  denotes phenyl which may optionally be substituted by  $C_{1-4}$ -alkyl, preferably methyl, -CN, -COOR<sup>9</sup>, NR<sup>7</sup>R<sup>8</sup>, -OR<sup>9</sup>, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>CONR<sup>7</sup>R<sup>8</sup>, -SO<sub>3</sub>H or halogen, or

- $R^1$  denotes phenyl- $C_{1-6}$ -alkyl, preferably phenyl- $C_{1-4}$ -alkyl,  
 10 phenyl- $C_{2-6}$ -alkenyl or phenyl- $C_{2-6}$ -alkynyl, wherein the phenyl ring may optionally be substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups  $C_{1-3}$ -alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>,  
 15 -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO- $C_{1-4}$ -Alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-  
 20 dioxolane or 1,3-dioxane, or

- $R^1$  denotes  $C_{3-7}$ -cycloalkyl- $C_{1-6}$ -alkyl,  $C_{3-7}$ -cycloalkyl- $C_{2-6}$ -alkenyl,  $C_{3-7}$ -cycloalkyl- $C_{2-6}$ -alkynyl, wherein the cycloalkyl group may optionally be substituted, either  
 25 directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups  $C_{1-3}$ -alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-OCONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO- $C_{1-4}$ -Alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>,  
 30 -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>,



-OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane or 1,3-dioxane, or

R<sup>1</sup> denotes a norbornane, norbornene, C<sub>3-6</sub>-dicycloalkyl-methyl, preferably dicyclopropylmethyl, adamantane or noradamantane group which may optionally be substituted by C<sub>1-4</sub>-alkyl, preferably methyl, or

R<sup>1</sup> denotes a group of formula A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenyl, A-C<sub>2-6</sub>-alkynyl or A-, where A is a C- or N-linked 5-, 6- or 7- membered heterocycle, which contains one or more heteroatoms selected from the group comprising nitrogen, oxygen or sulphur and may optionally be mono- or polysubstituted, preferably monosubstituted, by benzyl, optionally methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -COR<sup>10</sup>, -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, =O, a ketal, ethyleneketal, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup> or halogen;

20

R<sup>2</sup> or R<sup>3</sup> denotes a C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl or C<sub>2-8</sub>-alkynyl group which may optionally be mono- or polysubstituted by -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -CHO, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH=NOH, -CH=NOR<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -NHCONHPhenyl, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane or 1,3-dioxane, or

R<sup>2</sup> or R<sup>3</sup> denotes phenyl-C<sub>1-6</sub>-alkyl, preferably phenyl-C<sub>1-4</sub>-alkyl, phenyl-C<sub>2-6</sub>-alkenyl or phenyl-C<sub>2-6</sub>-alkynyl, wherein the phenyl ring may optionally be substituted, either



directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups C<sub>1-3</sub>-alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>,  
 5 -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane or 1,3-dioxane, or  
 10 R<sup>2</sup> or R<sup>3</sup> denotes a group of formula A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenyl, A-C<sub>2-6</sub>-alkynyl or A-, where A is a C- or N-linked 5-, 6- or 7- membered heterocycle, which contains one or more heteroatoms selected from the group comprising nitrogen, oxygen or sulphur and may optionally be mono- or polysubstituted, preferably monosubstituted, by benzyl, optionally methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, -CN,  
 15 -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -COR<sup>10</sup>, -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, =O, a ketal, ethyleneketal, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup> or halogen;

R<sup>4</sup> or R<sup>6</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl which may optionally be substituted by -NR<sup>7</sup>R<sup>8</sup>, benzyl, but preferably hydrogen;  
 25

R<sup>5</sup> denotes hydrogen, a C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl or C<sub>2-8</sub>-alkynyl group which may optionally be mono- or polysubstituted by -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -CHO, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH=NOH, -CH=NOR<sup>9</sup>,  
 30 -NR<sup>7</sup>R<sup>8</sup>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -NHCONHPhenyl, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, OCONR<sup>7</sup>R<sup>8</sup>, halogen,



optionally methyl-substituted 1,3-dioxolane or 1,3-dioxane, or

5  $R^5$  denotes  $C_{3-7}$ -cycloalkyl, preferably cyclopentyl or cyclohexyl, which may optionally be substituted by =O, -OH, -OR<sup>9</sup>, OCOR<sup>9</sup> or -OCOPyridyl, or

10  $R^5$  denotes phenyl which may optionally be substituted by -OH, halogen, -OR<sup>9</sup>,  $C_{1-4}$ -alkyl, preferably CH<sub>3</sub>, NH<sub>2</sub>, COOH, -SO<sub>3</sub>H, -COOR<sup>9</sup>, -OCH<sub>2</sub>COOR<sup>9</sup>, -CN or -OCH<sub>2</sub>CONR<sup>7</sup>R<sup>8</sup>, or

15  $R^5$  denotes phenyl- $C_{1-6}$ -alkyl, preferably phenyl- $C_{1-4}$ -alkyl, phenyl- $C_{2-6}$ -alkenyl or phenyl- $C_{2-6}$ -alkynyl, wherein the phenyl ring may optionally be substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups  $C_{1-3}$ -alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO- $C_{1-4}$ -alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, 20 -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane or 1,3-dioxane, or

25  $R^5$  denotes a norbornane, norbornene,  $C_{3-6}$ -dicycloalkyl-methyl, preferably dicyclopropylmethyl, adamantane or noradamantane group which may optionally be substituted by  $C_{1-4}$ -alkyl, preferably methyl, or

30  $R^5$  denotes -CHO, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup> or NR<sup>7</sup>R<sup>8</sup>, or



- R<sup>5</sup> denotes C<sub>3-7</sub>-cycloalkyl-C<sub>1-6</sub>-alkyl, C<sub>3-7</sub>-cycloalkyl-C<sub>2-6</sub>-alkenyl, C<sub>3-7</sub>-cycloalkyl-C<sub>2-6</sub>-alkynyl, wherein the cycloalkyl group may optionally be substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups C<sub>1-3</sub>-alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO-C<sub>1-4</sub>-Alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane or 1,3-dioxane, or
- R<sup>5</sup> denotes a group of formula A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenylene, A-C<sub>2-6</sub>-alkynylene or A-, where A is a C- or N-linked 5-, 6- or 7- membered heterocycle, which contains one or more heteroatoms selected from the group comprising nitrogen, oxygen or sulphur and may optionally be mono- or polysubstituted, preferably monosubstituted, by benzyl, optionally methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -COR<sup>10</sup>, -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, =O, a ketal, ethyleneketal, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup> or halogen;

R<sup>7</sup> denotes hydrogen, C<sub>1-8</sub>-alkyl, preferably C<sub>1-4</sub>-alkyl, which may optionally be substituted by -COOR<sup>9</sup>, -COR<sup>10</sup>, -OR<sup>9</sup>, OCOR<sup>9</sup>, amino, phenyl, methoxy-substituted phenyl or amino, or a C<sub>3-6</sub>-cycloalkyl, or



R<sup>7</sup> denotes a 5-, 6- or 7- membered heterocycle C-linked directly or via a C<sub>1-4</sub>-alkyl chain, which contains one, two or three heteroatoms selected from the group comprising nitrogen, oxygen or sulphur and which is optionally mono-  
 5 or polysubstituted, preferably monosubstituted, by benzyl, methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, halogen, -OR<sup>9</sup>, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, =O, SO<sub>3</sub>H or -COOR<sup>9</sup>;

R<sup>8</sup> denotes hydrogen, C<sub>1-8</sub>-alkyl, preferably C<sub>1-4</sub>-alkyl,  
 10 which may optionally be substituted by -COOR<sup>9</sup>, -COR<sup>10</sup>, -OR<sup>9</sup>, OCOR<sup>9</sup>, amino, phenyl, methoxy-substituted phenyl or amino, or a C<sub>3-6</sub>-cycloalkyl, or

R<sup>8</sup> denotes a 5-, 6- or 7- membered heterocycle C-linked  
 15 directly or via a C<sub>1-4</sub>-alkyl chain, which contains one, two or three heteroatoms selected from the group comprising nitrogen, oxygen or sulphur and which is optionally mono- or polysubstituted, preferably monosubstituted, by benzyl, methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, halogen, -OR<sup>9</sup>, -CN,  
 20 -NO<sub>2</sub>, -NH<sub>2</sub>, =O, SO<sub>3</sub>H or -COOR<sup>9</sup>;  
 or

R<sup>7</sup> and R<sup>8</sup> together with the nitrogen atom form a saturated or unsaturated 5- or 6-membered ring which may contain  
 25 nitrogen, oxygen or sulphur as further heteroatoms, whilst the heterocycle may be substituted by a branched or unbranched alkyl group having 1 to 4 carbon atoms, preferably methyl, or may carry one of the groups -CN, -COOR<sup>9</sup>, -CONH<sub>2</sub>, -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup>, halogen or  
 30 -(CH<sub>2</sub>)<sub>n</sub>-phenyl, -(CH<sub>2</sub>)<sub>n</sub>-NH<sub>2</sub>, =O, -OCH<sub>2</sub>-CH<sub>2</sub>-O, -OCH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O, -(CH<sub>2</sub>)<sub>n</sub>-NH-C<sub>1-4</sub>-alkyl, -(CH<sub>2</sub>)<sub>n</sub>-N(C<sub>1-4</sub>-alkyl)<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>-NHCOOR<sup>9</sup>, wherein n=1, 2, 3 or 4;



$R^9$  denotes hydrogen,  $C_{1-4}$ -alkyl,  $C_{2-4}$ -alkenyl,  $C_{2-4}$ -alkynyl, a benzyl or phenyl group which may optionally be mono- or polysubstituted by  $-OCH_3$ ;

5

$R^{10}$  denotes  $C_{1-4}$ -alkyl,  $C_{2-4}$ -alkenyl,  $C_{2-4}$ -alkynyl, optionally methoxy-substituted phenyl, optionally methoxy-substituted benzyl,  $C_{3-6}$ -cycloalkyl;

- 10  $R^{11}$  denotes hydrogen,  $C_{1-3}$ -alkyl,  $-\overset{44}{COOR}^9$ ,  $-CH_2OR^9$ ,  $-CH_2NR^7R^8$ ,  $-CONR^7R^8$  or optionally methoxy-substituted phenyl, optionally in the form of their racemates, their enantiomers, their diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition
- 15 salts thereof.

Preferred compounds of general formula (I) are those wherein

- 20  $R^1$  denotes hydrogen,  $C_{1-8}$ -alkyl which may optionally be substituted by  $-COOH$ ,  $-COO-C_{1-4}$ -alkyl,  $-COO$ -phenyl,  $-COO$ -benzyl,  $-CONR^7R^8$ ,  $-CO-C_{1-4}$ -alkyl- $NR^7R^8$ ,  $-CO-C_{1-4}$ -alkyl,  $-CHO$ ,  $-NR^7R^8$ ,  $=NOH$ ,  $-NHCO-C_{1-4}$ -alkyl,  $-NHCO$ -Phenyl, hydroxy,  $=O$ ,  $C_{1-4}$ -alkoxy, phenyloxy,  $O$ -phenyl- $C_{1-4}$ -alkyloxy, benzyloxy,
- 25  $O$ -benzyl- $O$ - $C_{1-4}$ -alkyloxy,  $-OCO-C_{1-4}$ -alkyl,  $-OCO$ -phenyl,  $-OCO$ -benzyl,  $-OCO$ -pyridyl,  $-O-C_{2-4}$ -alkenyl or halogen, or

$R^1$  denotes  $-CHO$ ,  $-COOH$ ,  $-COO-C_{1-4}$ -alkyl,  $-COO$ -phenyl,  $-COO$ -benzyl,  $-CONR^7R^8$  or an amine of general formula  $NR^7R^8$ , or

30

$R^1$  denotes phenyl which may optionally be substituted by  $C_{1-4}$ -alkyl,  $-CO-C_{1-4}$ -alkyl,  $C_{1-4}$ -alkyl- $NR^7R^8$ ,  $C_{1-4}$ -alkyl- $OH$ ,



C<sub>1-4</sub>-alkyl=NOH, -COOH, -COO-C<sub>1-4</sub>-alkyl, -COO-phenyl, -COO-benzyl, -CONR<sup>7</sup>R<sup>8</sup>, -CO-C<sub>1-4</sub>-alkyl-NH<sub>2</sub>, NR<sup>7</sup>R<sup>8</sup>, hydroxy, C<sub>1-4</sub>-alkyloxy, benzyloxy, phenyloxy, -OCO-C<sub>1-4</sub>-alkyl, -OCO-phenyl, -OCO-benzyl, -OCO-pyridyl, -O-C<sub>2-4</sub>-alkenyl or  
 5 halogen, preferably chlorine or fluorine, or

R<sup>1</sup> denotes a C<sub>3-6</sub>-cycloalkyl or C<sub>3-6</sub>-cycloalkyl-C<sub>1-4</sub>-alkyl group which may optionally be substituted by =O, hydroxy, C<sub>1-4</sub>-alkyl or C<sub>1-4</sub>-alkyloxy, or  
 10

R<sup>1</sup> denotes a norbornane, norbornene, adamantane or noradamantane group which may optionally be substituted by C<sub>1-4</sub>-alkyl, preferably methyl, or

15 R<sup>1</sup> denotes phenyl-C<sub>1-4</sub>-alkyl, preferably benzyl, phenyl-C<sub>2-6</sub>-alkenyl or phenyl-C<sub>2-6</sub>-alkynyl, wherein the phenyl ring may optionally be substituted by C<sub>1-4</sub>-alkyl, -CO-C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, O-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, C<sub>1-4</sub>-alkyl-OH, C<sub>1-4</sub>-alkyl=NOH, -COOH, -COO-C<sub>1-4</sub>-alkyl, -COO-phenyl, -COO-benzyl, -CONR<sup>7</sup>R<sup>8</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, hydroxy, C<sub>1-4</sub>-alkyloxy, benzyloxy, phenyloxy, -OCO-C<sub>1-4</sub>-alkyl, -OCO-phenyl, -OCO-benzyl, -OCO-pyridyl, -O-C<sub>2-4</sub>-alkenyl or  
 20 halogen, preferably chlorine or fluorine, or

25 R<sup>1</sup> denotes a 5- or 6-membered heterocycle optionally C- or N-linked either directly or via a C<sub>1-4</sub>-alkylene bridge, which contains one, two or three heteroatoms selected from the group comprising nitrogen, oxygen or sulphur and which is optionally mono- or polysubstituted by benzyl or C<sub>1-4</sub>-alkyl;  
 30



R<sup>2</sup> or R<sup>3</sup> denotes a C<sub>1-8</sub>-alkyl which may optionally be substituted by -NR<sup>7</sup>R<sup>8</sup>, OH, C<sub>1-4</sub>-alkyloxy, C<sub>3-6</sub>-cycloalkyl or COOH, C<sub>2-8</sub>-alkenyl, phenyl-C<sub>1-4</sub>-alkyl, preferably benzyl, phenyl-C<sub>2-6</sub>-alkenyl or phenyl-C<sub>2-6</sub>-alkynyl, whilst the  
5 phenyl ring may optionally be substituted by hydroxy, C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, -NR<sup>7</sup>R<sup>8</sup> or halogen, preferably chlorine or fluorine, or

R<sup>2</sup> or R<sup>3</sup> denotes a 5- or 6-membered heterocycle optionally  
10 C-or N-linked either directly or via a C<sub>1-4</sub>-alkylene bridge, which contains one, two or three heteroatoms selected from the group comprising nitrogen, oxygen or sulphur and which is optionally mono- or polysubstituted by benzyl or C<sub>1-4</sub>-alkyl;

15

R<sup>4</sup> or R<sup>6</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl which may optionally be substituted by -NR<sup>7</sup>R<sup>8</sup>, or benzyl;

R<sup>5</sup> denotes hydrogen, C<sub>1-8</sub>-alkyl, preferably C<sub>1-6</sub>-alkyl,  
20 which may optionally be substituted by halogen, or

R<sup>5</sup> denotes phenyl which may optionally be substituted by C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, hydroxy, -NR<sup>7</sup>R<sup>8</sup> or halogen, preferably chlorine or fluorine, or

25

R<sup>5</sup> denotes phenyl-C<sub>1-6</sub>-alkyl, preferably benzyl, whilst the phenyl ring may optionally be substituted by C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, hydroxy, -NR<sup>7</sup>R<sup>8</sup> or halogen, preferably chlorine or fluorine, or

30

R<sup>5</sup> denotes an amine of formula -NR<sup>7</sup>R<sup>8</sup>, or



R<sup>5</sup> denotes a 5- or 6-membered heterocycle optionally C- or N- linked either directly or via a C<sub>1-4</sub>-alkylene bridge, which contains one or more heteroatoms selected from the group comprising nitrogen or oxygen and which is optionally substituted by benzyl or C<sub>1-4</sub>-alkyl; or

R<sup>5</sup> denotes a C<sub>3-6</sub>-cycloalkyl which may optionally be substituted by =O, hydroxy, C<sub>1-4</sub>-alkyl or C<sub>1-4</sub>-alkyloxy, or

10 R<sup>5</sup> denotes a norbornane, norbornene, adamantane or noradamantane group which may optionally be substituted by C<sub>1-4</sub>-alkyl, preferably methyl;

15 R<sup>7</sup> denotes hydrogen, a branched or unbranched C<sub>1-4</sub>-alkyl group, or

R<sup>7</sup> denotes a C-linked 5- or 6-membered heterocycle which contains one, two or three heteroatoms selected from the group comprising nitrogen, oxygen or sulphur and which is optionally substituted by benzyl, C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, halogen, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, -OH or =O;

R<sup>8</sup> denotes hydrogen, a branched or unbranched C<sub>1-4</sub>-alkyl group, or

25

R<sup>8</sup> denotes a C-linked 5- or 6-membered heterocycle which contains one, two or three heteroatoms selected from the group comprising nitrogen, oxygen or sulphur and which is optionally substituted by benzyl, C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, halogen, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, -OH or =O;

30

or



R<sup>7</sup> and R<sup>8</sup> together with the nitrogen atom form a saturated or unsaturated 5- or 6-membered ring which may contain nitrogen or oxygen as further heteroatoms, whilst the  
5 heterocycle may be substituted by a branched or unbranched alkyl group having 1 to 4 carbon atoms, preferably methyl, or by a -(CH<sub>2</sub>)<sub>1-4</sub>-phenyl group, preferably benzyl, optionally in the form of their racemates, their enantiomers, their diastereomers and mixtures thereof, and  
10 optionally the pharmacologically acceptable acid addition salts thereof.

Also preferred are the compounds of general formula (I) wherein

15

R<sup>1</sup> denotes hydrogen, C<sub>1-6</sub>-alkyl, preferably C<sub>1-4</sub>-alkyl, which may optionally be substituted by -COO-C<sub>1-4</sub>-alkyl, -CHO, -COOH, COO-C<sub>1-4</sub>-alkyl, COO-phenyl, -COO-benzyl, -CONR<sup>7</sup>R<sup>8</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NHCO-C<sub>1-4</sub>-alkyl,  
20 -NHCO-Phenyl, hydroxy, =O, C<sub>1-4</sub>-alkoxy, phenyloxy, O-phenyl-O-C<sub>1-4</sub>-alkyloxy, benzyloxy, O-benzyl-O-C<sub>1-4</sub>-alkyloxy, -OCO-C<sub>1-4</sub>-alkyl, -OCO-phenyl, -OCO-pyridyl, -OCO-benzyl, -O-C<sub>2-4</sub>-alkenyl or halogen, or

25 R<sup>1</sup> denotes phenyl, whilst the phenyl ring may optionally be substituted by C<sub>1-4</sub>-alkyl, hydroxy, C<sub>1-4</sub>-alkyloxy, NR<sup>7</sup>R<sup>8</sup>, halogen, preferably fluorine or chlorine, or

R<sup>1</sup> denotes phenyl-C<sub>1-3</sub>-alkyl, preferably benzyl, whilst the  
30 phenyl ring may optionally be substituted by C<sub>1-4</sub>-alkyl, -CO-C<sub>1-4</sub>-alkyl, -O-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, C<sub>1-4</sub>-alkyl-OH, -COOH, -COO-C<sub>1-4</sub>-alkyl, -COO-phenyl, -COO-benzyl,



-CONR<sup>7</sup>R<sup>8</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, hydroxy, C<sub>1-4</sub>-alkyloxy, benzyloxy, phenyloxy, -OCO-C<sub>1-4</sub>-alkyl, -OCO-phenyl, -OCO-benzyl, -OCO-pyridyl, -O-C<sub>2-4</sub>-alkenyl or halogen, preferably chlorine or fluorine, or

5

R<sup>1</sup> denotes a cyclopentyl, cyclohexyl, cyclopentanone, cyclohexanone, hydroxycyclopentane or hydroxycyclohexane linked via a single bond or via an alkylene chain having 1 to 4 carbon atoms, or

10

R<sup>1</sup> denotes -CHO, -COOH, -COO-C<sub>1-4</sub>-alkyl, -COO-phenyl, -COO-benzyl, -CO-NH-C<sub>1-4</sub>-alkyl, -CO-N(C<sub>1-4</sub>-alkyl)<sub>2</sub> or -CO-NH-phenyl, or

15

R<sup>1</sup> denotes an amine of general formula NR<sup>7</sup>R<sup>8</sup>, or

R<sup>1</sup> denotes a furan, tetrahydrofuran,  $\alpha$ -pyran,  $\gamma$ -pyran, dioxolane, tetrahydropyran, dioxane, thiophene, thiolane, dithiolane, pyrrole, pyrroline, pyrrolidine, pyrazole, pyrazoline, imidazole, imidazoline, imidazolidine, triazole, pyridine, piperidine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, morpholine, thiomorpholine, oxazole, isoxazole, oxazine, thiazole, isothiazole, thiadiazole, oxadiazole or pyrazolidine  
 20 linked via a single bond or via an alkylene chain with 1 to 4 carbon atoms;  
 25

R<sup>2</sup> or R<sup>3</sup> denotes C<sub>1-7</sub>-alkyl, preferably C<sub>1-5</sub>-alkyl, which may optionally be substituted by -NR<sup>7</sup>R<sup>8</sup>, OH, C<sub>1-4</sub>-alkyloxy, C<sub>3-6</sub>-cycloalkyl, preferably cyclopropyl, or COOH, C<sub>2-5</sub>-alkenyl, C<sub>2-5</sub>-alkynyl, phenyl-C<sub>1-3</sub>-alkyl, preferably benzyl, whilst the phenyl ring may be substituted by C<sub>1-4</sub>-alkyl, -  
 30



NR<sup>7</sup>R<sup>8</sup>, hydroxy, C<sub>1-4</sub>-alkyloxy or halogen, preferably chlorine or fluorine, or

R<sup>2</sup> or R<sup>3</sup> denotes a furan, tetrahydrofuran, -pyran, -  
5 pyran, dioxolane, tetrahydropyran, dioxane, thiophene,  
thiolane, dithiolane, pyrrole, pyrroline, pyrrolidine,  
pyrazole, pyrazoline, imidazole, imidazoline,  
imidazolidine, triazole, pyridine, piperidine, pyridazine,  
pyrimidine, pyrazine, piperazine, triazine, morpholine,  
10 thiomorpholine, oxazole, isoxazole, oxazine, thiazole,  
isothiazole, thiadiazole, oxadiazole or pyrazolidine  
linked via a single bond or via an alkylene chain with 1  
to 4 carbon atoms;

15 R<sup>4</sup> or R<sup>6</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl, preferably C<sub>1-3</sub>-  
alkyl, C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup> or benzyl;

R<sup>5</sup> denotes hydrogen, C<sub>1-6</sub>-alkyl, preferably C<sub>1-4</sub>-alkyl,  
which may optionally be substituted by halogen, or

20

R<sup>5</sup> denotes cyclopentyl, cyclohexyl, cyclopentanone,  
cyclohexanone, hydroxycyclopentane or hydroxycyclohexane,  
or

