

1.116.692



PATENT SPECIFICATION

NO. DRAWINGS

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Int. Cl.:—C 07 d 85/50, C 07 d 99/02

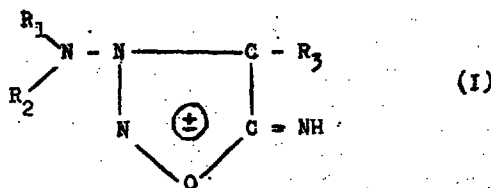
COMPLETE SPECIFICATION

A method for producing Sydnonimine Derivatives

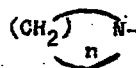
We, TAKEDA CHEMICAL INDUSTRIES LTD., a body corporate organised under the laws of Japan, of 27, Doshomachi 2-chome, Higashi-ku, Osaka, Japan, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to novel sydnonimine derivatives and pharmaceutically acceptable acid addition salts thereof having useful medicinal properties.

The present invention provides sydnonimine derivatives of the general formula (I) and acid addition salts thereof:



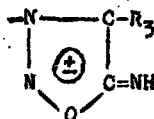
in which R_3 is a hydrogen atom or an alkyl group having one to five carbon atoms, and R_1 and R_2 each represent an alkyl group having one to five carbon atoms or an alkenyl group having two to five carbon atoms, or R_1 and R_2 , together with the nitrogen atom to which they are attached, represent a morpholino radical, a pipercolino radical, a



radical (wherein n is 4, 5 or 6), or a



radical (wherein R' is an alkyl group having one to five carbon atoms or a



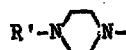
radical, wherein R_3 has the same meaning as above).

Although compounds containing a sydnonimine ring and substituents involving a C—N linkage at the nitrogen atom in the 3 position of the ring are known, compounds containing a sydnonimine ring and substituents involving an N—N linkage at the nitrogen atom in the 3 position of the ring have not previously been described,

[Price 4s. 6d.]

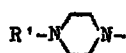
Price 25s.

wherein R_1 , R_2 and R_3 have the same meaning as above, R_1' and R_2' have the same meanings as R_1 and R_2 except that when R_1' and R_2' , together with the nitrogen atom, represent



5 R' represents an alkyl group of one to five carbon atoms or a radical of the formula $-\text{NH}-\text{CH}-\text{CN}$, R_3 having the meanings given above and R_1'' and R_2'' have the

same meanings as R_1 and R_2 except that when R_1'' and R_2'' , together with the nitrogen atom, represent



10 R' represents an alkyl group of one to five carbon atoms or a radical of the formula $-\text{N}-\text{CH}-\text{CN}$, R_3 having the meanings given above.



To prepare the cyanoalkyl hydrazine of the general formula (III), a hydrazine of the general formula (II) is subjected to cyanoalkylation. The reaction is generally conducted by reacting a hydrazine derivative of the formula (II) with an alkali metal or ammonium cyanide and an aldehyde of the formula $R_3\text{CHO}$ (V), wherein R_3 has the same meaning as above. Examples of hydrazines which can be used are N,N-dimethylhydrazine, N,N-diethylhydrazine, N,N-di-*n*-butylhydrazine, N-methyl-N-*n*-butylhydrazine, N-ethyl-N-*n*-butylhydrazine, N,N-diamylhydrazine, N-allyl-N-methylhydrazine, N-allyl-N-ethylhydrazine, N,N-diallylhydrazine, N-butenyl-N-methylhydrazine, N,N-dibutenylhydrazine, N-aminopiperidine, N-aminomorpholine, N-aminopyrrolidine, N-amino- α -pipecoline, N-aminohexahydroazepine, N-amino-N'-methylpiperazine, N-amino-N'-ethylpiperazine and N-amino-N'-sydnominopiperazine. Examples of aldehydes are formaldehyde, acetaldehyde, propionaldehyde, butyraldehyde, isobutyraldehyde, valeraldehyde and caproaldehyde. Sodium cyanide, potassium cyanide or ammonium cyanide can be employed advantageously as the cyanide. The reaction of the hydrazine with the aldehyde and cyanide is carried out, for example, by adding a cyanide solution and an aldehyde solution to a hydrazine solution while cooling or at room temperature. Water is generally employed as the reaction solvent but other solvents, may be used provided they do not unduly hinder the reaction. The reaction may be carried out in the presence of a catalyst (e.g., sodium bisulphite).

