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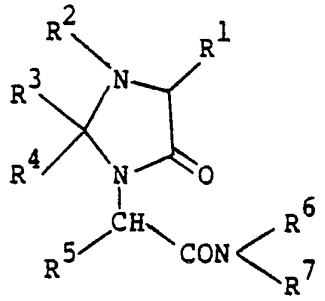
Description

This invention relates to new chemical compounds which have useful pharmacological activity, to processes and intermediates for making them, and pharmaceutical compositions containing them.

According to the invention we provide 5-oxo-1-imidazolidineacetamide derivatives of Structure (1)



(1)

in which

R^1 is H, C_{1-5} alkyl (straight or branched), or a phenyl or benzyl group optionally substituted by C_{1-5} alkyl (straight or branched), C_{1-4} alkoxy (straight or branched) or hydroxy;

R^2 is H, OH, C_{1-5} alkyl (straight or branched), aryl or acyl;

R^3 is H, C_{1-5} alkyl (straight or branched) or phenyl and R^4 is C_{1-5} alkyl (straight or branched) or phenyl, or R^3 and R^4 can together form a 1,4-butylene or 1,5-pentylene group;

R^5 is H or C_{1-5} alkyl (straight or branched);

R^6 is H, C_{1-5} alkyl (straight or branched), —CHR^8CONH_2 or —$CHR^8CONHCHR^9CONH_2$; where R^8 and R^9 (which can be the same or different) are H or C_{1-5} alkyl (straight or branched); and

R^7 is H or C_{1-5} alkyl (straight or branched),

and pharmaceutically acceptable salts thereof.

Preferably R^1 is H, methyl or isobutyl, particularly H.

Preferably R^2 is H, formyl or acetyl.

Examples of aryl groups are phenyl, and naphthyl which may be optionally substituted by C_{1-5} alkyl (straight or branched), C_{1-4} alkoxy (straight or branched) or hydroxy. Preferably the aryl groups are phenyl, 4-hydroxyphenyl, and 4-methoxyphenyl. Examples of acyl groups are C_{1-5} (straight or branched) alkanoyl groups, particularly formyl, acetyl and propionyl, and aroyl groups, particularly benzoyl and substituted benzoyl groups such as 4-methoxybenzoyl.

Preferably R^3 and R^4 are both methyl or together form a 1,4-butylene or 1,5-pentylene group, or R^3 is methyl or isopropyl and R^4 is hydrogen.

Preferably R^5 is H, methyl, isopropyl, 1-methylpropyl or isobutyl.

Preferably R^6 is H, —CHR^8CONH_2 or —$CHR^8CONHCHR^9CONH_2$.

Preferably R^7 is H.

Preferably R^8 is H, methyl, isopropyl, 1-methylpropyl or isobutyl.

Preferably R^9 is H, methyl, isopropyl, 1-methylpropyl or isobutyl.

It will be appreciated that there will be chiral centres present if R^1 is other than hydrogen, if R^3 and R^4 are different, and if any of R^5, R^8 and R^9 are other than hydrogen. The present invention includes all optical isomers of the compounds of Structure (1) in their resolved and partially resolved forms and in the forms of racemic mixtures. When the synthetic precursor for the substituent can be a natural amino acid then preferably that substituent will have the natural (L) configuration.

Particularly preferred compounds of Structure (1) are:

2,2-dimethyl-5-oxo-1-imidazolidineacetamide,

2-(1-methylethyl)-5-oxo-1-imidazolidineacetamide,

2-(2,2-dimethyl-5-oxo-1-imidazolidineacetamido)acetamide,

2-[2-(2,2-dimethyl-5-oxo-1-imidazolidineacetamido)acetamido]acetamide,

2,2,4-trimethyl-5-oxo-1-imidazolidineacetamide,

3-acetyl-2,2-dimethyl-5-oxo-1-imidazolidineacetamide,

3-formyl-2,2-dimethyl-5-oxo-1-imidazolidineacetamide,

(S)-2-[2,2-dimethyl-4-isobutyl-5-oxo-1-imidazolidine acetamido]acetamide,

2-methyl-5-oxo-1-imidazolidineacetamide,

2-(2-isopropyl-5-oxo-1-imidazolidineacetamido)acetamide, and

2-[4S-isobutyl-2-isopropyl-5-oxo-1-imidazolidineacetamido]acetamide,

and their pharmaceutically acceptable salts.

The compounds of Structure (1) can be prepared by reacting a compound of Structure (2)

$$R^{10}HNCHR^1CONHCHR^5CO—W—X \quad (2)$$

in which R^{10} is H, OH, C_{1-5} alkyl (straight or branched) or aryl, W is a bond, —$NHCHR^8CO$— or —$NHCHR^8CONHCHR^9CO$—, and X is —NR^6R^7 or —OH where R^6, R^7, R^8 and R^9 are as defined above provided that R^6 and R^7 are both hydrogen when W is other than a bond, with a carbonyl compound R^3COR^4, and when X is —OH the product is converted into the corresponding compound in which X is NR^6R^7, and when X is —OH and W is a bond or —$NHCHR^8CO$— the product is converted into a compound in which W is —$NHCHR^8CO$— or —$NHCHR^8CONHCHR^9CO$— and X is —NR^6R^7, and when R^2 in the product is hydrogen optionally the product is converted into a compound in which R^2 is acyl, and optionally the compound of Structure (1) is converted into a pharmaceutically acceptable salt.

When R^3 is H the carbonyl compound is an aldehyde and from equimolar to two molar equivalents of the aldehyde are used. When R^3 is other than H the carbonyl compound is a ketone and preferably a larger excess of the ketone is used, together with higher temperatures and/or longer reaction times than for the corresponding reactions with aldehydes.

Conversion of a compound in which X is —OH into a compound in which X is —NR^6R^7 requires the activation of the carboxyl group or the use of a peptide coupling reagent. This procedure will necessitate the temporary protection of the secondary amino groups in compounds in which R^2 is H. Suitable methods for activating carboxyl groups, suitable peptide coupling reagents and protecting groups are all well known to the art and are described for example in 'Peptide Synthesis' by M. Bodansky, Y Klausner and M. Ondetti (Wiley, 1976) and in 'Protective Groups in Organic Synthesis' by T. W. Greene (Wiley, 1981). Examples of activated derivatives of carboxyl groups are acyl chlorides, acyl azides, mixed anhydrides (e.g. formed with an alkyl chloroformate or pivaloyl chloride) and activated esters (e.g. trichlorophenyl, N-hydroxy-succinimido and 1-hydroxybenzotriazole esters). Examples of peptide coupling reagents are carbodiimides and Woodward's Reagent K (N-ethyl-5-phenylisoxazolium-3'-sulphonate). Examples of nitrogen-protecting groups are benzyloxycarbonyl and t-butyloxycarbonyl.

When the peptide side chain contains chiral centres (i.e. when R^5, R^8 and R^9 are other than hydrogen) then the route of synthesis and the reagents will be chosen to ensure that only a small degree of racemisation occurs under the reaction conditions. When racemisation is not a problem and R^6 is a monopeptide or dipeptide unit the preferred synthesis is that in which W is a bond and the monopeptide or dipeptide unit is incorporated at a later stage.

