

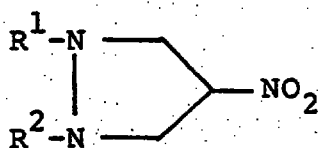
4-NITRO-1,2-HYDROCARBYL-PYRAZOLIDINES AND
METHODS OF SYNTHESIS OF 4-AMINO ANALOGUES THEREFROM

This invention is concerned with novel 4-nitro-1,2-hydrocarbyl pyrazolidines and with a novel process for preparing 4-amino-1,2-hydrocarbyl-pyrazolidines from these novel 4-nitro-1,2-hydrocarbyl-pyrazolidines, all intermediates to the preparation of N-(1,2-hydrocarbyl-4-pyrazolidinyl) benzamides, which latter compounds have utility in controlling emesis and gastric emptying in warm-blooded animals.

The 4-nitro-1,2-hydrocarbyl-pyrazolidines of this invention have not previously been disclosed and the method of preparation from 1,2-disubstituted hydrazines with 1,3-bis-(disubstituted amino)-2-nitropropanes is believed to be novel. The 4-amino-1,2-hydrocarbyl-pyrazolidines have not previously been prepared by the method of this invention, but are known compounds used in the preparation of the benzamides as described in U.S. application Serial No. 041,461 (U.S. Patent 4,207,327). In that disclosure, 4-amino-1,2-hydrocarbyl-pyrazolidines are prepared from 4-halo-1,2-hydrocarbyl-pyrazolidines and ammonia.

The process of this invention involves a novel reaction of 1,2-disubstituted hydrazine acid salts with 1,3-bis-(disubstituted amino)-2-nitropropanes to give novel 4-nitro-1,2-hydrocarbyl-pyrazolidines which are reduced to 4-amino-1,2-hydrocarbyl-pyrazolidines. The process does not require isolation of the 4-nitro-1,2-hydrocarbyl-pyrazolidines from the initial solution before reduction can be carried out.

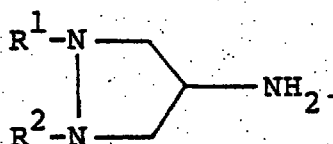
The novel precursors, the 4-nitro-1,2-hydrocarbyl-pyrazolidines, of this invention have the formula:



II

5 wherein R¹ and R² can each represent a loweralkyl, lower-cycloalkyl, phenyl-loweralkyl or substituted phenyl-loweralkyl group and may be the same or different and the hydrocarbyl
10 moieties are further defined in the definitions below.

The 4-amino-1,2-hydrocarbyl-pyrazolidines having the formula:



I

15 are produced as a final product of this invention and have utility in the preparation of hereinabove described
20 benzamides wherein R¹ and R² are as defined above and below.

It is therefore an object of the present invention to provide novel 4-nitro-1,2-hydrocarbyl-pyrazolidine inter-
mediates leading to 4-amino-1,2-hydrocarbyl pyrazolidine
25 intermediates for the preparation of N-(4-pyrazolidinyl) benzamides which have utility in controlling gastric disorders.

Another object is to provide novel methods of preparing both the 4-nitro and 4-amino-1,2-hydrocarbyl pyrazolidines.

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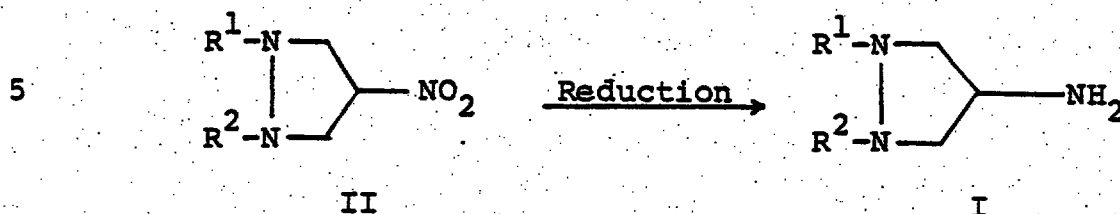
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corresponding 4-amino-1,2-hydrocarbyl-pyrazolidines (I) as represented by the following equation:



