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Heffe

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[54] **CYANOALKYL SUBSTITUTED-3-OXO-ALKAMIDINES**

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Feb. 28, 1973 Switzerland 2917/73

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[51] **Int. Cl.** **C07c 121/42,** C07c 121/66

[58] **Field of Search** ..... 260/465.5 R, 464, 465 E

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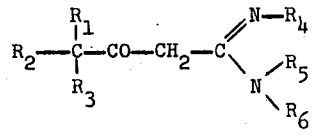
[57] **ABSTRACT**

The present invention relates to amidino ketones, which are useful as hypoglycemic agents, having the formula



wherein

R_1 is alkyl of 1 to 4 carbon atoms, phenyl or substituted phenyl,

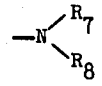
R_2 is alkyl of 1 to 4 carbon atoms, or

R_1 and R_2 together are $-(CH_2)_n-$, wherein n is an integer from 2 to 7, and

R_3 is alkyl of 1 to 4 carbon atoms, or

R_1, R_2 and R_3 together with the carbon atom to which they are bound form the adamantyl radical,

R_4 is alkyl of 1 to 8 carbon atoms, alkenyl of 2 to 8 carbon atoms, alkoxyalkyl of 2 to 8 carbon atoms in the aggregate thereof, cyanoalkyl wherein the alkyl radical is of 1 to 5 carbon atoms, or a group of formula



wherein

R_7 and R_8 are the same or different and each is alkyl of 1 to 4 carbon atoms, and

R_5 and R_6 are the same or different and each is alkyl of 1 to 8 carbon atoms, alkenyl of 2 to 8 carbon atoms, alkoxyalkyl of 2 to 8 carbon atoms in the aggregate thereof or cyanoalkyl wherein the alkyl is of 1 to 5 carbon atoms, or one of R_4, R_5 and R_6 is phenyl or substituted phenyl and the others of R_4, R_5 and R_6 are as defined above, provided at least one of R_4, R_5 and R_6 is cyanoalkyl wherein the alkyl is of 1 to 5 carbon atoms.

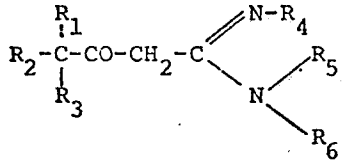
8 Claims, No Drawings

CYANOALKYL SUBSTITUTED-3-OXO-ALKAMIDINES

IMPROVEMENTS IN OR RELATING TO ORGANIC COMPOUNDS

The present invention relates to amidino ketones, especially 3-oxo-butanamidine derivatives.

The invention provides compounds of formula I,



I

wherein

R_1 is alkyl of 1 to 4 carbon atoms, phenyl or substituted phenyl, and

R_2 is alkyl of 1 to 4 carbon atoms, or

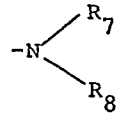
R_1 and R_2 together are $-(CH_2)_n-$, wherein n is an integer from 2 to 7,

and

R_3 is alkyl of 1 to 4 carbon atoms, or

R_1, R_2 and R_3 together with the carbon atom to which they are bound form the adamantyl radical,

R_4 is alkyl of 1 to 8 carbon atoms, alkenyl of 2 to 8 carbon atoms, alkoxyalkyl of 2 to 8 carbon atoms in the aggregate thereof, cyanoalkyl wherein the alkyl radical is of 1 to 5 carbon atoms, or a group of formula



wherein

R_7 and R_8 are the same or different and each is alkyl of 1 to 4 carbon atoms, or

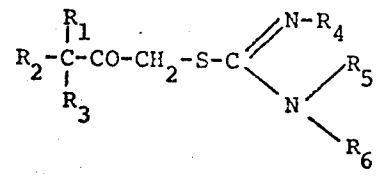
R_7 and R_8 together with the nitrogen atom are a heterocyclic ring, or a heterocyclic ring having a ring oxygen atom, and

R_5 and R_6 are the same or different and each is alkyl of 1 to 8 carbon atoms, alkenyl of 2 to 8 carbon atoms, alkoxyalkyl of 2 to 8 carbon atoms in the aggregate thereof or cyanoalkyl wherein the alkyl is of 1 to 5 carbon atoms, or one of R_4, R_5 and R_6 is phenyl or substituted phenyl and the others of R_4, R_5 and R_6 are as defined above.