The compounds of Structure (1) have useful nootropic activity, that is they help restore learning and memory difficulties associated with ageing and various pathologies including Alzheimer's disease. To evaluate the nootropic activity, the compounds were submitted to pharmacological tests designed to detect a positive action on cognitive processes disrupted by an experimental cerebral impairment.

In particular the protection against the amnesia induced by maximal electroconvulsive shock (ECS) was studied. The experimental procedure described by Banfi et al., J. Pharmacol. Methods, *8*; 255—264 (1982) was followed: Male albino CD Swiss mice from Charles River (Calco, Italy) are used. Mice were 35 days old. The apparatus is essentially the same as described by Essman [Pharm. Res. Commun., *5*, 295—302, (1973)]. The passage from a light box (10 × 10 × 12 cm) into a dark one (23 × 16 × 12 cm) was punished by unavoidable foot shocks (0.3 mA, 50 Hz, 5 sec). In order to erase newly encoded information in the memory, a maximal ECS (30 mA, 150 msec, 50 Hz) is given to the mice by corneal electrodes immediately after the trial. The retest is performed 24 hr after ECS. Mice that did not cross from the light box into the dark one in 60 sec were considered as not affected by the retrograde amnesic effect of ECS. Groups of control animals were submitted to sham ECS to demonstrate the amnesic action of ECS. Saline or tested compounds are injected i.p. to groups of at least 20 mice 1 hr before the conditioning trial. The number of animals showing retention over the total number in each treated group is compared with that of controls by the chi square test.

The compounds under study are tested at the doses of 0.3 mg/kg, 1 mg/kg, 10 mg/kg and 30 mg/kg. The difference in percentage retention between the control saline-treated mice submitted to ECS and those submitted to sham ECS demonstrated the amnesic action of ECS. The degree of protective activity of the compounds is evaluated by comparing the groups treated with the compounds plus ECS to the group treated with saline alone plus ECS. Significant protective action was observed, for example, after intraperitoneal administration of 2-(1-methylethyl)-5-oxo-1-imidazolidineacetamide or 2-(2,2-dimethyl-5-oxo-1-imidazolidineacetamido)acetamide in a dose range from 0.3 to 30 mg/kg.

The specific mechanism of action of the compounds can be characterised by high affinity choline uptake determinations using synaptosomal preparations from cortical and hippocampal rat tissues, for example as described by F. Pedata et al., Clinical Neuropharmacology, 7, (Suppl. 1), 772—3, (1984). Activity in this test indicates that the compounds might enhance cholinergic neurotransmission by increasing the amount of choline pre-synaptically available which in turn would lead to an increase in brain acetylcholine levels, thus improving the performance of brains in which choline and acetylcholine levels were abnormally low.

An alternative method for investigating the selective action of the compounds of Structure (1) is to test their activity in rats against both the disruptive action of scopolamine on mnestic trace and on the reduction of acetylcholine levels in hippocampus.

In order to use a compound of Structure (1) for the therapeutic treatment of humans and animals, it is normally formulated in accordance with standard pharmaceutical practice as a pharmaceutical composition. Therefore in another aspect the present invention provides a pharmaceutical composition which comprises a compound of Structure (1) and a pharmaceutically acceptable carrier.

The compounds of the Structure (1) may be administered in standard manner for the treatment of the indicated diseases, for example orally, parenterally, rectally, transdermally or via trans-mucosal (for example sub-lingual, or buccal or insufflatory) administration.

The compounds of the Structure (1) which are active when given orally or via sub-lingual or buccal administration can be formulated as syrups, tablets, capsules and lozenges. A syrup formulation will generally consist of a suspension or solution of the compound or salt in a liquid carrier for example, ethanol, glycerine or water with a flavouring or colouring agent. Where the composition is in the form of a tablet, any pharmaceutical carrier routinely used for preparing solid formulations may be used. Examples of such carriers include magnesium stearate, starch, lactose and sucrose. Where the composition is in the form of a capsule, any routine encapsulation is suitable, for example using the aforementioned carriers in a hard gelatin capsule shell. Where the composition is in the form of a soft gelatin shell capsule any pharmaceutical carrier routinely used for preparing dispersions or suspensions may be utilised, for example aqueous gums, celluloses, silicates or oils and are incorporated in a soft gelatin capsule shell.

Typical parenteral compositions consist of a solution or suspension of the compound of the Structure (1) in a sterile aqueous or non-aqueous carrier optionally containing a parenterally acceptable oil, for example polyethylene glycol, polyvinylpyrrolidone, lecithin, arachis oil, or sesame oil.

A typical suppository formulation comprises a compound of Structure (1) which is active when administered in this way, with a binding and/or lubricating agent, for example polymeric glycols, gelatins, cocoa-butter or other low melting vegetable waxes or fats.

Typical transdermal formulations comprise a conventional aqueous or non-aqueous vehicle, for example a cream, ointment, lotion or paste or can be in the form of a medicated plaster, patch or membrane.

Preferably the composition is in unit dosage form, for example a tablet or capsule, so that the patient may administer to himself a single dose.

Piracetam is a compound which is used in the treatment of senile dementia and related disease conditions. The compounds of Structure (1) can be administered in similar regimes to those established for piracetam with any appropriate adjustment in dose levels or frequency of dosing having regard to the greater activity and better pharmacological profile of the compounds of Structure (1).

Each dosage unit for oral administration contains suitably from 0.5 mg/kg to 50 mg/kg, and preferably from 1 mg/kg to 8 mg/kg, and each dosage unit for parenteral administration contains suitably from 0.1 mg/kg to 10 mg/kg, of a compound of Structure (1).

The daily dosage regimen for oral administration is suitably about 0.5 mg/kg to 100 mg/kg, more suitably about 1 mg/kg to 25 mg/kg of a compound of Structure (1) calculated as the free base. The active ingredient may be administered from 1 to 6 times daily. The compounds of Structure (1) may be co-administered with other pharmaceutically active compounds, for example in combination, concurrently or sequentially, particularly with other compounds used in the treatment of elderly patients e.g. tranquillisers, diuretics antihypertensives, vasodilator and inotropic agents.

The invention is illustrated by the following Examples.

Example 1

2,2-Dimethyl-5-oxo-1-imidazolidineacetamide

A. 1) To an ice cold solution of thionyl chloride (5 ml) in dry ethanol (50 ml) a solution of sodium 2,2-dimethyl-5-oxo-1-imidazolidineacetate (4 g) in dry ethanol (50 ml) was added dropwise. The mixture was stirred at 0°C for 1 hour, then at room temperature overnight. After evaporation under reduced pressure, the residue was taken up with a saturated solution of sodium hydrogen carbonate and extracted with 3 × 100 ml of dichloromethane. The organic layer was dried and evaporated, to yield ethyl 2,2-dimethyl-5-oxo-1-imidazolidineacetate (2.57 g) as a colorless oil (Rf. 0.49, methanol/acetone 1:1; silica gel plates). Oxalate salt m.p. 109—113°C (ethanol/diethyl ether).

