

UNITED STATES PATENT OFFICE

2,538,794

ALKAMINE ESTERS OF Δ^2 -CYCLOHEXENYL-
ALKYLACETIC ACIDS

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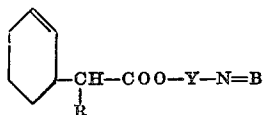
Serial No. 43,543

9 Claims. (Cl. 260—294.3)

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This invention relates to aminoalkyl esters of Δ^2 -cyclohexenylalkylacetic acids and to therapeutically acceptable salts thereof which are useful as antispasmodic agents. This is a continuation-in-part of our copending application, S. N. 642,427, filed January 19, 1946.

These esters have the formula



where R is an alkyl group of 4-6 carbon atoms, Y is an alkylene bridge having at least two carbon atoms separating the oxygen and nitrogen atoms, and $-N=B$ is a tertiary-amino group wherein B represents two alkyl groups or the atoms necessary to complete a heterocyclic ring. More specifically Y may be a divalent hydrocarbon radical such as ethylene, propylene, butylene, 1-methylethylene, 2-methylethylene or 1-methylbutylene; and $-N=B$ includes such structures as dimethylamino, ethylmethylamino, diethylamino, dipropylamino, dibutylamino, butylpropylamino, piperidyl, 2-methylpiperidyl, morpholinyl, thiomorpholinyl, beta-hydroxyethylethylamino, etc. These may be classed together as aliphatic tertiary-amino groups; the heterocyclic rings are distinctly non-aromatic in character and can be thought of as two alkyl groups joined together by a divalent bridge such as $-CH_2-$, $-O-$ or $-S-$.

These compounds are generally used in the form of water-soluble acid-addition salts or quaternary ammonium derivatives. The acids which may be used to prepare the salts are those which produce, when combined with the basic esters, salts whose anions are relatively innocuous to the animal organism in therapeutic doses of the salts, so that the beneficial physiological properties inherent in the basic esters are not vitiated by side-effects ascribable to the anions. Appropriate acid addition salts are those derived from mineral acids such as hydrochloric acid, hydrobromic acid, hydriodic acid, and sulfuric acid; and organic acids such as acetic acid, citric acid and tartaric acid. The quaternary ammonium derivatives are obtained by the addition of alkyl or aralkyl esters of inorganic acids or organic sulfonic acids, such as methyl chloride, methyl bromide, methyl iodide, ethyl bromide, propyl chloride, benzyl chloride, benzyl bromide, methyl sulfate, methyl benzenesulfonate, methyl-p-toluenesulfonate, etc.

Synthetic antispasmodics usually have both a musculotropic (papaverine-like) action and neurotropic (atropine-like) action. It is desirable that new compounds be introduced which have high neurotropic activity but which lack the characteristic undesirable physiological side-effects of atropine.

Our compounds are distinguished by high neu-

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rotropic activity, and, in addition, several members of the series show antihistaminic action.

Our compounds are conveniently prepared by esterification of the corresponding substituted acetic acid, $(C_6H_9)-CHR-COOH$. The acids themselves are prepared in the following manner. The sodio derivative of diethyl Δ^2 -cyclohexenylmalonate, $(C_6H_9)-CH-(COOC_2H_5)_2$, is alkylated with RX , where R is an alkyl group of 4-6 carbons and X is a halogen atom, i. e., chlorine, bromine or iodine. The resulting Δ^2 -cyclohexenylalkylmalonic ester, $(C_6H_9)-CR-(COOC_2H_5)_2$, is hydrolyzed by heating with 30% alcoholic potassium hydroxide in a bomb at 140-150° C., and decarboxylated at 180° C. at atmospheric pressure, giving the desired Δ^2 -cyclohexenylalkylacetic acid.

In some cases where the malonic esters are difficult to prepare because of the steric hindrance of the groups involved, an alternative procedure can be used. This is based on the method of Alexander and Cope [J. Am. Chem. Soc. 66, 886 (1944)], which involves condensation of an aldehyde or ketone with ethyl cyanoacetate and reduction of the resulting ethylenic double bond, all carried out in one step. In preparing the compounds of the present invention the carbonyl compound used has a structure such that the group R in the resulting substituted cyanoacetic ester, $R-CH(CN)-COOC_2H_5$, has 4-6 carbon atoms. For example, condensation of ethyl cyanoacetate and methyl isopropyl ketone in the presence of ammonium acetate, acetic acid and alladium-on-charcoal in an atmosphere of hydrogen gives ethyl (1,2-dimethylpropyl)-cyanoacetate. The sodio-derivative of the mono-substituted cyanoacetic ester is then alkylated with a Δ^2 -cyclohexenyl halide to give an ethyl Δ^2 -cyclohexenylalkylcyanoacetate,