The compound of formula (III) can also be obtained by reacting a hydrazine of the formula (II) with a hydroxyalkyl nitrile of the formula: $\text{HO}-\text{CH}-\text{CN}$ (wherein



R_3 has the same meaning as above), which is obtained, for example, by reaction of the corresponding aldehyde with an alkali metal cyanide or ammonium cyanide. The reaction between the hydrazine and the hydroxyalkyl nitrile may be carried out, for example, by mixing the two reaction components at room temperature with or without a solvent.

For the preparation of the nitroso compound of the formula (IV), a nitroso group is introduced into the cyanoalkyl hydrazine of the formula (III). The nitrosation can be effected in known manner, for example, (a) by reacting a cyanoalkyl hydrazine with a nitroso compound such as an alkali metal nitrite (e.g., sodium nitrite or potassium nitrite) or ammonium nitrite in an aqueous medium, preferably while cooling; (b) by passing nitrous fumes into a solution or suspension of cyanoalkyl hydrazine, preferably while cooling, using an organic solvent such as benzene, toluene, xylene, acetone, methyl alcohol, ethyl alcohol, diethyl ether, acetic acid, ethyl acetate or acetic anhydride; (c) by adding a solution of nitrosyl chloride to a solution of cyanoalkyl hydrazine in the presence of an alkali metal salt of a carboxylic acid such as sodium acetate or potassium acetate; or (d) by reacting an alkyl nitrite with the cyanoalkyl hydrazine.

Finally, to prepare the sydnonimine compounds of the general formula (I), the

nitroso compound of the formula (IV) is subjected to a ring-closure reaction. When the nitroso compound is unstable, the reaction mixture from the nitrosation may be subjected directly to the ring-closure reaction without separating the compound from the reaction mixture. The reaction is carried out, for example, by adding acid to the nitroso compound dissolved in water or in an organic solvent. Examples of acids which may be used are inorganic acids such as hydrochloric acid, sulphuric acid, nitric acid, or phosphoric acid, or strong organic acids such as picric acid. Organic solvents which may be used include, for example, methyl alcohol, ethyl alcohol, iso-propyl alcohol, diethyl ether, acetone, benzene, xylene, toluene or tetrahydrofuran. The reaction is generally carried out at room temperature. It is preferred to add an alcoholic solution of hydrochloric acid to the nitroso compound at room temperature to allow the reaction to take place, the alcohol used being, for example, methyl alcohol, ethyl alcohol or isopropyl alcohol. Thus, the desired sydnonimine compound is precipitated from the reaction system in the form of its salt with the acid used. After the ring-closure reaction has been completed, an organic solvent such as diethyl ether or acetone may be added to the reaction system in order to accelerate the precipitation of the desired product. The sydnonimine salt may be converted into its free base or into another pharmaceutically acceptable salt such as the formate, acetate, butyrate, oxalate, fumarate, maleate, succinate, glycolate, lactate, malate, tartrate, citrate, ascorbate, salicylate or para-minosolicylate.

Being highly soluble in water, the sydnonimine compounds and their salts are preferably administered in the form of an aqueous solution containing about 1 milligram of sydnonimine per millilitre of water; they are generally administered *per os* but may alternatively be applied as an injection. The dose for an adult is from 5 to 25 milligrams per day.

The following Examples illustrate the invention.

EXAMPLE 1

While ice-cooling and agitating, potassium cyanide (10 g.) dissolved in water (20 ml.) and a 37 per cent aqueous solution (12.5 g.) of formaldehyde were added to N-aminopiperidine hydrochloride (21 g.) dissolved in water (20 ml.), and the resulting mixture was agitated for 7 hours at room temperature to give an oily layer. After standing overnight, the oily layer was extracted with diethyl ether, and the ether was removed from the extract by evaporation to yield a reddish-brown, oily residue.

Fractional distillation of the oily residue under reduced pressure gave N-piperidino-cyanomethylamine as a light-yellow liquid (11.2 g.) at 80°C. to 89°C./3mmHg, or 120 to 128°C./22mmHg. Its hydrochloride melted at 157°C. to 158°C.