2) An ice cold solution of ethyl 2,2-dimethyl-5-oxo-1-imidazolidineacetate (2 g) in methanol (150 ml) was saturated with gaseous ammonia. The solution was stirred at room temperature for 36 hours. After evaporation the residue was chromatographed on a silica gel column, eluting with dichloromethane/methanol 6:4. The selected fractions were collecetd, evaporated and the residue was crystallized from ethanol, to give 1 g of the title compound, as a white powder, m.p. 144—146°C.

B) To a solution of glycylglycinamide acetate (10 g) in methanol (250 ml) and acetone (125 ml), was added Amberlite IRA—68 resin (20 g). Amberlite is a registered trade mark and IRA—68 is a weakly basic resin. The suspension was stirred at room temperature for 1 hour, then resin was filtered off and the solution was evaporated under reduced pressure. The residue was suspended in refluxing acetone (250 ml) and methanol was added to obtain a clear solution, which was refluxed for 2 hours. Evaporation and trituration of the residue with acetone gave 6.85 g of the title compound.

Example 2

1) To 50 ml of anhydrous ethanol stirred at 0—5°C, 2 ml thionyl chloride were added. At the same temperature 2.1 g (0.01 mol) of sodium 2-(1-methylethyl)-5-oxo-1-imidazolidineacetate were added. The suspension obtained was stirred at 0°C for 1 hour and at room temperature for 2 hours. The solvent was evaporated under reduced pressure and the residue taken up with ethyl acetate. The solid residue was filtered off and the solvent evaporated. The residue was dissolved in a saturated solution of sodium hydrogen carbonate and extracted with 3 × 50 ml of dichloromethane. The organic layers were dried and evaporated to give ethyl 2-(1-methylethyl)-5-oxo-1-imidazolidineacetate (0.9 g) as a pale-yellow oil (42%) (Rf 0.6, ethyl acetate/dichloromethane 6:4; silica gel plates). Hydrochloride salt, m.p. 148—149°C (methanol/ethyl acetate).

2) An ice cold solution of 3.8 g (0.018 mol) of ethyl 2-(1-methylethyl)-5-oxo-1-imidazolidineacetate in 100 ml of methanol was saturated with gaseous ammonia. The solution was stirred at room temperature overnight and the solvent was evaporated under reduced pressure, to give 2-(1-methylethyl)-5-oxo-1-imidazolidineacetamide (3.4 g) as a viscous oil (Rf 0.33; ethyl acetate/methanol 6:4; silica gel plates). Monohydrate of sulphate salt m.p. 64°C resolidifying with final decomposition at 114—118°C.

Example 3

2-(2,2-Dimethyl-5-oxo-1-imidazolidineacetamido)acetamide

To a solution of glycylglycylglycinamide acetate (800 mg) in methanol (8 ml) and acetone (15 ml), Amberlite IRA—68 resin (2 ml) was added. The suspension was stirred at room temperature for 1 hour, then the resin was filtered off and the solution was evaporated under reduced pressure. The residue was suspended in acetone and stirred at room temperature overnight. The precipitate was collected and crystallized from ethyl acetate, to give the title compound, as a white powder, m.p. 102—105°C dec.

Example 4

2-[2-(2,2-Dimethyl-5-oxo-1-imidazolidineacetamido)acetamido]acetamide

The same procedure of the Example 3 starting from triglycylglycinamide acetate afforded the title compound as a white powder, Rf 0.2 (dichloromethane/methanol 1:1; silica gel plates), m.p. 100—105°C dec.

Example 5

2,2,4-Trimethyl-5-oxo-1-imidazolidineacetamide

The same procedure of the Example 3 starting from alanylglycinamide acetate afforded the title compound as a white hygroscopic solid, Rf 0.48 (dichloromethane/methanol 1:1; silica gel plates). Maleate salt, m.p. 142—144°C dec.

Example 6

3-Acetyl-2,2-dimethyl-5-oxo-1-imidazolidineacetamide

A solution of 2,2 dimethyl-5-oxo-1-imidazolidineacetamide (1.7 g) in acetic anhydride (9 ml) was stirred at 70—80°C for 5 minutes. The precipitate was collected and washed with acetone, affording the title compound as a white powder, m.p. 188—189°C (ethyl acetate).

Example 7

3-Formyl-2,2-dimethyl-5-oxo-1-imidazolidineacetamide

The same procedure of Example 6, using mixed acetic-formic anhydride yielded the title compound as a white powder, m.p. 211—213°.

Example 8

(S)-2-[2,2-Dimethyl-4-isobutyl-5-oxo-1-imidazolidine acetamido]acetamide

The same procedure of Example 3 starting from L-leucylglycylglycinamide hydrochloride, afforded the title compound as a white hygroscopic solid (Rf 0.47 dichloromethane-methanol 7:3, silica gel plates).

Example 9

2-Methyl-5-oxo-1-imidazolidineacetamide

A solution of glycylglycinamide (0.5 g) and acetaldehyde (0.4 ml) in methanol (5 ml) was stirred at room temperature for 8 hours. Evaporation of the solvent gave a residue which was chromatographed on a silica gel column (eluant dichloromethane/methanol 75:25). The selected fractions were collected, evaporated to give the title compound (Rf = 0.3, dichloromethane/methanol 7:3, silica gel plates). Mass spectrum (E.I., 70 eV, 1.5 mA), m/z = 142 (M^+. —CH_3), 99.

Example 10

2-(2-Isopropyl-5-oxo-1-imidazolidineacetamido)acetamide

The same procedure of example 9, starting from glycylglycylglycinamide and isobutyraldehyde, afforded the title compound as a white hygroscopic solid, m.p. 65—70°C. Mass spectrum (E.I., 70 eV, 1.5 mA), m/z = 199 (M^+. —C_3H_7).

Example 11

2-[4S-Isobutyl-2-isopropyl-5-oxo-1-imidazolidineacetamido]acetamide

The same procedure of example 9, starting from L-leucylglycylglycinamide and isobutyraldehyde, afforded the title compound as a diastereoisomeric mixture, Rf 0.58 (dichloromethane-methanol 7:3) Mass spectrum (E.I., 70 eV, 1.5 mA), m/z = 255 (M^+. $-C_3H_7$).

Example 12

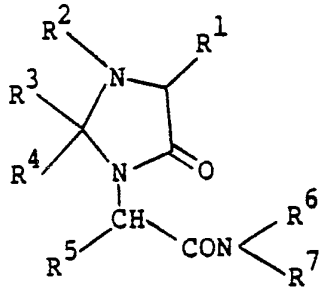
Composition for 1 tablet

2-(1-methylethyl)-5-oxo-1-imidazolidineacetamide	100 mg
lactose	100 mg
corn starch	80 mg
talcum	11.5 mg
silicon dioxide	4 mg
magnesium stearate	2.5 mg
gelatine	2.0 mg

For the manufacture of 1000 tablets, 100 g of active ingredient are mixed with 100 g of lactose and 70 g of corn starch. The mixture is moistened with an aqueous solution of gelatine and then granulated and dried. The granules are mixed with 10 g of corn starch, 11.5 g of talcum, 4.0 g of silicon dioxide and 2.5 g of magnesium stearate and the mixture is pressed into tablets each weighing 300 mg and having the active ingredient content of 100 mg. The tablets can have different shapes and breaking notches for finer adjustment of the dosage.