When in formula I R_1 or one of the substituents R_4, R_5 and R_6 is a substituted phenyl group, the substituted phenyl group preferably is alkylphenyl, the alkyl radical having from 1 to 4 carbon atoms, especially methylphenyl, the alkyl substituent being preferably in the p position, or halophenyl, especially chlorophenyl, the halo substituent being preferably in the p position.

When R_7 and R_8 together with the nitrogen atom are a heterocyclic ring, this is preferably a five or six membered heterocyclic ring, preferably saturated e.g. morpholine, pyrrolidine or piperazine.

Further, in accordance with the invention a compound of formula I may be obtained by a process comprising desulphurizing a compound of formula II,



II

wherein R_1 to R_6 are as defined above.

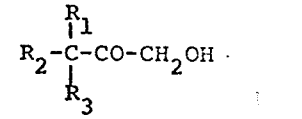
The process according to the invention may be effected in the presence of a desulphurizing agent, preferably triaryl derivatives, trialkyl derivatives or mixed alkyl/triaryl derivatives wherein each of the alkyl groups preferably is of 1 to 4 carbon atoms, of phosphorous, arsenic, antimony or bismuth, especially, however, of phosphorous or arsenic. Especially preferred are the phosphorus derivatives. Preferred examples of desulphurizing agents are triphenylphosphine or arsine and triethyl-phosphite.

The process according to the invention may be effected in the absence of a solvent or in an inert organic solvent, e.g. dimethyl formamide, dioxane or dimethyl acetamide. However, the reaction is preferably effected in the absence of a solvent. The reaction temperature may be from 70° to 120°C. After the reaction is complete, the reaction mixture may be acidified, e.g. with an acid capable of forming a water-soluble acid addition form of the compound of formula I, e.g. hydrobromic acid, the residue is conveniently filtered off and the resulting acid addition salt form of the compound of formula I is conveniently isolated from the resulting reaction mixture in known manner, e.g. by concentrating by evaporation, and may be purified, e.g. by recrystallization.

Free base forms of compounds of formula I may be converted into acid addition salt form in conventional manner, and vice versa.

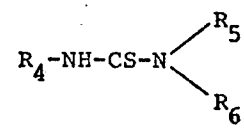
Examples of suitable acids for acid addition salt formation are the hydrohalic acids such as hydrochloric and hydrobromic acid, or perchloric acid, and organic acids such as oxalic acid and maleic acid.

The compounds of formula II, used as starting materials in the above process, may be obtained by reacting a reactive ester of an alcohol of formula III,



III

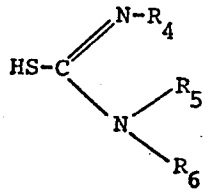
wherein R_1 to R_3 are as defined above, with a compound of formula IV,



IV

wherein R_4 to R_6 are as defined above.

In the above reaction the compounds of formula IV react in their tautomeric form of formula IV*a*,



IVa

wherein R_4 to R_6 are as defined above.

Suitable reactive esters of the alcohol of formula III, include esters of hydrohalic acids, e.g. hydrobromic or hydrochloric acid, or the tosylate. The reaction may be effected either in the absence of a solvent or in an inert organic solvent, e.g. a lower alcohol of 1 to 6 carbon atoms, acetone, or a cyclic or straight chain ether such as dioxane, tetrahydrofuran or diisopropyl ether. The reaction temperature conveniently is from 20° to 100°C. Free base forms of the resulting compounds of formula II are liberated from the acid addition salt forms in known manner, e.g. by treatment with an aqueous alkali metal hydroxide solution.

The compounds of formulae III and IV, used as starting materials in the above process, are either known or may be produced in known manner from known starting materials, for example a compound of formula IV wherein R_4, R_5 and R_6 are alkyl may be obtained by reacting an alkylisothiocyanate with a dialkyl amine in conventional manner.

In so far as the production of the starting material is not particularly described, these compounds are known or may be produced and purified in accordance

The compounds of formula I are useful because they possess pharmacological activity in animals. In particular the compounds are useful as hypoglycaemic agents as indicated by a lowering of the blood sugar content in the blood of rats on p.o. administration of from 100 to 300 mg/kg animal body weight, of the compounds, in accordance with the following test:

The compound to be tested is administered in increasing doses to groups of 5 to 10 animals. 2 hours after administration, a blood sample is taken from each animal, and the glucose content in the blood serum is established using the ferric cyanide test. The blood sugar lowering effect is determined by a comparison with a control group of 5 to 10 animals to which is administered a physiological common salt solution.