The N-piperidino-cyanomethylamine (5 g.) suspended in water (10 ml.) was dissolved homogeneously as its hydrochloric acid salt by the addition of hydrochloric acid (5 ml.) diluted with water (10 ml.). Sodium nitrite (2.5 g.) dissolved in water (5 ml.) was added to the aqueous solution while ice-cooling and agitating to give an oily layer, which was then extracted twice each with diethyl ether (50 ml.). The extract was dried with sodium sulphate, and the ether was then removed by evaporation to leave a yellow oil. A 4N-methyl alcoholic solution (30 ml.) of hydrochloric acid was added to the yellow oil and the alcohol was removed by evaporation to yield a white solid. The solid was recrystallised from ethyl alcohol-anhydrous diethyl ether to yield 3-piperidino-sydnonimine hydrochloride (2.6 g.) in the form of colourless crystals having a melting point of 160 to 163°C. (with decomposition).

Analysis. $C_7H_{13}N_4OCl$

	C	H	N
Calculated	41.08	6.40	27.86
Found	41.40	6.41	27.61

EXAMPLE 2

Potassium cyanide (10 g) dissolved in water (20 ml.) and a 37 per cent aqueous solution of formaldehyde were added to N-aminomorpholine hydrochloride (20 g) dissolved in water (20 ml.), under ice-cooling and while agitating, and the resulting mixture was further agitated for 6 hours at room temperature to allow the reaction to take place. The reaction mixture was continuously extracted with diethyl ether for 8 hours. After removing the ether from the extract by evaporation, the remaining yellow oil was subjected to a fractional distillation under reduced pressure to isolate N-morpholino-cyanomethylamine as light-yellow liquid (44 g) at 96°C. to 108°C./

0.4 mmHg., whose hydrochloric acid salt had a melting point of 178 to 181°C. (with decomposition).

Concentrated hydrochloric acid (2.8 ml) was added to the N-morpholino-cyanomethylamine (3.9 g) in water (5 ml) and then, while ice-cooling and agitating, sodium nitrite (2.5 g) dissolved in water was added (4 ml) to give an oily substance. The oily substance was extracted with diethyl ether and the extract was dried with sodium sulphate, followed by the removal of the ether by evaporation to leave a yellow oily substance. A 4 N methyl alcoholic solution (20 ml) of hydrochloric acid was added to the yellow oily substance. After removing the methyl alcohol from the solution by evaporation, anhydrous diethyl ether was added to the remnant to solidify it completely, followed by discarding the ether by decantation.

The remaining solid part was recrystallised from ethyl alcohol to yield 3-morpholino-sydnonimine hydrochloride (0.5 g) in the form of colourless crystals having a melting point of 171 to 173°C. (with decomposition).

Analysis. $C_6H_{11}N_4O_2Cl$

	C	H	N
Calculated	34.87	5.37	27.12
Found	34.83	5.04	26.99

The use of N-amino-N'-methylpiperazine hydrochloride instead of N-amino-morpholine hydrochloride gave 3-(N-methylpiperazino)-sydnonimine hydrochloride in a similar manner.

EXAMPLE 3

Potassium cyanide (1.3 g) in water (5 ml.) and a 37 per cent aqueous solution (1.6 g) of formaldehyde were added to N-amino-pyrrolidine hydrochloride (2.4 g), while ice-cooling and agitating and the mixture was then agitated for 4 hours at room temperature to allow reaction to take place. The reaction mixture was extracted with diethyl ether, and the ether was removed from the extract by evaporation to leave a reddish-brown oil, which was then subjected to fractional distillation under reduced pressure to isolate N-pyrrolidino-cyanomethylamine as a light-yellow liquid (1.2 g) at 65 to 67°C./0.3 mmHg, the hydrochloric acid salt of which had a melting point of 159 to 161°C. (with decomposition).

Hydrochloric acid (1.5 ml) was added to the N-pyrrolidino-cyanomethylamine (2.0 g) suspended in water (10 ml), while cooling, and then sodium nitrite (3 g) in water (5 ml.) was dropped into the mixture to give an oily substance, which was then extracted with diethyl ether. A 4 N methyl alcoholic solution (10 ml) of hydrochloric acid was added in the ether extract while cooling to precipitate 3-pyrrolidino-sydnonimine hydrochloride as colourless crystals with one mole of water of crystallisation.

The crystals recrystallised from ethyl alcohol had a melting point of 175 to 176°C. (with decomposition).