25 R<sup>5</sup> denotes pyridyl, tetrahydrofuranyl, tetrahydropyranyl,  
furyl or a morpholine, piperidine or piperazine group  
optionally substituted by C<sub>1-4</sub>-alkyl or benzyl, or

R<sup>5</sup> denotes a phenyl group which may optionally be  
30 substituted by C<sub>1-4</sub>-alkyl, halogen or hydroxy, or



R<sup>5</sup> denotes phenyl-C<sub>1-3</sub>-alkyl, preferably benzyl, whilst the phenyl ring may optionally be substituted by C<sub>1-4</sub>-alkyl, -NR<sup>7</sup>R<sup>8</sup>, hydroxy, C<sub>1-4</sub>-alkyloxy or halogen, preferably chlorine or fluorine, or

5

R<sup>5</sup> denotes an amine of general formula -NR<sup>7</sup>R<sup>8</sup>, or

R<sup>5</sup> denotes a norbornene, norbornane, adamantane or noradamantane group which may optionally be substituted by  
10 C<sub>1-4</sub>-alkyl, preferably methyl;

R<sup>7</sup> denotes hydrogen, a branched or unbranched C<sub>1-4</sub>-alkyl group, or

15 R<sup>7</sup> denotes a C-linked pyrrole, pyrrolidine, pyrazole, imidazole, imidazolidine, triazole, pyridine, piperidine, pyrimidine, pyrazine, piperazine, morpholine, oxazole, isoxazole, thiazole, isothiazole or thiadiazole optionally substituted by C<sub>1-4</sub>-alkyl, -NO<sub>2</sub>, -NH<sub>2</sub>, hydroxy, C<sub>1-4</sub>-  
20 alkyloxy, chlorine or bromine;

R<sup>8</sup> denotes hydrogen, a branched or unbranched C<sub>1-4</sub>-alkyl group, or

25 R<sup>8</sup> denotes a C-linked pyrrole, pyrrolidine, pyrazole, imidazole, imidazolidine, triazole, pyridine, piperidine, pyrimidine, pyrazine, piperazine, morpholine, oxazole, isoxazole, thiazole, isothiazole or thiadiazole optionally substituted by C<sub>1-4</sub>-alkyl, -NO<sub>2</sub>, -NH<sub>2</sub>, hydroxy, C<sub>1-4</sub>-  
30 alkyloxy, chlorine or bromine;

or



R<sup>7</sup> and R<sup>8</sup> together with the nitrogen atom form a saturated or unsaturated 5- or 6-membered ring which may contain nitrogen or oxygen as further heteroatoms, whilst the  
5 heterocycle may be substituted by a branched or unbranched alkyl group having 1 to 4 carbon atoms, preferably methyl, or by a -(CH<sub>2</sub>)<sub>1-4</sub>-phenyl group, preferably benzyl,

optionally in the form of their racemates, their  
10 enantiomers, their diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

Preferred compounds according to the invention are  
15 compounds of general formula (I) wherein

R<sup>1</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl, which may optionally be substituted by -NHCO-C<sub>1-4</sub>-alkyl, -NR<sup>7</sup>R<sup>8</sup>, hydroxy, C<sub>1-4</sub>-alkyloxy, fluorine, chlorine or bromine, -CHO, -COOH,  
20 -COO-C<sub>1-4</sub>-alkyl, phenyl, phenyl-C<sub>1-3</sub>-alkyl, preferably benzyl which may optionally be substituted by C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, -O-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, hydroxy, benzyloxy or fluorine, phenyloxy-C<sub>1-3</sub>-alkyl, preferably phenyloxymethyl, which may optionally be substituted by methoxy, benzyl  
25 -C<sub>1-3</sub>-alkyl, preferably [benzyloxymethyl] which may optionally be substituted by methoxy, benzoyloxymethyl, pyridylcarbonyloxymethyl, cyclohexylmethyl, pyridylmethyl, pyrrolylmethyl, morpholinomethyl, cyclopentyl or furyl;

30 R<sup>2</sup> or R<sup>3</sup> denotes C<sub>1-5</sub>-alkyl, which may optionally be substituted by hydroxy, methoxy or cyclopropyl, C<sub>2-4</sub>-alkenyl, C<sub>2-4</sub>-alkynyl or benzyl;



R<sup>4</sup> or R<sup>6</sup> denotes hydrogen, C<sub>1-3</sub>-alkyl, C<sub>1-3</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, N-morpholinoethyl or benzyl;

- 5 R<sup>5</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl, optionally fluorine-substituted, pyridyl, piperidinyl, morpholinyl, piperazinyl, 4-benzylpiperazinyl, furyl, tetrahydrofuranyl, tetrahydropyranyl, NR<sup>7</sup>R<sup>8</sup>, cyclopentyl, cyclohexyl, adamantyl, noradamantyl, norbornyl  
10 norbornenyl, phenyl or benzyl, wherein the phenyl ring may optionally be substituted by fluorine

R<sup>7</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl or pyridyl;

- 15 R<sup>8</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl or pyridyl

optionally in the form of their racemates, their enantiomers, their diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition  
20 salts thereof.

Also preferred according to the invention are compounds of general formula (I) wherein

- 25 R<sup>1</sup> denotes hydrogen, methyl, which may optionally be substituted by -NH<sub>2</sub>, -NHMe, -NMe<sub>2</sub>, -N(i-propyl)<sub>2</sub>, -NHAcetyl, hydroxy, methoxy, ethoxy, phenyloxy, methoxyphenyloxy, methoxybenzyloxy, morpholine, benzoyloxy, pyridylcarbonyloxy, pyridine, pyridylamino,  
30 methylpiperazine or pyrrole; ethyl which may optionally be substituted by -NH<sub>2</sub> or hydroxy, n-propyl, isopropyl, n-butyl, tert. butyl, cyclopentyl, cyclohexylmethyl, benzyl



which may optionally be substituted by hydroxy, methoxy, benzyloxy -C<sub>1-3</sub>-alkyl, preferably benzyloxymethyl, dimethylaminoethoxy, N-morpholinoethoxy or fluorine, phenyl, phenylethyl, -COOH, -COOMethyl, -COOPropyl,  
5 -COOButyl or furan;

R<sup>2</sup> or R<sup>3</sup> denotes methyl, which may optionally be substituted by cyclopropyl, ethyl which may optionally be substituted by hydroxy or methoxy, n-propyl, isopropyl, n-  
10 butyl, isobutyl, tert. butyl, butenyl, n-pentyl, allyl or propargyl;

R<sup>4</sup> or R<sup>6</sup> denotes hydrogen, methyl or ethyl, which may optionally be substituted by morpholine;  
15

R<sup>5</sup> denotes hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, tert. butyl, phenyl, benzyl, pyridine, piperidine, morpholine, piperazine, 4-benzylpiperazinyl, tetrahydrofuranyl, tetrahydropyranyl, -NMe<sub>2</sub>, cyclopentyl,  
20 cyclohexyl, adamantyl, noradamantyl, norbornanyl or norbornenyl,

optionally in the form of their racemates, their enantiomers, their diastereomers and mixtures thereof, and  
25 optionally the pharmacologically acceptable acid addition salts thereof.

Particularly preferred according to the invention are compounds of general formula (I) wherein  
30

R<sup>1</sup> denotes methyl which may optionally be substituted by -NH<sub>2</sub>, -NHMe, -N(i-propyl)<sub>2</sub>, -NHAcetyl, hydroxy, phenyloxy,



methylnpiperazine or pyrrole; ethyl which may optionally be substituted by -NH<sub>2</sub> or hydroxy, cyclopentyl, benzyl which may optionally be substituted by hydroxy, methoxy, benzyloxy, dimethylaminoethoxy, N-morpholinoethoxy or  
5 fluorine, phenylethyl, -COOH, -COOPropyl, -COOButyl or furan;

R<sup>2</sup> or R<sup>3</sup> denotes methyl which may optionally be substituted by cyclopropyl, ethyl which may optionally be substituted by hydroxy or methoxy, n-propyl, isopropyl, n-  
10 butyl, isobutyl, butenyl, n-pentyl/ allyl or propargyl;

R<sup>4</sup> or R<sup>6</sup> denotes hydrogen, methyl or ethyl, which may optionally be substituted by morpholine;

15

R<sup>5</sup> denotes methyl, ethyl, n-propyl, tert. butyl, cyclopentyl or norbornenyl,

optionally in the form of their racemates, their  
20 enantiomers, their diastereomers and mixtures thereof, and optionally the pharmacologically acceptable acid addition salts thereof.

Especially preferred according to the invention are  
25 compounds of general formula (I) wherein

R<sup>1</sup> denotes methyl, which may optionally be substituted by phenyloxy or pyrrole; benzyl which may optionally be substituted by hydroxy, methoxy, dimethylaminoethoxy or  
30 fluorine, cyclopentyl, furan or phenylethyl;

R<sup>2</sup> or R<sup>3</sup> denotes ethyl, n-propyl, allyl or propargyl;

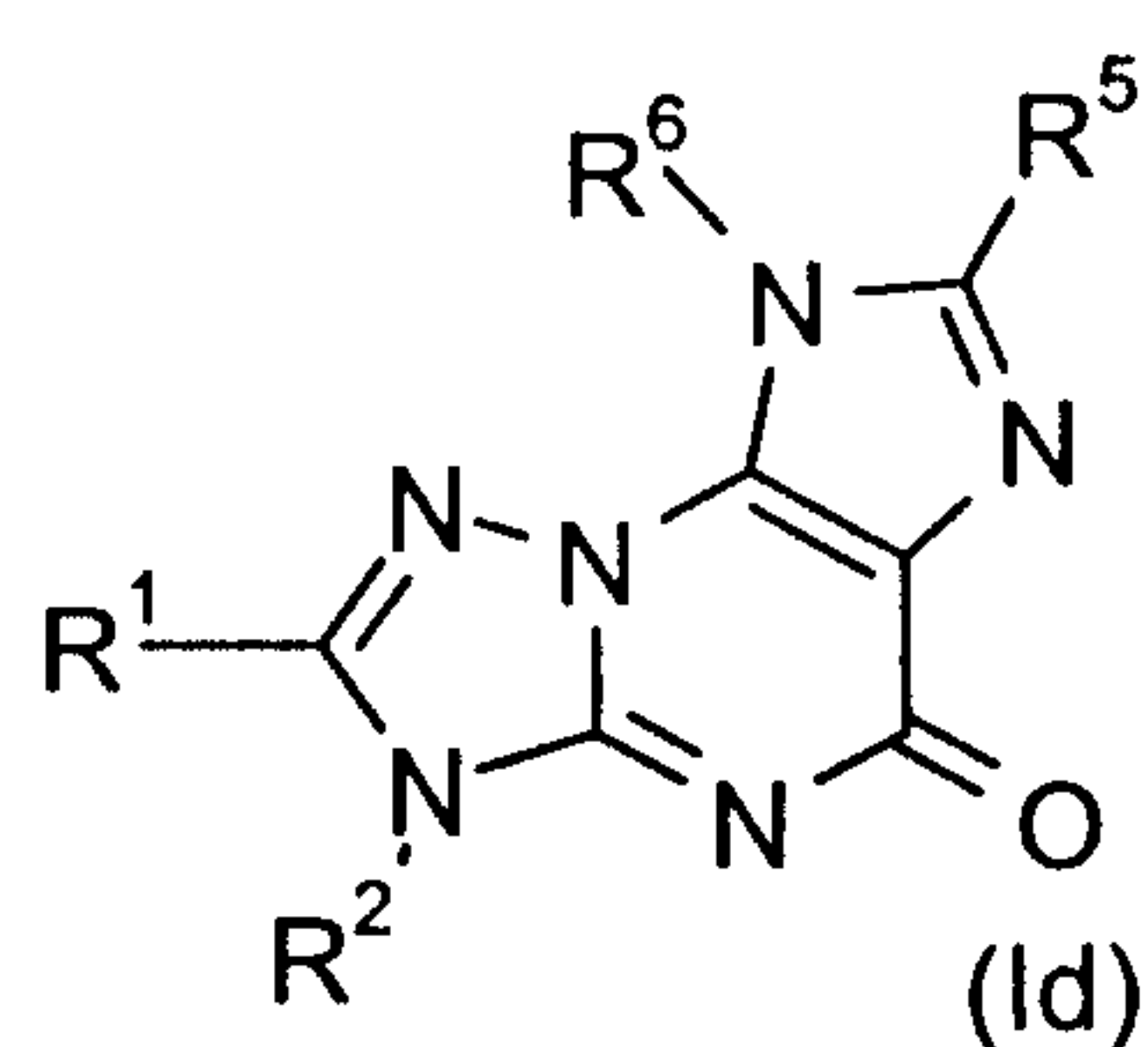
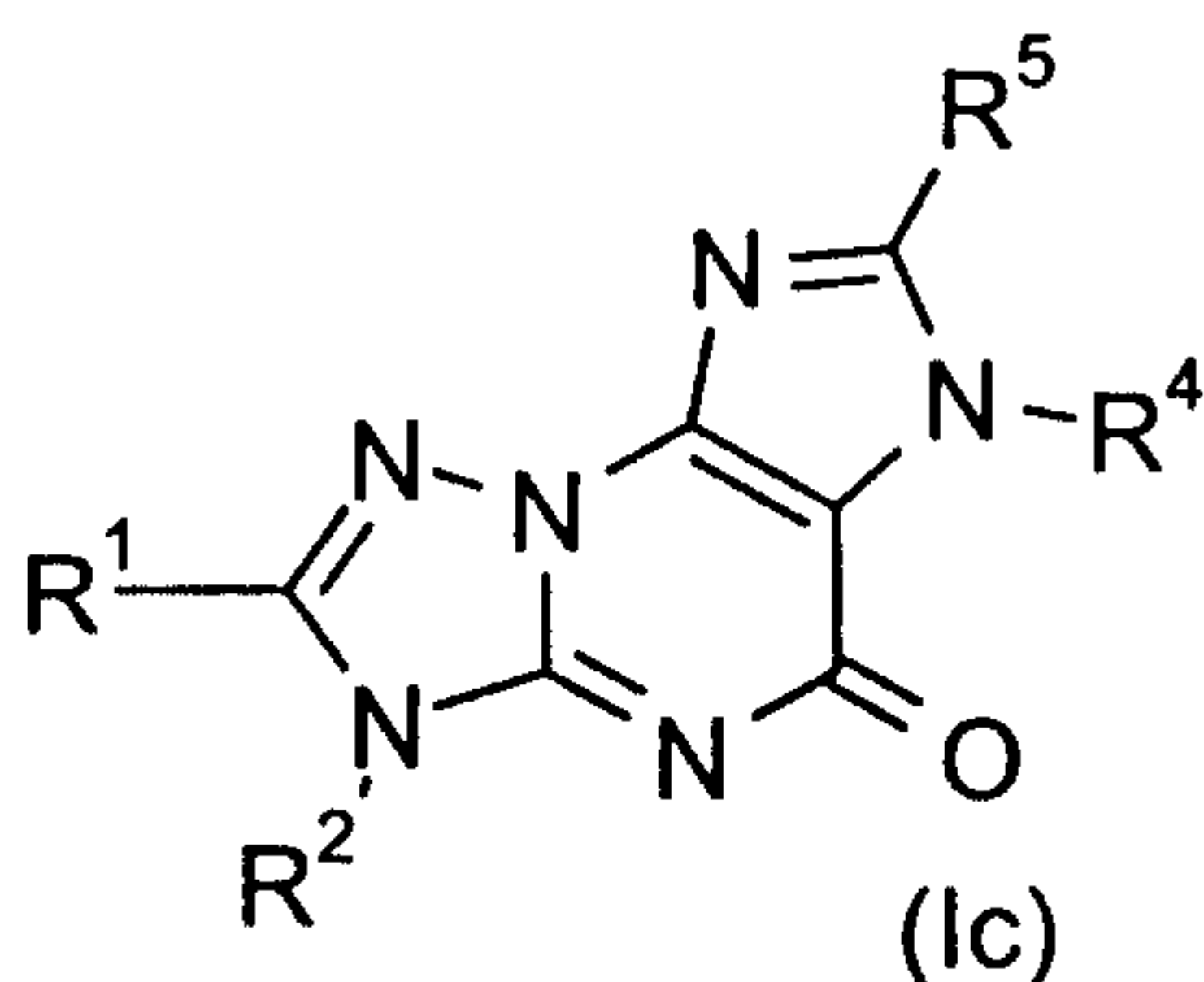
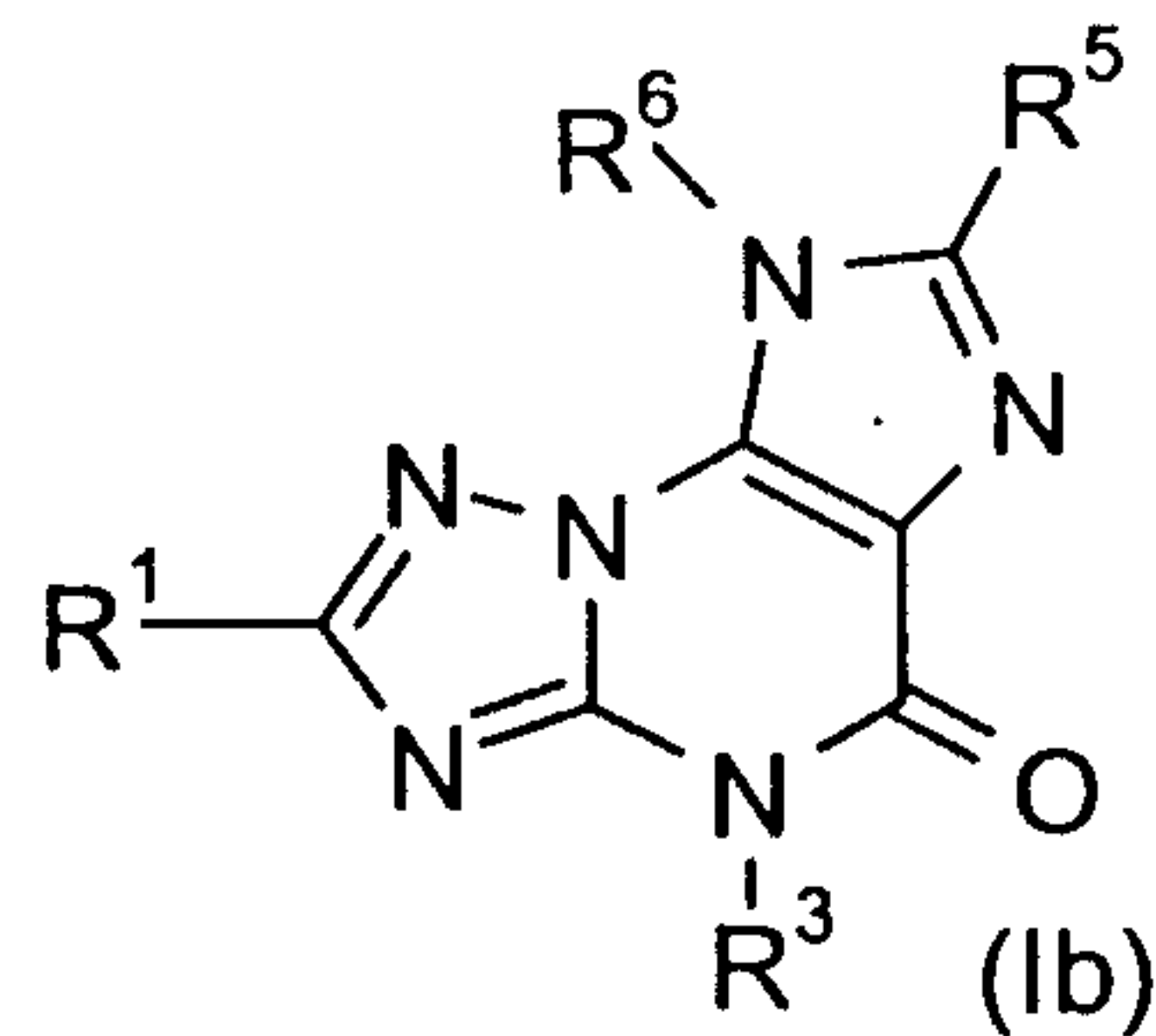
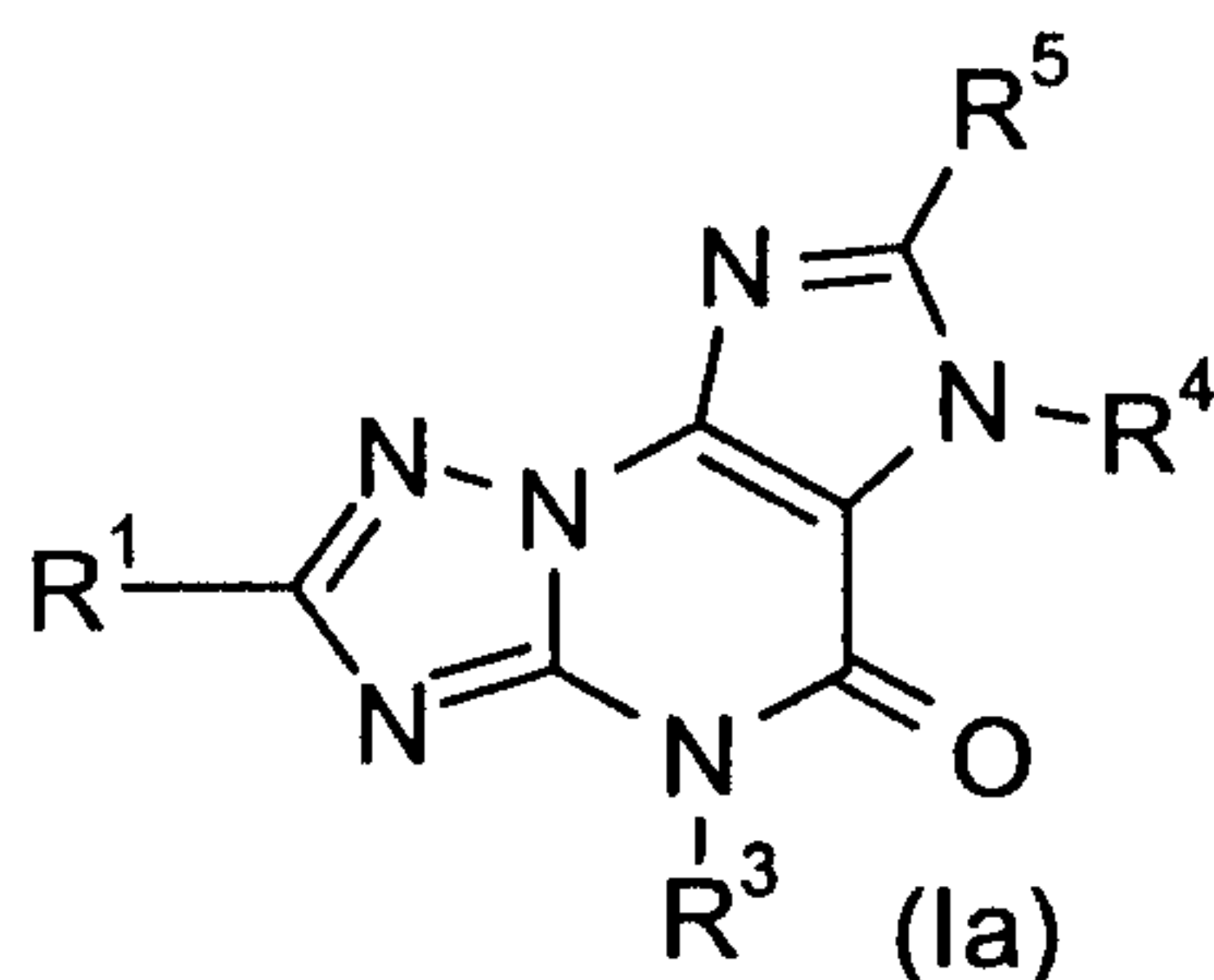


$R^4$  or  $R^6$  denotes hydrogen;

$R^5$  denotes methyl, ethyl, n-propyl, tert. butyl,  
5 cyclopentyl or norbornenyl,

optionally in the form of their racemates, their  
enantiomers, their diastereomers and mixtures thereof, and  
optionally the pharmacologically acceptable acid addition  
10 salts thereof.