For the above mentioned use the dosage will, of course, vary depending on the compounds employed, mode of administration and condition to be treated. However, in general, satisfactory results are obtained when administered at a daily dosage of from 1.5 mg to about 300 mg per kg animal body weight, conveniently given in divided doses 2 to 4 times a day or in sustained release form. For the larger mammals, the total daily dosage is in the range from about 100 to about 1000 mg, and dosage forms suitable for oral administration comprise from about 25 mg to about 500 mg of the compounds admixed with a solid or liquid pharmaceutical carrier or diluent.

As the free base forms of the compounds of formula I are usually oily at room temperature, the compounds are conveniently administered in pharmaceutically acceptable acid addition salt forms which have the same order of activity as the free base forms, and which are readily prepared in conventional manner. Representative acid addition salt forms include organic acid salt forms such as the hydrogen maleate, fumarate, tartrate and methane sulphonate and mineral acid salt forms

such as the hydrochloride, hydrobromide and sulphate. A pharmacetical composition may comprise a compound of formula I, in free base form or in pharmaceutically acceptable acid addition salt form, in association with a pharmaceutical carrier or diluent. Such compositions may be prepared by conventional techniques to be in the form of, for example, capsules, tablets, suppositories, suspensions or solutions, for enteral or parenteral administration. Aside from the usual pharmaceutical diluents or carriers, e.g. water, alcohols, natural or hardened oils and waxes, these pharmaceutical compositions may contain suitable preserving, stabilizing, wetting, solubilizing, sweetening, flavouring or colouring agents.

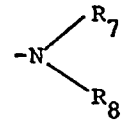
An example of a tablet composition comprises 136 mg of N^1-butyl-N^2,N^2-diallyl-4,4-dimethyl-3-oxo-pentanamidine hydrobromide, 1 mg of magnesium stearate, 4 mg of polyvinyl pyrrolidone, 0.5 mg of dimethyl silicone oil, 5 mg of talc, 10 mg of maize starch, 137.8 mg of lactose and 1.5 mg of polyethylene glycol - 6000.

The tablets are produced in conventional manner and are provided with a double slit.

In a preferred class of compounds, R_1, R_2 and R_3 are independently alkyl, R_4 is alkyl, alkenyl, phenyl, or substituted phenyl and R_5 and R_6 are, independently, alkyl, alkenyl, alkoxyalkyl or cyanoalkyl. More especially R_1, R_2 and R_3 are alkyl, especially methyl, and R_4, R_5 and R_6 are independently alkenyl especially of 3 to 4 carbon atoms or especially alkyl of 1 to 4 carbon atoms.

In another preferred class of compounds R_5 and R_6 are identical.

In another class of compounds R_1 is phenyl or substituted phenyl and R_2 is alkyl, or R_1 and R_2 together are $-(CH_2)_n-$ and R_3 is alkyl, or R_1, R_2 and R_3 together with the carbon atom to which they are bound form the adamantyl radical, R_4 is a group of formula;



wherein

R_7 and R_8 are the same or different and each is alkyl of 1 to 4 carbon atoms, or

R_7 and R_8 together with the nitrogen atom are a heterocyclic ring, or a heterocyclic ring having a ring oxygen atom, and

R_5 and R_6 are phenyl or substituted phenyl.

In the following non-limitative Examples the temperatures are indicated in degrees Centigrade, room temperature is between 20° and 30°C, unless otherwise indicated. The commonly used vacuum is between 8 and 20 mm of Hg, unless otherwise indicated.

EXAMPLE 1

N^1,N^2-triethyl-4,4-dimethyl-3-oxo-pentanamidine

a. N^1,N^2-triethyl-5,5-dimethyl-4-oxo-2-thiahexanamidine

A mixture of 14.3 g of bromopinacoline, 12.8 g of N^1,N^2-triethyl thiourea and 120 cc of acetone is heated to the boil at reflux for 8 hours. The reaction mixture is subsequently concentrated by evaporation in a vacuum. 80 cc of an aqueous 1 N sodium hydroxide solution are added to the resulting residue, and the result-

ing mixture is extracted with diethyl ether. The ethereal solution is dried with potassium carbonate and is subsequently concentrated by evaporation. N^1,N^2-triethyl-5,5-dimethyl-4-oxo-2-thiahexanamidine is obtained as oily residue.