Claims for the Contracting States: BE CH DE FR GB IT LI LU NL SE

1. A compound of Structure (1)



(1)

wherein

R^1 is H, C_{1-5} alkyl (straight or branched), or a phenyl or benzyl group optionally substituted by C_{1-5} alkyl (straight or branched), C_{1-4} alkoxy (straight or branched) or hydroxy;

R^2 is H, OH, C_{1-5} alkyl (straight or branched), aryl or acyl;

R^3 is H, C_{1-5} alkyl (straight or branched) or phenyl and R^4 is C_{1-5} alkyl (straight or branched) or phenyl, or R^3 and R^4 can together form a 1,4-butylene or 1,5-pentylene group;

R^5 is H or C_{1-5} alkyl (straight or branched);

R^6 is H, C_{1-5} alkyl (straight or branched), $—CHR^8CONH_2$ or $—CHR^8CONHCHR^9CONH_2$; where R^8 and R^9 (which can be the same or different) are H or C_{1-5} alkyl (straight or branched); and

R^7 is H or C_{1-5} alkyl (straight or branched),

or a pharmaceutically acceptable salt thereof.

2. A compound according to Claim 1 in which R^1 is H, methyl or isobutyl.

3. A compound according to Claim 1 or Claim 2 in which R^2 is H, formyl or acetyl.

4. A compound according to any one of Claims 1 to 3 in which R^3 and R^4 are both methyl or together form a 1,4-butylene or 1,5-pentylene group, or R^3 is hydrogen and R^4 is isopropyl, or R^3 is hydrogen and R^4 is methyl.

5. A compound according to any one of Claims 1 to 4 in which R^5 is H, methyl, isopropyl, 1-methylpropyl or isobutyl.

6. A compound according to any one of Claims 1 to 5 in which R^6 is H, $—CHR^8CONH_2$ or $—CHR^8CONHCHR^9CONH_2$.

7. A compound according to any one of Claims 1 to 6 in which R^7 is H.

8. A compound according to any one of Claims 1 to 7 in which R^8 is H, methyl, isopropyl, 1-methylpropyl or isobutyl.

9. A compound according to any one of Claims 1 to 8 in which R^9 is H, methyl, isopropyl, 1-methylpropyl or isobutyl.

10. A compound according to Claim 1 which is
2-(1-methylethyl)-5-oxo-1-imidazolidineacetamide, or
2-(2,2-dimethyl-5-oxo-1-imidazolidineacetamido)acetamide.

11. A compound according to Claim 1 selected from the group
2,2-dimethyl-5-oxo-1-imidazolidineacetamide,
2-[2-(2,2-dimethyl-5-oxo-1-imidazolidineacetamido)acetamido]acetamide,
2,2,4-trimethyl-5-oxo-1-imidazolidineacetamide,
3-acetyl-2,2-dimethyl-5-oxo-1-imidazolidineacetamide,
3-formyl-2,2-dimethyl-5-oxo-1-imidazolidineacetamide,
(S)-2-[2,2-dimethyl-4-isobutyl-5-oxo-1-imidazolidine acetamido]acetamide,
2-methyl-5-oxo-1-imidazolidineacetamide,
2-(2-isopropyl-5-oxo-1-imidazolidineacetamido)acetamide, and
2-[4S-isobutyl-2-isopropyl-5-oxo-1-imidazolidineacetamido]acetamide.

12. A pharmaceutical composition comprising a compound according to any one of Claims 1 to 11 and a pharmaceutical carrier.

13. A compound according to any one of Claims 1 to 11 for use as a therapeutic agent.

14. A process for preparing a compound according to Claim 1 which comprises reacting a compound of Structure (2)

$$R^{10}HNCHR^1CONHCHR^5CO—W—X \qquad (2)$$

in which R^{10} is H, OH, C_{1-5} alkyl (straight or branched) or aryl, W is a bond, $—NHCHR^8CO—$ or $—NHCHR^8CONHCHR^9CO—$, and X is $—NR^6R^7$ or —OH where R^6, R^7, R^8 and R^9 are as defined in any one of Claims 1 to 9 provided that R^6 and R^7 are both hydrogen when W is other than a bond; with a carbonyl compound R^3COR^4; and

i) when X is —OH converting the product into the corresponding compound in which X is NR^6R^7;

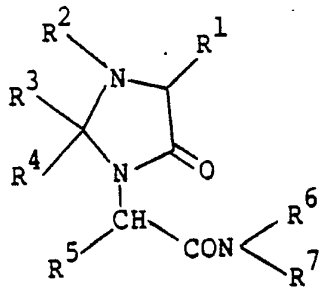
ii) when X is —OH and W is a bond or $—NHCHR^8CO—$ converting the product into a compound in which W is $—NHCHR^8CO—$ or $—NHCHR^8CONHCHR^9CO—$ and X is $—NR^6R^7$;

iii) when R^2 is hydrogen optionally converting the product into a compound in which R^2 is acyl;

iv) optionally forming a pharmaceutically acceptable salt.

Claims for the Contracting State: AT

1. A process for preparing a compound of Structure (1)



(1)

wherein

R^1 is H, C_{1-5} alkyl (straight or branched), or a phenyl or benzyl group optionally substituted by C_{1-5} alkyl (straight or branched), C_{1-4} alkoxy (straight or branched) or hydroxy;

R^2 is H, OH, C_{1-5} alkyl (straight or branched), aryl or acyl;

R^3 is H, C_{1-5} alkyl (straight or branched) or phenyl and R^4 is C_{1-5} alkyl (straight or branched) or phenyl, or R^3 and R^4 can together form a 1,4-butylene or 1,5-pentylene group;

R^5 is H or C_{1-5} alkyl (straight or branched);

R^6 is H, C_{1-5} alkyl (straight or branched), $—CHR^8CONH_2$ or $—CHR^8CONHCHR^9CONH_2$; where R^8 and R^9 (which can be the same or different) are H or C_{1-5} alkyl (straight or branched); and

R^7 is H or C_{1-5} alkyl (straight or branched),

which comprises reacting a compound of Structure (2)

$$R^{10}HNCHR^1CONHCHR^5CO—W—X \quad (2)$$

in which R^{10} is H, OH, C_{1-5} alkyl (straight or branched) or aryl, W is a bond, —$NHCHR^8CO$— or —$NHCHR^8CONHCHR^9CO$—, and X is —NR^6R^7 or —OH where R^6, R^7, R^8 and R^9 are as hereinbefore defined provided that R^6 and R^7 are both hydrogen when W is other than a bond; with a carbonyl compound R^3COR^4; and

i) when X is —OH converting the product into the corresponding compound in which X is NR^6R^7;

ii) when X is —OH and W is a bond or —$NHCHR^8CO$— converting the product into a compound in which W is —$NHCHR^8CO$— or —$NHCHR^8CONHCHR^9CO$— and X is —NR^6R^7;

iii) when R^2 is hydrogen optionally converting the product into a compound in which R^2 is acyl;

iv) optionally forming a pharmaceutically acceptable salt.