10 wherein R¹ and R² are as defined hereinabove. Examples of reducing agents which will serve to convert the nitro compounds to the amino derivatives involve catalytic hydrogenation with hydrogen using metal catalysts, iron powder in acetic acid solvent, zinc dust in basic aqueous alcohol solution, tin-hydrochloric acid, hydrides such as
15 lithium aluminum hydride and diborane, sodium thiosulphate or ammonium sulphide. See Beuler, C.A. & Pearson, D.E. "Survey of Organic Synthesis" I and II (1970 and 1977) Chapter 8 each volume, Wiley Interscience Publ., N.Y., N.Y.

20 In further definition of symbols, the term "lower-alkyl" includes straight and branched chain radicals containing 1 to 8 carbon atoms such as, for example, methyl, ethyl, propyl, isopropyl, n-butyl, tertiary butyl, amyl, isoamyl, n-hexyl, n-heptyl, and n-octyl radicals. A "lower-alkoxy" radical has the formula -O-loweralkyl.

25 The term "lower cycloalkyl" as used herein includes primarily cyclic alkyl radicals containing from three up to twelve carbon atoms inclusive and includes such groups as cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, methyl-cyclopentyl, and ethyl-cyclohexyl.
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The term "phenyl-loweralkyl" as used herein includes the unsubstituted phenyl-loweralkyl radical and phenyl-loweralkyl radicals wherein phenyl is substituted by any radical or radicals which are not reactive or otherwise interfering under the conditions of reaction described herein and include such as loweralkyl, lower-alkoxy, tri-fluoromethyl, halo, acetamido, and sulphamoxyl. The substituted phenyl-loweralkyl radicals have preferably no more than three substituents on the phenyl group and their substituents are preferably such as those given above. These substituents can be in various available positions of the phenyl nucleus and when more than one substituent is present, can be the same or different and can be in various position combinations relative to each other. The loweralkyl and lower-alkoxy substituents each have preferably from one to four carbon atoms which can be arranged as straight or branched chains. Examples of the preferred substituents on phenyl or phenyl-lower alkyl groups are methyl, ethyl, propyl, butyl, fluoro, bromo, chloro, methoxy, ethoxy, propoxy, and butoxy radicals.

Included in the term "phenyl-loweralkyl" are such groups as benzyl, phenethyl, phenpropyl and α -methylbenzyl.

The term heterocyclic residue includes such radicals as pyrrolidino, morpholino, piperidino and piperazino.

The starting 1,2-disubstituted hydrazines (IV) of step I may be prepared by known methods. Symmetrical 1 and 2 disubstituted loweralkyl hydrazines may be prepared by methods given in the book "Organic Synthesis II, (referred to above at p.208-211, unsymmetrical 1 and 2-disubstituted-loweralkyl and cyclo-alkyl hydrazines may be prepared by methods given in "Chemistry

of Open Chain Organic Nitrogen Compounds" by Smith, P.A.S., Vol. 2, Chapter 2, publ. W.A. Benjamin, Inc., N.Y. (1966). Symmetrical phenyl-loweralkyl and substituted-phenyl-lower alkyl hydrazines may be prepared by reacting corresponding phenyl and substituted phenyl-loweralkyl azines with diborane. Unsymmetrical 1-phenyl-loweralkyl-2-loweralkyl or 1-phenyl-loweralkyl-2-cycloalkyl hydrazines may be prepared by the method of U.S. Patent 3,660,426. Symmetrical 1,2-cycloalkyl-hydrazines may be prepared by the method of Cope, A.C. and Engelhart, J.E. in J. Amer. Chem. Soc. 90, 7092-7096.

