ESTERS OF AMINO ALCOHOLS

Carl D. Lunsford, Richmond, Va., assignor to A. H. Robins Company, Inc., Richmond, Va., a corporation of Virginia

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The present invention relates to esters of amino alcohols, more particularly certain esters of N- or 1-substituted 3-pyridinolinos. These novel compounds include the cycloalkyl-aryl-acetates and glycolates of 3-pyridinolinos. The concept constituting the present invention is illustrated by the following structural formula:

\[ \text{R'} \quad \text{R''} \quad \text{O} \quad \text{C} \quad \text{O} \quad \text{R} \]

wherein

- R is a hydrocarbon radical, such as alkyl, cycloalkyl and aralkyl
- R' is a cycloalkyl radical, and
- R'' is hydrogen or a hydroxyl radical.

Nontoxic organic and inorganic acid addition salts of the compounds having the general structural formula shown above may be readily prepared as illustrated in the examples below and include salts formed with such inorganic and organic acids as hydrochloric, hydrobromic, hydriodic, sulfuric, sulfamic, phosphoric, acetic, glycolic, succinic, maleic, malic, citric, tartaric, ascorbic, benzoic, cinnamic, mandelic, benzoic, diphenylacetic and the like.

Quaternary ammonium salts such as alkyl salts, aralkyl salts, and the like, of the organic bases illustrated in the general structural formula appearing above may be readily formed by treatment of the organic bases with the appropriate quaternary salt forming substances, which include, for example, methyl chloride, methyl bromide, methyl iodide, methyl sulfide, methyl benzene-sulfonate, methyl p-toluensulfonate, ethyl chloride, ethyl bromide, ethyl iodide, n-propyl chloride, n-propyl bromide, n-propyl iodide, isopropyl bromide, n-butyl chloride, n-butyl bromide, isobutyl bromide, sec-butyl bromide, n-amyl bromide, n-hexyl chloride, benzyl chloride, benzyl bromide, and ethyl sulfate, yielding respectively the methochloride, methobromide, methiodide, methyl methosulfate, methobenzenesulfonate, metho-p-toluensulfonate, ethochloride, ethobromide, ethiodide, n-propochloride, n-propobromide, n-propoiodide, isopropobromide, n-butochloride, n-butobromide, isobutobromide, sec-butoxochloride, n-amobromide, n-hexochloride, benzochloride, benzobromide, ethosulfate, etc.

In the structural formula given above, the asterisks (*) serve to point out the asymmetric carbon atoms present in many of the compounds of the present invention. When two asymmetric centers are present, pairs of diastereoisomers are possible. These diastereoisomers, together with their optically active forms are included within the scope of the present invention.

The two pairs of diastereoisomers are separated and resolution of the diastereoisomers into their optically active forms may be accomplished by combining the basic diastereoisomers with an optically active organic acid and separating by fractional crystallization the d-and l-forms.

Evaluations of the compounds of the above concept by standard pharmacological tests have indicated the utility thereof as inhibitors of gastrointestinal motility, comparing favorably in potency with Methanethiolone bromide. The compounds are predominantly antagonists of acetylcholine.

This application is a continuation-in-part of Serial No. 666,520, Lunsford, filed June 17, 1957, entitled "Esters of Amino Alcohols," now abandoned.

The present invention is characterized by a particular esterification of a secondary alcohol attached directly to a ring carbon in the 3 position of the pyridoline ring fraction. The prior art into which the compounds of the present invention fall can be distinguished. United States Patent 2,655,511, Woodruff, describes N- or 1-pyrrolidyl esters where the alkoxy group is extra-cyclic to the pyridoline ring where there is a methylene bridge attached to the heterocyclic nitrogen; United States Patent 2,695,301, Blicke, teaches benzilates proceeding from the 2 position of the pyridoline ring but differs from the present invention in that the alcohol group is primary and extra-cyclic; United States Patent 2,738,847, Blicke, describes diphenyl acetates proceeding from the N or 1 position in the pyridoline ring and involves extra-cyclic esterification.

Therefore, it is an object of this invention to provide novel cycloalkyl-aryl-acetic acid esters of 3-pyridinolinos. It is a further object of the present invention to provide such esters wherein the alpha carbon of the acetate group may be substituted by an additional radical such as hydroxyl and wherein the 3-pyridinoline portion of the molecule is substituted in the N or 1 position.

It is an additional object of the present invention to provide novel acetylcholine antagonists having satisfactory activity when compared with known compounds currently in use as inhibitors of gastrointestinal motility.