This is hydrolyzed and decarboxylated to the corresponding Δ^2 -cyclohexenylalkylacetic acid, $(C_6H_9)-CHR-COOH$, although in lower yield than the hydrolysis and decarboxylation of the corresponding malonic ester. Substituted acetamides appear as byproducts and more drastic conditions of hydrolysis lead to decomposition.

Instead of alkylating malonic ester, a substituted malonic ester or substituted cyanoacetic ester with a Δ^2 -cyclohexenyl halide, it is often preferable to use the more readily available 1,2-dibromocyclohexane. The simple alkylation product, a 2-bromocyclohexylmalonic or cyanoacetic ester, is not obtained. Under the conditions of the reaction, hydrogen bromide is lost giving rise to the desired 2-3 double bond.

The preferred method, the malonic ester or cyanoacetic ester synthesis, in a given case depends upon the nature of the alkyl group to be introduced. If the alkyl group to be introduced is of the straight chain type or is branched at the end, the malonic ester synthesis is preferred.

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If the alkyl group is branched, particularly near its point of juncture with the rest of the molecule, the cyanoacetic ester method is preferred.

The esters of our invention, having the general formula $C_6H_5-CH(R)-COO-Y-N=B$ as described above, and their acid addition salts, are prepared from the free acid by one of the following methods.

(1) An acid halide or anhydride of a Δ^2 -cyclohexenylalkylacetic acid is reacted with a tertiary-aminoalkanol of the formula $HO-Y-N=B$, where Y is an alkylene bridge of at least 2 carbon atoms and $-N=B$ is a tertiary-amino group. The reaction is effected by simple admixture of the two components although heating is generally used to accelerate the reaction. The free basic ester is obtained by addition of alkali to the reaction mixture. The basic ester may be converted to an acid addition salt by the addition, preferably in non-aqueous medium, of a therapeutically acceptable acid, such as hydrogen chloride in alcoholic solution.

(2) The Δ^2 -cyclohexenylalkylacetic acid is reacted with a tertiary-aminoalkanol using a mineral acid, such as sulfuric acid, as a catalyst, present in an amount greater than that necessary to neutralize the amino alcohol. The free basic ester and its acid addition salts are obtained as in method 1.

(3) The Δ^2 -cyclohexenylalkylacetic acid is heated with a tertiary-aminoalkyl halide of the formula $Z-Y-N=B$, where Z is halogen (preferably chlorine or bromine) and Y and B have the same meaning as before. The free basic ester and its acid addition salts are obtained as in method 1.

(4) A metallic salt of a Δ^2 -cyclohexenylalkylacetic acid is heated or simply mixed with a tertiary-aminoalkyl halide. In this case the free basic ester is formed directly.

Quaternary ammonium salts are prepared by mixing the free basic ester with a lower alkyl or aralkyl ester of a strong inorganic acid or organic sulfonic acid, preferably in an inert organic solvent such as benzene or ether, with or without gentle heating. The salt either crystallizes immediately or can be obtained by concentration of the solvent.

EXAMPLE 1

(a) *Diethyl Δ^2 -cyclohexenylmalonate*.—To a solution of 184 g. (8 m.) of sodium in 2.8 liters of absolute ethanol is added 641 g. (4 m.) of diethyl malonate and then 968 g. (4 m.) of 1,2-dibromocyclohexane is slowly run in. After refluxing for six hours the mixture is practically neutral. Most of the alcohol is then removed by distillation and the residue is diluted with 1 liter of water. The layers are separated and the organic layer is washed with water, dried over anhydrous sodium sulfate and distilled from a Claisen flask. The fraction distilling at 88–130° (0.1 mm.), is redistilled through an efficient column, giving about 625 g. (65%) of diethyl Δ^2 -cyclohexenylmalonate, B. P. 87° C. (0.11 mm.); $n_D^{25}=1.4595$; $d_4^{25}=1.0443$.