b. N^1,N^2-triethyl-4,4-dimethyl-3-oxo-pentanamidine

13.5 g of the oily N^1,N^2-triethyl-5,5-dimethyl-4-oxo-2-thiahexanamidine obtained in section a) are mixed with 13.5 g of triphenyl phosphine, and the mixture is heated in an oil bath to 120° for 6 hours in a flask provided with an upright tube. The reaction mixture is subsequently cooled and triturated with 1 N hydrobromic acid until the acid reaction is maintained. The undissolved triphenyl phosphine sulphide is filtered off and washed with water. The aqueous filtrate is extracted with diethyl ether and purified with charcoal. After the charcoal is filtered off, the aqueous filtrate is evaporated to dryness in a vacuum. After recrystallization from 2 parts by volume of isopropanol/g of compound, or from 4.5 parts by volume of acetone/g of compound, the resulting N^1,N^2-triethyl-4,4-dimethyl-3-oxo-pentanamidine hydrobromide has a M.P. of 138°–140°.

Treatment of the hydrobromide with an aqueous 2 N sodium hydroxide solution, extraction of the alkaline solution with diethyl ether and concentration by evaporation of the ethereal mixture yields oily N^1,N^2-triethyl-4,4-dimethyl-3-oxo-pentanamidine.

EXAMPLE 2

N^2,N^2-di-isobutyl-N^1,4,4-trimethyl-3-oxo-pentanamidine.

a. N^2,N^2-di-isobutyl-N^1-methyl thiourea

A solution of 7.3 g of methyl isothiocyanate in 20 cc of benzene is added to a solution of 12.9 g of di-isobutylamine in 50 cc of benzene, and the resulting mixture is allowed to stand at 20° for 4 days. The mixture is subsequently concentrated by evaporation, and N^2,N^2-di-isobutyl-N^1-methyl thiourea, having a M.P. of 98°–100°, is obtained as residue.

b. N^2,N^2-di-isobutyl-4-oxo-2-thia-N^1,5,5-trimethyl-hexanamidine hydrobromide

19.5 g of N^2,N^2-di-isobutyl-N^1-methyl thiourea are dissolved in 100 cc of acetone, and 17.3 g of bromopinacoline are added to the solution. The resulting mixture is allowed to stand at 20° for 12 hours. The mixture is subsequently heated to the boil for 4 hours, is subsequently cooled, and the resulting precipitate is filtered off. The N^2,N^2-di-isobutyl-4-oxo-2-thia-N^1,5,5-trimethylhexanamidine hydrobromide, obtained as filter residue, has a M.P. of 202°–204°.

c. N^2,N^2-di-isobutyl-N^1,4,4-trimethyl-3-oxo-pentanamidine

11.8 g of N^2,N^2-di-isobutyl-4-oxo-2-thia-N^1,5,5-trimethyl-hexanamidine (obtained from the hydrobromide by treatment with caustic soda solution and extraction of the liberated base with ether) are heated to 120° for 8 hours together with 12.5 g of triphenyl arsine. The resulting melted material is neutralized with 1 N hydrobromic acid (about 28 cc). The aqueous solution is poured off and cold alcohol is added to the smeary crystalline product until the solid components are filterable. Filtration is subsequently effected. The filter residue contains about 11.6 g of a mixture of triphenyl arsine and triphenyl arsine sulphide. The filtrate is extracted with 100 cc of diethyl ether, and the aqueous solution is concentrated by evaporation in a vacuum. The evaporation residue is heated to 80° together with 150 cc of ethyl acetate, whereby after initial solution crystals are formed. Cooling is then effected to 0°, and the residue N^2,N^2-di-isobutyl-N^1,4,4-trimethyl-3-oxo-pentamidine hydrobromide (M.P. 151°–156°) is filtered off.

The compounds of formula I, indicated in the following Tables, are obtained by using the processes exemplified in the above Examples 1 and 2 and the corresponding starting materials. The indicated melting points refer to the corresponding salt forms. The free base forms of the compounds of formula I are obtained from the salt forms in known manner, e.g. by treatment with caustic soda solution and extraction with ether.

The substituents are in the ω-position except where otherwise stated.