Analysis $C_6H_{11}N_4OCl \cdot H_2O$

	C	H	N
Calculated	34.52	6.23	26.85
Found	34.36	6.23	26.72

EXAMPLE 4

N,N-dimethyl-hydrazine (6 g) dissolved in water (10 ml) was mixed with concentrated hydrochloric acid (10 ml). Potassium cyanide (7 g) dissolved in water (10 ml) and a 37 per cent aqueous solution (8.1 g) of formaldehyde were added while cooling and agitating, followed by further agitation for two and a half hours at room temperature to allow the reaction to take place. After the reaction mixture had been extracted with diethyl ether, the ether was removed by evaporation to leave a yellow oil, which was subjected to fractional distillation under reduced pressure to give N,N-dimethyl-N'-cyanomethyl-hydrazine as a light-yellow liquid (4.8 g) at 53 to 55°C./2mmHg.

The N,N-dimethyl-N'-cyanomethyl-hydrazine (4 g) dissolved in water (5 ml) was mixed with hydrochloric acid (3.6 g).

Sodium nitrite (4 g) dissolved in water (5 ml) was added dropwise to the mixture while cooling with dry ice-acetone solution, whereupon a white powdery substance precipitated out. The precipitate was separated out, washed with cold water and dissolved in methyl alcoholic-hydrochloric acid.

The alcohol was removed from the solution by evaporation to leave a white solid

substance. The white solid substance was then recrystallised from ethyl alcohol to obtain 3-dimethylamino-sydnonimine hydrochloride (3.3 g) in the form of colourless crystals having a melting point of 180 to 181°C. (with decomposition).

	Analysis	$C_4H_8N_4OCl$		
		C	H	N
Calculated		29.19	5.51	34.04
Found		28.91	5.56	33.85

EXAMPLE 5

Potassium cyanide (11.5 g) dissolved in a small amount of water was added to N-amino- α -pipecoline (20 g) dissolved in a mixture of water (20 ml) and concentrated hydrochloric acid (19 g) while ice-cooling and agitating. A 37 per cent aqueous solution (14.5 g) of formaldehyde was added dropwise to the mixture, while agitating, followed by further agitation. The resulting oily substance was extracted with diethyl ether. After drying with anhydrous potassium carbonate and removing the ether by evaporation, the extract was subjected to fractional distillation under reduced pressure to isolate N- α -pipecoline-cyanomethylamine (22 g) at 76 to 80°C./1mmHg., whose picrate had a melting point of 138°C. (with decomposition).

Sodium nitrite (2.5 g) dissolved in a small amount of water, was added to the N- α -pipecoline-cyanomethylamine (5 g) dissolved in a mixture of water (5 ml) and hydrochloric acid (3.7 g) while cooling and agitating followed by further agitation to give a brown oily substance, which was extracted with diethyl ether. The extract was dried with anhydrous potassium carbonate, and the ether was removed from the extract by evaporation to leave an oily product (5 g), which was mixed with a methyl alcoholic solution of hydrochloric acid.

After leaving to stand for a while, the methyl alcohol was removed from the mixture by evaporation at room temperature to give white needle-like crystals (3 g), which were recrystallised from ethyl alcohol to yield 3- α -pipecoline-sydnonimine hydrochloride (1.5 g) having a melting point of 157°C. (with decomposition).

	Analysis	$C_8H_{15}N_4OCl$		
		C	H	N
Calculated		43.94	6.91	25.62
Found		43.45	7.08	26.16

EXAMPLE 6

Hydroxyacetonitrile (2.8 g) was added dropwise to N,N-(di-*n*-butyl)-hydrazine (7.2 g) to allow reaction to take place. After about 15 hours, the upper part of the reaction mixture which was divided into two layers was subjected to fractional distillation under reduced pressure, which gave N-(di-*n*-butylamino)cyanomethylamine (3.3 g) at 85°C./0.2 mmHg. Sodium nitrite (2 g) dissolved in a small amount of water was added to the N-(di-*n*-butylamino)-cyanomethyl amine (5 g) dissolved in a mixture of water (10 ml) and hydrochloric acid (3 ml) to produce a yellow oily substance, which was then extracted with diethyl ether. The extract was dried with anhydrous potassium carbonate, and the ether was removed from the ether extract by evaporation to leave an oily substance. The oily substance was washed two or three times with anhydrous diethyl ether to obtain white solid matter.