(b) *Diethyl Δ^2 -cyclohexenyl-isoamylmalonate*.—To 17.3 g. (0.75 m.) of sodium melted under 150 cc. of dry toluene in a 1 liter flask is slowly added, with vigorous stirring, 180 g. (0.75 m.) of diethyl Δ^2 -cyclohexenylmalonate. The mixture is refluxed until practically all of the sodium has reacted, and then 136 g. (0.9 m.) of isoamyl bromide is added. After refluxing for twelve hours the reaction mixture is cooled and neutralized with acetic acid. Enough water is added

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to dissolve soluble salts and the organic layer is separated, washed with water and dried over anhydrous sodium sulfate. After removal of low-boiling solvents, the product is distilled at reduced pressure, first from a modified Claisen flask and then through an efficient column giving about 113 g. (48.5%) of diethyl Δ^2 -cyclohexenyl-isoamylmalonate, B. P. 97° C. (0.02 mm.); $n_D^{25}=1.4643$; $d_4^{25}=0.9993$.

(c) *Δ^2 -cyclohexenyl-isoamylacetic acid*.—A mixture of 40 g. of diethyl Δ^2 -cyclohexenyl-isoamylmalonate with a solution of 40 g. of potassium hydroxide in 100 cc. of 95% ethanol is heated on a bomb in an oil bath at 140–160° C. for three hours. After cooling, the contents are diluted with water, extracted with ether and acidified with hydrochloric acid. The product is extracted with ether, and the ether solutions then washed thoroughly with water and dried over anhydrous sodium sulfate. After removing the solvent, the product is heated to 180° C. until carbon dioxide ceases to be evolved, and then is distilled at reduced pressure from a Claisen flask, giving about 28 g. of Δ^2 -cyclohexenyl-isoamylacetic acid, B. P. 104° C. (0.07 mm.); $n_D^{25}=1.4746$; $d_4^{25}=0.9669$.

(d) *Beta-diethylaminoethyl Δ^2 -cyclohexenyl-isoamylacetate and its hydrochloride*.— Δ^2 -cyclohexenyl-isoamylacetic acid (21.8 g., 0.104 m.) is neutralized to phenolphthalein with alcoholic sodium ethoxide, and 14.1 g. (0.014 m.) of beta-diethylaminoethyl chloride in 40 cc. of isopropyl alcohol is then added. After standing for several days (or refluxing for several hours), the sodium chloride is removed by filtration, and the volatile solvents are distilled off. The basic ester is dissolved in ether, washed with water and extracted with cold dilute hydrochloric acid. The acid solution is washed with ether and made basic with sodium carbonate. The liberated basic ester is extracted with ether and the ether solution is dried over anhydrous sodium sulfate. Distillation of the product at reduced pressure after removal of the ether gives about 17.4 g. (54%) of beta-diethylaminoethyl Δ^2 -cyclohexenyl-isoamylacetate, B. P. 109° C. (0.029 mm.); $n_D^{25}=1.4660$; $d_4^{25}=0.9285$.

The hydrochloride of beta-diethylaminoethyl Δ^2 -cyclohexenyl-isoamylacetate is prepared by passing dry hydrogen chloride gas into a solution of 16.1 g. of the free basic ester in absolute ether. A colloidal precipitate forms which crystallizes upon stirring. After filtering, washing with ether and drying, the hydrochloride is obtained; weight 10.8 g. (60%). Upon recrystallization from methyl isobutyl ketone it has the M. P. 101–105° C.

EXAMPLE 2

(a) *Δ^2 -cyclohexenyl-isoamylacetyl chloride*.—A solution of 44 g. (0.21 m.) of Δ^2 -cyclohexenyl-isoamylacetic acid in 36.3 cc. of thionyl chloride is warmed at 50° C. until the reaction is complete. The excess thionyl chloride is removed at reduced pressure and the product is distilled giving about 45 g. (94%) of Δ^2 -cyclohexenyl-isoamylacetyl chloride, B. P. 85° C. (0.07 mm.); $n_D^{25}=1.4800$; $d_4^{25}=1.0017$.