Other objects of the invention will become apparent to those skilled in the art to which this invention pertains.

Members of the new group of compounds include the alpha-cycloalkyl-aryl acetic and glycolic acid esters of 3-pyridinolinos where the N or 1 position of the pyridoline ring is substituted by a hydrocarbon radical such as alkyl, cycloalkyl, aralkyl and the like, preferably lower alkyl.

Referring to R in the above structural formula, the preferred hydrocarbon radicals are alkyl, especially straight and branched chain lower alkyl radicals, cycloalkyl and aralkyl.

The term lower alkyl is defined to include straight and branched chain radicals of 1—6 carbon atoms inclusive and includes such substituents as methyl, ethyl, isopropyl, tertiary butyl, isobutyl and the like. The term cycloalkyl is defined to include primarily cyclic alkyl radicals containing 5 to 8 carbon atoms inclusive and encompasses such substituents as cyclohexyl, cyclopentyl, methyl cyclohexyl, ethyl cyclohexyl, dimethyl cyclohexyl, and cycloheptyl. Included in the term aralkyl are such radicals as lower alkyl-substituted mono-carboxylic aryl compounds such as benzyl, phenethyl, phenylpropyl and the like. Preferably, R is a hydrocarbon radical containing less than 8 carbon atoms and is selected from the group consisting of lower alkyl, cycloalkyl and aralkyl.

Referring to R' in the above structural formula the cycloalkyl hydrocarbon radicals are defined as above, preferably, the cycloalkyl radical contains at least 5 and less than 8 carbon atoms.

Referring to R" in the above structural formula, (in column 1), R" is preferably an hydroxy radical.

Generally, for reasons of activity, the esters in the form of nontoxic, pharmaceutically acceptable acid addition and quaternary ammonium salt compounds, where-
in referring to the structural formula in column 1, R is lower alkyl, R’ is cyclopentyl and R’’ is hydroxy, are preferred. Among the specifically preferred compounds are:

1 - ethyl - 3 - pyrrolidyl alpha-cyclopentylphenylacetate methobromide.
1 - methyl - 3 - pyrrolidyl alpha-cyclopentyl-mandelate hydrochloride
1 - methyl - 3 - pyrrolidyl alpha-cyclopentyl-mandelate methobromide

The cycloalkylaryl acetic acids are one of the preferred group of esterifying agents, i.e., wherein R’ is cycloalkyl and especially cyclopentyl. Thus, the 1-lower alkyl-3-pyrrolidyl cycloalkyl-arylacetic acids as acid addition salts and quaternary salts are preferred members of the series.

A preferred compound of this type is 1-ethyl-3-pyrrolidyl alpha-cyclopentylphenylacetate methobromide. Also of increased activity but not as preferred are:

1-ethyl-3-pyrrolidyl alpha-cyclohexylphenylacetate hydrochloride
1-methyl - 3 - pyrrolidyl alpha-cyclohexylphenylacetate methobromide
1 - ethyl - 3 - pyrrolidyl alpha-cyclohexylphenylacetate methobromide
1 - benzyl - 3 - pyrrolidyl alpha-cyclohexylphenylacetate methobromide

The alpha carbon of the acetate group preferably is further substituted by a hydroxy radical, i.e., wherein R” is a hydroxy radical. Such compounds may be alternatively viewed as substituted glycolates or mandelates.

A highly preferred compound by reason of activity from these esters having a hydroxy radical on the alpha carbon of the acetate is the 1-methyl-3-pyrrolidyl alpha-cyclopentyl-mandelate methobromide (1-methyl-3-(alpha-cyclopentylphenylhydroxyacetoxyl) pyrrolidine methobromide). This compound was found to be active at a dilution of about one part in 100,000,000 in counter-acting symptoms induced by acetylcholine in isolated intestinal strips. Other preferred compounds include 1-methyl-3-pyrrolidyl alpha-cyclopentyl-mandelate hydrochloride and 1-ethyl-3-pyrrolidyl alpha-cyclopentyl-mandelate hydrochloride.

Generally, the N or 1 lower alkyl substituted compounds indicated greater activity and generally the alpha-cycloalkyl-mandelates were preferred.

The esters of the present invention may be prepared by reaction of a 1-hydrocarbon substituted-3-pyrrolidinol of the formula—

![Structural formula]

wherein R is as above with an alpha aryl acetic acid compound of the formula:

![Structural formula]

wherein R’ and R’’ are as above and B is hydroxy, halogen or lower alkoxy.