The starting 1,3-bis-(disubstituted amino)-2-nitropropanes of Formula III may be prepared by the method of Zief, M. and Mason, J.P. in J. Org. Chem. 8, 1-5 (1943) wherein, for example, morpholine and formaldehyde are reacted followed by reaction with nitromethane.

In step 1, an acid salt of 1,2-disubstituted hydrazine (IV) and the 1,3-bis-(disubstituted amino)-2-nitropropanes (III) are reacted in any non-interfering solvent or solvent mixtures at temperatures between room temperature and 150°C, preferably 60-80°C. Suitable solvents include methanol, ethanol, 2-methoxy ethanol and isopropanol and mixtures of such alcohols with aromatic solvents such as toluene, and benzene. Halogenated solvents in mixtures with alcohols may also be used. Any suitable acid salts of the hydrazines may be used such as the hydrochloride or hydrogen sulphate salts. The amine hydrochlorides, V and VI, may be separated by filtration.

In the reaction of step 1 as will be readily realised by one skilled in the art, the $-NR^3R^4$ and $-NR^5R^6$ radicals in the 1,3 positions on the nitro propane are transient and

serve as proton acceptors and do not appear in the pyrazolidine structure. Thus, any member of $-NR^3R^4$ or $-NR^5R^6$ combinations on nitropropane within the scope of the definitions can be reacted with a given 1,2-disubstituted hydrazine acid salt to produce the same 4-nitro-1,2-hydrocarbyl-pyrazolidine. However, the preferred structures are the heterocyclic residues formed by R^3 and R^4 and R^5 and R^6 with the adjacent nitrogen atom such as morpholine, pyrrolidine, and piperidine, inasmuch as fewer side reactions occur. Of these heterocyclic residues, the use of the 1,3-di-morpholine combination is a preferred embodiment of the invention. Thus, the preferred nitropropane starting reagent is 1,3-dimorpholino-2-nitropropane. A preferred 1,2-disubstituted hydrazine is 1,2-diethylhydrazine and a preferred acid salt thereof is the dihydrochloride.

As mentioned above, it is not essential to totally isolate the 4-nitro-1,2-hydrocarbyl-pyrazolidines from the solution in step 1 before proceeding to the next step, it being only necessary to filter off the amine salts V and VI. However, if it is intended to separate these 4-nitro-1,2-hydrocarbyl-pyrazolidines as individual entities in substantially pure form, the solvent of the reaction mixture may be evaporated off, the residue dissolved in a non-polar solvent such as toluene and the resulting amine hydrochlorides V and VI then filtered off. The non-polar solvent may then be evaporated off to give the 4-nitro-1,2-hydrocarbyl-pyrazolidines (II). The compound may then be further purified by column chromatography. When the preferred 1,3-dimorpholino-2-nitropropane is used, V and VI will, of course, be identical, i.e. morpholino hydrochloride.

The invention may be put into practice in various ways and a number of specific embodiments will be described to illustrate the invention with reference to the accompanying examples.

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Example 1

4-Nitro-1,2-diethyl-pyrazolidine

A stirred solution of 4.03 g (0.025 moles) of 1,2-diethyl hydrazine dihydrochloride and 6.72 g (0.026 moles) of 1,3-dimorpholino-2-nitropropane in a mixture of 28 ml of methanol and 16 ml of toluene was heated at reflux for 3 hours. The solvents were evaporated under reduced pressure and the residue was re-suspended in toluene. The solid (mostly morpholine hydrochloride) was removed by filtration, leaving a solution of the title compound in toluene. Evaporation of the toluene gave an oil weighing 5.1 g, the free base of the title compound with minor impurities. Column chromatography on Florisil (Trade Mark), eluting with toluene, gave pure title compound which was obtained as an oil by evaporation of the toluene under reduced pressure. The product was characterised as follows: Infra Red (CHCl_3 , microns) 6.46 (S), 6.94 (M), 7.27 (S) and 9.82 (M); Nuclear Magnetic Resonance (CDCl_3 , δ) = 5.18 (m, 1H), 3.16-3.75 with weight center at 3.47 (m, 4H), 2.56 (q, 7.7H₂, 4H), 1.07 (t, 7.7H₂, 6H); Mass Spec: M^+ 173.