Example	R_1	R_2	R_3	R_4	R_5	R_6	M.P.	Salt form
3	Methyl	Methyl	Methyl	Methyl	Methyl	Methyl	197–199°	Bromide
4	Methyl	Methyl	Methyl	Methyl	Methyl	Ethyl	174–175°	Bromide
5	Methyl	Methyl	Methyl	Methyl	Ethyl	Ethyl	165–167°	Bromide
6	Methyl	Methyl	Methyl	Methyl	CH_3O-ethyl	CH_3O-ethyl	130–131°	Bromide
7	Methyl	Methyl	Methyl	Methyl	Propyl	Propyl	175–177°	Bromide
8	Methyl	Methyl	Methyl	Methyl	Isopropyl	Isopropyl	160–161°	Bromide
9	Methyl	Methyl	Methyl	Methyl	Allyl	Allyl	88–90°	Bromide
10	Methyl	Methyl	Methyl	Methyl	Butyl	Butyl	119–120°	Bromide
11	Methyl	Methyl	Methyl	Methyl	Isobutyl	Isobutyl	155–157°	Bromide
12	Methyl	Methyl	Methyl	Ethyl	Methyl	Methyl	190–192°	Bromide
13	Methyl	Methyl	Methyl	Ethyl	Methyl	Ethyl	144–145°	Bromide
14	Methyl	Methyl	Methyl	Ethyl	CH_3O-ethyl	CH_3O-ethyl	91–93°	Oxalate
15	Methyl	Methyl	Methyl	Ethyl	Propyl	Propyl	143–145°	Bromide
16	Methyl	Methyl	Methyl	Ethyl	Isopropyl	Isopropyl	132–134°	Bromide
17	Methyl	Methyl	Methyl	Ethyl	Butyl	Butyl	121–122°	Bromide
18	Methyl	Methyl	Methyl	Ethyl	Isobutyl	Isobutyl	160–162°	Bromide
19	Methyl	Methyl	Methyl	Ethyl	Allyl	Allyl	119–121°	Bromide
20	Methyl	Methyl	Methyl	Propyl	Methyl	Methyl	125–127°	Bromide
21	Methyl	Methyl	Methyl	Propyl	Ethyl	Ethyl	125–127°	Bromide
22	Methyl	Methyl	Methyl	Propyl	CH_3O-ethyl	CH_3O-ethyl	54–56°	Bromide
23	Methyl	Methyl	Methyl	Propyl	Propyl	Propyl	101–102°	Bromide
24	Methyl	Methyl	Methyl	Propyl	Isopropyl	Isopropyl	137–138°	Bromide
25	Methyl	Methyl	Methyl	Propyl	Isobutyl	Isobutyl	169–170°	Bromide
26	Methyl	Methyl	Methyl	Propyl	Allyl	Allyl	102–104°	Oxalate
27	Methyl	Methyl	Methyl	Isopropyl	Ethyl	Ethyl	151–152°	Bromide
28	Methyl	Methyl	Methyl	Isopropyl	Propyl	Propyl	119–120°	Bromide
29	Methyl	Methyl	Methyl	Isopropyl	Isopropyl	Isopropyl	171–172°	Bromide
30	Methyl	Methyl	Methyl	Isopropyl	Allyl	Allyl	126–128°	Oxalate
31	Methyl	Methyl	Methyl	Allyl	Methyl	Methyl	140–142°	Bromide
32	Methyl	Methyl	Methyl	Allyl	Ethyl	Ethyl	136–137°	Bromide
33	Methyl	Methyl	Methyl	Allyl	Propyl	Propyl	140–141°	Bromide
34	Methyl	Methyl	Methyl	Allyl	Isopropyl	Isopropyl	140–142°	Bromide