When B is lower alkoxy, the transesterification reaction is conducted in the presence of a sodium metal catalyst until the theoretical amount of lower alkanol separates. With this exception, the reaction conditions are similar for all variants of starting compounds, i.e., the reactants, used in approximately equimolar amounts, are heated at reflux temperatures for periods of at least about one hour and usually from one to two hours, preferably using a hydrocarbon solvent as the reaction medium. The resulting reaction product is extracted with dilute mineral acid, e.g., hydrochloric acid, and the resulting extract basified (e.g., with aqueous sodium hydroxide) to yield the free base upon extraction with the appropriate solvent. The acid addition salts and quaternary salts are produced from the base by reaction in solution of the base and the appropriate acid or quaternizing reagent.

The preparation of the starting N-substituted-3-pyrroolidinols used in the present invention has been previously described in United States Patents 2,830,997 and 2,838,521, Lunsford.

The following examples illustrate the preparation of the compounds of the present invention:

**EXAMPLE 1.—1-METHYL-3-PYRROLIDYL ALPHA- CYCLOHEXYLPHENYLACETATE**

To a solution of 71 grams (0.3 mole) of alpha-cyclohexylphenylacetate chloride in toluene were added 35.5 grams (0.35 mole) of 1-methyl-3-pyrrolidinol at a dropwise rate with stirring. After complete addition the mixture was refluxed for four hours, cooled and extracted with 3 N hydrochloric acid. The acid extract was basified with aqueous sodium hydroxide and extracted with chloroform. The chloroform layer was washed, dried over sodium sulfate and concentrated. The residue was distilled at reduced pressure. Yield 50 grams (55 percent); boiling point 144–147°C at 0.5 mm.

The hydrochloride was precipitated from an ethereal solution of the base with ethereal hydrogen chloride and crystallized from butanone; melting point 153.5–154.5°C.

The methiodide quaternary precipitated from an ethereal solution was the base and excess methyl iodide after standing for several hours. It was crystallized from butanone; melting point 169.5–170.5°C.

**EXAMPLE 2.—1-N-BUTYL-3-PYRROLIDYL ALPHA- CYCLOPENTYLPHENYLACETATE**

To a solution of 89 grams (0.4 mole) of alpha-cyclopentylphenylacetyl chloride in benzene were added 71.5 grams (0.30 mole) of 1-n-butyl-3-pyrrolidinol at a dropwise rate with stirring. After complete addition the mixture was refluxed for two hours, cooled and extracted with 3 N hydrochloric acid. The acid extract was basified with aqueous sodium hydroxide and extracted with ether. The layer was washed, dried over sodium sulfate, and concentrated. The residue was distilled at reduced pressure. Yield 110 grams (67 percent); boiling point 150–155°C at 0.1 mm.

The hydrochloride was precipitated from an ethereal solution of the base with ethereal hydrogen chloride and crystallized from butanone; melting point 107.5–109.5°C.

The methobromide quaternary was precipitated from an ethereal solution of the base and excess methyl bromide after standing for thirty-six hours. It was crystallized first from an ethyl acetate-ether mixture and then from butanone; melting point 104–106°C.

**EXAMPLE 3.—1-BENZYL-3-PYRROLIDYL ALPHA- CYCLOHEXYLPHENYL-ACETATE**

To a solution of 71 grams (0.3 mole) of alpha-cyclohexylphenylacetly chloride in toluene were added 62 grams (0.35 mole) of 1-benzyl-3-pyrrolidinol, at a dropwise rate with stirring. After complete addition the mixture was refluxed for four hours, cooled and extracted with 3 N hydrochloric acid. The acid extract was basified with aqueous sodium hydroxide and extracted with chloroform.

The chloroform layer was washed, dried over sodium sulfate and concentrated. The residue was distilled at reduced pressure. Yield 45.5 grams (40 percent); boiling point 187–189°C at 0.01 mm.

The hydrochloride was precipitated from an ethereal solution of the base with ethereal hydrogen chloride and...
crystallized from butanone; melting point 142-143.5°C. The methyl bromide quaternary precipitated from an ethereal solution of the base and excess methyl bromide, after standing for twenty-four hours, as an oil. This was crystallized from an ethyl acetate-ether-methanol mixture; melting point 183-185°C.  