(b) *Beta-dimethylaminoethyl Δ^2 -cyclohexenyl-isoamylacetate and its hydrochloride*.—Beta-dimethylaminoethanol (7.8 g., 0.088 m.) is dissolved in 70 cc. of dry pyridine and 20 g. (0.088 m.) of Δ^2 -cyclohexenyl-isoamylacetyl chloride is added, and the mixture is allowed to stand for a few minutes and finally heated on a steam bath for four hours. After cooling the mixture, it is shaken with a solution of 8 g. of sodium car-

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bonate monohydrate in 150 cc. of water and the water layer is separated and extracted with ether. The combined organic layers are concentrated using a water aspirator and the residue distilled at reduced pressure, giving about 21.7 g. (89%) of beta-dimethylaminoethyl Δ^2 -cyclohexenyl-isoamylacetate, B. P. 93° C. (0.015 mm.);

$$n_D^{25}=1.4665; d_4^{25}=0.9373$$

The hydrochloride is prepared in the manner described in Example 1, part d by passing dry hydrogen chloride gas through a solution of the basic ester in anhydrous ether. The hydrochloride is obtained in about 46% yield and has the M. P. 114–115° C.

EXAMPLE 3

Beta-(N-piperidyl)-ethyl Δ^2 -cyclohexenyl-isoamylacetate.—This is prepared by the same method described in Example 2, using as starting materials Δ^2 -cyclohexenyl-isoamylacetyl chloride and beta-(N-piperidyl)-ethanol. The product is obtained in about 77% yield and has the B. P. 130° C. (0.01 mm.); $n_D^{25}=1.4832$; $d_4^{25}=0.9768$.

The hydrochloride of beta-(N-piperidyl)-ethyl Δ^2 -cyclohexenyl-isoamylacetate is prepared in the usual manner from the free basic ester and hydrogen chloride gas in ether solution. It is obtained in about 76% yield and has the M. P. 157–159° C.

EXAMPLE 4

(a) **Ethyl Δ^2 -cyclohexenyl-sec-butylcyanoacetate.**—To sodium ethoxide prepared in a 1 liter flask from 36.8 g. (1.6 m.) of sodium and 600 cc. of absolute ethanol is added 127 g. (0.75 m.) of ethyl sec-butylcyanoacetate [Alexander and Cope, J. Am. Chem. Soc. 66, 886 (1944)], and then 194 g. (0.8 m.) of 1,2-dibromocyclohexane. After refluxing for three and one-half hours, most of the solvent is removed by distillation, water is added and the layers separated. The aqueous layer is extracted with ether, and the combined organic layers are washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. After removing the solvent, the product is distilled at reduced pressure, first from a Claisen flask and then through a 12-inch column packed with $\frac{1}{8}$ -inch glass helices, giving about 110 g. of ethyl Δ^2 -cyclohexenyl-sec-butylcyanoacetate, B. P. 94° C. (0.02 mm.); $n_D^{25}=1.4750$; $d_4^{25}=1.0015$.

(b) **Δ^2 -cyclohexenyl-sec-butylacetic acid.**—A mixture of 40 g. (0.16 m.) of ethyl Δ^2 -cyclohexenyl-sec-butylcyanoacetate with a solution of 70 g. of potassium hydroxide in 120 cc. of 90% ethanol is heated in a bomb in an oil bath at 140–180° C. for 43 hours. After cooling, the contents of the bomb are diluted with water, extracted with ether to remove considerable neutral material, and acidified. The acidic oil is extracted with ether, washed three times with water and once with saturated sodium chloride solution containing a little sodium bicarbonate, and finally dried over anhydrous sodium sulfate. After removal of solvent, the product is distilled at reduced pressure from a Claisen flask, giving about 21.6 g. (69%) of Δ^2 -cyclohexenyl-sec-butylacetic acid, B. P. 92° (0.01 mm.); $n_D^{25}=1.4800$; $d_4^{25}=0.9912$.

(c) **Beta-diethylaminoethyl Δ^2 -cyclohexenyl-sec-butylacetate and its hydrochloride.**—This is prepared from the substituted acetic acid using sodium ethoxide and beta-diethylaminoethyl chloride according to the method shown in Example 1, part d. Nine and six-tenths grams of

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acid results in about 8.6 g. (60%) of beta-diethylaminoethyl Δ^2 -cyclohexenyl-sec-butylacetate, B. P. 109° C. (0.04 mm.); $n_D^{25}=1.4701$;

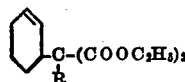
$$d_4^{25}=0.9428$$

The hydrochloride is prepared in the usual manner from the basic-ester and dry hydrogen chloride gas in ether solution. When recrystallized from methyl isobutyl ketone, the hydrochloride melts at 105–110° C.

Additional compounds have been made by the methods outlined in the preceding examples and are disclosed in the following table.