The compounds of general formula (I) form the following  
isomers:



the isomers of general formulae (Ia) and (Ib) being  
particularly preferred, especially those wherein  $R^4$  or  $R^6$   
20 are hydrogen or  $C_{1-4}$ -alkyl. Particularly preferred are  
compounds of general formula (Ia) and (Ib) wherein  $R^4$  and  
 $R^6$  denote hydrogen - in this case the isomers (Ia) and  
(Ib) are tautomers. According to the invention, the



particularly preferred compounds are the isomers (Ia), especially those which have a substituent in positions 2, 4 and 7.

5 The following compounds are of special interest according to the invention:

- 2-cyclopentyl-4,7-di-n-propyl-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one
- 10 2-benzyl-7-methyl-4-n-propyl-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one /
- 4-ethyl-7-methyl-2-(2-phenylethyl)-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one
- 4-ethyl-2-(2-phenylethyl)-7-n-propyl-imidazo[4,5-e]-s-
- 15 triazolo[1,5-a]pyrimidin-5-one
- 7-t-butyl-4-ethyl-2-(4-hydroxybenzyl)-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one
- 7-t-butyl-4-ethyl-2-(4-methoxybenzyl)-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one
- 20 7-cyclopentyl-4-ethyl-2-phenyloxymethyl-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one
- 7-cyclopentyl-4-ethyl-2-(N-pyrrolylmethyl)-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one
- 2-(2-furanyl)-7-methyl-4-n-propyl-imidazo[4,5-e]-s-
- 25 triazolo[1,5-a]pyrimidin-5-one
- 2-(2-furanyl)-4,7-di-n-propyl-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one
- 2-cyclopentyl-7-ethyl-4-(1-propen-3-yl)-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one
- 30 2-cyclopentyl-7-ethyl-4-(1-propyn-3-yl)-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one



If desired, the compounds of general formula (I) may be converted into their salts, more particularly, for pharmaceutical use, into their physiologically acceptable salts with an inorganic or organic acid. Suitable acids include for example succinic acid, hydrobromic acid, acetic acid, fumaric acid, maleic acid, methanesulphonic acid, lactic acid, phosphoric acid, hydrochloric acid, sulphuric acid, tartaric acid or citric acid. Mixtures of the abovementioned acids may also be used.

Suitable alkyl groups (including those which are components of other groups) are branched and unbranched alkyl groups having 1 to 8 carbon atoms, preferably 1 to 4 carbon atoms, such as: methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec. butyl, tert. butyl, pentyl, isopentyl, hexyl, heptyl and octyl. In some cases the abbreviations Me, Et, n-Pr, i-Pr, n-Bu, i-Bu, t-Bu, etc. are used for the abovementioned groups.

Suitable alkenyl groups (including those which are components of other groups) are branched and unbranched alkenyl groups having 2 to 8 carbon atoms, preferably 2 to 4 carbon atoms, provided that they have at least one double bond, as well as the abovementioned alkyl groups, for example, provided that they have at least one double bond, such as vinyl (provided that no unstable enamines or enolethers are formed), propenyl, isopropenyl, butenyl, pentenyl and hexenyl.

Suitable alkynyl groups (including those which are components of other groups) are alkynyl groups having 2 to



8 carbon atoms, provided that they have at least one triple bond, such as ethynyl, propargyl, butynyl, pentynyl and hexynyl.

- 5 Suitable cycloalkyl groups having 3 to 6 carbon atoms include, for example, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, which may also be substituted by branched or unbranched alkyl having 1 to 4 carbon atoms, hydroxy, and/or halogen or as hereinbefore defined. Halogen  
10 generally denotes fluorine, chlorine, bromine or iodine.

Examples of N-linked cyclic groups of general formula  $NR^7R^8$  include: pyrrole, pyrroline, pyrrolidine, piperidine, morpholine, thiomorpholine, imidazole,  
15 imidazoline, imidazolidine, pyrazole, pyrazoline, pyrazolidine, preferably morpholine, piperazine and piperidine, whilst the abovementioned heterocycles may also be substituted by benzyl, alkyl having 1 to 4 carbon atoms, preferably methyl, or as specified in the  
20 definitions.

Examples of C-linked 5- or 6-membered heterocyclic rings which may contain, nitrogen, oxygen or sulphur as heteroatoms, include, for example, furan, tetrahydrofuran,  
25 tetrahydrofuranone, -butyrolactone, -pyran, -pyran, dioxolane, tetrahydropyran, dioxane, thiophene, dihydrothiophene, thiolane, dithiolane, pyrrole, pyrroline, pyrrolidine, pyrazole, pyrazoline, imidazole, imidazoline, imidazolidine, triazole, tetrazole, pyridine,  
30 piperidine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, tetrazine, morpholine, thiomorpholine, oxazole, isoxazole, oxazine, thiazole, isothiazole, thiadiazole,

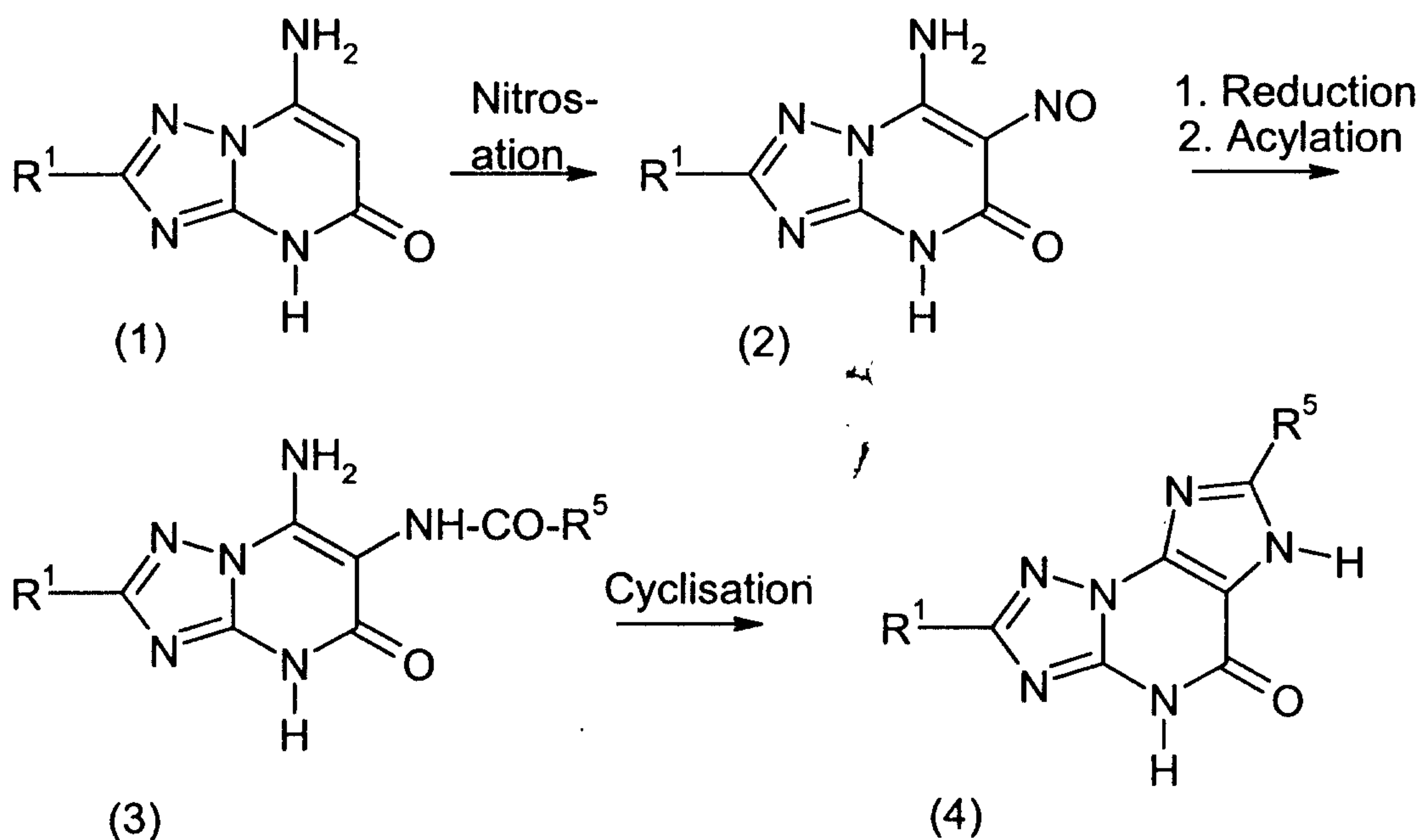


oxadiazole or pyrazolidine, whilst the heterocycle may be substituted as specified in the definitions.

=O denotes an oxygen atom linked via a double bond.



The compounds according to the invention may be prepared as described in the prior art (Tenor et al., Chem. Ber. Vol. 97 (1964) p. 1373-1382), to which reference is hereby made (diagram 1).



5

#### Diagram 1:

The above method of synthesis already disclosed in the prior art can be used to prepare the compounds of general formula (I) according to the invention wherein the groups  $R^2$  or  $R^3$  and  $R^4$  or  $R^6$  denote hydrogen. In this case, the compounds of general formula (I) are tautomers, one tautomeric form of which is represented by formula (4) in diagram 1. The triazolopyrimidones referred to as compounds (1) in diagram 1 may be prepared by reacting cyanoacetic ester derivatives with suitably substituted 3-amino-1,2,4-triazoles as described by Tenor et al. In the introduction. The latter compounds can be obtained by methods known from the literature (J. Org. Chem. 1926, p.

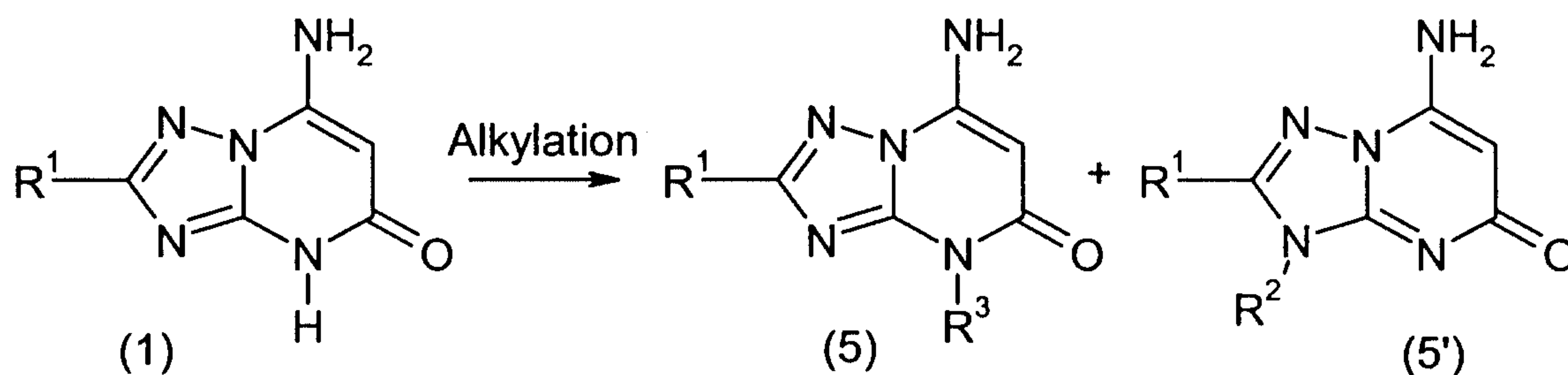
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1729; Org. Synthesis 26, p. 11; J. Chem. Soc. 1929, p. 816).

In order to obtain the compounds of general formula (I) wherein the groups  $R^4$  or  $R^6$  and  $R^2$  or  $R^3$  denote something other than hydrogen, the following procedure may be followed:

Before the reaction sequence described in the prior art and shown in diagram 1, the compounds (1) may be derivatised according to diagram 2. According to the invention, alkylation or benzylation is preferred as derivatisation.



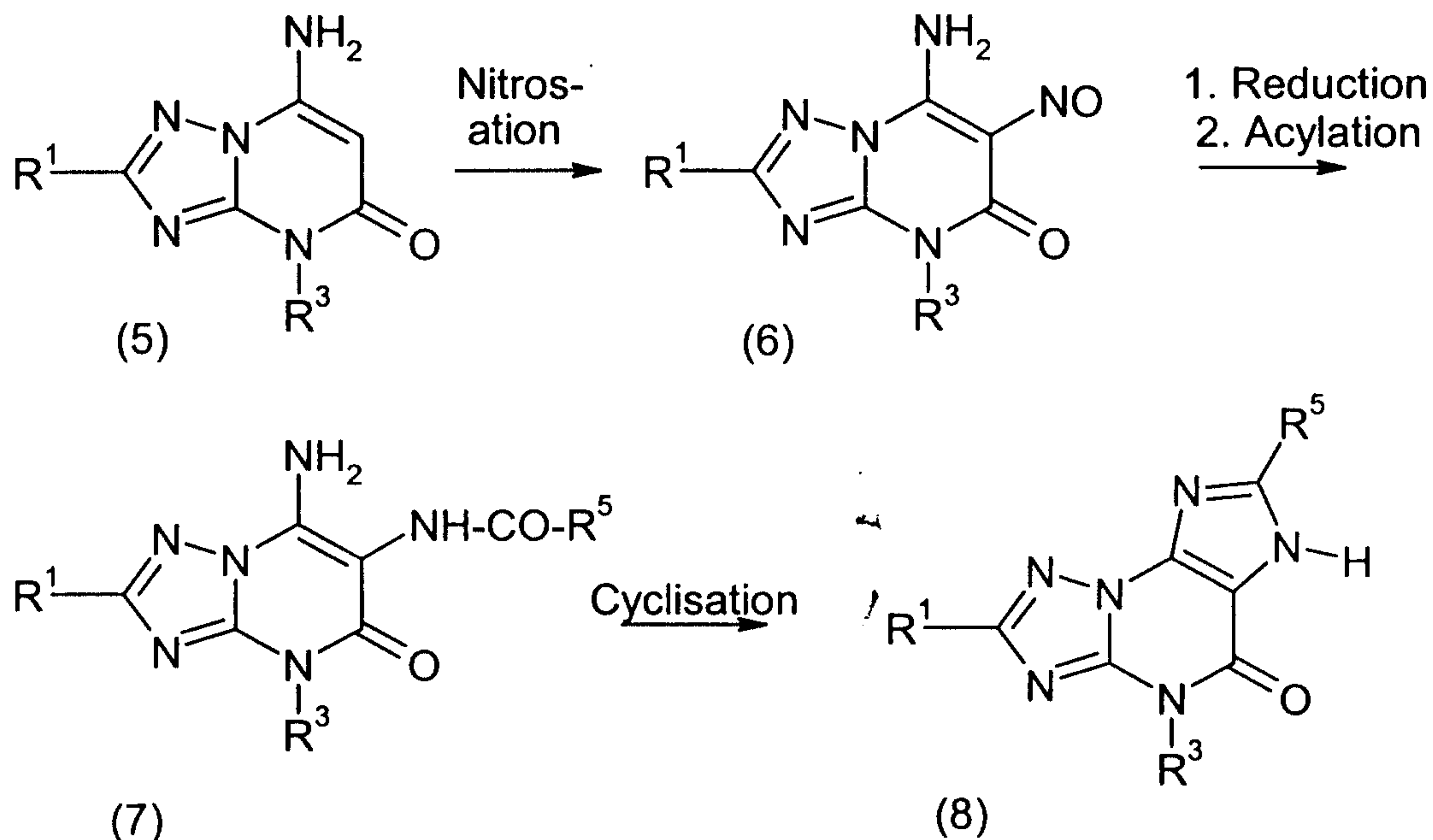
#### Diagram 2:

The alkylation or benzylation to be carried out leads to the compounds (5). The isomeric alkylation products (5') may possibly be obtained as well. Any mixtures of products (5) and (5') obtained can be separated into the pure alkylation products (5) and (5') using purification methods known to the skilled person, such as fractional crystallisation or chromatography.

The compounds (5) and (5') are then subjected to the reaction sequence described by Tenor et al., as shown



diagrammatically for the reaction of compounds (5) in diagram 3.



5

#### Diagram 3:

The procedure described above which can be carried out analogously to the prior art can be used to prepare the compounds of general formula (I) according to the invention wherein the groups  $R^4$  or  $R^6$  denote hydrogen. In this case, the compounds of general formula (I) are tautomers, one tautomeric form of which is represented by formula (8) in diagram 3.

Starting from the alkylation products (5') the compounds (8') may be obtained accordingly (diagram 4).



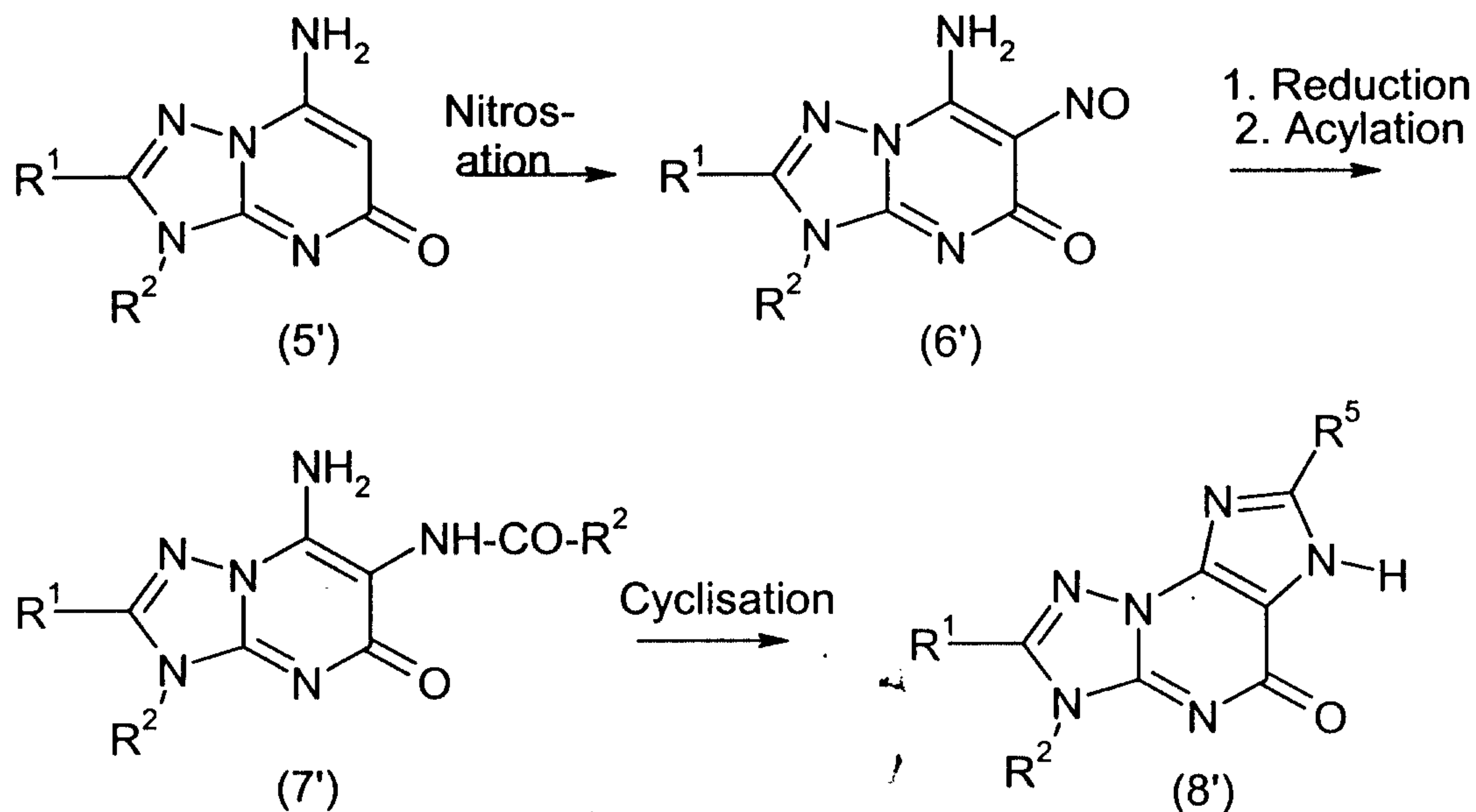


Diagram 4:

- 5 The method of synthesis described above which can be carried out analogously to the prior art can be used to prepare the compounds of general formula (I) according to the invention wherein the groups  $R^4$  or  $R^6$  denote hydrogen. In this case, the compounds of general formula (I) are
- 10 tautomers, one tautomeric form of which is represented by formula (8') in diagram 4.

Compounds (Ia) and (Ib) may be obtained by re-alkylation of the compounds (8) (Diagram 5).

15

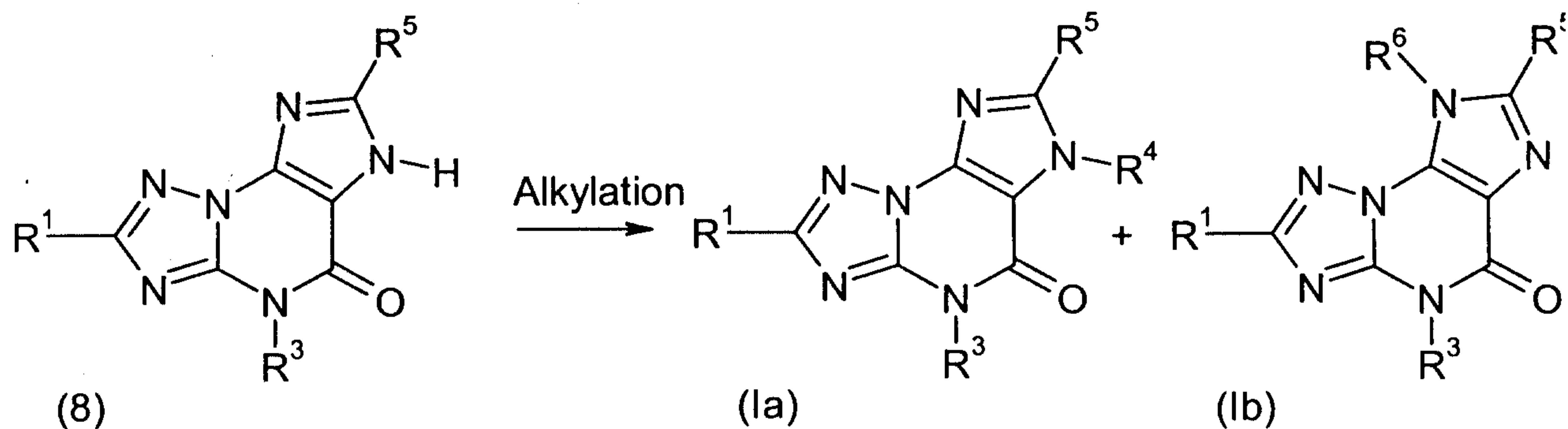


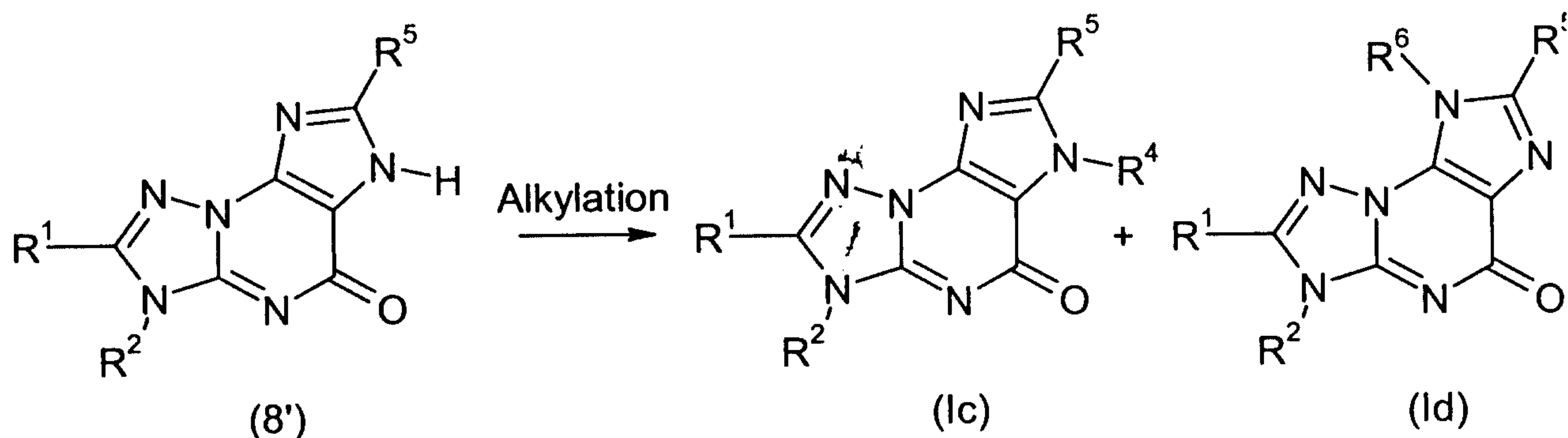


Diagram 5:

Mostly the compounds (Ia) are isolated as the main products.