2. A process according to Claim 1 in which R^1 is H, methyl or isobutyl.

3. A process according to Claim 1 or Claim 2 in which R^2 is H, formyl or acetyl.

4. A process according to any one of Claims 1 to 3 in which R^3 and R^4 are both methyl or together form a 1,4-butylene or 1,5-pentylene group, or R^3 is hydrogen and R^4 is isopropyl, or R^3 is hydrogen and R^4 is methyl.

5. A process according to any one of Claims 1 to 4 in which R^5 is H, methyl, isopropyl, 1-methylpropyl or isobutyl.

6. A process according to any one of Claims 1 to 5 in which R^6 is H, —CHR^8CONH_2 or —$CHR^8CONHCHR^9CONH_2$.

7. A process according to any one of Claims 1 to 6 in which R^7 is H.

8. A process according to any one of Claims 1 to 7 in which R^8 is H, methyl, isopropyl, 1-methylpropyl or isobutyl.

9. A process according to any one of Claims 1 to 8 in which R^9 is H, methyl, isopropyl, 1-methylpropyl or isobutyl.

10. A process according to claim 1 in which the compound of Structure (1) is
2-(1-methylethyl)-5-oxo-1-imidazolidineacetamide, or
2-(2,2-dimethyl-5-oxo-1-imidazolidineacetamido)acetamide.

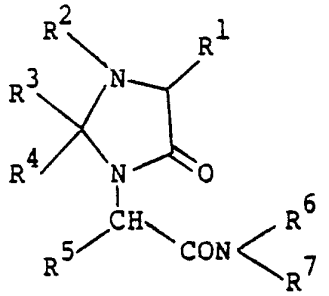
11. A process according to claim 1 in which the compound of Structure (1) is
2,2-dimethyl-5-oxo-1-imidazolidineacetamide,
2-[2-(2,2-dimethyl-5-oxo-1-imidazolidineacetamido)acetamido]acetamide,
2,2,4-trimethyl-5-oxo-1-imidazolidineacetamide,
3-acetyl-2,2-dimethyl-5-oxo-1-imidazolidineacetamide,
3-formyl-2,2-dimethyl-5-oxo-1-imidazolidineacetamide,
(S)-2-[2,2-dimethyl-4-isobutyl-5-oxo-1-imidazolidine acetamido]acetamide,
2-methyl-5-oxo-1-imidazolidineacetamide,
2-(2-isopropyl-5-oxo-1-imidazolidineacetamido)acetamide, and
2-[4S-isobutyl-2-isopropyl-5-oxo-1-imidazolidineacetamido]acetamide.

12. A process for preparing a pharmaceutical composition which comprises bringing into association a compound of Structure (1) in claim 1 and a pharmaceutical carrier.

13. A process according to claim 12 in which the compound of Structure (1) is
2-(1-methylethyl)-5-oxo-1-imidazolidineacetamide, or
2-(2,2-dimethyl-5-oxo-1-imidazolidineacetamido)acetamide.

Patentansprüche für die Vertragsstaaten: BE CH DE FR GB IT LI LU NL SE

1. Verbindung der Struktur (1):



(1)

in der

R^1 ein Wasserstoffatom, einen geradkettigen oder verzweigten C_{1-5}-Alkylrest oder eine Phenyl- oder Benzylgruppe, gegebenenfalls substituiert mit einem geradkettigen oder verzweigten C_{1-5}-Alkylrest, einem geradkettigen oder verzweigten C_{1-4}-Alkoxyrest oder einer Hydroxylgruppe, bedeutet;

R^2 ein Wasserstoffatom, eine Hydroxylgruppe, einen geradkettigen oder verzweigten C_{1-5}-Alkyl-, Aryl- oder Acylrest bedeutet;

R^3 ein Wasserstoffatom, einen geradkettigen oder verzweigten C_{1-5}-Alkylrest oder eine Phenylgruppe bedeutet und R^4 einen geradkettigen oder verzweigten C_{1-5}-Alkylrest oder eine Phenylgruppe bedeutet, oder R^3 und R^4 zusammen eine 1,4-Butylen- oder 1,5-Pentylengruppe bilden;

R^5 ein Wasserstoffatom oder einen geradkettigen oder verzweigten C_{1-5}-Alkylrest bedeutet;

R^6 ein Wasserstoffatom, einen geradkettigen oder verzweigten C_{1-5}-Alkylrest, einen Rest $—CHR^8CONH_2$ oder $—CHR^8CONHCHR^9CONH_2$ bedeutet; wobei R^8 und R^9, die gleich oder unterschiedlich sein können, Wasserstoffatome oder geradkettige oder verzweigte C_{1-5}-Alkylreste bedeuten; und

R^7 ein Wasserstoffatom oder einen geradkettigen oder verzweigten C_{1-5}-Alkylrest bedeutet,

oder ein pharmazeutisch verträgliches Salz davon.

2. Verbindung nach Anspruch 1, in der R^1 ein Wasserstoffatom, eine Methyl- oder Isobutylgruppe bedeutet.

3. Verbindung nach Anspruch 1 oder 2, in der R^2 ein Wasserstoffatom, eine Formyl- oder Acetylgruppe bedeutet.

4. Verbindung nach einem der Ansprüche 1 bis 3, in der sowohl R^3 als auch R^4 Methylgruppen bedeuten oder zusammen eine 1,4-Butylen- oder 1,5-Pentylengruppe bilden, oder R^3 ein Wasserstoffatom und R^4 eine Isopropylgruppe bedeuten, oder R^3 ein Wasserstoffatom und R^4 eine Methylgruppe bedeuten.

5. Verbindung nach einem der Ansprüche 1 bis 4, in der R^5 ein Wasserstoffatom, eine Methyl-, Isopropyl, 1-Methylpropyl- oder Isobutylgruppe bedeutet.

6. Verbindung nach einem der Ansprüche 1 bis 5, in der R^6 ein Wasserstoffatom, einen Rest $—CHR^8CONH_2$ oder $—CHR^8CONHCHR^9CONH_2$ bedeutet.

7. Verbindung nach einem der Ansprüche 1 bis 6, in der R^7 ein Wasserstoffatom ist.

8. Verbindung nach einem der Ansprüche 1 bis 7, in der R^8 ein Wasserstoffatom, eine Methyl-, Isopropyl-, 1-Methylpropyl- oder Isobutylgruppe bedeutet.

9. Verbindung nach einem der Ansprüche 1 bis 8, in der R^9 ein Wasserstoffatom, eine Methyl-, Isopropyl, 1-Methylpropyl- oder Isobutylgruppe bedeutet.

10. Verbindung nach Anspruch 1, nämlich 2-(1-Methylethyl)-5-oxo-1-imidazolidinacetamid oder 2-(2,2-Dimethyl-5-oxo-1-imidazolidinacetamido)-acetamid.