—Continued

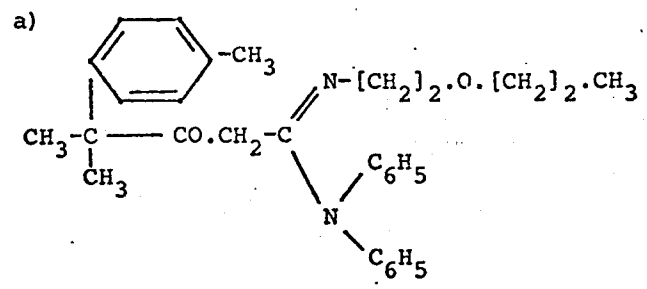
Example	R_1	R_2	R_3	R_4	R_5	R_6	M.P.	Salt form
35	Methyl	Methyl	Methyl	Allyl	Isobutyl	Isobutyl	148–149°	Bromide
36	Methyl	Methyl	Methyl	Allyl	Allyl	Allyl	93–94°	Oxalate
37	Methyl	Methyl	Methyl	Butyl	Methyl	Methyl	113–114°	Bromide
38	Methyl	Methyl	Methyl	Butyl	Ethyl	Ethyl	117–118°	Bromide
39	Methyl	Methyl	Methyl	Butyl	Propyl	Propyl	79–80°	Bromide
40	Methyl	Methyl	Methyl	Butyl	Isopropyl	Isopropyl	130–132°	Bromide
41	Methyl	Methyl	Methyl	Butyl	Butyl	Butyl	78–82°	Bromide
42	Methyl	Methyl	Methyl	Butyl	Allyl	Allyl	80–81°	Bromide
43	Methyl	Methyl	Methyl	Isobutyl	Ethyl	Ethyl	192–194°	Bromide
44	Methyl	Methyl	Methyl	Isobutyl	Propyl	Propyl	103–104°	Bromide
45	Methyl	Methyl	Methyl	Isobutyl	Allyl	Allyl	96–98°	Bromide
46	Methyl	Methyl	Methyl	sec-Butyl	Ethyl	Ethyl	128–131°	Bromide
47	Methyl	Methyl	Methyl	sec-Butyl	CH_3O-ethyl	CH_3O-ethyl	83–84°	Oxalate
48	Methyl	Methyl	Methyl	sec-Butyl	Propyl	Propyl	113–114°	Oxalate
49	Methyl	Methyl	Methyl	sec-Butyl	Allyl	Allyl	104–105°	Oxalate
50	Methyl	Methyl	Methyl	tert-Butyl	Ethyl	Ethyl	138–139°	Bromide
51	Methyl	Methyl	Methyl	tert-Butyl	Isopropyl	Isopropyl	134–135°	Bromide
52	Methyl	Methyl	Methyl	Amyl	Methyl	Methyl	128–130°	Bromide
53	Methyl	Methyl	Methyl	Amyl	Ethyl	Ethyl	74–76°	Oxalate
54	Methyl	Methyl	Methyl	Amyl	Propyl	Propyl	60–61°	Bromide
55	Methyl	Methyl	Methyl	Amyl	Allyl	Allyl	82–84°	Oxalate
56	Methyl	Methyl	Methyl	Isoamyl	Ethyl	Ethyl	119–120°	Bromide
57	Methyl	Methyl	Methyl	Octyl	Ethyl	Ethyl	84–85°	Bromide
58	Methyl	Methyl	Ethyl	Ethyl	Ethyl	107–109°	Bromide	
59	Methyl	Methyl	Ethyl	Methyl	Isobutyl	Isobutyl	143–145°	Bromide
60	Methyl	Methyl	Ethyl	Ethyl	Propyl	Propyl	125–126°	Oxalate
61	Methyl	Methyl	Ethyl	Ethyl	Allyl	Allyl	87–88°	Oxalate
62	Methyl	Methyl	Ethyl	sec-Butyl	Ethyl	Ethyl	100–102°	Bromide
63	Methyl	Methyl	Methyl	Methyl	Methyl	Phenyl	189–192°	Bromide
64	Methyl	Methyl	Methyl	Ethyl	Ethyl	Phenyl	213–216°	Bromide
65	Methyl	Methyl	Methyl	Phenyl	Methyl	Methyl	179–182°	Bromide
66	Methyl	Methyl	Methyl	Phenyl	Ethyl	Ethyl	169–172°	Bromide
67	Methyl	Methyl	Methyl	Phenyl	Propyl	Propyl	181–182°	Bromide
68	Methyl	Methyl	Methyl	Phenyl	Allyl	Allyl	113–115°	Bromide
69	Methyl	Methyl	Methyl	p-Cl-phenyl	Ethyl	Ethyl	181–183°	Bromide
70	Methyl	Methyl	Methyl	p-CH_3-phenyl	Ethyl	Ethyl	162–163°	Bromide
71	Methyl	Methyl	Phenyl	Ethyl	Ethyl	Ethyl	143–144°	Bromide
72	Methyl	Methyl	Ethyl	Butyl	Ethyl	Ethyl	113–114°	Bromide
73	Methyl	Methyl	Ethyl	sec-Butyl	Allyl	Allyl	92–93°	Oxalate
74	Methyl	Methyl	Methyl	sec-Butyl	Isopropyl	Isopropyl	163–164°	Bromide
75	Methyl	Methyl	Methyl	Octyl	Methyl	Methyl	127–128°	Bromide
76	Methyl	Methyl	Methyl	β-Methallyl	Methyl	Methyl	135–137°	Bromide
77	Methyl	Methyl	Methyl	β-Methallyl	Ethyl	Ethyl	153–155°	Bromide
78	Methyl	Methyl	Methyl	β-Methallyl	Propyl	Propyl	142–143°	Bromide
79	Methyl	Methyl	Methyl	Hexyl	Ethyl	Ethyl	90–91°	Oxalate
80	Methyl	Methyl	Methyl	Butyl	Methyl	Ethyl	108–109°	Bromide
81	Methyl	Methyl	Methyl	Hexyl	Methyl	Methyl	128–129°	Bromide
82	Methyl	Methyl	Methyl	Isobutyl	Methyl	Methyl	185–186°	Bromide
83	Methyl	Methyl	Methyl	sec-Butyl	Methyl	Ethyl	98–100°	Bromide
84	Methyl	Methyl	Methyl	tert-Butyl	Methyl	Ethyl	163–164°	Bromide
85	Methyl	Methyl	Methyl	sec-Hexyl	Methyl	Methyl	81–82°	Oxalate
86	Methyl	Methyl	Methyl	Methyl	Isoamyl	Isoamyl	164–165°	Bromide
87	Methyl	Methyl	Methyl	Isoamyl	Allyl	Allyl	74–75°	Oxalate
88	Methyl	Methyl	Methyl	sec-Hexyl	Methyl	Ethyl	108–110°	Oxalate
89	Methyl	Methyl	Methyl	Ethyl	2-Cyanoethyl	2-cyanoethyl	167–168°	Bromide
90	Methyl	Methyl	Methyl	sec-Butyl	Methyl	2-cyanoethyl	95–96°	Oxalate