5

Analogously, the reaction of the derivatives (8') leads to the compounds (Ic) and (Id) (Diagram 6).



10

Diagram 6:

Mostly the compounds (Ic) are isolated as the main products. Depending on the substitution pattern, the compounds (Ia), (Ib), (Ic) or (Id) wherein the groups R<sup>1</sup> to R<sup>6</sup> may be defined as hereinbefore, can be further functionalised using methods known from the literature.

15

These functionalisations comprise the processes familiar to the skilled person, namely oxidation, reduction, ether splitting, acylation, alkylation, etc. Moreover, the use of common protecting groups, especially common hydroxyl and amino protecting groups may be necessary. It is particularly preferable to use the p-methoxybenzyl group as a protecting group for a hydroxyl function, for example, in conjunction with the benzyl group as an amino protecting group.

20  
25



Major differences between the procedure according to the invention and the methods known from the prior art are explained in more detail in the Experimental section which follows, by means of important key stages. The Examples  
5 which follow serve to illustrate the invention without restricting its scope.

Synthesis Example I: 7-cyclopentyl-4-ethyl-2-phenyloxymethyl)-imidazo[4,5-e]-s-triazolo[1,5-a]-  
10 pyrimidin-5-one

Preliminary stages:

Starting with anise alcohol and chloroacetic acid, 4-methoxybenzyloxyacetic acid may be obtained under alkaline  
15 reaction conditions. The experimental procedure for synthesising ethers in this way is known in the art and requires no detailed experimental study. Using methods known from the literature (J. Org. Chem. 1926, p. 1729; Org. Synthesis 26, p. 11; J. Chem. Soc. 1929, p. 816) the  
20 correspondingly substituted 3-aminotriazole derivative may be obtained therefrom by reacting with aminoguanidine, and is then converted into the 7-amino-2-[(4-methoxybenzyl-oxy)methyl]-s-triazolo-[1,5-a]-pyrimidin-5-one by the method disclosed by Tenor et al. (see above).

25

7-amino-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-s-triazolo-  
[1,5-a]-pyrimidin-5-one:

145.6 g of 7-amino-2-[(4-methoxybenzyl-oxy)methyl]-s-triazolo-[1,5-a]-pyrimidin-5-one is dissolved in 1500 ml  
30 of dimethylformamide and mixed with 76.8 g of potassium carbonate. After the addition of 45.2 ml of ethyl iodide



the mixture is stirred for about 1.5 days at ambient temperature. For working up, the dimethylformamide is distilled off *in vacuo* and the residue remaining is taken up in 500 ml of water (distilled), 500 ml of saturated NaCl solution and 1000 ml of dichloromethane. After separation of the organic phase the aqueous phase remaining is extracted three more times with 200 ml of dichloromethane. The combined organic phases are dried over magnesium sulphate and then freed from solvent. About 180 g of a solid remain, which is used in the next step without further purification.

7-amino-4-ethyl-2-[(4-methoxybenzyl-oxy)methyl]-6-nitroso-s-triazolo-[1,5-a]-pyrimidin-5-one

3.7 g of the precursor (7-amino-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-s-triazolo-[1,5-a]-pyrimidin-5-one) are dissolved in 17 ml of dimethylformamide, and 2.69 ml of isoamyl nitrite are added whilst cooling with ice. After the reaction is complete (about 3 hours) 34 ml of water are added at 5-10°C. The solid obtained is separated off, washed with water and diethyl ether and recrystallised from 80 ml of ethanol. 2.0 g of 7-amino-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-6-nitroso-s-triazolo-[1,5-a]-pyrimidin-5-one are left.

6,7-diamino-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-s-triazolo-[1,5-a]-pyrimidin-5-one

At ambient temperature, 1.5 g of 7-amino-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-6-nitroso-s-triazolo-[1,5-a]-pyrimidin-5-one are added to 64 ml of aqueous ammonia solution (25%) and 13 ml of ethanol and dissolved therein. At 30-35°C a solution of 3.3 g of Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> in 30 ml of water is added dropwise. The resulting mixture is stirred



at ambient temperature until the reaction is complete (about 3-4 hours). After cooling in an ice bath, the crystals obtained are suction filtered and dried. 1.2 g of 6,7-diamino-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-s-triazolo-[1,5-a]-pyrimidin-5-one are obtained, which is used in the next step without further purification.

7-amino-6-cyclopentylcarbonylamino-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-s-triazolo-[1,5-a]-pyrimidin-5-one

1.1 g of 6,7-diamino-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-s-triazolo-[1,5-a]-pyrimidin-5-one are taken up in 19 ml of dimethylformamide and 0.7 g of dimethylaminopyridine (DMAP) are added. At 3-5°C 0.5 ml of cyclopentanecarboxylic acid chloride (dissolved in 2 ml of dimethylformamide) are added with stirring. The resulting mixture is stirred for 2 hours at constant temperature. The mixture is kept at ambient temperature with stirring until the reaction is complete (about 12-16 hours). For working up, the dimethylformamide is distilled off in vacuo and the residue remaining is taken up in 20 ml of water and 20 ml of diethyl ether. The solid precipitated is separated off and washed with water and diethyl ether. After the crystals obtained (1.27 g) have been dried, the acylation product thus obtained is used in the next step without further purification.

7-cyclopentyl-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one

1.25 g of the acylation product synthesised earlier are



taken up in 15 ml of water and 7 ml of ethanol and then 3.5 ml of an aqueous sodium hydroxide solution (50%) and 0.95 g of calcium hydroxide are added successively. The mixture thus obtained is stirred at elevated temperature (about 95°C) until the reaction is complete (about 6 hours). For working up, it is cooled (with ice) and mixed with about 20 ml of aqueous 4N HCl solution. The solid precipitated is separated and dried. 1.1 g of 7-cyclopentyl-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one is obtained, pure enough for the following reactions.

6-benzyl-7-cyclopentyl-4-ethyl-2-[(4-methoxybenzyloxy)-methyl]-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one

2.11 g of 7-cyclopentyl-4-ethyl-2-[(4-methoxybenzyloxy)methyl]-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one and 0.76 g of potassium carbonate are taken up in 50 ml of dimethylformamide. 0.65 ml of benzyl bromide are added dropwise with cooling and stirring. The solution obtained is then stirred for 2 to 3 days at ambient temperature. For working up, the dimethylformamide is distilled off *in vacuo* and the residue remaining is taken up in 20 ml of dichloromethane and washed with 20 ml of water. The organic phase is separated off and dried over magnesium sulphate. After the solvent has been distilled off the residue remaining is stirred in 20 ml of diethyl ether. The solid precipitated is separated and dried. 2.6 g of 6-benzyl-7-cyclopentyl-4-ethyl-2-[(4-methoxybenzyloxy)-methyl]-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one are obtained. No further purification is carried out.



6-benzyl-7-cyclopentyl-4-ethyl-2-hydroxymethyl-  
imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one

5 6-benzyl-7-cyclopentyl-4-ethyl-2-[(4-methoxybenzyloxy)-  
methyl]-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one  
(1.03 g) is dissolved in 20 ml of dichloromethane and 1.2  
ml of water are added. At ambient temperature, 2,3-  
dichloro-5,6-dicyanobenzoquinone (DDQ, 0.68 g) is added  
10 with stirring and the mixture is stirred for a further 4  
hours. After the 2,3-dichloro-5,6-dicyanobenzoquinone  
precipitate has been separated off, the remaining solution  
is washed with saturated aqueous sodium hydrogen carbonate  
solution and saturated aqueous sodium chloride solution  
15 and dried over sodium sulphate. The solvent is distilled  
off and the residue remaining is crystallised from diethyl  
ether. 0.74 g of 6-benzyl-7-cyclopentyl-4-ethyl-2-  
hydroxymethyl-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-  
5-one are obtained in the form of slightly reddish  
20 crystals which can be used in the next step without  
further purification.

6-benzyl-2-bromomethyl-7-cyclopentyl-4-ethyl-imidazo[4,5-  
e]-s-triazolo-[1,5-a]-pyrimidin-5-one

25

0.6 g of 6-benzyl-7-cyclopentyl-4-ethyl-2-hydroxymethyl-  
imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one are  
taken up in 7 ml of dichloromethane and 0.25 ml of  
triethylamine are added at ambient temperature with  
30 stirring. Then 0.15 ml of thionyl bromide are added.  
After 2 hours' stirring at constant temperature the  
reaction is complete. For working up, the mixture is  
diluted with 20 ml of dichloromethane and washed



successively with 15 ml of water and 15 ml of aqueous sodium chloride solution. The organic phase is dried over magnesium sulphate and the solvent is distilled off in vacuo. The residue remaining is recrystallised from diethyl ether. 0.45 g of the title compound remain, pure enough to be used in the subsequent reactions.

6-benzyl-7-cyclopentyl-4-ethyl-2-phenyloxymethyl-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one

10

66 mg of sodium hydride (66% in mineral oil) are added to a solution of 0.16 g of phenol in 15 ml of dimethylformamide. After 30 minutes' stirring at ambient temperature, 0.68 g of 6-benzyl-2-bromomethyl-7-cyclopentyl-4-ethyl-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one are added. The mixture is stirred at elevated temperature (about 100°C) until the reaction is complete (about 8 hours). For working up, some water is added and then the solvent is distilled off in vacuo. The residue remaining is taken up in 20 ml of dichloromethane and 20 ml of water. After acidification with aqueous 1N HCl solution, the organic phase is separated off, washed with water and dried over magnesium sulphate. The solvent is distilled off and the residue remaining is recrystallised from diethyl ether. 0.6 g of the title compound remain, pure enough to be used in the subsequent reactions.

30

7-cyclopentyl-4-ethyl-2-phenyloxymethyl-imidazo[4,5-e]-s-triazolo[1,5-a]pyrimidin-5-one

0.6 g of 6-benzyl-7-cyclopentyl-4-ethyl-2-phenyloxymethyl-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one are hydrogenated in 30 ml of methanol on 0.1 g of Pearlman catalyst (60°C, 5 bar). After separation of the catalyst,



the residue is evaporated to dryness. The title compound is purified by chromatography on silica gel (dichloromethane:methanol 99:1). Using the above method, 0.2 g of the title compounds were obtained (melting point 5 229°C).

Synthesis Example II: 7-cyclopentyl-4-ethyl-2-(methylaminomethyl)-imidazo[4,5-e]-s-triazolo[1,5-a]-pyrimidin-5-one

10

6-benzyl-7-cyclopentyl-4-ethyl-2-formyl-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one

0.3 g of 6-benzyl-7-cyclopentyl-4-ethyl-2-hydroxymethyl-  
15 imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one (for preparation see Synthesis Example I) are dissolved in 1.1 ml of dichloromethane and 0.45 g of pyridinium dichromate are added. The brown suspension obtained is stirred for about 24 hours at ambient temperature. The solvent is  
20 distilled off and the residue remaining is stirred with an ethyl acetate/cyclohexane mixture (2:1.5 ml). The clear, light yellow supernatant solution is filtered through silica gel. After the solvent has been distilled off, 0.15 g of the title compound are left in the form of a  
25 colourless resin.

6-benzyl-7-cyclopentyl-4-ethyl-2-(methylaminomethyl)-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one

30 0.5 g of 6-benzyl-7-cyclopentyl-4-ethyl-2-formyl-imidazo[4,5-e]-s-triazolo-[1,5-a]-pyrimidin-5-one are hydrogenated, together with 0.1 g of methylamine, in 30 ml



of methanol on 50 mg of 10% palladium on charcoal (5 bar, 20°C, 3 hours). For working up, the catalyst is filtered off and the solvent is distilled off *in vacuo*. The product is purified by chromatography on silica gel  
5 (dichloromethane:methanol 95:5) and yields 0.42 g of the title compound in the form of a colourless oil.

7-Cyclopentyl-4-ethyl-2-(methylaminomethyl)-  
imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one:

10

0.37 g of 2-aminomethyl-6-benzyl-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one are hydrogenated in 30 ml of glacial acetic acid on 50 mg of palladium on charcoal (10%) (5 bar, 20°C, 19 hours). For  
15 working up, the catalyst is filtered off and the solvent is distilled off *in vacuo*. The crude product is purified by chromatography on silica gel (dichloromethane:methanol 90:10) and yields 0.18 g of the title compound in the form of colourless crystals (melting point: 172-175 °C).

20

Synthesis Example III: 2-(N-Acetylaminoethyl)-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one

25

6-Benzyl-2-(N-acetylaminoethyl)-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one:

0.5 g of 2-aminomethyl-6-benzyl-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one (for  
30 preparation see synthesis example II) are dissolved in 10 ml of dichloromethane and 0.2 ml of pyridine and 0.1 ml of acetyl chloride is added dropwise whilst cooling. After 2 hours' stirring at constant temperature the mixture is  
35 diluted with 10 ml of dichloromethane for working up and



washed twice with dilute aqueous hydrochloric acid. The organic phase is separated off, dried over magnesium sulphate and the solvent is distilled off *in vacuo*. 0.7 g of the title compound are left in the form of an amorphous colourless solid.

2-(N-Acetylaminomethyl)-7-cyclopentyl-4-ethyl-  
imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one:

0.7 g of 6-benzyl-2-(N-acetylaminomethyl)-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one are hydrogenated in 30 ml of glacial acetic acid on 50 mg of Pearlman catalyst (5 bar, 60°C, 5.3 hours). For working up, the catalyst is filtered off and the solvent is distilled off *in vacuo*. The crude product is purified by chromatography on silica gel (dichloromethane:methanol 95:5) and yields 0.3 g of the title compound in the form of colourless crystals (melting point: 269-271°C).

**Synthesis Example IV: 2-Aminomethyl-7-cyclopentyl-4-ethyl-**  
**imidazo[4.5-e]-s-triazolo[1.5-a] pyrimidin-5-one**

2-Aminomethyl-6-benzyl-7-cyclopentyl-4-ethyl-  
imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one:

2 g of 6-benzyl-7-cyclopentyl-4-ethyl-2-formyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one (for preparation see synthesis example II) are hydrogenated together with 1 g of ammonia in 30 ml of methanol on 0.2 g palladium on charcoal (10%) (5 bar, 20°C, 2.3 hours). For working up, the catalyst is filtered off and the solvent is distilled off *in vacuo*. The crude product is purified by chromatography on silica gel (dichloromethane : methanol 95:5) and yields 0.65 g of the title compound in the form of a colourless amorphous solid.



2-Aminomethyl-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one:

0.56 g of 2-aminomethyl-6-benzyl-7-cyclopentyl-4-ethyl-  
5 imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one are  
hydrogenated in 30 ml of glacial acetic acid on 1 g of  
palladium on charcoal (10%) (5 bar, 60°C, 6.4 hours). For  
working up, the catalyst is filtered off and the solvent  
is distilled off in vacuo. The crude product is purified  
10 by chromatography on silica gel (dichloromethane:methanol  
90:10) and yields 0.18 g of the title compound in the form  
of colourless crystals (melting point: 240-245°C).

Synthesis Example V: 7-Cyclopentyl-4-ethyl-2-(N-  
15 pyrrolylmethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-  
5-one

6-Benzyl-7-cyclopentyl-4-ethyl-2-(N-pyrrolylmethyl)-  
imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one:

20 48 mg of sodium hydride (60% in mineral oil) are added to  
a solution of 0.8 g of pyrrole in 10 ml of  
dimethylformamide. After 30 minutes' stirring at ambient  
temperature, 0.46 g of 6-benzyl-2-bromomethyl-7-  
25 cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]-  
pyrimidin-5-one is obtained (for preparation see Synthesis  
Example 1). The mixture is stirred at elevated temperature  
(about 60°C) until the reaction is complete (about 6  
hours). For working up, some water is added and then the  
30 solvent is distilled off in vacuo. The residue remaining  
is taken up in 15 ml of dichloromethane and 10 ml of  
water. After acidification with aqueous, 1N HCl solution  
the organic phase is separated off, washed with water and  
dried over magnesium sulphate. The solvent is distilled  
35 off and the residue remaining is purified by  
chromatography on silica gel (ethyl acetate:cyclohexane



1:1). 0.2 g of the title compound are obtained in the form of a colourless solid.

5 7-Cyclopentyl-4-ethyl-2-(N-pyrrolylmethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one:

1 g of 6-benzyl-7-cyclopentyl-4-ethyl-2-(N-pyrrolylmethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one is hydrogenated in 100 ml of methanol on 0.1 g of  
10 Pearlman catalyst (60°C, 5 bar, 4.5 hours). After the catalyst has been separated off the residue is evaporated to dryness. The title compound is purified by chromatography on silica gel (dichloromethane : methanol 97:3).

15 Using the above method 0.67 g of the title compound (melting point:282-283°C) was obtained.

20 Synthesis Example VI: 2-(2-Aminoethyl)-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a] pyrimidin-5-one

6-Benzyl-2-cyanomethyl-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one:

25 0.46 g of 6-benzyl-2-bromomethyl-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one (for preparation see Synthesis example 1) are added to a solution of 0.72 g of KCN in 0.7 ml of water and 2.4 ml of ethanol heated to boiling. The mixture is boiled for a  
30 further 30 minutes until the reaction is complete. For working up the mixture is diluted with 10 ml of water and extracted with 15 ml of dichloromethane. The organic phase is separated off, washed with saturated sodium chloride solution and dried over magnesium sulphate. The solvent is  
35 distilled off and the residue remaining is purified by chromatography on silica gel (dichloromethane:methanol



99:1). 0.3 g of the title compound is obtained in the form of a colourless solid.

5 2-(2-Aminoethyl)-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one:

0.26 g of 6-benzyl-2-cyanomethyl-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one is hydrogenated in 30 ml of methanol and 1 ml of concentrated  
10 hydrochloric acid (32%) on 50 mg of palladium catalyst (10%) (60°C, 5 bar, 3.3 hours). After the catalyst has been separated of the residue is evaporated to dryness. The title compound is purified by crystallisation from methanol. Using the above method, 0.23 g of the title  
15 compound were obtained (melting point: 272-275°C).



The compounds of general formula (I) listed in Table 1 were prepared using the methods described above or by adopting analogous methods.

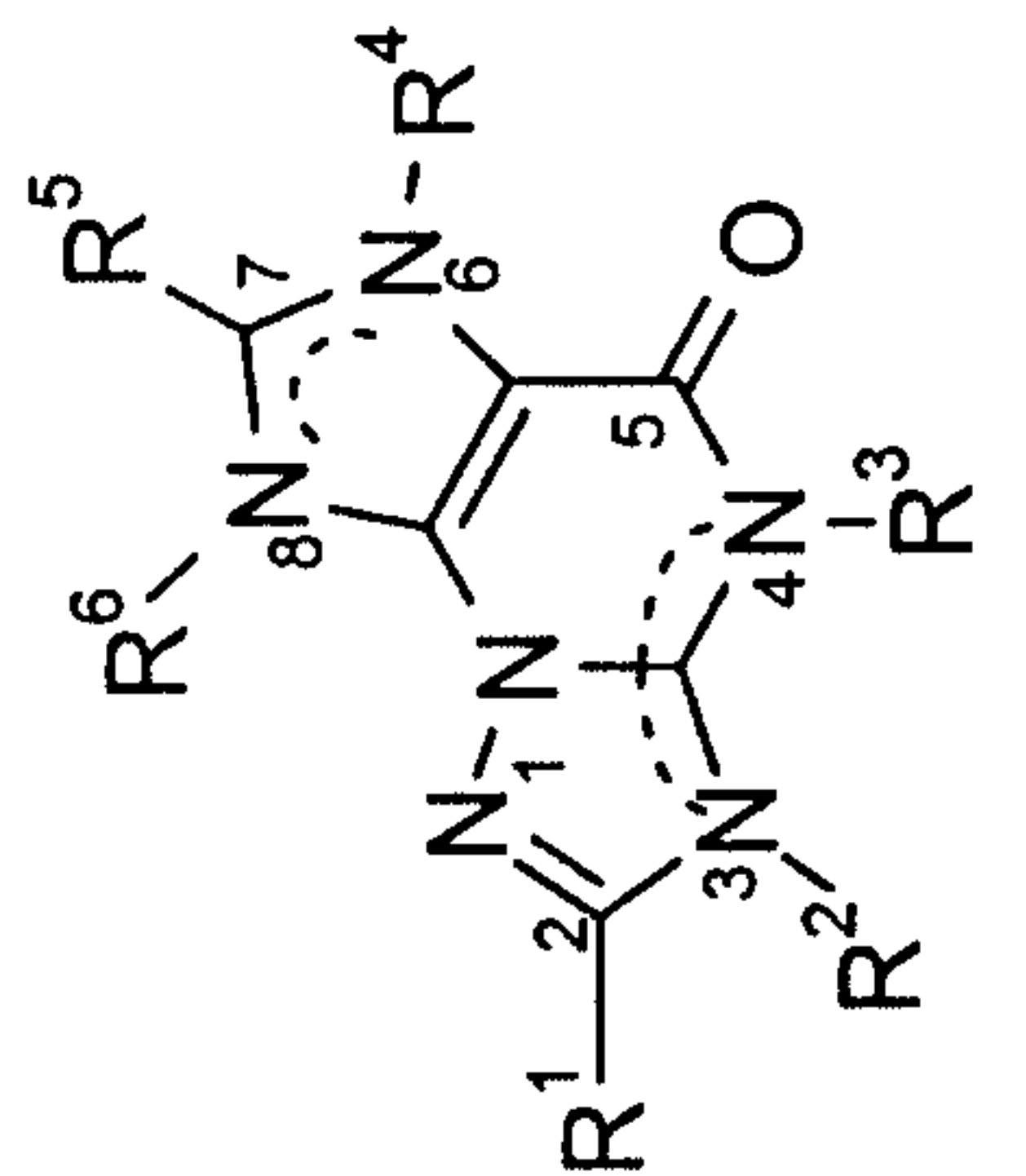
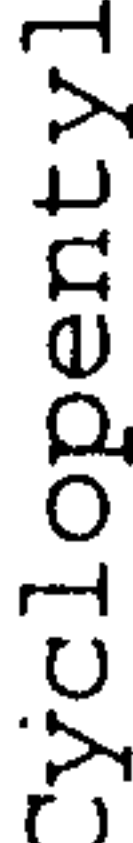
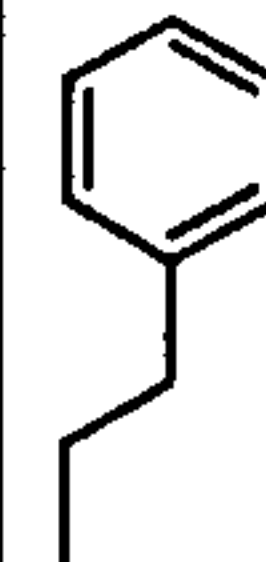
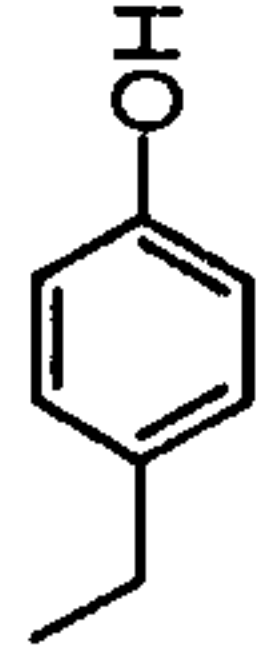
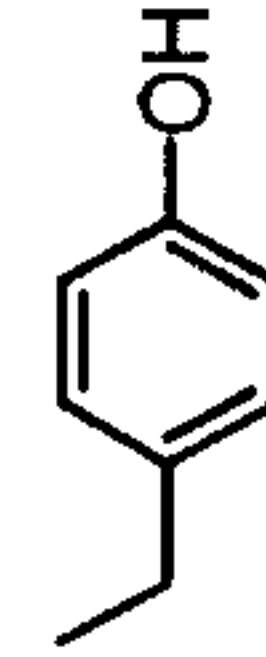
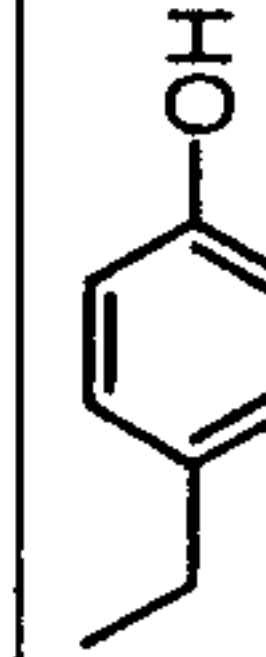
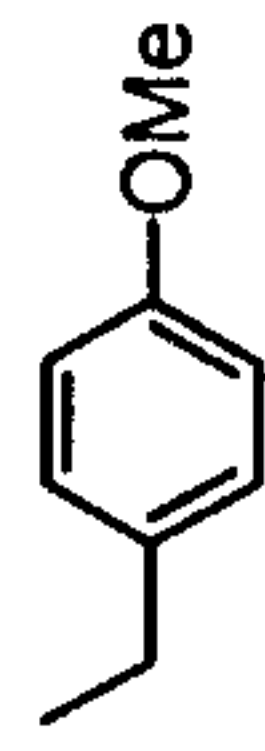