11. Verbindung nach Anspruch 1, nämlich
2,2-Dimethyl-5-oxo-1-imidazolidinacetamid,
2-[2-(2,2-Dimethyl-5-oxo-1-imidazolidinacetamido)-acetamido]-acetamid,
2,2,4-Trimethyl-5-oxo-1-imidazolidinacetamid,
3-Acetyl-2,2-dimethyl-5-oxo-1-imidazolidinacetamid,
3-Formyl-2,2-dimethyl-5-oxo-1-imidazolidinacetamid,
(S)-2-[2,2-Dimethyl-4-isobutyl-5-oxo-1-imidazolidinacetamido]-acetamid,
2-Methyl-5-oxo-1-imidazolidinacetamid,
2-(2-Isopropyl-5-oxo-1-imidazolidinacetamido)-acetamid, oder
2-[4S-Isobutyl-2-isopropyl-5-oxo-1-imidazolidinacetamido]-acetamid.

12. Arzneimittel, enthaltend eine Verbindung nach einem der Ansprüche 1 bis 11 und einen pharmazeutischen Träger.

13. Verbindung nach einem der Ansprüche 1 bis 11 zur Verwendung als therapeutischen Wirkstoff.

14. Verfahren zur Herstellung einer Verbindung nach Anspruch 1, umfassend die Umsetzung einer Verbindung der Struktur (2)

$$R^{10}HNCHR^1CONHCHR^5CO—W—X \qquad (2)$$

in der R^{10} ein Wasserstoffatom, eine Hydroxylgruppe, einen geradkettigen oder verzweigten C_{1-5}-Alkylrest oder einen Arylrest bedeutet, W eine Bindung oder die Reste $—NHCHR^8CO—$ oder $—NHCHR^8CONHCHR^9CO—$ bedeutet und X den Rest $—NR^6R^7$ oder eine Hydroxylgruppe bedeutet, wobei R^6, R^7, R^8 und R^9 die in einem der Ansprüche 1 bis 9 angegebene Bedeutung haben, mit der Maßgabe, daß R^6 und R^7 beide Wasserstoffatome sind, falls W etwas anderes als eine Bindung bedeutet; mit einer Carbonylverbindung R^3COR^4; und

i) falls X eine Hydroxylgruppe bedeutet, Umwandlung des Produktes in die entsprechende Verbindung, in der X den Rest $—NR^6R^7$ bedeutet;

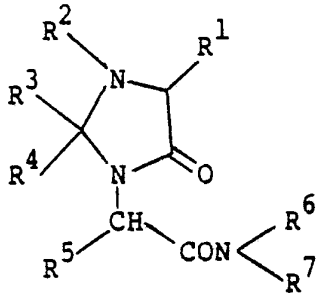
ii) falls X eine Hydroxylgruppe und W eine Bindung oder einen Rest $—NHCHR^8CO—$ bedeutet, Umwandlung des Produktes in eine Verbindung, in der W die Reste $—NHCHR^8CO—$ oder $—NHCHR^8CONHCHR^9CO—$ bedeutet und X den Rest $—NR^6R^7$ darstellt;

iii) falls R^2 ein Wasserstoffatom bedeutet, gegebenenfalls Umwandlung des Produktes in eine Verbindung, in der R^2 eine Acylgruppe ist;

iv) gegebenenfalls Erzeugung eines pharmazeutisch verträglichen Salzes.

Patentansprüche für den Vertragsstaat: AT

1. Verfahren zur Herstellung einer Verbindung der Struktur (1):



(1)

in der

R^1 ein Wasserstoffatom, einen geradkettigen oder verzweigten C_{1-5}-Alkylrest oder eine Phenyl- oder Benzylgruppe, gegebenenfalls substituiert mit einem geradkettigen oder verzweigten C_{1-5}-Alkylrest, einem geradkettigen oder verzweigten C_{1-4}-Alkoxyrest oder einer Hydroxylgruppe, bedeutet;

R^2 ein Wasserstoffatom, eine Hydroxylgruppe, einen geradkettigen oder verzweigten C_{1-5}-Alkyl-, Aryl- oder Acylrest bedeutet;

R^3 ein Wasserstoffatom, einen geradkettigen oder verzweigten C_{1-5}-Alkylrest oder eine Phenylgruppe bedeutet und R^4 einen geradkettigen oder verzweigten C_{1-5}-Alkylrest oder eine Phenylgruppe bedeutet, oder R^3 und R^4 zusammen eine 1,4-Butylen- oder 1,5-Pentylengruppe bilden;

R^5 ein Wasserstoffatom oder einen geradkettigen oder verzweigten C_{1-5}-Alkylrest bedeutet;

R^6 ein Wasserstoffatom, einen geradkettigen oder verzweigten C_{1-5}-Alkylrest, einen Rest $—CHR^8CONH_2$ oder $—CHR^8CONHCHR^9CONH_2$ bedeutet; wobei R^8 und R^9, die gleich oder unterschiedlich sein können, Wasserstoffatome oder geradkettige oder verzweigte C_{1-5}-Alkylreste bedeuten; und

R^7 ein Wasserstoffatom oder einen geradkettigen oder verzweigten C_{1-5}-Alkylrest bedeutet,

dadurch umfassend die Umsetzung einer Verbindung der Struktur (2)

$$R^{10}HNCHR^1CONHCHR^5CO—W—X \qquad (2)$$

in der R^{10} ein Wasserstoffatom, eine Hydroxylgruppe, einen geradkettigen oder verzweigten C_{1-5}-Alkylrest oder einen Arylrest bedeutet, W eine Bindung oder die Reste $—NHCHR^8CO—$ oder $—NHCHR^8CONHCHR^9CO—$ bedeutet und X den Rest $—NR^6R^7$ oder eine Hydroxylgruppe bedeutet, wobei R^6, R^7, R^8 und R^9 wie vorstehend definiert sind, mit der Maßgabe, daß R^6 und R^7 beide Wasserstoffatome bedeuten, falls W etwas anderes als eine Bindung bedeutet; mit einer Carbonylverbindung R^3COR^4; und

i) falls X eine Hydroxylgruppe bedeutet, Umwandlung des Produktes in die entsprechende Verbindung, in der X den Rest $—NR^6R^7$ bedeutet;

ii) falls X eine Hydroxylgruppe und W eine Bindung oder einen Rest $—NHCHR^8CO—$ bedeutet, Umwandlung des Produktes in eine Verbindung, in der W die Reste $—NHCHR^8CO—$ oder $—NHCHR^8CONHCHR^9CO—$ bedeutet und X den Rest $—NR^6R^7$ darstellt;

iii) falls R^2 ein Wasserstoffatom bedeutet, gegebenenfalls Umwandlung des Produktes in eine Verbindung, in der R^2 eine Acylgruppe ist;

iv) gegebenenfalls Erzeugung eines pharmazeutisch verträglichen Salzes.

2. Verfahren nach Anspruch 1, wobei R^1 ein Wasserstoffatom, eine Methyl- oder Isobutylgruppe bedeutet.

3. Verfahren nach einem der Ansprüche 1 oder 2, wobei R^2 ein Wasserstoffatom, eine Formyl- oder Acetylgruppe bedeutet.

4. Verfahren nach einem der Ansprüche 1 bis 3, wobei sowohl R^3 als auch R^4 Methylgruppen bedeuten oder zusammen eine 1,4-Butylen- oder 1,5-Pentylengruppe bilden, oder R^3 ein Wasserstoffatom und R^4 eine Isopropylgruppe bedeuten, oder R^3 ein Wasserstoffatom und R^4 eine Methylgruppe bedeuten.