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Example 2

4-Nitro-1,2-diisopropyl-pyrazolidine

Following the procedure of Example 1, but substituting an equal molar amount of 1,2-diisopropyl hydrazine dihydro-

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chloride for 1,2-diethyl hydrazine dihydrochloride, the title compound was obtained.

Example 3

4-Nitro-1,2-diethyl-pyrazolidine

To a suspension of 3 g (0.022 moles) potassium carbonate in 20 ml ethanol in an ice bath was added 1.8 g (0.011 moles) of diethyl hydrazine dihydrochloride monohydrate with stirring for about 5 minutes. To this mixture was added 1.92 (0.011 moles) of 1,3-bis-dimethylamino-2-nitropropane and stirring was continued at room temperature for 2.5 hours. The alcoholic solution was decanted from the solid and evaporated to give a dark oil. Diethyl ether was added to give a suspension. Magnesium sulphate was added and the liquid portion separated and evaporated to an oil. Nuclear Magnetic Resonance confirmed the presence of the product with some contamination by starting nitro compound.

Example 4

4-Nitro-1,2-Bis(4-methoxybenzyl)pyrazolidine.

Di-(4-methoxybenzyl) azine was first prepared by reacting 2 moles of p-methoxybenzaldehyde with 1 mole hydrazine in isopropyl alcohol at 10°C. Di-(4-methoxybenzyl) hydrazine was obtained by reacting the azine with diborane in tetrahydrofuran under nitrogen atmosphere at or below 10°C and isolated as an oil. The dihydrochloride salt of bis-(4-methoxybenzyl) hydrazine was obtained as white solid by mixing with hydrogen chloride gas in isopropanol followed by addition of methylene chloride and toluene (81% yield

based on azine). 1,2-Di-(4-methoxybenzyl)hydrazine (3.5 g, 0.01 mole) and 1,3-dimorpholine-1,2-nitropropane (2.6 g, 0.01 mole) were suspended in a mixture of 30 ml of methanol and 20 ml of toluene and heated to reflux for 3 hours. The reaction mixture was evaporated to dryness and the residue extracted with toluene and filtered. The toluene filtrate was evaporated to give 3.5 g of brown oil which was purified by column chromatography using 10% diethyl ether - 90% methylene chloride on silica gel. Nuclear Magnetic Resonance and mass spectra confirmed the structure of the product as being that of title compound. The oil solidified after one day standing at room temperature.

Examples 5A to 5J

Following the procedure of Example 1, but substituting an equal molar amount of the following for 1,2-di-ethyl hydrazine hydrochloride:

1,2-dicyclohexyl hydrazine dihydrochloride, (Example 5A)
1-cyclohexyl-2-methyl hydrazine dihydrochloride, (Example 5B)
1-isopropyl-2-methyl hydrazine dihydrochloride, (Example 5C)
1-ethyl-2-methyl hydrazine dihydrochloride, (Example 5D)
1-isopropyl-2-ethyl hydrazine dihydrochloride, (Example 5E)
1-benzyl-2-methyl hydrazine dihydrochloride, (Example 5F)
1-benzyl-2-ethyl hydrazine dihydrochloride, (Example 5G)
1-cyclohexyl-2-ethyl hydrazine dihydrochloride, (Example 5H)
1,2-dibenzyl hydrazine dihydrochloride, (Example 5I) and
1-(4-methoxybenzyl)-2-ethyl hydrazine dihydrochloride
(Example 5J)

there are obtained:

- 4-nitro-1,2-dicyclohexyl-pyrazolidine, (Example 5A)
4-nitro-1-cyclohexyl-2-methyl-pyrazolidine, (Example 5B)
4-nitro-1-isopropyl-2-methyl-pyrazolidine, (Example 5C)
4-nitro-1-ethyl-2-methyl-pyrazolidine, (Example 5D)
5 4-nitro-1-isopropyl-2-ethyl-pyrazolidine, (Example 5E)
4-nitro-1-benzyl-2-methyl-pyrazolidine, (Example 5F)
4-nitro-1-benzyl-2-ethyl-pyrazolidine, (Example 5G)
4-nitro-1-cyclohexyl-2-ethyl-pyrazolidine (Example 5H)
4-nitro-1,2-dibenzyl-pyrazolidine, (Example 5I) and
10 4-nitro-1-(4-methoxybenzyl)-2-ethyl-pyrazolidine, (Example 5J)

Examples 6A to 6E

Following the procedure of Example 4, but substituting equal molar amounts of the following for di(4-methoxybenzyl) hydrazine:

- 15 di-(3,4,5-trimethoxybenzyl)hydrazine, (Example 6A)
bis-(2,4-dimethoxybenzyl)hydrazine, (Example 6B)
bis-(2,4-dimethylbenzyl)hydrazine, (Example 6C)
di-(α -methylbenzyl)hydrazine, (Example 6D)
20 bis-(2,4-dimethoxyphenylethyl)hydrazine, (Example 6E)
there are obtained:
4-nitro-1,2-di [(3',4',5'-trimethoxy)benzyl] pyrazolidine,
(Example 6A)
4-nitro-1,2-bis [(2',4'-dimethoxy)benzyl] pyrazolidine,
(Example 6B).
25 4-nitro-1,2-bis [(2',4'-dimethyl)benzyl] pyrazolidine,
(Example 6C)
4-nitro-1,2-di [(α -methylbenzyl)] pyrazolidine,
(Example 6D)
30 4-nitro-1,2-bis [(2',4'-dimethoxy)phenylethyl] pyrazolidine,
(Example 6E)

Example 7

4-Amino-1,2-diethyl-pyrazolidine.

To a solution of approximately 3.0 g (0.016 mole) of 4-nitro-1,2-diethyl-pyrazolidine in 100 ml of toluene was added 60 ml of anhydrous ethanol and 2 g Raney nickel (washed three times with anhydrous ethanol). This mixture was hydrogenated for three hours at about 30 psi. The mixture was filtered to give a light yellow solution. The solvents were evaporated off at reduced pressure giving a colourless liquid, namely 1.95 g of the title product, b.p. 113-115°C at 40 mm Hg. The dimaleate salt melted at 119-120°C.

Example 8

4-Amino-1,2-diethyl-pyrazolidine.

A stirred solution of 4.03 g (0.025 moles) of 1,2-diethylhydrazine dihydrochloride and 6.72 g (0.026 moles) of 1,3-dimorpholino-2-nitropropane in a mixture of 28 ml of methanol and 16 ml of toluene was heated at reflux for 3 hours. The solvents were evaporated off under reduced pressure and the residue was resuspended in 100 ml of toluene. The solid morpholine hydrochloride was removed by filtration, leaving a solution of 4-nitro-1,2-diethyl-pyrazolidine in toluene. To this toluene solution was added 60 ml anhydrous ethanol and 2 g of Raney Nickel which had been washed three times with anhydrous ethanol. This mixture was hydrogenated at about 30 psi. hydrogen pressure. The mixture was filtered carefully under nitrogen to prevent ignition. Evaporation off of the solvents and distillation at reduced pressure gave a colourless liquid product weighing 1.95 g.

(54% yield calculated on diethylhydrazine), b.p. 113-115°C at 40 mm Hg.