The white solid matter was recrystallised from methyl alcohol-anhydrous diethyl ether to give 3-(di-*n*-butylamino)-sydnonimine hydrochloride having a melting point of 108°C. (with decomposition).

	Analysis	$C_{10}H_{21}N_4OCl$		
		C	H	N
Calculated		48.28	8.51	22.52
Found		48.29	8.50	22.47

EXAMPLE 7

Potassium cyanide (8 g) dissolved in a small amount of water was added to N-aminopiperidine hydrochloride (15 g) dissolved in water (15 ml) while cooling and agitating. After further agitation of the mixture, an 80 per cent aqueous solution (6 g) of acetaldehyde was added dropwise to the mixture. Half an hour later, an oily substance separated out, and was extracted with diethyl ether. The extract was dried, and the ether was removed by evaporation. The residue was subjected to fractional

distillation under reduced pressure to distil N-piperidino- α -cyanoethylamine (6 g) at 60 to 67°C./6 to 7 mmHg. The picric acid salt of the N-piperidino- α -cyano-ethylamine had a melting point of 131°C.

5 Sodium nitrite (3 g) dissolved in a small amount of water was added under agitation to the N-piperidino- α -cyanoethylamine (6 g) dissolved in a mixture of water (20 ml) and hydrochloric acid (4 g) to yield an oily substance, which was extracted with diethyl ether. The extract was dried with anhydrous potassium carbonate, and the ether was removed from the extract by evaporation to leave the nitroso compound as an oily substance. The nitroso compound was mixed with a methyl alcoholic solution of hydrochloric acid, and then left to stand, the methyl alcohol being thereafter removed from the mixture by evaporation. The remaining oily substance was washed several times with anhydrous diethyl ether. The solid substance obtained was recrystallised from methyl alcohol-diethyl ether to obtain 3-piperidino-4-methyl-sydnonimine hydrochloride having a melting point of 167 to 170°C. (with decomposition).

15	Analysis	$C_8H_{15}N_4OCl$			15
		C	H	N	
	Calculated	43.94	6.91	25.62	
	Found	44.21	6.89	25.31	

20 The nitroso compound obtained as above was dissolved in diethyl ether and the solution was mixed with picric acid dissolved in ethyl alcohol-diethyl ether, followed by removing the solvent by evaporation. The yellow oily substance obtained was washed with diethyl ether to produce a yellow solid.

25 The solid was recrystallised from diethyl ether-ethyl alcohol to obtain 3-piperidino-4-methyl sydnonimine picrate having a melting point of 148°C. (with decomposition).

	Analysis	$C_{14}H_{17}N_7O_8$			
		C	H	N	
	Calculated	40.88	4.17	23.84	
	Found	41.02	4.23	23.58	

30 **EXAMPLE 8**
N,N'-diaminopiperazine hydrochloride (3.8 g) dissolved in water (30 ml) was neutralised with sodium bicarbonate (3.5 g).

35 Formaldehyde-sodium bisulphite monohydrate (6.1 g) dissolved in water (20 ml) was added to the neutralised solution and the mixture was heated at 70°C. for 3 hours on a water bath, followed by evaporation to dryness, to leave a white solid substance.

The white solid substance was dissolved in water (20 ml) and potassium cyanide (3.0 g) was added. The mixture was heated at 60°C. for about one hour on a water bath to precipitate out N,N'-bis-(cyanomethylamino)-piperazine in the form of colourless needle-like crystals (2.3 g).

40 Sodium nitrite (2.0 g) dissolved in water (7 ml) was added to the N,N'-bis-(cyanomethylamino)piperazine (2.0 g) dissolved in a mixture of water (30 ml) and hydrochloric acid (2 ml) to precipitate out a nitroso compound in the form of a white powder.

45 Hydrochloric acid (10 ml) was added under agitation to the nitroso compound after the latter had been separated by filtration. The mixture was dissolved in water (50 ml) while heating and allowed to stand for a while to precipitate out 3,3'-(1,4-piperazine-diyl)-bis-sydnonimine hydrochloride in the form of colourless crystals having a melting point of 242 to 243°C. (with decomposition).