5. Verfahren nach einem der Ansprüche 1 bis 4, wobei R^5 ein Wasserstoffatom, eine Methyl-, Isopropyl-, 1-Methylpropyl- oder Isobutylgruppe bedeutet.

6. Verfahren nach einem der Ansprüche 1 bis 5, wobei R^6 ein Wasserstoffatom, einen Rest $—CHR^8CONH_2$ oder $—CHR^8CONHCHR^9CONH_2$ bedeutet.

7. Verfahren nach einem der Ansprüche 1 bis 6, wobei R^7 ein Wasserstoffatom ist.

8. Verfahren nach einem der Ansprüche 1 bis 7, wobei R^8 ein Wasserstoffatom, eine Methyl-, Isopropyl-, 1-Methylpropyl- oder Isobutylgruppe bedeutet.

9. Verfahren nach einem der Ansprüche 1 bis 8, wobei R^9 ein Wasserstoffatom, eine Methyl-, Isopropyl-, 1-Methylpropyl- oder Isobutylgruppe bedeutet.

10. Verfahren nach Anspruch 1, wobei die Verbindung der Struktur (1)
2-(1-Methylethyl)-5-oxo-1-imidazolidinacetamid oder
2-(2,2-Dimethyl-5-oxo-1-imidazolidinacetamido)-acetamid ist.

11. Verfahren nach Anspruch 1, wobei die Verbindung der Struktur (1)
2,2-Dimethyl-5-oxo-1-imidazolidinacetamid,
2-[2-(2,2-Dimethyl-5-oxo-1-imidazolidinacetamido)acetamido]-acetamid,

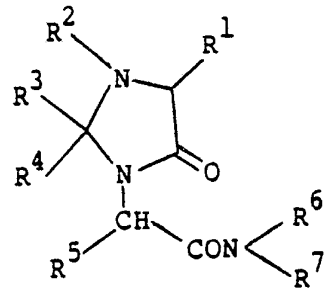
2,2,4-Trimethyl-5-oxo-1-imidazolidinacetamid,
3-Acetyl-2,2-dimethyl-5-oxo-1-imidazolidinacetamid,
3-Formyl-2,2-dimethyl-5-oxo-1-imidazolidinacetamid,
(S)-2-[2,2-Dimethyl-4-isobutyl-5-oxo-1-imidazolidinacetamido]-acetamid,
2-Methyl-5-oxo-1-imidazolidinacetamid,
2-(2-Isopropyl-5-oxo-1-imidazolidinacetamido)-acetamid, oder
2-[4S-Isobutyl-2-isopropyl-5-oxo-1-imidazolidinacetamido]-acetamid ist.

12. Verfahren zur Herstellung eines Arzneimittels, umfassend das Zusammenbringen einer Verbindung der Struktur (1) nach Anspruch 1 und eines pharmazeutischen Trägers.

13. Verfahren nach Anspruch 12, wobei die Verbindung der Struktur (1)
2-(1-Methylethyl)-5-oxo-1-imidazolidinacetamid oder
2-(2,2-Dimethyl-5-oxo-1-imidazolidinacetamido)-acetamid ist.

Revendications pour les Etats contractants: BE CH DE FR GB IT LI LU NL SE

1. Composé de structure (1)



(1)

dans laquelle
R^1 est H, C_{1-5} alkyle (droit ou ramifié), ou un groupe phényle ou benzyle éventuellement substitués par un C_{1-6} alkyle (droit ou ramifié), C_{1-4} alkoxy (droit ou ramifié) ou hydroxy;
R^2 est H, OH, C_{1-5} alkyle (droit ou ramifié), aryle ou acyle;
R^3 est H, C_{1-5} alkyle (droit ou ramifié) ou phényle et R^4 est C_{1-5} alkyle (droit ou ramifié) ou phényle ou R^3 et R^4 forment ensemble un groupe 1,4-butylène ou 1,5-pentylène;
R^5 est H ou C_{1-5} alkyle (droit ou ramifié);
R^6 est H, C_{1-5} alkyle (droit ou ramifié), —CHR^8CONH_2 ou —$CHR^8CONHCHR^9CONH_2$; où R^8 et R^9 (qui peuvent être identiques ou différents) sont H ou C_{1-5} alkyle (droit ou ramifié), et
R^7 est H ou C_{1-5} alkyle (droit ou ramifié), ou son sel pharmaceutiquement acceptables.

2. Composé selon la revendication 1 dans laquelle R^1 est H, méthyle ou isobutyle.

3. Composé selon la revendication 1 ou 2 dans laquelle R^2 est H, formyle ou acétyle.

4. Composé selon l'une quelconque des revendications 1 à 3 dans laquelle R^3 et R^4 sont chacun un méthyle ou forment ensemble un groupe 1,4-butylène ou 1,5-pentylène, ou R^3 est hydrogène et R^4 est isopropyle, ou R^3 est hydrogène et R^4 est méthyle.

5. Composé selon la revendication 4 dans laquelle R^5 est H, méthyle, isopropyle, 1-méthylpropyle ou isobutyle.

6. Composé selon la revendication 5 dans laquelle R^6 est H, —CHR^8CONH_2 ou —$CHR^8CONHCHR^9CONH_2$.

7. Composé selon la revendication 6 dans laquelle R^7 est H.

8. Composé selon la revendication 7 dans laquelle R^8 est H, méthyle, isopropyle, 1-méthylpropyle ou isobutyle.

9. Composé selon la revendication 8 dans laquelle R^9 est H, méthyle, isopropyle, 1-méthylpropyle ou isobutyle.

10. Composé selon la revendication 1 qui est le: 2-(1-méthyléthyl)-5-oxo-1-imidazolidineacétamide, ou le 2-(2,2-diméthyl-5-oxo-1-imidazolidineacétamido)acétamide.

11. Composé selon la revendication 1 choisi parmi le groupe:
2,2-diméthyl-5-oxo-1-imidazolidineacétamide,
2-[2-(2,2-diméthyl-5-oxo-1-imidazolidineacétamido)acétamido]acétamide,
2,2,4-triméthyl-5-oxo-2-imidazolidineacétamide,
3-acétyl-2,2-diméthyl-5-oxo-1-imidazolidineacétamide,
3-formyl-2,2-diméthyl-5-oxo-1-imidazolidineacétamide,
(S)-2-[2,2-diméthyl-4-isobutyl-5-oxo-1-imidazolidine acétamido]acétamide,
2-méthyl-5-oxo-1-imidazolidineacétamide,
2-(2-isopropyl-5-oxo-1-imidazolidineacétamido)acétamide, et
2-[4S-isobutyl-2-isopropyl-5-oxo-1-imidazolidineacétamido]acétamide.