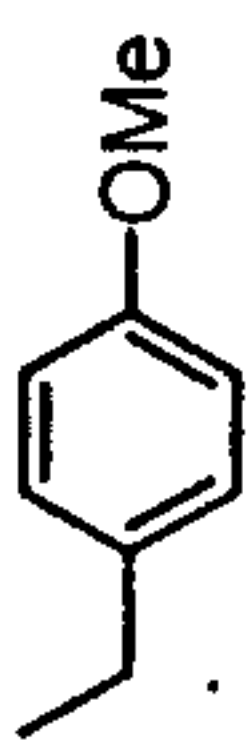
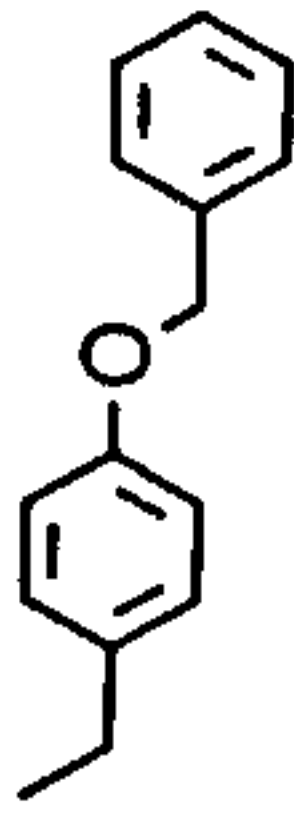
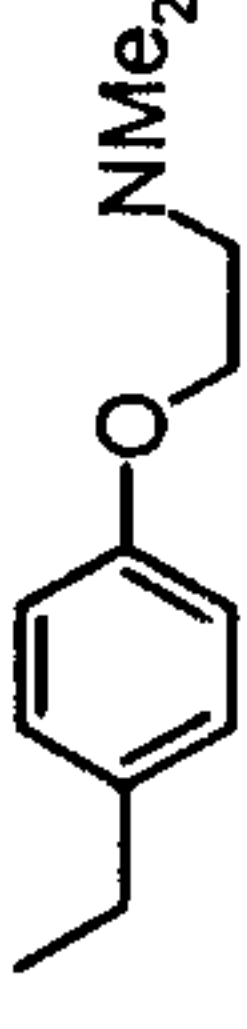
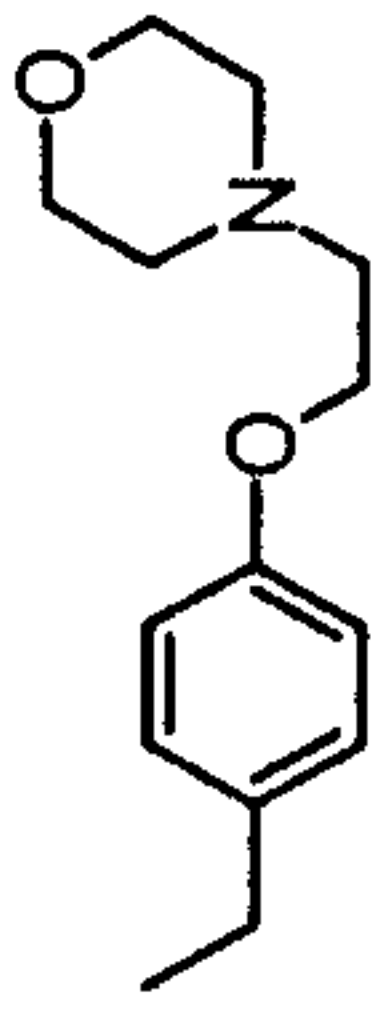
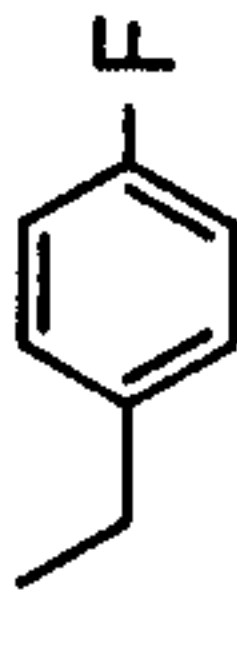
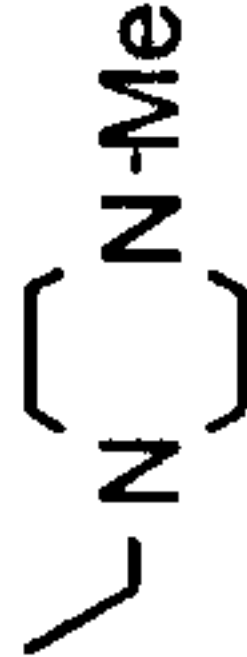
Table 1:

| No. | R <sup>1</sup> | R <sup>2</sup> | R <sup>3</sup> | R <sup>4</sup> (or R <sup>6</sup> ) | R <sup>5</sup> | m.p. [°C] | name                                                                                         |
|-----|----------------|----------------|----------------|-------------------------------------|----------------|-----------|----------------------------------------------------------------------------------------------|
| 1   | Cyclopentyl    | -              | n-Propyl       | Methyl                              | Ethyl          | 155-157   | 2-Cyclopentyl-7-ethyl-6-methyl-4-n-propyl-imidazo [4.5-e] -s-triazolo [1.5-a]pyrimidin-5-one |
| 2   | Cyclopentyl    | -              | n-Propyl       | H                                   | n-Propyl       | 244-246   | 2-Cyclopentyl-4,7-di-n-propyl-imidazo [4.5-e] -s-triazolo [1.5-a]pyrimidin-5-one             |
| 3   | Cyclopentyl    | -              | i-Propyl       | H                                   | Ethyl          | 260-262   | 2-Cyclopentyl-7-ethyl-4-i-propyl-imidazo [4.5-e] -s-triazolo [1.5-a]pyrimidin-5-one          |
| 4   | Cyclopentyl    | -              | n-Butyl        | H                                   | Ethyl          | 265       | 4-n-Butyl-2-cyclopentyl-7-ethyl-imidazo [4.5-e] -s-triazolo [1.5-a]pyrimidin-5-one           |
| 5   | Cyclopentyl    | -              | i-Butyl        | H                                   | Ethyl          | 297       | 4-i-Butyl-2-cyclopentyl-7-ethyl-imidazo [4.5-e] -s-triazolo [1.5-a]pyrimidin-5-one           |
| 6   | Cyclopentyl    | -              | n-Pentyl       | H                                   | Ethyl          | 255       | 2-Cyclopentyl-7-ethyl-4-n-pentyl-imidazo [4.5-e] -s-triazolo [1.5-a]pyrimidin-5-one          |



| No. | R <sup>1</sup>                                                                        | R <sup>2</sup> | R <sup>3</sup> | R <sup>4</sup> (or R <sup>6</sup> )                                                   | R <sup>5</sup> | m.p. [°C]   | name                                                                                                             |
|-----|---------------------------------------------------------------------------------------|----------------|----------------|---------------------------------------------------------------------------------------|----------------|-------------|------------------------------------------------------------------------------------------------------------------|
| 7   |    | -              | 1-Buten-4-yl   | H                                                                                     | Ethyl          | 243         | 4-(1-Buten-4-yl)-2-cyclopentyl-7-ethyl-imidazo [4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                          |
| 8   |    | -              | n-Propyl       | H                                                                                     | Methyl         | 231-233     | 2-Benzyl-7-methyl-4-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                                     |
| 9   |    | -              | n-Propyl       | Methyl                                                                                | Ethyl          | 167-169     | 2-Benzyl-7-ethyl-6-methyl-4-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                             |
| 10  |    | -              | Ethyl          | H                                                                                     | Methyl         | 283-284     | 4-Ethyl-7-methyl-2-(2-phenylethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                               |
| 11  |   | -              | Ethyl          | H                                                                                     | n-Propyl       | 250-253     | 4-Ethyl-2-(2-phenylethyl)-7-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                             |
| 12  |  | -              | Ethyl          | H                                                                                     | t-Butyl        | 297-298     | 7-t-Butyl-4-ethyl-2-(4-hydroxybenzyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                            |
| 13  |  | -              | Ethyl          | Methyl                                                                                | t-Butyl        | 202-204     | 7-t-Butyl-4-ethyl-2-(4-hydroxybenzyl)-6-methyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                   |
| 14  |  | -              | Ethyl          |  | t-Butyl        | -           | 7-t-Butyl-4-ethyl-2-(4-hydroxybenzyl)-6-[2-(N-morpholino)-ethyl]-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one |
| 15  |  | -              | Ethyl          | H                                                                                     | t-Butyl        | 204 decomp. | 7-t-Butyl-4-ethyl-2-(4-methoxybenzyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                            |



| No. | R <sup>1</sup>                                                                        | R <sup>2</sup> | R <sup>3</sup> | R <sup>4</sup> (or R <sup>6</sup> ) | R <sup>5</sup>                                                                        | m.p. [°C]      | name                                                                                                        |
|-----|---------------------------------------------------------------------------------------|----------------|----------------|-------------------------------------|---------------------------------------------------------------------------------------|----------------|-------------------------------------------------------------------------------------------------------------|
| 16  |    | -              | Ethyl          | Methyl                              | t-Butyl                                                                               | 127-128        | 7-t-Butyl-4-ethyl-2-(4-methoxybenzyl)-6-methyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one              |
| 17  |    | -              | Ethyl          | H                                   | t-Butyl                                                                               | 245-246        | 2-(4-Benzyloxy-benzyl)-7-t-butyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                    |
| 18  |    | -              | Ethyl          | H                                   | t-Butyl                                                                               | 204<br>decomp. | 7-t-Butyl-2-{4-[2-(dimethylamino)-ethyloxy]-benzyl}-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one |
| 19  |   | -              | Ethyl          | H                                   | t-Butyl                                                                               | 228-230        | 7-t-Butyl-4-ethyl-2-{4-[2-(N-morpholino)-ethyloxy]-benzyl}-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one  |
| 20  |  | -              | Ethyl          | H                                   |  | 255-257        | 4-Ethyl-2-(4-fluorobenzyl)-7-(5-norbornen-2(S)-yl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one          |
| 21  | -CH <sub>2</sub> -NH <sub>2</sub>                                                     | -              | Ethyl          | H                                   | Cyclopropyl                                                                           | 240-245        | 2-Aminomethyl-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                         |
| 22  | -CH <sub>2</sub> -NHMe                                                                | -              | Ethyl          | H                                   | Cyclopropyl                                                                           | 172-175        | 7-Cyclopentyl-4-ethyl-2-(methylaminomethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                 |
| 23  | -CH <sub>2</sub> -N(i-Pr) <sub>2</sub>                                                | -              | Ethyl          | H                                   | t-Butyl                                                                               | 262-264        | 7-t-Butyl-4-ethyl-2-(diisopropylamino-methyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one               |
| 24  |  | -              | Ethyl          | H                                   | t-Butyl                                                                               | 283<br>decomp. | 7-t-Butyl-4-ethyl-2-[(4-methylpiperazin-1-yl)methyl]-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one        |



| No. | R <sup>1</sup>                                    | R <sup>2</sup> | R <sup>3</sup> | R <sup>4</sup> (or R <sup>6</sup> ) | R <sup>5</sup> | m.p. [°C] | name                                                                                         |
|-----|---------------------------------------------------|----------------|----------------|-------------------------------------|----------------|-----------|----------------------------------------------------------------------------------------------|
| 25  | -CH <sub>2</sub> -NHAC                            | -              | Ethyl          | H                                   | Cyclophenyl    | 269-271   | 2-(N-Acetylaminoethyl)-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one |
| 26  | -CH <sub>2</sub> CH <sub>2</sub> -NH <sub>2</sub> | -              | Ethyl          | H                                   | Cyclophenyl    | 272-275   | 2-(2-Aminoethyl)-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one       |
| 27  | -CH <sub>2</sub> -OH                              | -              | Ethyl          | H                                   | t-Butyl        | 236       | 7-t-Butyl-4-ethyl-2-hydroxymethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one            |
| 28  | -CH(OH)Me                                         | -              | Ethyl          | H                                   | Cyclophenyl    | 264-266   | 7-Cyclopentyl-4-ethyl-2-(1-hydroxyethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one     |
| 29  | -CH <sub>2</sub> -Ophenyl                         | -              | Ethyl          | H                                   | Cyclophenyl    | 229       | 7-Cyclopentyl-4-ethyl-2-phenyloxymethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one      |
| 30  | -COOH                                             | -              | Ethyl          | H                                   | Cyclophenyl    | >300      | 2-Carboxy-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one              |
| 31  | COO-iPropyl                                       | -              | Ethyl          | H                                   | t-Butyl        | 298-302   | 7-t-Butyl-2-carboxyisopropyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one         |
| 32  | COO-iPropyl                                       | -              | Ethyl          | H                                   | Cyclophenyl    | 304-305   | 2-Carboxyisopropyl-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one     |
| 33  | COO-t-Butyl                                       | -              | Ethyl          | H                                   | t-Butyl        | >300      | 7-t-Butyl-2-(carboxy-tert.butyl)-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one     |



| No. | R <sup>1</sup>                                                                      | R <sup>2</sup> | R <sup>3</sup>    | R <sup>4</sup> (or<br>R <sup>6</sup> ) | R <sup>5</sup> | m.p.<br>[°C] | name                                                                                         |
|-----|-------------------------------------------------------------------------------------|----------------|-------------------|----------------------------------------|----------------|--------------|----------------------------------------------------------------------------------------------|
| 34  | COO-t-Butyl                                                                         | -              | Ethyl             | H                                      | Cyclopentyl    | >300         | 2-(Carboxy-tert.butyl)-7-cyclopentyl-4-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one |
| 35  |  | -              | Ethyl             | H                                      | Cyclopentyl    | 282-283      | 7-Cyclopentyl-4-ethyl-2-(N-pyrrolylmethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one   |
| 36  | 2-Furanyl                                                                           | -              | n-Propyl          | H                                      | Methyl         | >300         | 2-(2-Furanyl)-7-methyl-4-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one            |
| 37  | 2-Furanyl                                                                           | -              | n-Propyl          | H                                      | n-Propyl       | >300         | 2-(2-Furanyl)-4,7-di-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one                |
| 38  | Cyclopentyl                                                                         | -              | Allyl             | H                                      | Ethyl          | 231-232      | 2-Cyclopentyl-7-ethyl-4-(1-propen-3-yl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one      |
| 39  | Cyclopentyl                                                                         | -              | Propargyl         | H                                      | Ethyl          | 274          | 2-Cyclopentyl-7-ethyl-4-(1-propin-3-yl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one      |
| 40  | Cyclopentyl                                                                         | -              | 2-Methoxyethyl    | H                                      | Ethyl          | 220          | 2-Cyclopentyl-7-ethyl-4-(2-methoxyethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one     |
| 41  | Cyclopentyl                                                                         | -              | Cyclopropylmethyl | H                                      | Ethyl          | ???          | 2-Cyclopentyl-4-cyclopropylmethyl-7-ethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one    |
| 42  | Cyclopentyl                                                                         | -              | n-Butyl           | H                                      | Methyl         | 260          | 4-n-Butyl-2-cyclopentyl-7-methyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one             |



| No. | R <sup>1</sup> | R <sup>2</sup> | R <sup>3</sup>  | R <sup>4</sup> (or<br>R <sup>6</sup> ) | R <sup>5</sup> | m.p.<br>[°C] | name                                                                                       |
|-----|----------------|----------------|-----------------|----------------------------------------|----------------|--------------|--------------------------------------------------------------------------------------------|
| 43  | Cyclopentyl    | -              | 2-Hydroxy-ethyl | H                                      | Ethyl          | 285          | 2-Cyclopentyl-7-ethyl-4-(2-hydroxyethyl)-imidazo [4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one  |
| 44  | Cyclopentyl    | -              | 2-Methoxy-ethyl | H                                      | Methyl         | 212-214      | 2-Cyclopentyl-4-(2-methoxyethyl)-7-methyl-imidazo [4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one |



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The receptor binding values described hereinafter were determined analogously to Ensinger et al. in "Cloning and functional characterisation of human A<sub>1</sub> adenosine Receptor - Biochemical and Biophysical Communications, Vol 187, No. 2, 919-926, 1992".

The Table which follows contains KiA<sub>1</sub> (human) receptor binding values.

10 Table 2:

| Example No.: | K <sub>i</sub> A <sub>1</sub> [nM] |
|--------------|------------------------------------|
| 11           | 8.1                                |
| 12           | 6.0                                |
| 15           | 2.1                                |
| 29           | 3.6                                |
| 35           | 2.6                                |

The A<sub>3</sub> receptor binding values given hereinafter were determined analogously to Salvatore et al. "Molecular cloning and characterization of the human A<sub>3</sub>-adenosine receptor" (Proc. Natl. Acad. Sci. USA 90, 10365-10369, 1993).

Table 3 contains KiA<sub>3</sub> (human) receptor binding values.

Table 3:

| Example No. | K <sub>i</sub> A <sub>3</sub> [nM] |
|-------------|------------------------------------|
| 2           | 5.6                                |
| 8           | 0.9                                |
| 10          | 7.2                                |
| 36          | 2.2                                |
| 37          | 8.3                                |

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The new compounds of general formula (Ia) to (Id) may be administered orally, transdermally, by inhalation or parenterally. The compounds according to the invention occur as active ingredients in conventional preparations, e.g. in compositions consisting essentially of an inert pharmaceutical carrier and an effective dose of the active substance, such as plain or coated tablets, capsules, lozenges, powders, solutions, suspensions, emulsions, syrups, suppositories, transdermal systems, etc. An effective dose of the compounds according to the invention is between 1 and 100, preferably between 1 and 50, more especially between 5 and 30 mg per/dose for oral administration, and between 0.001 and 50, preferably between 0.1 and 10 mg per dose for intravenous or intramuscular use. For inhalation, according to the invention it is appropriate to use solutions which contain 0.01 to 1.0, preferably 0.1 to 0.5% of active substance. For administration by inhalation it is preferable to use powders. It is also possible to use the compounds according to the invention as a solution for infusion, preferably in physiological saline solution or nutrient saline.

The compounds of general formula (I) may be used on their own or in conjunction with other active substances according to the invention, optionally also in conjunction with other pharmacologically active substances. Suitable preparations include for example tablets, capsules, suppositories, solutions, elixirs, emulsions or dispersible powders. Suitable tablets may be obtained, for example, by mixing the active substance(s) with known excipients, for example inert diluents such as calcium carbonate, calcium phosphate or lactose, disintegrants such as corn starch or alginic acid, binders such as starch or gelatine, lubricants such as magnesium stearate or talc and/or agents for delaying release, such as



carboxymethyl cellulose, cellulose acetate phthalate, or polyvinyl acetate. The tablets may also comprise several layers.

- 5 Coated tablets may be prepared accordingly by coating cores produced analogously to the tablets with substances normally used for tablet coatings, for example collidone or shellac, gum arabic, talc, titanium dioxide or sugar. To achieve delayed release or prevent incompatibilities  
10 the core may also consist of a number of layers. Similarly the tablet coating may consist of a number of layers to achieve delayed release, possibly using the excipients mentioned above for the tablets.
- 15 Syrups or elixirs containing the active substances or combinations thereof according to the invention may additionally contain a sweetener such as saccharine, cyclamate, glycerol or sugar and a flavour enhancer, e.g. a flavouring such as vanilline or orange extract. They may  
20 also contain suspension adjuvants or thickeners such as sodium carboxymethyl cellulose, wetting agents such as, for example, condensation products of fatty alcohols with ethylene oxide, or preservatives such as p-hydroxybenzoates.

- 25 Solutions for injection are prepared in the usual way, e.g. with the addition of preservatives such as p-hydroxybenzoates, or stabilisers such as alkali metal salts of ethylenediamine tetraacetic acid, and transferred  
30 into injection vials or ampoules.

- Capsules containing one or more active substances or combinations of active substances may for example be prepared by mixing the active substances with inert  
35 carriers such as lactose or sorbitol and packing them into gelatine capsules.



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Suitable suppositories may be made for example by mixing with carriers provided for this purpose, such as neutral fats or polyethyleneglycol or the derivatives thereof.

- 5 A therapeutically effective daily dose is between 1 and 800 mg, preferably 10 - 300 mg per adult.

The Examples which follow illustrate the present invention without restricting its scope:

10



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Examples of pharmaceutical formulationsA)            Tablets    per tablet

|   |                      |        |
|---|----------------------|--------|
| 5 | active substance     | 100 mg |
|   | lactose              | 140 mg |
|   | corn starch          | 240 mg |
|   | polyvinylpyrrolidone | 15 mg  |
|   | magnesium stearate   | 5 mg   |

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 500 mg

The finely ground active substance, lactose and some of the corn starch are mixed together. The mixture is screened, then moistened with a solution of

15 polyvinylpyrrolidone in water, kneaded, wet-granulated and dried. The granules, the remaining corn starch and the magnesium stearate are screened and mixed together. The mixture is compressed to produce tablets of suitable shape and size.