Examples 9A to 9K

- 5 Following the procedure of Example 7 but substituting an equal molar amount of the following for 4-nitro-1,2-diethyl-pyrazolidine:
- 4-nitro-1,2-dicyclohexyl-pyrazolidine, (Example 9A)
4-nitro-1-cyclohexyl-2-methyl-pyrazolidine, (Example 9B)
10 4-nitro-1-isopropyl-2-methyl-pyrazolidine, (Example 9C)
4-nitro-1-ethyl-2-methyl-pyrazolidine, (Example 9D)
4-nitro-1-isopropyl-2-ethyl-pyrazolidine, (Example 9E)
4-nitro-1-benzyl-2-methyl-pyrazolidine, (Example 9F)
4-nitro-1-benzyl-2-ethyl-pyrazolidine, (Example 9G)
15 4-nitro-1-cyclohexyl-2-ethyl-pyrazolidine, (Example 9H)
4-nitro-1,2-dibenzyl-pyrazolidine, (Example 9I)
4-nitro-1,2-di(4-methoxybenzyl)pyrazolidine, (Example 9J) and
4-nitro-1-(4-methoxybenzyl)-2-ethyl-pyrazolidine, (Example 9K)
 there are obtained:
- 20 4-amino-1,2-dicyclohexyl-pyrazolidine, (Example 9A)
4-amino-1-cyclohexyl-2-methyl-pyrazolidine, (Example 9B)
4-amino-1-isopropyl-2-methyl-pyrazolidine, (Example 9C)
4-amino-1-ethyl-2-methyl-pyrazolidine, (Example 9D)
4-amino-1-isopropyl-2-ethyl-pyrazolidine, (Example 9E)
25 4-amino-1-benzyl-2-methyl-pyrazolidine, (Example 9F)
4-amino-1-benzyl-2-ethyl-pyrazolidine, (Example 9G)
4-amino-1-cyclohexyl-2-ethyl-pyrazolidine, (Example 9H)
4-amino-1,2-dibenzyl-pyrazolidine, (Example 9I)
4-amino-1,2-di(4-methoxybenzyl)pyrazolidine, (Example 9J) and
30 4-amino-1-(4-methoxybenzyl)-2-ethyl-pyrazolidine, (Example 9K)

Examples 10A to 10F

Following the procedure of Example 8 but substituting an equal molar amount of the following for 1,2-diethylhydrazinedihydrochloride:

- 5 1-(4-chlorobenzyl)-2-ethyl hydrazine dihydrochloride
(Example 10A)
1,2-di(4-chlorobenzyl)hydrazine dihydrochloride, (Example 10B)
1,2-di(4-trifluoromethylbenzyl)hydrazine dihydrochloride,
(Example 10C)
10 1,2-di(4-acetamidobenzyl) hydrazine hydrogen sulphate,
(Example 10D)
1,2-di(4-sulphamoxybenzyl)hydrazine dihydrochloride,
(Example 10E) and
1,2-di(4-butoxybenzyl)hydrazine phosphoric acid salt,
15 (Example 10F)

there are obtained:

- 4 -amino-1-(4-chlorobenzyl)-2-ethyl pyrazolidine, (Example 10A)
4-amino-1,2-di(4-chlorobenzyl)pyrazolidine, (Example 10B)
4-amino-1,2-di(4-trifluoromethylbenzyl)pyrazolidine,
20 (Example 10C)
4-amino-1,2-di(4-acetamidobenzyl)pyrazolidine, (Example 10D)
4-amino-1,2-di(4-sulphamoxybenzyl)pyrazolidine, (Example 10E and
4-amino-1,2-di(butoxybenzyl)pyrazolidine, (Example 10F)

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Example 11

4-Amino-1,2-diisopropyl-pyrazolidine.

Following the procedure of Example 7, but substituting an equal molar amount of 4-nitro-1,2-diisopropyl-pyrazolidine for 4-nitro-1,2-diethyl-pyrazolidine, the title compound is
30 obtained.