12. Composition pharmaceutique comprenant un composé selon l'une quelconque des revendications 1 à 11 et un véhicule pharmaceutique.

13. Composé selon l'une quelconque des revendications 1 à 11 utilisé comme agent thérapeutique.

14. Procédé de préparation d'un composé selon la revendication 1 comprenant la réaction d'un composé de structure (2)

$$R^{10}HNCHR^1CONHCHR^5CO—W—X \qquad (2)$$

dans laquelle R^{10} est H, OH, C_{1-5} alkyle (droit ou ramifié) ou aryle, W est une liaison, —$NHCHR^8CO$— ou —$NHCHR^8CONHCHR^9CO$—, et X est —NR^6R^7 ou —OH où R^6, R^7, R^8 et R^9 sont comme définis dans l'une quelconque des revendications 1 à 9 sous réserve que R^6 et R^7 sont chacun un hydrogène quand W est autre qu'une liaison; avec un composé carbonyle R^3COR^4; et

i) lorsque X est —OH, conversion du produit en le composé correspondant dans lequel X est NR^6R^7;

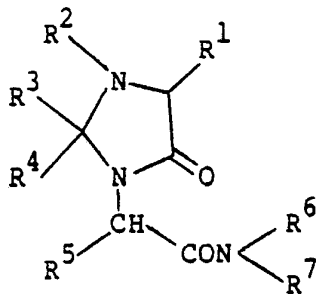
ii) lorsque X est —OH et W est une liaison ou —$NHCHR^8CO$— conversion du produit en un composé dans lequel W est —$NHCHR^8CO$— ou —$NHCHR^8CONHCHR^9CO$— et X est —NR^6R^7;

iii) lorsque R^2 est hydrogène, conversion éventuelle du produit en un composé dans lequel R^2 est acyle;

iv) formation éventuelle d'un sel pharmaceutiquement acceptable.

Revendications pour l'Etat contractant: AT

1. Procédé de préparation d'un composé de structure



(1)

dans laquelle

R^1 est H, C_{1-5} alkyle (droit ou ramifié), ou un groupe phényle ou benzyle éventuellement substitués par un C_{1-5} alkyle (droit ou ramifié), C_{1-4} alkoxy (droit ou ramifié) ou hydroxy;

R^2 est H, OH, C_{1-5} alkyle (droit ou ramifié), aryle ou acyle;

R^3 est H, C_{1-5} alkyle (droit ou ramifié) ou phényle et R^4 est C_{1-5} alkyle (droit ou ramifié) ou phényle ou R^3 et R^4 forment ensemble un groupe 1,4-butylène ou 1,5-pentylène;

R^5 est H ou C_{1-5} alkyle (droit ou ramifié);

R^6 est H, C_{1-5} alkyle (droit ou ramifié), —CHR^8CONH_2 ou —$CHR^8CONHCHR^9CONH_2$; où R^8 et R^9 (qui peuvent être identiques ou différents) sont H ou C_{1-5} alkyle (droit ou ramifié) et

R^7 est H ou C_{1-5} alkyle (droit ou ramifié) comprenant la réaction d'un composé de structure (2)

$$R^{10}HNCHR^1CONHCHR^5CO—W—X \qquad (2)$$

dans laquelle R^{10} est H, OH, C_{1-5} alkyle (droit ou ramifié) ou aryle, W est une liaison, —$NHCHR^8CO$— ou —$NHCHR^8CONHCHR^9CO$—, et X est —NR^6R^7 ou —OH où R^6, R^7, R^8 et R^9 sont comme définis ci-dessus sous réserve que R^6 et R^7 sont chacun un hydrogène quand W est autre qu'une liaison; avec un composé carbonyle R^3COR^4; et

i) lorsque X est —OH, conversion du produit en le composé correspondant dans lequel X est NR^6R^7;

ii) lorsque X est —OH et W est une liaison ou —$NHCHR^8CO$— conversion du produit en un composé dans lequel W est —$NHCHR^8CO$— ou —$NHCHR^8CONHCHR^9CO$— et X est —NR^6R^7;

iii) lorsque R^2 est hydrogène, conversion éventuelle du produit en un composé dans lequel R^2 est acyle;

iv) formation éventuelle d'un sel pharmaceutiquement acceptable.

2. Procédé selon la revendication 1 dans laquelle R^1 est H, méthyle ou isobutyle.

3. Procédé selon la revendication 1 ou 2 dans laquelle R^2 est H, formyle ou acétyle.

4. Procédé selon l'une quelconque des revendications 1 à 3 dans laquelle R^3 et R^4 sont chacun méthyle ou forment ensemble un groupe 1,4-butylène ou 1,5-pentylène ou R^3 est hydrogène et R^4 est isopropyle, ou R^3 est hydrogène et R^4 est méthyle.

5. Procédé selon l'une quelconque des revendications 1 à 4 dans laquelle R^5 est H, méthyle, isopropyle, 1-méthylpropyle, ou isobutyle.

6. Procédé selon l'une quelconque des revendications 1 à 5 dans laquelle R^6 est H, $—CHR^8CONH_2$ ou $—CHR^8CONHCHR^9CONH_2$.

7. Procédé selon l'une quelconque des revendications 1 à 6 dans laquelle R^7 est H.

8. Procédé selon l'une quelconque des revendications 1 à 7 dans laquelle R^8 est H, méthyle, isopropyle, 1-méthylpropyle ou isobutyle.

9. Procédé selon l'une quelconque des revendication 1 à 8 dans laquelle R^9 est H, méthyle, isopropyle, 1-méthylpropyle ou isobutyle.

10. Procédé selon la revendication 1 dans laquelle le composé de structure (1) est 2-(1-méthyléthyl)-5-oxo-1-imidazolidineacétamide, ou le 2-(2,2-diméthyl-5-oxo-1-imidazolidineacétamido)acétamide.

11. Procédé selon la revendication 1 dans laquelle le composé de structure (1) est
2,2-diméthyl-5-oxo-1-imidazolidineacétamide,
2-[2-(2,2-diméthyl-5-oxo-1-imidazolidineacétamido)acétamido]acétamide,
2,2,4-triméthyl-5-oxo-2-imidazolidineacétamide,
3-acétyl-2,2-diméthyl-5-oxo-1-imidazolidineacétamide,
3-formyl-2,2-diméthyl-5-oxo-1-imidazolidineacétamide,
(S)-2-[2,2-diméthyl-4-isobutyl-5-oxo-1-imidazolidine acétamido]acétamide,
2-méthyl-5-oxo-1-imidazolidineacétamide,
2-(2-isopropyl-5-oxo-1-imidazolidineacétamido)acétamide, et
2-[4S-isobutyl-2-isopropyl-5-oxo-1-imidazolidineacétamido]acétamide.

12. Procédé de préparation d'une composition pharmaceutique qui comprend l'association d'un composé de structure (1) selon la revendication 1 et d'un véhicule pharmaceutique.

13. Procédé selon la revendication 12 dans laquelle le composé de structure (1) est:
2-(1-méthyléthyl)-5-oxo-1-imidazolidineacétamide, ou
2-(2,2-diméthyl-5-oxo-1-imidazolidineacétamido)acétamide.