20

B)            Tablets                            per tablet

|    |                             |        |
|----|-----------------------------|--------|
|    | active substance            | 80 mg  |
|    | corn starch                 | 190 mg |
| 25 | lactose                     | 55 mg  |
|    | microcrystalline cellulose  | 35 mg  |
|    | polyvinylpyrrolidone        | 15 mg  |
|    | sodium-carboxymethyl starch | 23 mg  |
|    | magnesium stearate          | 2 mg   |

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 400 mg

The finely ground active substance, some of the corn starch, lactose, microcrystalline cellulose and

35 polyvinylpyrrolidone are mixed together, the mixture is screened and worked with the remaining corn starch and



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water to form a granulate which is dried and screened. The sodiumcarboxymethyl starch and the magnesium stearate are added and mixed in and the mixture is compressed to form tablets of a suitable size.

5

| C) | <u>Coated tablets</u> | <u>per coated tablet</u> |
|----|-----------------------|--------------------------|
|    | Active substance      | 5 mg                     |
|    | Corn starch           | 41.5 mg                  |
| 10 | lactose               | 30 mg                    |
|    | Polyvinylpyrrolidone  | 3 mg                     |
|    | Magnesium stearate    | 0.5 mg                   |
|    |                       | <hr/> 80 mg              |

15 The active substance, corn starch, lactose and polyvinylpyrrolidone are mixed thoroughly and moistened with water. The moist mass is forced through a screen with a mesh size of 1 mm, dried at about 45°C and the granules are then passed through the same screen. After the  
20 magnesium stearate has been mixed in, convex tablet cores with a diameter of 6 mm are compressed in a tablet making machine. The tablet cores thus produced are coated in known manner with a coating consisting essentially of sugar and talc. The finished coated tablets are polished  
25 with wax.

| D) | <u>Capsules</u>    | <u>per capsule</u> |
|----|--------------------|--------------------|
|    | Active substance   | 50 mg              |
| 30 | Corn starch        | 268.5 mg           |
|    | Magnesium stearate | 1.5 mg             |
|    |                    | <hr/> 320 mg       |

The substance and cornstarch are mixed and moistened with  
35 water. The moist mass is screened and dried. The dry granules are screened and mixed with magnesium



stearate. The finished mixture is packed into size 1 hard gelatine capsules.

E) Ampoule solution

5

|                  |       |
|------------------|-------|
| active substance | 50 mg |
| sodium chloride  | 50 mg |
| water for inj.   | 5 ml  |

10 The active substance is dissolved in water at its own pH or optionally at pH 5.5 to 6.5 and sodium chloride is added to make it isotonic. The solution obtained is filtered free from pyrogens and the filtrate is transferred under aseptic conditions into ampoules which  
15 are then sterilised and sealed by fusion. The ampoules contain 5 mg, 25 mg and 50 mg of active substance.

F) Suppositories

|    |                  |                |
|----|------------------|----------------|
| 20 | Active substance | 50 mg          |
|    | Solid fat        | <u>1650 mg</u> |
|    |                  | 1700 mg        |

The hard fat is melted. At 40°C the ground active  
25 substance is homogeneously dispersed. It is cooled to 38°C and poured into slightly chilled suppository moulds.

G) Oral Suspension

|    |                       |        |
|----|-----------------------|--------|
| 30 | Active substance      | 50 mg  |
|    | Hydroxyethylcellulose | 50 mg  |
|    | Sorbic acid           | 5 mg   |
|    | Sorbitol (70%)        | 600 mg |
|    | Glycerol              | 200 mg |
| 35 | Flavouring            | 15 mg  |
|    | water ad              | 5 ml   |



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Distilled water is heated to 70°C. Hydroxyethylcellulose is dissolved therein with stirring. After the addition of sorbitol solution and glycerol the mixture is cooled to ambient temperature. At ambient temperature, sorbic acid, 5 flavouring and substance are added. The suspension is evacuated with stirring in order to eliminate air.

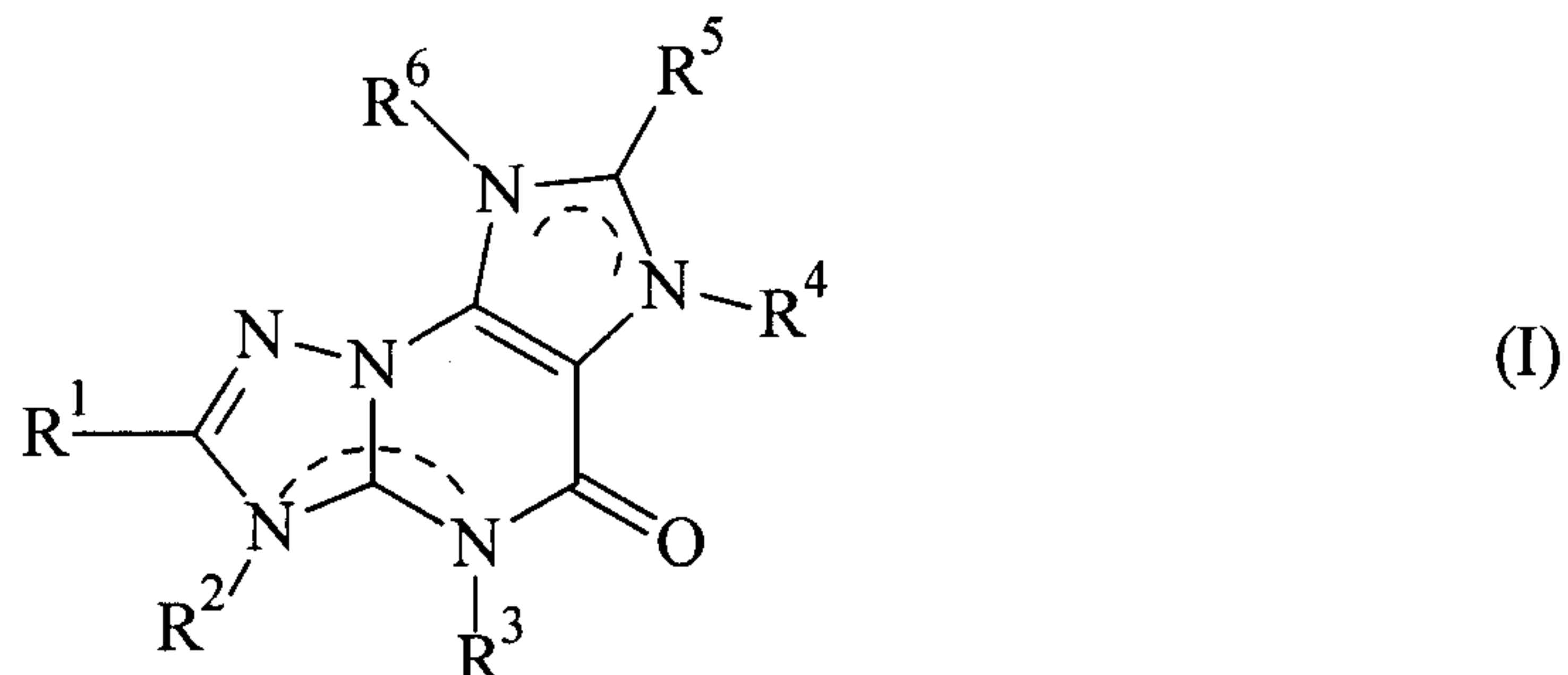


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CLAIMS:

1. A compound of general formula (I)



wherein the dotted lines between the nitrogen atoms of the above general formula I indicate the existence of a double bond in one of two possible positions, so that the groups  
 10 R<sup>4</sup> and R<sup>6</sup> and R<sup>3</sup> and R<sup>2</sup> need not be present simultaneously and wherein

R<sup>1</sup> denotes hydrogen, a C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl or C<sub>2-8</sub>-alkynyl group which is optionally mono- or polysubstituted by -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -CHO, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>,  
 15 -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH=NOH, -CH=NOR<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -NHCONHPhenyl, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane or 1,3-dioxane;

20 R<sup>1</sup> denotes -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>; =O; O-phenyl-C<sub>1-4</sub>-alkoxy, O-phenyl-O-C<sub>1-4</sub>-alkoxy, or -COO-C<sub>1-4</sub>-alkyl;

R<sup>1</sup> denotes -CHO, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup> or NR<sup>7</sup>R<sup>8</sup>;

R<sup>1</sup> denotes C<sub>3-7</sub>-cycloalkyl which is optionally substituted by =O, -OR<sup>9</sup>, OCOR<sup>9</sup> or -OCOPyridyl;

25 R<sup>1</sup> denotes cyclopentanone or cyclohexanone;



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$R^1$  denotes phenyl which is optionally substituted by  $C_{1-4}$ -alkyl, -CN, -COOR<sup>9</sup>, NR<sup>7</sup>R<sup>8</sup>, -OR<sup>9</sup>, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>CONR<sup>7</sup>R<sup>8</sup>, -CO- $C_{1-4}$ -alkyl-NH<sub>2</sub>, -SO<sub>3</sub>H or halogen;

$R^1$  denotes phenyl- $C_{1-6}$ -alkyl, phenyl- $C_{2-6}$ -alkenyl or  
 5 phenyl- $C_{2-6}$ -alkynyl, wherein the phenyl ring is optionally substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups selected from  $C_{1-3}$ -alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>,  
 10 -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO- $C_{1-4}$ -alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane and  
 15 1,3-dioxane;

$R^1$  denotes  $C_{3-7}$ -cycloalkyl- $C_{1-6}$ -alkyl,  $C_{3-7}$ -cycloalkyl- $C_{2-6}$ -alkenyl,  $C_{3-7}$ -cycloalkyl- $C_{2-6}$ -alkynyl, wherein the cycloalkyl group is optionally substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one  
 20 or more of the groups selected from  $C_{1-4}$ -alkyl,  $C_{1-4}$ -alkoxy, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO- $C_{1-4}$ -alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>,  
 25 -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane and 1,3-dioxane;

$R^1$  denotes a norbornane, norbornene,  $C_{3-6}$ -dicycloalkylmethyl, adamantane or noradamantane group which is optionally  
 30 substituted by  $C_{1-4}$ -alkyl; or



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$R^1$  denotes a group of formula A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenyl, A-C<sub>2-6</sub>-alkynyl or A-, where A is a C- or N-linked 5-,  
 5 6- or 7-membered heterocycle, which contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and is optionally mono- or polysubstituted by benzyl, optionally methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -COR<sup>10</sup>,  
 10 -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, =O, a ketal, ethyleneketal, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup> or halogen;

$R^2$  or  $R^3$  denotes a C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl or C<sub>2-8</sub>-alkynyl group which is optionally mono-or polysubstituted by one or more groups selected from -CN, C<sub>3-6</sub>-cycloalkyl, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>,  
 15 -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -CHO, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH=NOH, -CH=NOR<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -NHCONHPhenyl, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-  
 20 substituted 1,3-dioxolane and 1,3-dioxane;

$R^2$  or  $R^3$  denotes phenyl-C<sub>1-6</sub>-alkyl, phenyl-C<sub>2-6</sub>-alkenyl or phenyl-C<sub>2-6</sub>-alkynyl, wherein the phenyl ring is optionally substituted, either directly or via an alkylene bridge having 1 to 4 carbon atoms, by one or more of the groups  
 25 selected from C<sub>1-3</sub>-alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>, -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CO-R<sup>9</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>,  
 30 -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane and 1,3-dioxane;



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$R^2$  or  $R^3$  denotes a group of formula A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenyl, A-C<sub>2-6</sub>-alkynyl or A-, where A is a C- or N-linked 5-, 6- or 7-membered heterocycle, which contains one or more heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and is optionally mono- or polysubstituted by benzyl, optionally methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -COR<sup>10</sup>,  
 5 -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, =O, a ketal, ethleneketal, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup> or halogen;

$R^4$  or  $R^6$  denotes hydrogen, C<sub>1-4</sub>-alkyl which is optionally substituted by -NR<sup>7</sup>R<sup>8</sup> or benzyl;

$R^5$  denotes hydrogen, a C<sub>1-8</sub>-alkyl, C<sub>2-8</sub>-alkenyl or C<sub>2-8</sub>-alkynyl group which may optionally be mono- or polysubstituted by  
 15 -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -CHO, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>, -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH=NOH, -CH=NOR<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>, -NHCOOR<sup>9</sup>, -NHCONHPhenyl, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>,  
 20 -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, OCONR<sup>7</sup>R<sup>8</sup>, halogen, optionally methyl-substituted 1,3-dioxolane or 1,3-dioxane;

$R^5$  denotes C<sub>3-7</sub>-cycloalkyl, which is optionally substituted by =O, -OR<sup>9</sup>, OCOR<sup>9</sup> or -OCOPyridyl;

$R^5$  denotes phenyl which may optionally be substituted by -OH, halogen, -OR<sup>9</sup>, C<sub>1-4</sub>-alkyl, NH<sub>2</sub>, COOH, -SO<sub>3</sub>H, -COOR<sup>9</sup>,  
 25 -OCH<sub>2</sub>COOR<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -CN or -OCH<sub>2</sub>CONR<sup>7</sup>R<sup>8</sup>;

$R^5$  denotes phenyl-C<sub>1-6</sub>-alkyl, phenyl-C<sub>2-6</sub>-alkenyl or phenyl-C<sub>2-6</sub>-alkynyl, wherein the phenyl ring is optionally substituted, either directly or via an alkylene bridge  
 30 having 1 to 4 carbon atoms, by one or more of the groups selected from C<sub>1-3</sub>-alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>,



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-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>,  
 -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>,  
 -CO-R<sup>9</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>,  
 -NHCOOR<sup>9</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>,  
 5 -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>,  
 halogen, optionally methyl-substituted 1,3-dioxolane and  
 1,3-dioxane;

R<sup>5</sup> denotes a norbornane, norbornene, C<sub>3-6</sub>-dicycloalkylmethyl,  
 adamantane or noradamantane group which is optionally  
 10 substituted by C<sub>1-4</sub>-alkyl;

R<sup>5</sup> denotes -CHO, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup> or NR<sup>7</sup>R<sup>8</sup>;

R<sup>5</sup> denotes C<sub>3-7</sub>-cycloalkyl-C<sub>1-6</sub>-alkyl, C<sub>3-7</sub>-cycloalkyl-  
 C<sub>2-6</sub>-alkenyl, C<sub>3-7</sub>-cycloalkyl-C<sub>2-6</sub>-alkynyl, wherein the  
 cycloalkyl group is optionally substituted, either directly  
 15 or via an alkylene bridge having 1 to 4 carbon atoms, by one  
 or more of the groups C<sub>1-3</sub>-alkyl, -CN, -CH<sub>2</sub>OCOR<sup>9</sup>, -COOR<sup>9</sup>, -CF<sub>3</sub>,  
 -CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CHO, -CH=NOR<sup>9</sup>, -COR<sup>10</sup>, -CH(OH)R<sup>10</sup>,  
 -CH(OR<sup>9</sup>)<sub>2</sub>, -CH=CH-R<sup>11</sup>, -CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>, -CH<sub>2</sub>-CH<sub>2</sub>-O-CONR<sup>7</sup>R<sup>8</sup>,  
 -CO-R<sup>9</sup>, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, NR<sup>7</sup>R<sup>8</sup>, -NO<sub>2</sub>, -NHCOR<sup>9</sup>, -NHCONR<sup>7</sup>R<sup>8</sup>,  
 20 -NHCOOR<sup>9</sup>, -OCOR<sup>9</sup>, -OCOPyridyl, -OCH<sub>2</sub>COOR<sup>9</sup>, -OCH<sub>2</sub>-CONR<sup>7</sup>R<sup>8</sup>,  
 -OCH<sub>2</sub>-CH<sub>2</sub>-NR<sup>7</sup>R<sup>8</sup>, -OCH<sub>2</sub>CH<sub>2</sub>OR<sup>9</sup>, -OCH<sub>2</sub>-CH<sub>2</sub>OCOR<sup>9</sup>, -OCONR<sup>7</sup>R<sup>8</sup>,  
 halogen, optionally methyl-substituted 1,3-dioxolane or  
 1,3-dioxane; or

R<sup>5</sup> denotes a group of formula A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl,  
 25 A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl,  
 A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenylene,  
 A-C<sub>2-6</sub>-alkynylene or A-, where A is a C- or N-linked 5-,  
 6- or 7-membered heterocycle, which contains one or more  
 heteroatoms selected from the group consisting of nitrogen,  
 30 oxygen and sulphur and is optionally mono- or  
 polysubstituted by benzyl, optionally methoxy-substituted  
 benzyl, C<sub>1-4</sub>-alkyl, -CN, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -COOR<sup>9</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -COR<sup>10</sup>,



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-NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, =O, a ketal, ethyleneketal, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup> or halogen;

R<sup>7</sup> denotes hydrogen, C<sub>1-8</sub>-alkyl which is optionally substituted by -COOR<sup>9</sup>, -COR<sup>10</sup>, -OR<sup>9</sup>, OCOR<sup>9</sup>, amino, phenyl,  
5 methoxy-substituted phenyl or amino, or a C<sub>3-6</sub>-cycloalkyl, or

R<sup>7</sup> denotes a 5-, 6- or 7-membered heterocycle C-linked directly or via a C<sub>1-4</sub>-alkyl chain, which contains one, two or three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and which is optionally mono-  
10 or polysubstituted by benzyl, methoxy-substituted benzyl, C<sub>1-4</sub>-alkyl, halogen, -OR<sup>9</sup>, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, =O, SO<sub>3</sub>H or -COOR<sup>9</sup>;

R<sup>8</sup> denotes hydrogen, C<sub>1-8</sub>-alkyl which is optionally substituted by -COOR<sup>9</sup>, -COR<sup>10</sup>, -OR<sup>9</sup>, -OCOR<sup>9</sup>, amino, phenyl, methoxy-substituted phenyl or amino, or a C<sub>3-6</sub>-cycloalkyl, or

15 R<sup>8</sup> denotes a 5-, 6- or 7-membered heterocycle C-linked directly or via a C<sub>1-4</sub>-alkyl chain, which contains one, two or three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and which is optionally mono- or polysubstituted by benzyl, methoxy-substituted benzyl,  
20 C<sub>1-4</sub>-alkyl, halogen, -OR<sup>9</sup>, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, =O, SO<sub>3</sub>H or -COOR<sup>9</sup>;

R<sup>7</sup> and R<sup>8</sup> together with the nitrogen atom form a saturated or unsaturated 5- or 6-membered ring which optionally comprises nitrogen, oxygen or sulphur as a further heteroatom, wherein the heterocycle is optionally substituted by a branched or  
25 unbranched alkyl group having 1 to 4 carbon atoms, -CN, -COOR<sup>9</sup>, -CONH<sub>2</sub>, -NO<sub>2</sub>, -NH<sub>2</sub>, -OR<sup>9</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>-R<sup>9</sup>, halogen or -(CH<sub>2</sub>)<sub>n</sub>-phenyl, -(CH<sub>2</sub>)<sub>n</sub>-NH<sub>2</sub>, =O, -OCH<sub>2</sub>-CH<sub>2</sub>-O, -OCH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-O, -(CH<sub>2</sub>)<sub>n</sub>-NH-C<sub>1-4</sub>-alkyl, -(CH<sub>2</sub>)<sub>n</sub>-N(C<sub>1-4</sub>-alkyl)<sub>2</sub>, or -(CH<sub>2</sub>)<sub>n</sub>-NHCOOR<sup>9</sup>, wherein n=1, 2, 3 or 4;



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R<sup>9</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl, C<sub>2-4</sub>-alkynyl, a benzyl or phenyl group which is optionally mono- or polysubstituted by -OCH<sub>3</sub>;

R<sup>10</sup> denotes C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl, C<sub>2-4</sub>-alkynyl, optionally methoxy-substituted phenyl, optionally methoxy-substituted benzyl, C<sub>3-6</sub>-cycloalkyl;

R<sup>11</sup> denotes hydrogen, C<sub>1-3</sub>-alkyl, -COOR<sup>9</sup>, -CH<sub>2</sub>OR<sup>9</sup>, -CH<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -CONR<sup>7</sup>R<sup>8</sup> or optionally methoxy-substituted phenyl,

or a racemate thereof, an enantiomer thereof, a diastereomer thereof, a mixture thereof or a pharmacologically acceptable acid addition salt thereof.

2. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein the C<sub>3-7</sub> cycloalkyl in the definition of R<sup>1</sup> is cyclopentyl or cyclohexyl.

3. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein the C<sub>1-4</sub>-alkyl substituent or the phenyl in the definition of R<sup>1</sup> is methyl.

4. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein the phenyl-C<sub>1-6</sub>-alkyl in the definition of R<sup>1</sup> is phenyl-C<sub>1-4</sub>-alkyl.

5. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein the C<sub>3-6</sub>-dicycloalkylmethyl in the definition of R<sup>1</sup> is dicyclopropylmethyl.

6. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein the C<sub>1-4</sub>-alkyl substituent on the norbornane, norbornene,



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C<sub>3-6</sub>-dicycloalkylmethyl, adamantane or noradamantane group in the definition of R<sup>1</sup> is methyl.

7. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein the optionally  
5 mono or polysubstituted group selected from A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenyl, A-C<sub>2-6</sub>-alkynyl and A- in the definition of R<sup>1</sup> is mono substituted.
- 10 8. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 7, wherein the phenyl-C<sub>1-6</sub>-alkyl in the definition of R<sup>2</sup> and R<sup>3</sup> is phenyl-C<sub>1-4</sub>-alkyl.
9. A compound, racemate, enantiomer, diastereomer,  
15 mixture or salt according to any one of claims 1 to 7, wherein the optionally mono or polysubstituted group selected from A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenyl,  
20 A-C<sub>2-6</sub>-alkynyl and A- in the definition of R<sup>2</sup> and R<sup>3</sup> is mono substituted.
10. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 9 wherein R<sup>4</sup> or R<sup>6</sup> is hydrogen.
- 25 11. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 10, wherein the C<sub>3-7</sub> cycloalkyl in the definition of R<sup>5</sup> is cyclopentyl or cyclohexyl.
12. A compound, racemate, enantiomer, diastereomer,  
30 mixture or salt according to any one of claims 1 to 10,



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wherein the C<sub>1-4</sub>-alkyl substituent or the phenyl in the definition of R<sup>5</sup> is methyl.

13. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 10, wherein the phenyl-C<sub>1-6</sub>-alkyl in the definition of R<sup>5</sup> is phenyl-C<sub>1-4</sub>-alkyl.

14. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 10, wherein the C<sub>3-6</sub>-dicycloalkylmethyl in the definition of R<sup>5</sup> is dicyclopropylmethyl.

15. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 10, wherein the C<sub>1-4</sub>-alkyl substituent on the norbornane, norbornene, C<sub>3-6</sub>-dicycloalkylmethyl, adamantane or noradamantane group in the definition of R<sup>5</sup> is methyl.

16. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 10, wherein the optionally mono or polysubstituted group selected from A-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>1-6</sub>-alkyl, A-CONH-C<sub>2-6</sub>-alkenyl, A-CONH-C<sub>2-6</sub>-alkynyl, A-NH-CO-C<sub>1-6</sub>-alkyl, A-NH-CO-C<sub>2-6</sub>-alkenyl, A-NH-CO-C<sub>2-6</sub>-alkynyl, A-C<sub>2-6</sub>-alkenyl, A-C<sub>2-6</sub>-alkynyl and A- in the definition of R<sup>5</sup> is mono substituted.

17. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 16 wherein the C<sub>1-8</sub>-alkyl in the definition of R<sup>7</sup> is C<sub>1-4</sub>-alkyl.

18. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 16, wherein the mono- or polysubstituted heterocycle in the definition of R<sup>7</sup> is mono-substituted.



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19. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 18, wherein the C<sub>1-8</sub>-alkyl in the definition of R<sup>8</sup> is C<sub>1-4</sub>-alkyl.

20. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 18, wherein the mono- or polysubstituted heterocycle in the definition of R<sup>8</sup> is mono-substituted.

21. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 16, wherein, in the definition of R<sup>7</sup> and R<sup>8</sup>, when taken together, the C<sub>1-4</sub>-alkyl substituent in the heterocycle is methyl.

22. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein:

R<sup>1</sup> denotes hydrogen, C<sub>1-8</sub>-alkyl which is optionally substituted by -COOH, -COO-C<sub>1-4</sub>-alkyl, -COO-phenyl, -COO-benzyl, -CO-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, -CO-C<sub>1-4</sub>-alkyl, -CHO, -NR<sup>7</sup>R<sup>8</sup>, =NOH, -NHCO-C<sub>1-4</sub>-alkyl, -NHCO-phenyl, hydroxy, =O, C<sub>1-4</sub>-alkoxy, phenyloxy, O-phenyl-C<sub>1-4</sub>-alkyloxy, benzyloxy, O-benzyl-O-C<sub>1-4</sub>-alkyloxy, -OCO-C<sub>1-4</sub>-alkyl, -OCO-phenyl, -OCO-benzyl, -OCO-pyridyl, -O-C<sub>2-4</sub>-alkenyl or halogen;

R<sup>1</sup> denotes -CHO, -COOH, -COO-C<sub>1-4</sub>-alkyl, -COO-phenyl, -COO-benzyl, -CONR<sup>7</sup>R<sup>8</sup> or an amine of general formula NR<sup>7</sup>R<sup>8</sup>;

R<sup>1</sup> denotes phenyl which is optionally substituted by C<sub>1-4</sub>-alkyl, -CO-C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, C<sub>1-4</sub>-alkyl-OH, C<sub>1-4</sub>-alkyl=NOH, -COOH, -COO-C<sub>1-4</sub>-alkyl, -COO-phenyl, -COO-benzyl, -CONR<sup>7</sup>R<sup>8</sup>, CO-C<sub>1-4</sub>-alkyl-NH<sub>2</sub>, NR<sup>7</sup>R<sup>8</sup>, hydroxy, C<sub>1-4</sub>-alkyloxy, benzyloxy, phenyloxy, -OCO-C<sub>1-4</sub>-alkyl, -OCO-phenyl, -OCO-benzyl, -OCO-pyridyl, -O-C<sub>2-4</sub>-alkenyl or halogen;



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$R^1$  denotes a  $C_{3-6}$ -cycloalkyl or  $C_{3-6}$ -cycloalkyl- $C_{1-4}$ -alkyl group which is optionally substituted by =O, hydroxy,  $C_{1-4}$ -alkyl or  $C_{1-4}$ -alkyloxy;

$R^1$  denotes a norbornane, norbornene, adamantane or  
5 noradamantane group which is optionally substituted by  $C_{1-4}$ -alkyl;

$R^1$  denotes phenyl- $C_{1-4}$ -alkyl, phenyl- $C_{2-6}$ -alkenyl or phenyl- $C_{2-6}$ -alkynyl, wherein the phenyl ring is optionally substituted by  $C_{1-4}$ -alkyl, -CO- $C_{1-4}$ -alkyl,  $C_{1-4}$ -alkyl- $NR^7R^8$ ,  
10 O- $C_{1-4}$ -alkyl- $NR^7R^8$ ,  $C_{1-4}$ -alkyl-OH,  $C_{1-4}$ -alkyl=NOH, -COOH, -COO- $C_{1-4}$ -alkyl, -COO-phenyl, -COO-benzyl, -CONR<sup>7</sup>R<sup>8</sup>, -CO- $C_{1-4}$ -alkyl- $NR^7R^8$ ,  $NR^7R^8$ , hydroxy,  $C_{1-4}$ -alkyloxy, benzyloxy, phenyloxy, -OCO- $C_{1-4}$ -alkyl, -OCO-phenyl, -OCO-benzyl, -OCO-pyridyl, -O- $C_{2-4}$ -alkenyl or halogen; or

15  $R^1$  denotes a 5- or 6-membered heterocycle optionally C- or N-linked either directly or via a  $C_{1-4}$ -alkylene bridge, which contains one, two or three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and which is optionally mono- or polysubstituted by benzyl or  
20  $C_{1-4}$ -alkyl;

$R^2$  or  $R^3$  denotes a  $C_{1-8}$ -alkyl which is optionally substituted by - $NR^7R^8$ , OH,  $C_{1-4}$ -alkyloxy,  $C_{3-6}$ -cycloalkyl or COOH,  $C_{2-8}$ -alkenyl, phenyl- $C_{1-4}$ -alkyl, phenyl- $C_{2-6}$ -alkenyl or phenyl- $C_{2-6}$ -alkynyl, whilst the phenyl ring is optionally  
25 substituted by hydroxy,  $C_{1-4}$ -alkyl,  $C_{1-4}$ -alkyloxy, - $NR^7R^8$  or halogen; or

$R^2$  or  $R^3$  denotes a 5- or 6-membered heterocycle optionally C- or N-linked either directly or via a  $C_{1-4}$ -alkylene bridge, which comprises one, two or three heteroatoms selected from  
30 the group consisting of nitrogen, oxygen and sulphur and



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which is optionally mono- or polysubstituted by benzyl or C<sub>1-4</sub>-alkyl;

R<sup>4</sup> or R<sup>6</sup> denotes hydrogen, C<sub>1-4</sub>-alkyl which is optionally substituted by -NR<sup>7</sup>R<sup>8</sup>, or benzyl;

- 5 R<sup>5</sup> denotes hydrogen, C<sub>1-8</sub>-alkyl, which is optionally substituted by halogen;

R<sup>5</sup> denotes phenyl which is optionally substituted by C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, hydroxy, -NR<sup>7</sup>R<sup>8</sup> or halogen;

- 10 R<sup>5</sup> denotes phenyl-C<sub>1-6</sub>-alkyl, wherein the phenyl ring is optionally substituted by C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, hydroxy, -NR<sup>7</sup>R<sup>8</sup> or halogen;

R<sup>5</sup> denotes an amine of formula -NR<sup>7</sup>R<sup>8</sup>;

- 15 R<sup>5</sup> denotes a 5- or 6-membered heterocycle optionally C- or N-linked either directly or via a C<sub>1-4</sub>-alkylene bridge, which comprises one or more heteroatoms selected from the group consisting of nitrogen and oxygen and which is optionally substituted by benzyl or C<sub>1-4</sub>-alkyl;

R<sup>5</sup> denotes a C<sub>3-6</sub>-cycloalkyl which is optionally substituted by =O, hydroxy, C<sub>1-4</sub>-alkyl or C<sub>1-4</sub>-alkyloxy; or

- 20 R<sup>5</sup> denotes a norbornane, norbornene, adamantane or noradamantane group which is optionally substituted by C<sub>1-4</sub>-alkyl;

R<sup>7</sup> denotes hydrogen, a branched or unbranched C<sub>1-4</sub>-alkyl group, or

- 25 R<sup>7</sup> denotes a C-linked 5- or 6-membered heterocycle which comprises one, two or three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and which



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is optionally substituted by benzyl, C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, halogen, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, -OH or =O;

R<sup>8</sup> denotes hydrogen, a branched or unbranched C<sub>1-4</sub>-alkyl group, or

- 5 R<sup>8</sup> denotes a C-linked 5- or 6-membered heterocycle which comprises one, two or three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur and which is optionally substituted by benzyl, C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, halogen, -CN, -NO<sub>2</sub>, -NH<sub>2</sub>, -OH or =O;

10 or

- R<sup>7</sup> and R<sup>8</sup> together with the nitrogen atom form a saturated or unsaturated 5- or 6-membered ring which optionally comprises nitrogen or oxygen as a further heteroatom, wherein the heterocycle is optionally substituted by a branched or  
15 unbranched alkyl group having 1 to 4 carbon atoms, or by a -(CH<sub>2</sub>)<sub>1-4</sub>-phenyl group.

23. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 22, wherein the halogen substituent on the phenyl in the definition of R<sup>1</sup> is chlorine  
20 or fluorine.

24. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 22, wherein the C<sub>1-4</sub>-alkyl substituent on the norbornane, norbornene, adamantane or noradamantane group is methyl.

- 25 25. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 22, wherein the phenyl-C<sub>1-4</sub>-alkyl group in the definition of R<sup>1</sup> is benzyl.

26. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 22, wherein the halogen



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substituent on the phenyl-C<sub>1-4</sub>-alkyl, phenyl-C<sub>2-6</sub>-alkenyl or phenyl-C<sub>2-6</sub>-alkynyl group in the definition of R<sup>1</sup> is chlorine or fluorine.

27. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 22 to 26, wherein the phenyl-C<sub>1-4</sub>-alkyl substituent on the C<sub>1-8</sub>-alkyl group in the definition of R<sup>2</sup> or R<sup>3</sup> is benzyl.

28. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 22 to 26, wherein the halogen substituent on the C<sub>1-8</sub>-alkyl group in the definition of R<sup>2</sup> or R<sup>3</sup> is chlorine or fluorine.

29. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 22 to 28, wherein the C<sub>1-8</sub>-alkyl group in the definition of R<sup>5</sup> is C<sub>1-6</sub>-alkyl.

30. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 22 to 28, wherein the halogen substituent on the phenyl group in the definition of R<sup>5</sup> is chlorine or fluorine.

31. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 22 to 28, wherein the phenyl-C<sub>1-6</sub>-alkyl group in the definition of R<sup>5</sup> is benzyl.

32. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 22 to 28, wherein the halogen substituent on the phenyl-C<sub>1-6</sub>-alkyl group in the definition of R<sup>5</sup> is chlorine or fluorine.

33. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 22 to 28, wherein the C<sub>1-4</sub>-alkyl substituent on the norbornane,



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norbornene, adamantane or noradamantane group in the definition of  $R^5$  is methyl.

34. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 22 to 33, wherein the  $C_{1-4}$  substituent on the heterocycle of the definition of  $R^7$  and  $R^8$  when taken together is methyl.

35. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 22 to 33, wherein the  $-(CH_2)_{1-4}$ -phenyl substituent on the heterocycle of the definition of  $R^7$  and  $R^8$  when taken together is benzyl.

36. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein:

$R^1$  denotes hydrogen,  $C_{1-6}$ -alkyl, which is optionally substituted by  $-COO-C_{1-4}$ -alkyl,  $-CHO$ ,  $-COOH$ ,  $COO-C_{1-4}$ -alkyl,  $COO$ -phenyl,  $-COO$ -benzyl,  $-CONR^7R^8$ ,  $-CO-C_{1-4}$ -alkyl- $NR^7R^8$ ,  $-NR^7R^8$ ,  $-NHCO-C_{1-4}$ -alkyl,  $-NHCO$ -phenyl, hydroxy,  $=O$ ,  $C_{1-4}$ -alkoxy, phenyloxy,  $O$ -phenyl- $O-C_{1-4}$ -alkyloxy, benzyloxy,  $O$ -benzyl- $O-C_{1-4}$ -alkyloxy,  $-OCO-C_{1-4}$ -alkyl,  $-OCO$ -phenyl,  $-OCO$ -pyridyl,  $-OCO$ -benzyl,  $-O-C_{2-4}$ -alkenyl or halogen;

$R^1$  denotes phenyl, wherein the phenyl ring is optionally substituted by  $C_{1-4}$ -alkyl, hydroxy,  $C_{1-4}$ -alkyloxy,  $NR^7R^8$ , or halogen;

$R^1$  denotes phenyl- $C_{1-3}$ -alkyl, wherein the phenyl ring is optionally substituted by  $C_{1-4}$ -alkyl,  $-CO-C_{1-4}$ -alkyl,  $-O-C_{1-4}$ -alkyl- $NR^7R^8$ ,  $C_{1-4}$ -alkyl- $NR^7R^8$ ,  $C_{1-4}$ -alkyl- $OH$ ,  $-COOH$ ,  $-COO-C_{1-4}$ -alkyl,  $-COO$ -phenyl,  $-COO$ -benzyl,  $-CONR^7R^8$ ,  $-CO-C_{1-4}$ -alkyl- $NR^7R^8$ ,  $NR^7R^8$ , hydroxy,  $C_{1-4}$ -alkyloxy, benzyloxy, phenyloxy,  $-OCO-C_{1-4}$ -alkyl,  $-OCO$ -phenyl,  $-OCO$ -benzyl,  $-OCO$ -pyridyl,  $-O-C_{2-4}$ -alkenyl or halogen;



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$R^1$  denotes a cyclopentyl, cyclohexyl, cyclopentanone, cyclohexanone, hydroxycyclopentane or hydroxycyclohexane linked via a single bond or via an alkylene chain having 1 to 4 carbon atoms;

- 5  $R^1$  denotes -CHO, -COOH, -COO- $C_{1-4}$ -alkyl, -COO-phenyl, -COO-benzyl, -CO-NH- $C_{1-4}$ -alkyl, -CO-N( $C_{1-4}$ -alkyl)<sub>2</sub> or -CO-NH-phenyl;

$R^1$  denotes an amine of general formula  $NR^7R^8$ ; or

- $R^1$  denotes a furan, tetrahydrofuran, -pyran, dioxolane, 10 tetrahydropyran, dioxane, thiophene, thiolane, dithiolane, pyrrole, pyrroline, pyrrolidine, pyrazole, pyrazoline, imidazole, imidazoline, imidazolidine, triazole, pyridine, piperidine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, morpholine, thiomorpholine, oxazole, isoxazole, 15 oxazine, thiazole, isothiazole, thiadiazole, oxadiazole or pyrazolidine linked via a single bond or via an alkylene chain with 1 to 4 carbon atoms;

- $R^2$  or  $R^3$  denotes a  $C_{1-7}$ -alkyl, which is optionally substituted by - $NR^7R^8$ , OH,  $C_{1-4}$ -alkyloxy,  $C_{3-6}$ -cycloalkyl, or COOH, 20  $C_{2-5}$ -alkenyl,  $C_{2-5}$ -alkynyl, phenyl- $C_{1-3}$ -alkyl, wherein the phenyl ring is optionally substituted by  $C_{1-4}$ -alkyl, - $NR^7R^8$ , hydroxy,  $C_{1-4}$ -alkyloxy or halogen; or

- $R^2$  or  $R^3$  denotes a furan, tetrahydrofuran, -pyran, dioxolane, tetrahydropyran, dioxane, thiophene, thiolane, dithiolane, 25 pyrrole, pyrroline, pyrrolidine, pyrazole, pyrazoline, imidazole, imidazoline, imidazolidine, triazole, pyridine, piperidine, pyridazine, pyrimidine, pyrazine, piperazine, triazine, morpholine, thiomorpholine, oxazole, isoxazole, oxazine, thiazole, isothiazole, thiadiazole, oxadiazole or 30 pyrazolidine linked via a single bond or via an alkylene chain with 1 to 4 carbon atoms;



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$R^4$  or  $R^6$  denotes hydrogen,  $C_{1-4}$ -alkyl,  $C_{1-4}$ -alkyl- $NR^7R^8$  or benzyl;

$R^5$  denotes hydrogen,  $C_{1-6}$ -alkyl, which is optionally substituted by halogen;

- 5  $R^5$  denotes cyclopentyl, cyclohexyl, cyclopentanone, cyclohexanone, hydroxycyclopentane or hydroxycyclohexane;

$R^5$  denotes pyridyl, tetrahydrofuranyl, tetrahydropyranyl, furyl or a morpholine, piperidine or piperazine group optionally substituted by  $C_{1-4}$ -alkyl or benzyl;

- 10  $R^5$  denotes a phenyl group which is optionally substituted by  $C_{1-4}$ -alkyl, halogen or hydroxy, or

$R^5$  denotes phenyl- $C_{1-3}$ -alkyl, whilst the phenyl ring is optionally substituted by  $C_{1-4}$ -alkyl,  $-NR^7R^8$ , hydroxy,  $C_{1-4}$ -alkyloxy or halogen;

- 15  $R^5$  denotes an amine of general formula  $-NR^7R^8$ ; or

$R^5$  denotes a norbornene, norbornane, adamantane or noradamantane group which is optionally substituted by  $C_{1-4}$ -alkyl;

- 20  $R^7$  denotes hydrogen, a branched or unbranched  $C_{1-4}$ -alkyl group, or

- $R^7$  denotes a C-linked pyrrole, pyrrolidine, pyrazole, imidazole, imidazolidine, triazole, pyridine, piperidine, pyrimidine, pyrazine, piperazine, morpholine, oxazole, isoxazole, thiazole, isothiazole or thiadiazole optionally substituted by  $C_{1-4}$ -alkyl,  $-NO_2$ ,  $-NH_2$ , hydroxy,  $C_{1-4}$ -alkyloxy, chlorine or bromine;
- 25

$R^8$  denotes hydrogen, a branched or unbranched  $C_{1-4}$ -alkyl group, or



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R<sup>8</sup> denotes a C-linked pyrrole, pyrrolidine, pyrazole, imidazole, imidazolidine, triazole, pyridine, piperidine, pyrimidine, pyrazine, piperazine, morpholine, oxazole, isoxazole, thiazole, isothiazole or thiadiazole optionally substituted by C<sub>1-4</sub>-alkyl, -NO<sub>2</sub>, -NH<sub>2</sub>, hydroxy, C<sub>1-4</sub>-alkyloxy, chlorine or bromine;

or

R<sup>7</sup> and R<sup>8</sup> together with the nitrogen atom form a saturated or unsaturated 5- or 6-membered ring which optionally comprises nitrogen or oxygen as a further heteroatom, wherein the heterocycle is optionally substituted by a branched or unbranched alkyl group having 1 to 4 carbon atoms, or by a -(CH<sub>2</sub>)<sub>1-4</sub>-phenyl group.

37. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 36, wherein the C<sub>1-6</sub>-alkyl group in the definition of R<sup>1</sup> is C<sub>1-4</sub>-alkyl.

38. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 36, wherein the halogen substituent on the phenyl group in the definition of R<sup>1</sup> is chlorine or fluorine.

39. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 36, wherein the phenyl-C<sub>1-3</sub>-alkyl group in the definition of R<sup>1</sup> is benzyl.

40. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 36, wherein the halogen substituent on the phenyl-C<sub>1-3</sub>-alkyl group in the definition of R<sup>1</sup> is chlorine or fluorine.

41. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 40,



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wherein the C<sub>1-7</sub>-alkyl group in the definition of R<sup>2</sup> and R<sup>3</sup> when taken together is C<sub>1-5</sub>-alkyl.

42. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 40, wherein the C<sub>3-6</sub>-cycloalkyl group in the definition of R<sup>2</sup> and R<sup>3</sup> when taken together is cyclopropyl.

43. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 40, wherein the phenyl-C<sub>1-3</sub>-alkyl group in the definition of R<sup>2</sup> and R<sup>3</sup> when taken together is benzyl.

44. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 40, wherein the halogen substituent on the phenyl-C<sub>1-3</sub>-alkyl group in the definition of R<sup>2</sup> and R<sup>3</sup> when taken together is chlorine or fluorine.

45. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 44, wherein the C<sub>1-4</sub>-alkyl in the definition of R<sup>4</sup> or R<sup>6</sup> is C<sub>1-3</sub>-alkyl.

46. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 45, wherein the C<sub>1-6</sub>-alkyl group in the definition of R<sup>5</sup> is C<sub>1-4</sub>-alkyl.

47. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 45, wherein the phenyl-C<sub>1-3</sub>-alkyl group in the definition of R<sup>5</sup> is benzyl.

48. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 45,



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wherein the halogen substituent on the phenyl-C<sub>1-3</sub>-alkyl group in the definition of R<sup>5</sup> is chlorine or fluorine.

49. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 45, wherein the C<sub>1-4</sub>-alkyl substituent on the norbornene, norbornane, adamantane or noradamantane group in the definition of R<sup>5</sup> is methyl.

50. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 48, wherein the C<sub>1-4</sub>-alkyl substituent on the heterocycle in the definition of R<sup>7</sup> and R<sup>8</sup> when taken together is methyl.

51. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 36 to 48, wherein the -(CH<sub>2</sub>)<sub>1-4</sub>-phenyl substituent on the heterocycle in the definition of R<sup>7</sup> and R<sup>8</sup> when taken together is benzyl.

52. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein:

R<sup>1</sup> denotes hydrogen; C<sub>1-4</sub>-alkyl, which is optionally substituted by -NHCO-C<sub>1-4</sub>-alkyl, -NR<sup>7</sup>R<sup>8</sup>, hydroxy, C<sub>1-4</sub>-alkyloxy, fluorine, chlorine or bromine; -CHO; -COOH, -COO-C<sub>1-4</sub>-alkyl; phenyl; phenyl-C<sub>1-3</sub>-alkyl, which is optionally substituted by C<sub>1-4</sub>-alkyl, C<sub>1-4</sub>-alkyloxy, -O-C<sub>1-4</sub>-alkyl-NR<sup>7</sup>R<sup>8</sup>, hydroxy, benzyloxy or fluorine; phenyloxy-C<sub>1-3</sub>-alkyl, which is optionally substituted by methoxy; benzyloxymethyl which is optionally substituted by methoxy; benzoyloxymethyl; pyridylcarbonyloxymethyl; cyclohexylmethyl; pyridylmethyl; pyrrolylmethyl; morpholinomethyl; cyclopentyl or furyl;



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$R^2$  or  $R^3$  denotes  $C_{1-5}$ -alkyl, which is optionally substituted by hydroxy, methoxy or cyclopropyl;  $C_{2-4}$ -alkenyl;  $C_{2-4}$ -alkynyl or benzyl;

$R^4$  or  $R^6$  denotes hydrogen,  $C_{1-3}$ -alkyl,  $C_{1-3}$ -alkyl- $NR^7R^8$ ,  
5 N-morpholinoethyl or benzyl;

$R^5$  denotes hydrogen,  $C_{1-4}$ -alkyl, optionally fluorine-substituted, pyridyl, piperidinyl, morpholinyl, piperazinyl, 4-benzylpiperazinyl, furyl, tetrahydrofuranyl, tetrahydropyranyl,  $NR^7R^8$ , cyclopentyl, cyclohexyl, adamantyl,  
10 noradamantyl, norbornyl, norbornenyl, benzyl or phenyl, wherein the phenyl ring is optionally substituted by fluorine;

$R^7$  denotes hydrogen,  $C_{1-4}$ -alkyl or pyridyl; and

$R^8$  denotes hydrogen,  $C_{1-4}$ -alkyl or pyridyl.

15 53. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 52, wherein the phenyl- $C_{1-3}$ -alkyl group in the definition of  $R^1$  is benzyl.

54. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 52, wherein the  
20 phenyl- $C_{1-3}$ -alkyl group in the definition of  $R^1$  is phenoxymethyl.

55. A compound, racemate, enantiomer, mixture or salt according to claim 1, wherein:

$R^1$  denotes hydrogen, methyl, which is optionally substituted  
25 by  $-NH_2$ ,  $-NHMe$ ,  $-NMe_2$ ,  $-N(i\text{-propyl})_2$ ,  $-NHAcetyl$ , hydroxy, methoxy, ethoxy, phenyloxy, methoxyphenyloxy, methoxybenzyloxy, morpholine, benzoyloxy, pyridylcarbonyloxy, pyridine, pyridylamino, methylpiperazine or pyrrole; ethyl which is optionally substituted by  $-NH_2$  or



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hydroxy; n-propyl; isopropyl; n-butyl; tert. butyl;  
 cyclopentyl; cyclohexylmethyl; benzyl which is optionally  
 substituted by hydroxy, methoxy, benzyloxy,  
 dimethylaminoethoxy, N-morpholinoethoxy or fluorine; phenyl;  
 5 phenylethyl; -COOH; -COOethyl; -COOpropyl; -COObutyl or  
 furan;

$R^2$  or  $R^3$  denotes methyl, which is optionally substituted by  
 cyclopropyl; ethyl which is optionally substituted by  
 hydroxy or methoxy; n-propyl; isopropyl; n-butyl; isobutyl;  
 10 tert. butyl; butenyl; n-pentyl; allyl or propargyl;

$R^4$  or  $R^6$  denotes hydrogen, methyl or ethyl, which is  
 optionally substituted by morpholine;

$R^5$  denotes hydrogen, methyl, ethyl, n-propyl, isopropyl,  
 n-butyl, tert. butyl, phenyl, benzyl, pyridine, piperidine,  
 15 morpholine, piperazine, 4-benzylpiperazinyl,  
 tetrahydrofuranyl, tetrahydropyranyl, -NMe<sub>2</sub>, cyclopentyl,  
 cyclohexyl, adamantyl, noradamantyl, norbornanyl or  
 norbornenyl.