Example 12

4-Amino-1,2-diisopropyl-pyrazolidine Fumarate [1:2],
Hemihydrate.

5 The free base obtained in Example 11 is reacted with
fumaric acid to obtain the title compound m.p. 157-161°C.

Examples 13A to 13E

10 Following the procedure of Example 7, but substituting
equal molar amounts of the following for 4-nitro-1,2-
diethyl-pyrazolidine:

4-nitro-1,2-di [(3',4',5'-trimethoxy)benzyl] pyrazolidine,
(Example 13A)

4-nitro-1,2-bis [(3',4'-dimethoxy)benzyl] pyrazolidine,
(Example 13B)

15 4-nitro-1,2-bis [(2',4'-dimethyl)benzyl] pyrazolidine,
(Example 13C)

4-nitro-1,2-di (α-methylbenzyl)pyrazolidine, (Example 13D)

4-nitro-1,2-bis [(2',4'-dimethoxy)phenylethyl] pyrazolidine,
(Example 13E)

20 there are obtained:

4-amino-1,2-di [(3',4',5'-trimethoxy)benzyl] pyrazolidine,
(Example 13A)

4-amino-1,2-bis [(3',4'-dimethoxy)benzyl] pyrazolidine,
(Example 13B)

25 4-amino-1,2-bis [(2',4'-dimethyl)benzyl] pyrazolidine,
(Example 13C)

4-amino-1,2-bis (α-methylbenzyl)pyrazolidine, (Example 13D) and

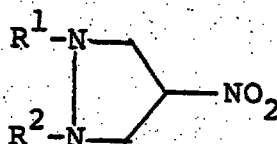
4-amino-1,2-bis [(2',4'-dimethoxy)phenylethyl] pyrazolidine,
(Example 13D)

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CLAIMS:

1. A compound having the formula:



5. wherein;

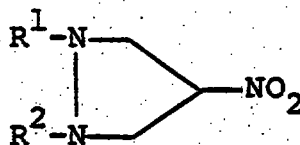
R^1 and R^2 each represent a loweralkyl, lowercycloalkyl, phenyl-loweralkyl or substituted phenyl-loweralkyl group and may be the same or different.

10. 2. 4-Nitro-1,2-diethyl-pyrazolidine.
3. 4-Nitro-1,2-diisopropyl-pyrazolidine.
15. 4. 4-Nitro-1,2-bis(4-methoxybenzyl)pyrazolidine.
5. 4-Nitro-1,2-dicyclohexyl-pyrazolidine.
6. 4-Nitro-1-cyclohexyl-2-methyl-pyrazolidine.
20. 7. 4-Nitro-1-isopropyl-2-methyl-pyrazolidine.
8. 4-Nitro-1-ethyl-2-methyl-pyrazolidine.
9. 4-Nitro-1-isopropyl-2-ethyl-pyrazolidine.
25. 10. 4-Nitro-1-benzyl-2-methyl-pyrazolidine.
11. 4-Nitro-1-benzyl-2-ethyl-pyrazolidine.



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12. 4-Nitro-1-cyclohexyl-2-ethyl-pyrazolidine.
13. 4-Nitro-1,2-dibenzyl-pyrazolidine.
14. 4-Nitro-1-(4-methoxybenzyl)-2-ethyl-pyrazolidine.
15. 4-Nitro-1,2-di [(3',4',5'-trimethoxy)benzyl]
pyrazolidine.
16. 4-nitro-1,2-bis [(2',4'-dimethoxy)benzyl]
pyrazolidine.
17. 4-Nitro-1,2-bis [(2',4'-dimethyl)benzyl]
pyrazolidine.
18. 4-Nitro-1,2-di [(α -methylbenzyl)] pyrazolidine.
19. 4-Nitro-1,2-bis [(2',4'-dimethoxy)phenylethyl]
pyrazolidine.
20. A process for the preparation of a 4-nitro-1,2-
hydrocarbyl-pyrazolidine having the formula:



wherein,

R^1 and R^2 each represent a loweralkyl, lowercycloalkyl or phenyl-loweralkyl group and may be the same or different, which comprises reacting a disubstituted hydrazine acid salt having the formula:



wherein R^1 and R^2 are as defined above and X represents an acid anion, with a 1,3-bis(disubstituted amino)-2-nitropropane having the formula:

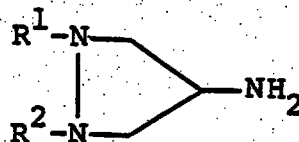


to produce the said 4-nitro-1,2-hydrocarbyl-pyrazolidine, wherein R^3 , R^4 , R^5 and R^6 each represent a loweralkyl group and may be the same or different and R^3 and R^4 or R^5 and R^6 taken together with the adjacent nitrogen atom may form a heterocyclic residue.

21. A method as claimed in Claim 20 substantially as specifically described herein with reference to any one of Examples 1, 2, 3, 4, 5A to 5J, or 6A to 6E.

22. A compound as claimed in any one of Claims 1 to 19 whenever made by a process claimed in Claim 20 or Claim 21.

23. A process for the preparation of a 4-amino-1,2-hydrocarbyl-pyrazolidine having the formula:





wherein R^1 and R^2 each represent a loweralkyl, lower-cycloalkyl, or phenyl-loweralkyl group and may be the same or different, which comprises reducing a 4-nitro-1,2-hydrocarbyl-pyrazolidine having the formula:



wherein R^1 and R^2 are as defined above, to produce the said 4-amino-1,2-hydrocarbyl-pyrazolidine.

24. A process for the preparation of 4-amino-1,2-hydrocarbyl-pyrazolidines having the formula:



wherein R^1 and R^2 each represent a lower alkyl, lower-cycloalkyl or phenyl-loweralkyl group and may be the same or different; which comprises the steps of

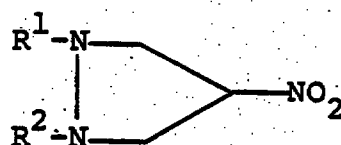
1) reacting a disubstituted hydrazine acid salt having the formula:



wherein R^1 and R^2 are as defined above and X represents an acid anion with a 1,3-bis(disubstituted amino)-2-nitropropane having the formula:



wherein R^3 , R^4 , R^5 and R^6 each represent a loweralkyl group and may be the same or different and R^3 and R^4 or R^5 and R^6 taken together with the adjacent nitrogen atom may form a heterocyclic residue, to produce a 4-nitro-1,2-hydrocarbyl-pyrazolidine having the formula:



wherein R^1 and R^2 are as defined above, and

2) reducing the said 4-nitro-1,2-hydrocarbyl-pyrazolidine to produce the said 4-amino-1,2-hydrocarbyl-pyrazolidine.

25. A process as claimed in Claim 23 or Claim 24 in which the 1,3-bis(disubstituted amino)-2-nitropropane is 1,3-dimorpholino-2-nitropropane.

26. A process as claimed in Claim 23 or Claim 24 in which the disubstituted hydrazine acid salt is an acid salt of 1,2-diethyl hydrazine.

27. A process as claimed in Claim 23 or Claim 24 in which the disubstituted hydrazine acid salt is 1,2-diethyl hydrazine dihydrochloride.



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28. A process as claimed in any one of Claims 23 to 27 in which the reduction is carried out with hydrogen over a Raney Nickel catalyst.

29. A method as claimed in Claim 23 or Claim 24 substantially as specifically described herein with reference to any one of Examples 7, 8, 9A to 9K, 10A to 10F, 11, 12, or 13A to 13E.

30. A 4-amino-1,2-hydrocarbyl-pyrazolidine whenever made by a process as claimed in any one of Claims 23 to 29.

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