50	Analysis	$C_8H_{14}O_2N_8Cl_2 \cdot 2H_2O$			50
		C	H	N	
	Calculated	26.59	4.99	31.02	
	Found	27.03	5.09	30.42	

55 **EXAMPLE 9**
First, formaldehyde-sodium bisulphite monohydrate (5.0 g) under agitation, then potassium cyanide (4.0 g) was added to N-methyl-N-allyl-hydrazine (5.2 g) dissolved in water (30 ml), and the mixture was heated at 60°C. on a water bath to give an oily layer, which was extracted with diethyl ether. The extract was dehydrated with anhydrous potassium carbonate, and the ether was evaporated. The resulting mixture

was subjected to fractional distillation under reduced pressure to give N-(methylallyl-amino)-cyanomethylamine (3.0 g) at 101 to 105°C./20 mmHg.

Sodium nitrite (1.5 g) dissolved in water (4 ml) was added dropwise to the N-(methylallylamino)-cyanomethylamine (1.9 g) dissolved in a mixture of water (10 ml) and hydrochloric acid (1.5 ml) while cooling to produce a brown oily layer, which was then extracted with diethyl ether. The extract was dried with anhydrous potassium carbonate and the ether was removed by evaporation to leave a residue, which was immediately dissolved in anhydrous methyl alcohol. Dry hydrogen chloride was introduced into the solution, and the methyl alcohol was removed from the solution by evaporation to leave a syrupy substance.

The syrupy substance was washed with diethyl ether, dissolved in a small amount of water and mixed with an aqueous solution of picric acid to produce yellow, needle-like crystals of 3-methylallylamino-sydnonimine picrate.

3-methylallylamino-sydnonimine picrate recrystallised from hot water had a melting point of 131 to 134°C.

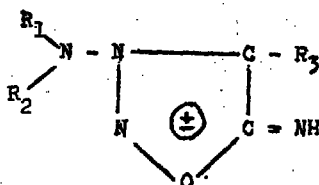
Analysis	$C_{12}H_{13}N_3O_8$		
	C	H	N
Calculated	37.60	3.42	25.58
Found	37.36	3.56	25.50

Compounds of the formula III above are described and claimed in our copending Application No. 9271/68, Serial No. 1,116,693.

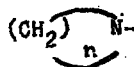
Compounds of the formula IV above are described and claimed in our copending application No. 9272/68, Serial No. 1,116,694.

WHAT WE CLAIM IS:—

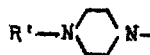
1. A sydnonimine compound of the general formula:



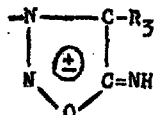
in which R_3 represents a hydrogen atom or an alkyl group having one to five carbon atoms, and R_1 and R_2 each represent an alkyl group having one to five carbon atoms or a lower alkenyl group having two to five carbon atoms, or R_1 and R_2 , together with the nitrogen atom to which they are attached, represent a morpholino radical, a piperidino radical, a



radical (wherein n is 4, 5, or 6), or a



radical (wherein R' is an alkyl group having one to five carbon atoms or a



radical, wherein R_3 has the same meaning as above).

- The pharmaceutically acceptable salts of the compounds claimed in claim 1.
- 3-piperidino-sydnonimine and acid addition salts thereof.
- 3-morpholino-sydnonimine and acid addition salts thereof.
- 3- α -piperidino-sydnonimine and acid addition salts thereof.
- 3-dimethylamino-sydnonimine and acid addition salts thereof.

was subjected to fractional distillation under reduced pressure to give N-(methylallyl-amino)-cyanomethylamine (3.0 g) at 101 to 105°C./20 mmHg.

Sodium nitrite (1.5 g) dissolved in water (4 ml) was added dropwise to the N-(methylallyl-amino)-cyanomethylamine (1.9 g) dissolved in a mixture of water (10 ml) and hydrochloric acid (1.5 ml) while cooling to produce a brown oily layer, which was then extracted with diethyl ether. The extract was dried with anhydrous potassium carbonate and the ether was removed by evaporation to leave a residue, which was immediately dissolved in anhydrous methyl alcohol. Dry hydrogen chloride was introduced into the solution, and the methyl alcohol was removed from the solution by evaporation to leave a syrupy substance.

The syrupy substance was washed with diethyl ether, dissolved in a small amount of water and mixed with an aqueous solution of picric acid to produce yellow, needle-like crystals of 3-methylallylamino-sydnonimine picrate.