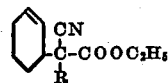
TABLE I

A. Malonates



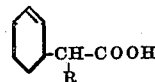
R	B. P. °C. (mm.)	n_D^{25}	d_4^{25}
$\text{CH}_3(\text{CH}_2)_4-$	95 (0.09)	1.4638	1.0071
$\text{CH}_3\text{CHCH}_2\text{CH}_2-$ CH_3	97 (0.02)	1.4643	0.9993
$\text{CH}_3\text{CH}_2\text{CHCH}_2-$ CH_3	98 (0.018)	1.4648	1.0071
$\text{CH}_3\text{CH}_2\text{CHCH}_2-$ CH_2CH_3	106 (0.026)	1.4684	0.9984

B. Cyanoacetates



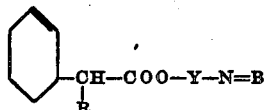
R	B. P. °C. (mm.)	n_D^{25}	d_4^{25}
$\text{CH}_3\text{CHCH}_2-$ CH_3	92 (0.05)	1.4727	0.9913
$\text{CH}_3\text{CH}_2\text{CH}-$ CH_3	94 (0.02)	1.4750	1.0015
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}-$ CH_3	101 (0.05)	1.4750	0.9882
$\text{CH}_3\text{CH}-\text{CH}-$ $\text{CH}_3 \quad \text{CH}_3$	96 (0.045)	1.4778	0.9974

C. Acetic acids



R	B. P. °C. (mm.)	n_D^{25}	d_4^{25}
$\text{CH}_3(\text{CH}_2)_4-$	102 (0.006)	1.4770	0.9818
$\text{CH}_3\text{CHCH}_2\text{CH}_2-$ CH_3	104 (0.07)	1.4746	0.9669
$\text{CH}_3\text{CH}_2\text{CHCH}_2-$ CH_3	103 (0.03)	1.4758	0.9715
$\text{CH}_3\text{CH}_2\text{CH}-\text{CH}_2-$ CH_2CH_3	111 (0.026)	1.4775	0.9660
$\text{CH}_3\text{CHCH}_2-$ CH_3	110 (0.013)	1.4754	0.9810
$\text{CH}_3\text{CH}_2\text{CH}-$ CH_3	92 (0.01)	1.4800	0.9912
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}-$ CH_3	106 (0.046)	1.4790	0.9778
$\text{CH}_3\text{CH}-\text{CH}-$ $\text{CH}_3 \quad \text{CH}_3$	108 (0.04)	1.4806	-----

TABLE II
Basic esters

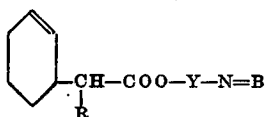


Compound	R	Y-N=B	B.P. °C (mm.)
1.....	$\text{CH}_3(\text{CH}_2)_4-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_2\text{CH}_3 \\ \text{CH}_2\text{CH}_3 \end{array}$	118 (0.2)
2.....	$\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_2\text{CH}_3 \\ \text{CH}_2\text{CH}_3 \end{array}$	108 (0.01)
3.....	$\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_2\text{CH}_3 \\ \text{CH}_2\text{CH}_3 \end{array}$	109 (0.029)
4.....	$\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_3 \\ \text{CH}_3 \end{array}$	93 (0.015)
5.....	$\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_2\text{CH}_2 \\ \text{CH}_2\text{CH}_2 \end{array}$	130 (0.01)
6.....	$\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_2\text{CH}_3 \\ \text{CH}_2\text{CH}_3 \end{array}$	109 (0.04)
7.....	$\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}_2-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_2\text{CH}_3 \\ \text{CH}_2\text{CH}_3 \end{array}$	110 (0.025)
8.....	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_2\text{CH}_3 \\ \text{CH}_2\text{CH}_3 \end{array}$	130 (0.5)
9.....	$\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_2\text{CH}_3 \\ \text{CH}_2\text{CH}_3 \end{array}$	124 (0.15)
10.....	$\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}_2-$	$-\text{CH}_2\text{CH}_2\text{N} \begin{array}{l} \text{CH}_2\text{CH}_3 \\ \text{CH}_2\text{CH}_3 \end{array}$	114 (0.016)

Compound	n_D^{25}	d_4^{25}	Hydrochloride, M. P. °C.
1.....	1.4670	0.9335	103-104.5
2.....	1.4669	0.9305	116-118
3.....	1.4680	0.9285	101-105
4.....	1.4665	0.9373	114-115
5.....	1.4832	0.9768	157-159
6.....	1.4701	0.9428	105-110
7.....	1.4684	0.9324	102-104
8.....	1.4695	0.9319	102-107
9.....	1.4720	0.9454	128-132
10.....	1.4690	0.9358	100-102