EXAMPLE 4.—1-METHYL-3-PYRROLIDYL ALPHA-CYCLOPENTYLPHENYLACETATE  
To a solution of 52 grams (0.244 mole) of alpha-cyclopentylphenylacetyl chloride in benzene were added 25 grams (0.248 mole) of 1-methyl-3-pyrrolidinol, at a dropwise rate, with stirring. After complete addition the mixture was refluxed for two hours, cooled and extracted with 3 N hydrochloric acid. The acid extract was basified with aqueous sodium hydroxide and extracted with ether. The ether layer was washed, dried over sodium sulfate, and concentrated. The residue was distilled at reduced pressure. Yield 40 grams (63 percent); boiling point 144-147°C at 0.2 mm. The hydrochloride was precipitated as an oil from an ethereal solution of the base with ethereal hydrogen chloride. This was crystallized from a methanol-ethyl acetate mixture and melted at 114-115°C.

The methyl bromide quaternary was precipitated from an ethereal solution of the base and excess methyl bromide after standing for seventy-two hours. It was purified by recrystallization from butanone and melted at 166.5-168°C.

EXAMPLE 5.—1-N-BUTYL-3-PYRROLIDYL ALPHA-CYCLOPENTYLAMENDATE  
A mixture of 54 grams (0.216 mole) of methyl alpha-cyclopentylamendate and 39 grams (0.272 mole) of 1-n-butyl-3-pyrrolidinol in 500 ml. of heptane was refluxed under a Dean and Stark moisture trap, with the addition of four 0.1 gram pieces of sodium at one hour intervals. After five hours refluxing the solution was concentrated at one half volume, diluted with ether and washed with water. The ether layer was dried over sodium sulfate and concentrated. The residue was fractionally distilled at reduced pressure. Yield 60 grams (80.5 percent); boiling point 160-165°C at 0.04 mm. The hydrochloride was precipitated from an ethereal solution of the base and excess methyl bromide after standing for one week. The solid was crystallized from butanone and melted at 129-130°C.

Analysis.—Calc'd for C₂₅H₄₁NO₅.HCl: C, 60.63; H, 7.93; N, 4.47; Cl, 10.1. Found: C, 60.57; H, 7.95; N, 4.43; Cl, 10.0.  

The methyl bromide quaternary was precipitated from an ethereal solution of the base and excess methyl bromide after standing for one week. The solid was crystallized from butanone and melted at 176-177°C.  

Analysis.—Calc'd for C₂₅H₄₁NO₅.HCl: C, 60.63; H, 7.93; N, 4.47; Cl, 10.1. Found: C, 60.57; H, 7.95; N, 4.43; Cl, 10.0.  

EXAMPLE 6.—1-METHYL-3-PYRROLIDYL ALPHA-CYCLOPENTYLAMENDATE  
A mixture of 42.5 grams (0.17 mole) of methyl alpha-cyclopentylamendate and 18 grams (0.175 mole) of 1-methyl-3-pyrrolidinol in 500 ml. of heptane was refluxed under a Dean and Stark moisture trap, with the addition of four 0.1 gram pieces of sodium at one hour intervals. After five hours refluxing the solution was concentrated to one half volume, and extracted with cold 3 N HCl. The acid extract was made alkaline with aqueous sodium hydroxide and extracted with ether which was washed, dried, and concentrated. The residue was fractionated at reduced pressure. Yield 33 grams (64%); boiling point 151-154°C at 0.2 mm. Rf 1.5265.  

The hydrochloride salt was precipitated as an oil from an ethereal solution of the base with ethereal hydrogen chloride. It was crystallized from butanone; melting 170-171°C.

Analysis.—Calc'd for C₂₅H₄₁NO₅.HCl: C, 60.63; H, 7.93; N, 4.47; Cl, 10.1. Found: C, 60.57; H, 7.95; N, 4.43; Cl, 10.0.  

The methyl bromide quaternary was prepared by saturating a solution of the base in dry ethyl acetate with methyl bromide. After standing for nine days the resulting crystalline solid was filtered and recrystallized from butanone and from ethyl acetate; melting point 193-194.5°C.  

Analysis.—Calc'd for C₂₅H₄₁NO₅.Br: Br, 20.06. Found: Br, 19.78.

EXAMPLE 7.—1-ETHYL-3-PYRROLIDYL ALPHA-CYCLOPENTYLAMENDATE HYDROCHLORIDE  
This compound was prepared according to the method outlined for the methyl derivative above (see Example 6). The base boiled at 162-165°C at 0.25 mm. After recrystallization from butanone, the salt melted 160-161.5°C.

Analysis.—Calc'd for C₂₅H₄₁NO₅.Cl: Cl, 9.82. Found: Cl, 9.81.