56. A compound, racemate, enantiomer, mixture or salt  
 20 according to claim 1, wherein:

$R^1$  denotes methyl which is optionally substituted by -NH<sub>2</sub>,  
 -NHMe, -N(i-propyl)<sub>2</sub>, -NHAcetyl, hydroxy, phenyloxy,  
 methylpiperazine or pyrrole; ethyl which is optionally  
 substituted by -NH<sub>2</sub> or hydroxy; cyclopentyl; benzyl which is  
 25 optionally substituted by hydroxy, methoxy, benzyloxy,  
 dimethylaminoethoxy, N-morpholinoethoxy or fluorine;  
 phenylethyl; -COOH; -COOpropyl; -COObutyl or furan;

$R^2$  or  $R^3$  denotes methyl which is optionally substituted by  
 cyclopropyl; ethyl which is optionally substituted by



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hydroxy or methoxy; n-propyl; isopropyl; n-butyl; isobutyl; butenyl; n-pentyl; allyl or propargyl;

$R^4$  or  $R^6$  denotes hydrogen, methyl or ethyl, which is optionally substituted by morpholine;

5  $R^5$  denotes methyl, ethyl, n-propyl, tert. butyl, cyclopentyl or norbornenyl.

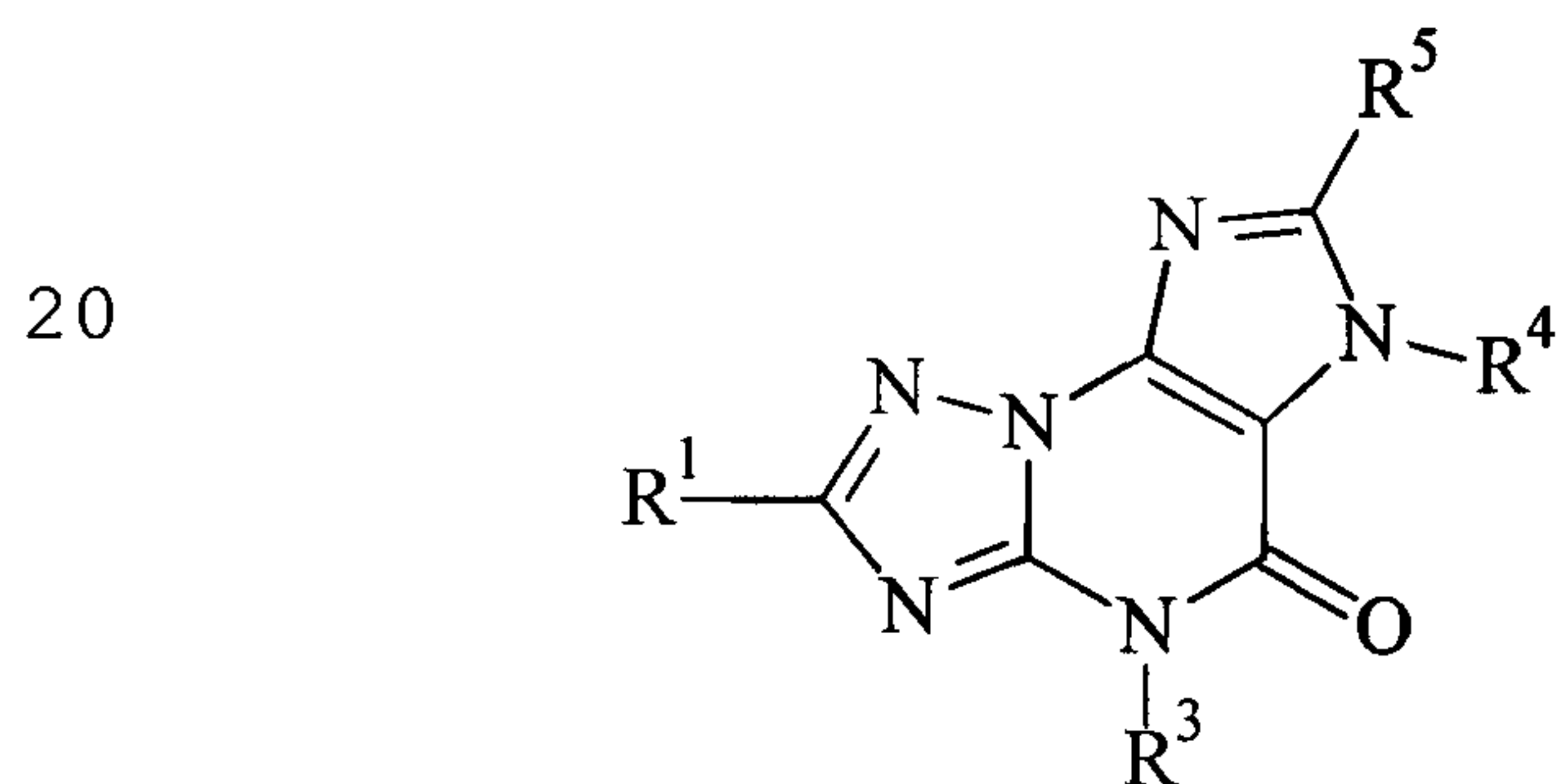
57. A compound, racemate, enantiomer, diastereomer, mixture or salt according to claim 1, wherein  $R^1$  denotes methyl, which is optionally substituted by phenyloxy or  
10 pyrrole; benzyl which is optionally substituted by hydroxy, methoxy, dimethylaminoethoxy or fluorine; cyclopentyl; furan or phenylethyl;

$R^2$  or  $R^3$  denotes ethyl, n-propyl, allyl or propargyl;

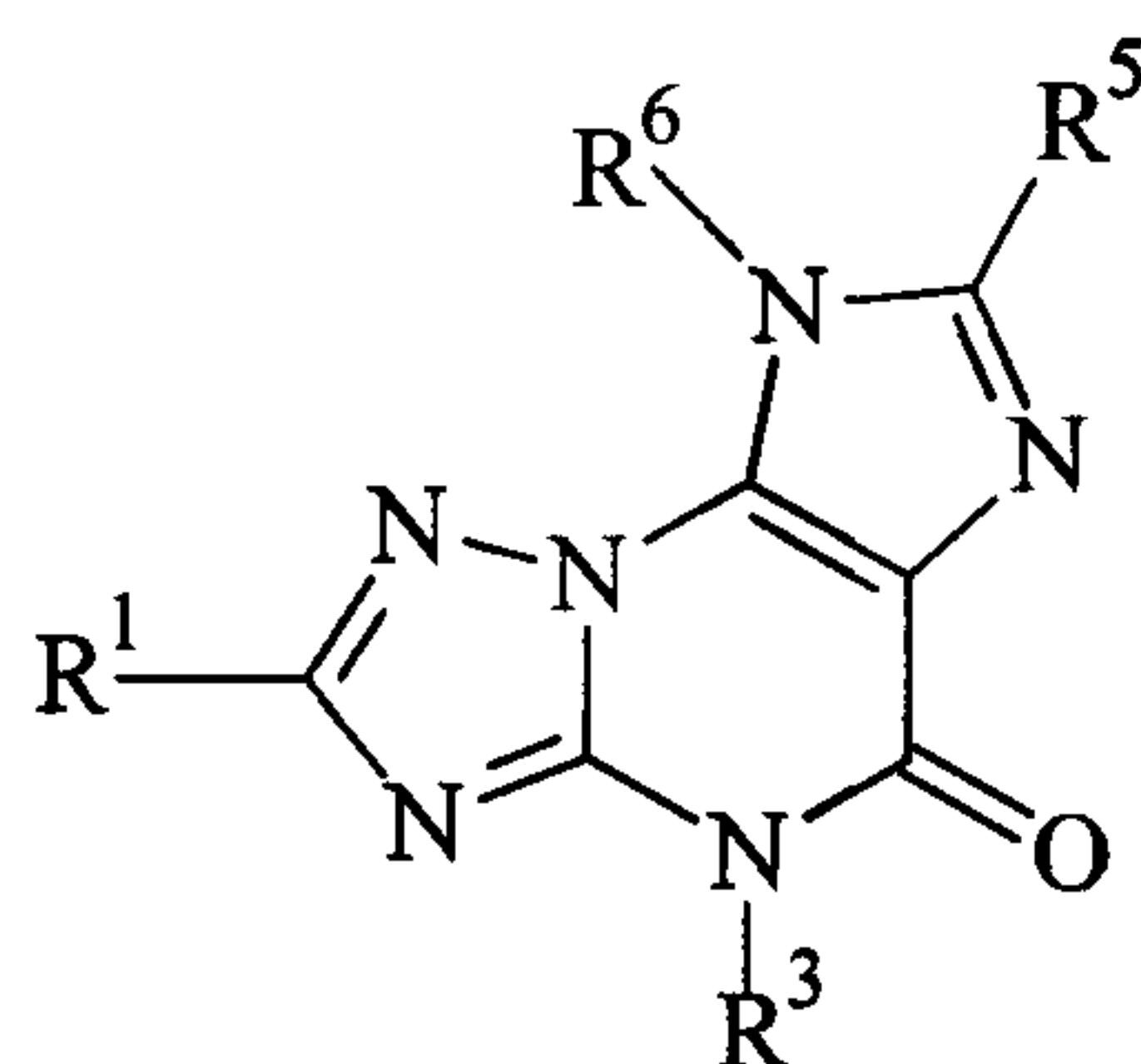
$R^4$  or  $R^6$  denotes hydrogen;

15  $R^5$  denotes methyl, ethyl, n-propyl, tert. butyl, cyclopentyl or norbornenyl.

58. A compound which is an isomer of formulae (Ia) or (Ib)



(Ia)



(Ib)

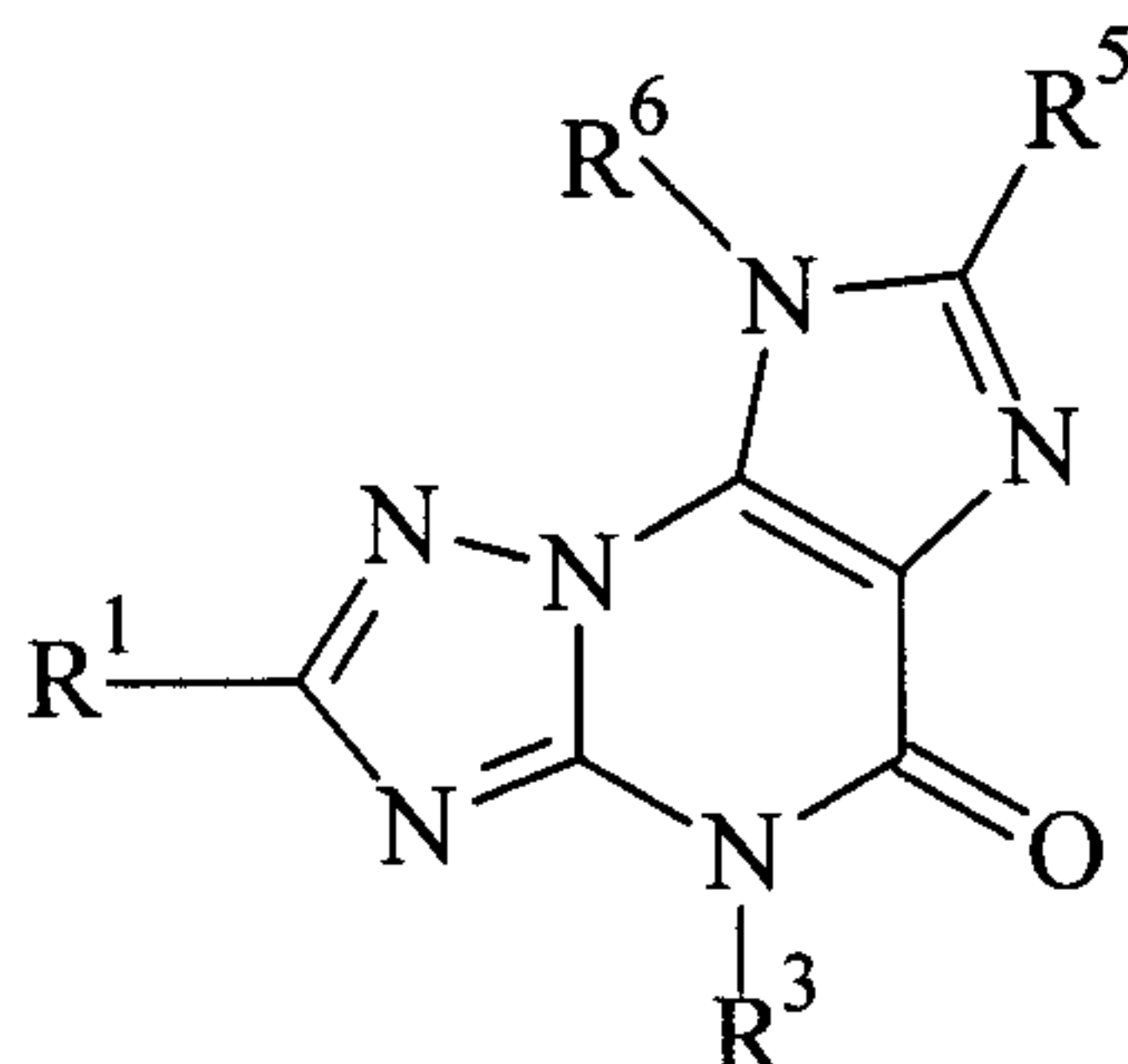
wherein  $R^1$ ,  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^6$  are as defined in any one of  
25 claims 1 to 57.



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59. An isomer of a compound of formula (Ib)

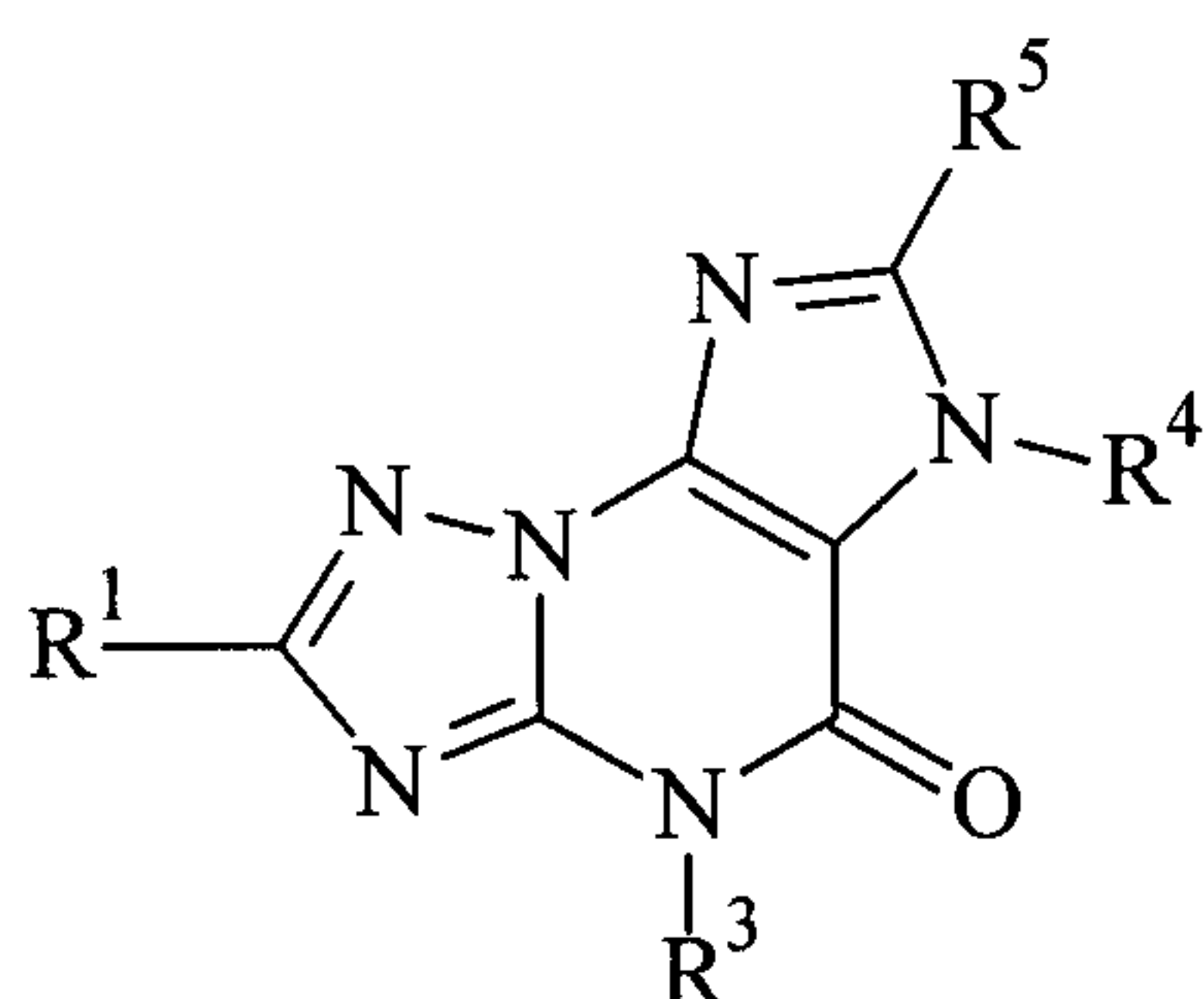


5

(Ib)

wherein R¹, R³, R⁵ and R⁶ are as defined in any one of claims 1 to 57.

60. An isomer of a compound of formula (Ia)



(Ia)

10

15 wherein R¹, R³, R⁴ and R⁵ are as defined in any one of claims 1 to 57.

61. 2-Cyclopentyl-4,7-di-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

20 62. 2-Benzyl-7-methyl-4-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

25 63. 4-Ethyl-7-methyl-2-(2-phenylethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a racemate thereof, an



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enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

64. 4-Ethyl-2-(2-phenylethyl)-7-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a  
5 racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

65. 7-t-Butyl-4-ethyl-2-(4-hydroxybenzyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a  
10 racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

66. 7-t-Butyl-4-ethyl-2-(4-methoxybenzyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a  
15 racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

67. 7-Cyclopentyl-4-ethyl-2-phenyloxymethyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a  
20 racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

68. 7-Cyclopentyl-4-ethyl-2-(N-pyrrolylmethyl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a  
25 racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

69. 2-(2-Furanyl)-7-methyl-4-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a racemate thereof, an



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enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

70. 2-(2-Furanyl)-4,7-di-n-propyl-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

71. 2-Cyclopentyl-7-ethyl-4-(1-propen-3-yl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

72. 2-Cyclopentyl-7-ethyl-4-(1-propin-3-yl)-imidazo[4.5-e]-s-triazolo[1.5-a]pyrimidin-5-one; or a racemate thereof, an enantiomer thereof; a diastereomer thereof, a mixture thereof, or a pharmacologically acceptable salt thereof.

73. A pharmaceutical composition comprising a compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 57 and 61 to 72 or an isomer according to any one of claims 58 to 60 and a pharmaceutically acceptable carrier or diluent.

74. A pharmaceutical composition according to claim 73 with an adenosine-antagonistic activity.

75. Use of a compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 57 and 61 to 72 or an isomer according to any one of claims 58 to 60 in preparation of a pharmaceutical composition with adenosine-antagonistic activity.

76. Use of a compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of



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claims 1 to 57 and 61 to 72 or an isomer according to any one of claims 58 to 60 for treatment of a disease or condition responsive to a substance with adenosine-antagonistic activity.

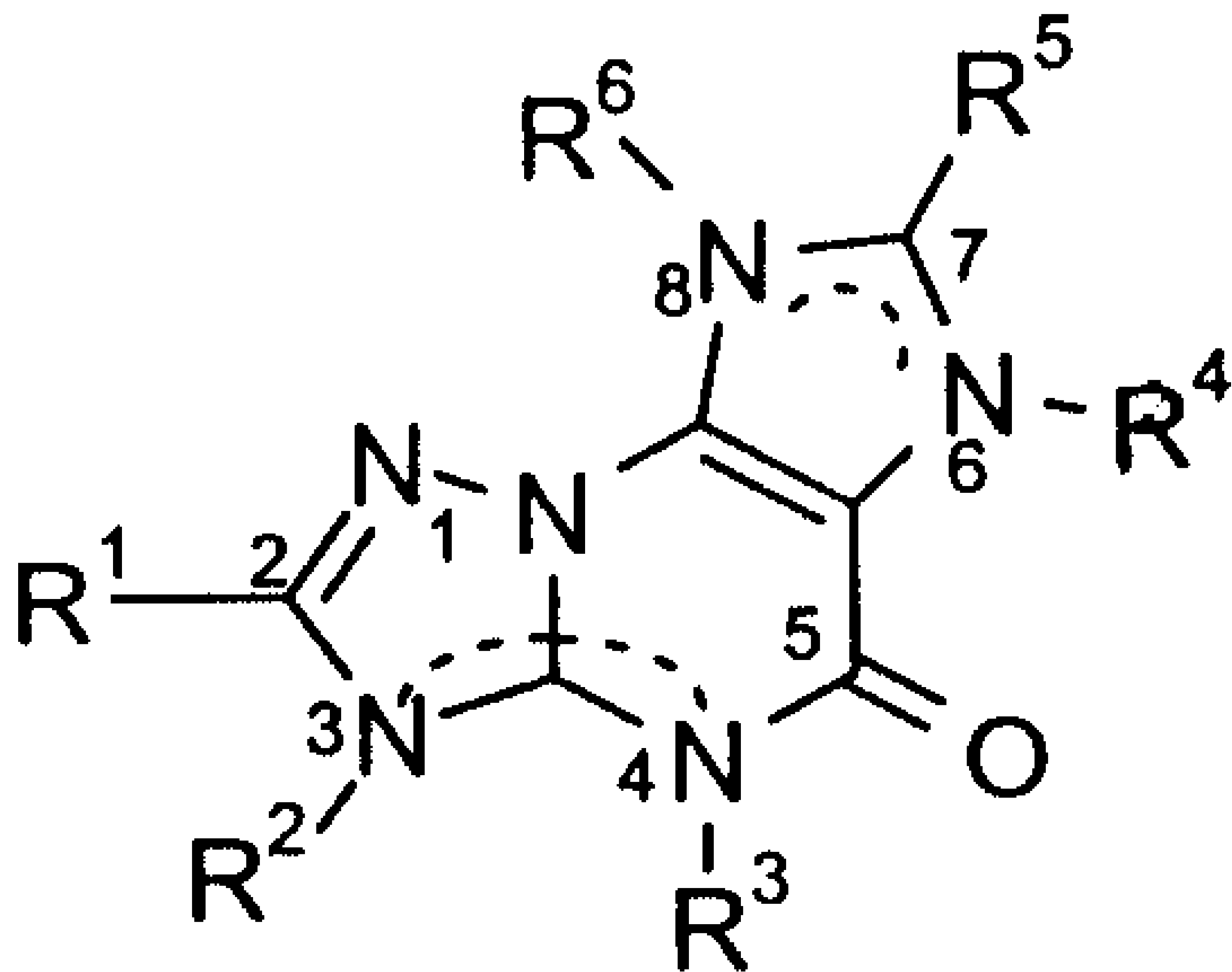
5 77. A compound, racemate, enantiomer, diastereomer, mixture or salt according to any one of claims 1 to 57 and 61 to 72 or an isomer according to any one of claims 58 to 60 for treatment of a disease or condition responsive to a substance with adenosine-antagonistic  
10 activity.

FETHERSTONHAUGH &amp; CO.

OTTAWA, CANADA

PATENT AGENTS





(I)