We claim:

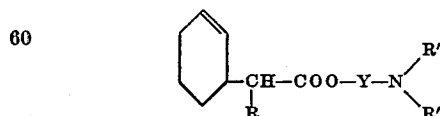
1. A substance of the group consisting of basic esters of the formula



wherein R is an alkyl group of 4-6 carbon atoms, Y is an alkylene bridge of 2-5 carbon atoms and

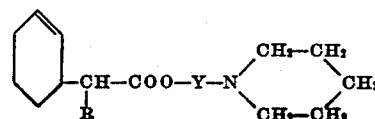
—N=B is a tertiary-amino group of the class consisting of di-lower-alkylamino, piperidyl and morpholinyl radicals; and acid addition and quaternary ammonium salts thereof.

2. A substance of the group consisting of basic esters of the formula



65 wherein R is an alkyl group of 4-6 carbon atoms, Y is an alkylene bridge of 2-5 carbon atoms and R' and R'' are lower alkyl groups; and acid addition and quaternary ammonium salts thereof.

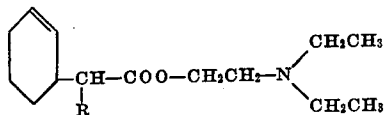
3. A substance of the group consisting of basic esters of the formula



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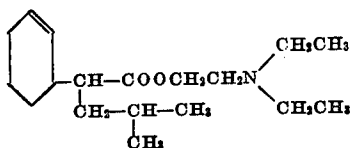
wherein R is an alkyl group of 4-6 carbon atoms and Y is an alkylene bridge of 2-5 carbon atoms; and acid addition and quaternary ammonium salts thereof.

4. A substance of the group consisting of the formula



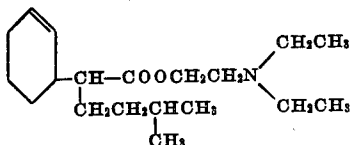
wherein R is an alkyl group of 4-6 carbon atoms, and acid addition and quaternary ammonium salts thereof.

5. A substance of the group consisting of beta-diethylaminoethyl Δ^2 -cyclohexenyl-isoamylacetate of the formula



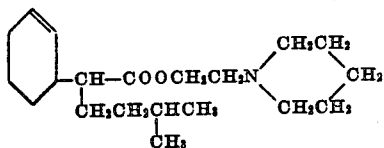
and acid addition and quaternary ammonium salts thereof.

6. A substance of the group consisting of beta-diethylaminoethyl Δ^2 -cyclohexenyl-isoamylacetate of the formula



and acid addition and quaternary ammonium salts thereof.

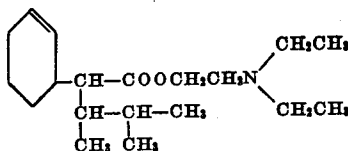
7. A substance of the group consisting of beta-(N-piperidyl)-ethyl Δ^2 -cyclohexenyl-isoamylacetate of the formula



and acid addition and quaternary ammonium salts thereof.

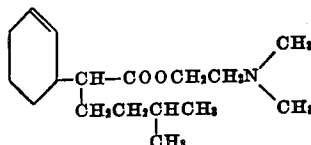
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8. A substance of the group consisting of beta-diethylaminoethyl Δ^2 -cyclohexenyl-(1,2-dimethylpropyl)-acetate of the formula



and acid addition and quaternary ammonium salts thereof.

9. A substance of the group consisting of beta-dimethylaminoethyl Δ^2 -cyclohexenyl-isoamylacetate of the formula



and acid addition and quaternary ammonium salts thereof.

ROBERT BRUCE MOFFETT.
CHARLOTTE ANNE HART.

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Certificate of Correction

Patent No. 2,538,794

January 23, 1951

ROBERT BRUCE MOFFETT ET AL.

It is hereby certified that error appears in the printed specification of the above numbered patent requiring correction as follows:

Column 2, line 33, for "alladium-on-charcoal" read *palladium-on-charcoal*;
column 9, line 5, after "of", second occurrence, insert *a compound of*;

and that the said Letters Patent should be read as corrected above, so that the same may conform to the record of the case in the Patent Office.

Signed and sealed this 3rd day of April, A. D. 1951.

[SEAL]**THOMAS F. MURPHY,***Assistant Commissioner of Patents.*