3-methylallylamino-sydnonimine picrate recrystallised from hot water had a melting point of 131 to 134°C.

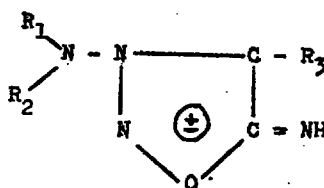
	Analysis $C_{12}H_{13}N_7O_8$		
	C	H	N
Calculated	37.60	3.42	25.58
Found	37.36	3.56	25.50

Compounds of the formula III above are described and claimed in our copending Application No. 9271/68, Serial No. 1,116,693.

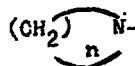
Compounds of the formula IV above are described and claimed in our copending application No. 9272/68, Serial No. 1,116,694.

WHAT WE CLAIM IS:—

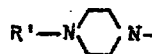
1. A sydnonimine compound of the general formula:



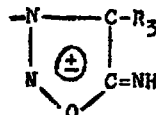
in which R_3 represents a hydrogen atom or an alkyl group having one to five carbon atoms, and R_1 and R_2 each represent an alkyl group having one to five carbon atoms or a lower alkenyl group having two to five carbon atoms, or R_1 and R_2 , together with the nitrogen atom to which they are attached, represent a morpholino radical, a pipercolino radical, a



radical (wherein n is 4, 5, or 6), or a



radical (wherein R' is an alkyl group having one to five carbon atoms or a



radical, wherein R_3 has the same meaning as above).

2. The pharmaceutically acceptable salts of the compounds claimed in claim 1.
3. 3-piperidino-sydnonimine and acid addition salts thereof.
4. 3-morpholino-sydnonimine and acid addition salts thereof.
5. 3- α -pipecolino-sydnonimine and acid addition salts thereof.
6. 3-dimethylamino-sydnonimine and acid addition salts thereof.



7. 3-(di-*n*-butylamino)-sydnonimine and acid addition salts thereof.
 8. 3-pyrrolidino-sydnonimine and acid addition salts thereof.
 9. 3-piperidino-4-methyl-sydnonimine and acid addition salts thereof.
 10. 3,3'-(1,4-piperazine-diyl)-bis-sydnonimine and acid addition salts thereof.
 11. 3-hexahydroazepin-1-yl-sydnonimine and acid addition salts thereof.
 12. 3-methylallylamino-sydnonimine and acid addition salts thereof.
 13. A process for the preparation of a compound of the general formula claimed in claim 1, which may be in acid addition salt form, which comprises treating a nitroso compound of the general formula



with an acid, the radicals R_1'' , R_2'' and R_3 being as hereinbefore defined.

14. A process as claimed in claim 13, wherein the acid is hydrochloric acid.
 15. A process as claimed in claim 13 or claim 14, wherein the reaction is carried out in an alcohol.
 16. A process as claimed in any of claims 13 to 15, wherein the compound of the general formula



is obtained by treating a cyanoalkyl hydrazine of the general formula:



(in which R_1' , R_2' , R_1'' , R_2'') and R_3 are as hereinbefore defined with an alkali metal or ammonium nitrite or with nitrous fumes or an alkyl nitrite.

17. A process for the preparation of the compounds claimed in claim 1, which may be in pharmaceutically acceptable acid addition salt form, which comprises reacting a hydrazine of the general formula:



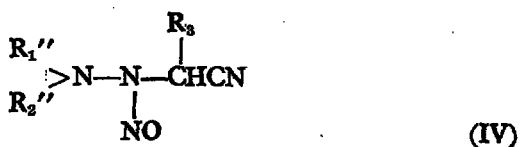
with an alkali metal or ammonium cyanide and an aldehyde of the general formula:



to prepare a compound of the general formula:



treating this compound with a nitrosation agent to produce a compound of the general formula:



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and treating this product with an acid, R_1' , R_2' , R_1'' , R_2'' and R_3 in these formulae being as hereinbefore defined.

18. A process for the preparation of the compounds claimed in claim 1 or claim 2, substantially as described with reference to any of the Examples.

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19. Sydnonimines and their salts when prepared by the process claimed in any of claims 13 to 18.

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20. Compounds as claimed in claim 1 or 2 substantially as herein described.

21. Compounds as claimed in claim 1 or 2 substantially as herein described with reference to any of the specific examples.

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