Using the process exemplified in Example 1 or 2 and the appropriate starting materials, there are obtained the following compounds

50

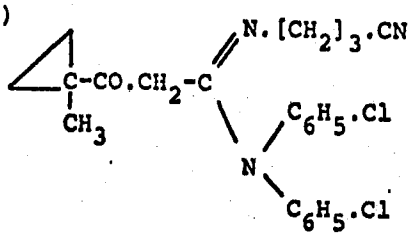
Structure:

a)

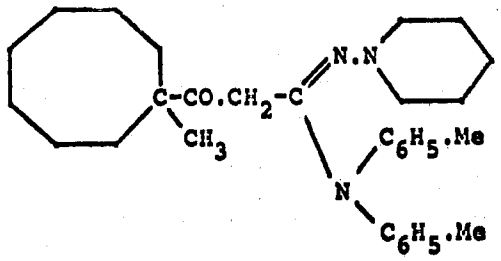


– Continued

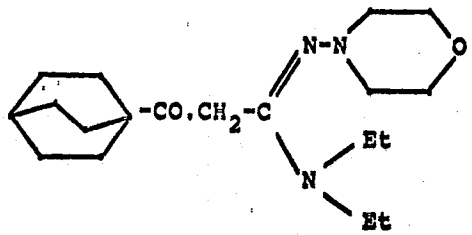
b)



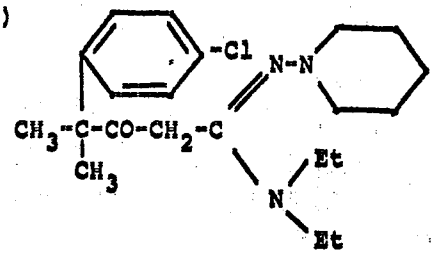
c)



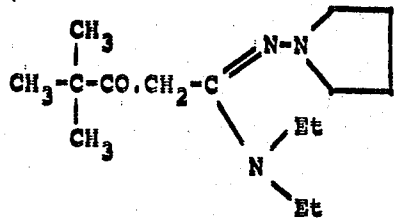
d)



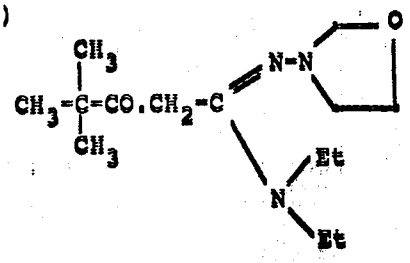
e)



f)

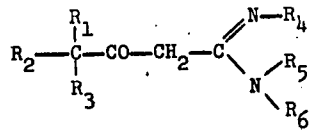


g)



What is claimed is:

1. A compound of the formula



wherein

R_1 is alkyl of 1 to 4 carbon atoms, phenyl or phenyl substituted with alkyl of 1 to 4 carbon atoms or chloro,

R_2 is alkyl of 1 to 4 carbon atoms, or

R_1 and R_2 together are $-(CH_2)_n-$, wherein n is an integer from 2 to 7, and

R_3 is alkyl of 1 to 4 carbon atoms, or

R_1, R_2 and R_3 together with the carbon atom to which they are bound form the adamantyl radical,

R_4 is alkyl of 1 to 8 carbon atoms, alkenyl of 2 to 8 carbon atoms, alkoxyalkyl of 2 to 8 carbon atoms in the aggregate thereof, cyanoalkyl wherein the alkyl radical is of 1 to 5 carbon atoms, or a group of formula

wherein

R_7 and R_8 are the same or different and each is alkyl of 1 to 4 carbon atoms, and

R_5 and R_6 are the same or different and each is alkyl of 1 to 8 carbon atoms, alkenyl of 2 to 8 carbon atoms, alkoxyalkyl of 2 to 8 carbon atoms in the aggregate thereof or cyanoalkyl wherein the alkyl is of 1 to 5 carbon atoms, or one of R_4, R_5 and R_6 is phenyl or phenyl substituted with alkyl of 1 to 4 carbon atoms or halo and the others of R_4, R_5 and R_6 are as defined above, provided at least one of R_4, R_5 and R_6 is cyanolkyl wherein the alkyl is of 1 to 5 carbons.

2. A compound of claim 1, wherein R_1 or one of R_4, R_5 and R_6 is, when substituted phenyl, alkylphenyl, the alkyl radical thereof having 1 to 4 carbon atoms, or halophenyl.

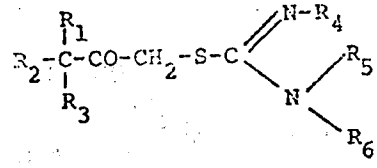
3. A compound of claim 1, wherein R_1, R_2 and R_3 are methyl.

4. The compound of claim 3, wherein R_4 is ethyl, R_5 is 2-cyanoethyl, R_6 is 2-cyanoethyl.

5. The compound of claim 3, wherein R_4 is sec-butyl, R_5 is methyl and R_6 is 2-cyanoethyl.

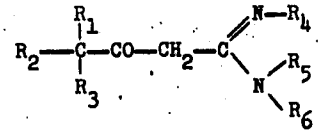
6. A compound of claim 1, wherein R_1 and R_2 are methyl and R_3 is ethyl.

7. A compound of the formula,



wherein R_1 to R_6 and the proviso are as stated in claim 1.

8. A compound according to claim 1 having the structure



wherein

R_1 is alkyl of 1 to 4 carbon atoms, phenyl or phenyl substituted with alkyl of 1 to 4 carbon atoms or chloro, and

R_2 is alkyl of 1 to 4 carbon atoms, or

R_1 and R_2 together are $-(CH_2)_n-$, wherein n is an integer from 2 to 7, and

R_3 is alkyl of 1 to 4 carbon atoms, or

R_1, R_2 and R_3 together with the carbon atom to which they are bound form the adamantyl radical,

R_4 is alkyl of 1 to 8 carbon atoms, alkenyl of 3 to 4 carbon atoms, methoxyethyl or cyanoethyl or a group of formula

wherein

R_7 and R_8 are the same or different and each is alkyl of 1 to 4 carbon atoms, and

R_5 and R_6 are the same or different and each is alkyl of 1 to 8 carbon atoms, alkenyl of 3 to 4 carbon atoms, methoxyethyl or cyanoethyl, or one of R_4, R_5 and R_6 is phenyl or phenyl substituted with alkyl of 1 to 4 carbon atoms or chloro and the others of R_4, R_5 and R_6 are as defined above,

provided at least one of R_4, R_5 and R_6 is cyanoethyl.

* * * * *