EXAMPLE 8.—1-CYCLOHEXYL-3-PYRROLIDYL ALPHA-CYCLOPENTYLAMENDATE HYDROCHLORIDE  
This compound was prepared according to the method outlined for the methyl derivative above. The base boiled at 193-195°C at 0.038 mm. After recrystallization from butanone and absolute ethanol, the salt melted 212-213.5°C.

Analysis.—Calc'd for C₂₅H₄₁NO₅.HCl: Cl, 8.69. Found: Cl, 8.81.

EXAMPLE 9.—1-METHYL-3-PYRROLIDYL ALPHA-CYCLOHEXYLAMENDATE  
A mixture of 10 grams (0.0403 mole) of methyl alpha-cyclohexylamendate and 5 grams (0.0493 mole) of N-methyl-3-pyrrolidinol in 125 ml. of n-heptane was refluxed for five hours under a Dean and Stark moisture trap. At approximately equal intervals starting at zero time three approximately 0.1 gram pieces of sodium metal were added to the reaction. At completion of the reflux time the heptane solution was extracted with ice-cold 3 N hydrochloric acid. The acid extract was basified with saturated aqueous potassium carbonate and extracted with ether. The ether extract was washed, dried over magnesium sulfate and concentrated. The residual oil was distilled at 160-163°C at 0.03 mm. giving an amber oil product. Yield 8.7 grams (68%).

The hydrochloride salt precipitated as a crystalline solid from an ethereal solution of the base with ethereal hydrogen chloride. It was crystallized from a butanone-methanol mixture; M.P. 206-207°C.

Analysis.—Calc'd for C₂₅H₄₁NO₅.HCl: Cl, 10.02. Found: Cl, 10.00.

The methyl bromide quaternary was prepared by saturating a solution of the free base in dry ethyl ether with methyl bromide and allowing the solution to stand 15 hours. The product precipitated as white crystals and was recrystallized from butanone; M.P. 253-255 (d). This decomposition range varies with the rate at which the sample is heated.


As pointed out in column 1, those compounds which have two asymmetric centers are capable of existing in two diastereoisomeric forms. These two forms can be separated by fractional crystallization as shown in the following example:

EXAMPLE 10.—1-ETHYL-3-PYRROLIDYL ALPHA-CYCLOHEXYLAMENDATE HYDROCHLORIDE  
A mixture of 41 grams (0.17 mole of methyl alpha-cyclohexylamendate and 23 grams (0.20 mole of N-ethyl-3-pyrrolidinol in 300 ml. of n-heptane was refluxed for 5 hours and a half hours under a Dean and Stark mois-
tured trap. At approximately equal intervals, starting at zero time, three approximately 0.1 gram pieces of sodium metal were added to the reaction. At completion of the reflux time the heptane solution was extracted with ice cold 3 N hydrochloric acid. The acid extract was basi-
field with aqueous sodium carbonate and extracted with ether. The ether extract was washed, dried over sodium sulfate and concentrated. The residual oil was distilled at 157–160° C./0.05 mm., giving an amber oil product. Yield 31.7 grams (56%).

This material was converted to the hydrochloride salt by precipitation as a crystalline solid from an ethereal solution of the base with ethereal hydrogen chloride. This material was fractionally crystallized from methyl ethyl ketone and from an ethyl acetate methanol mixture. High and low melting isomers were obtained:

2.956,062

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<th>R'</th>
<th>A</th>
<th>Salt</th>
<th>Calculated for</th>
<th>Percent X</th>
<th>Found</th>
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<td>H</td>
<td>HCl</td>
<td>C₆H₅NO₂H-HCl</td>
<td>10.42</td>
<td>10.39</td>
<td>490.46</td>
<td>160-164</td>
</tr>
<tr>
<td>n-C₆H₅</td>
<td>cy-C₆H₅</td>
<td>H</td>
<td>HCl</td>
<td>C₆H₅NO₂H-HCl</td>
<td>10.02</td>
<td>10.00</td>
<td>338.88</td>
<td>200-207</td>
</tr>
<tr>
<td>n-C₆H₅</td>
<td>cy-C₆H₅</td>
<td>H</td>
<td>HCl</td>
<td>C₆H₅NO₂H-HCl</td>
<td>9.81</td>
<td>9.83</td>
<td>316.69</td>
<td>250-255</td>
</tr>
<tr>
<td>CH₃</td>
<td>cy-C₆H₅</td>
<td>H</td>
<td>HCl</td>
<td>C₆H₅NO₂H-HCl</td>
<td>9.64</td>
<td>9.68</td>
<td>367.91</td>
<td>184-185</td>
</tr>
<tr>
<td>CH₃</td>
<td>cy-C₆H₅</td>
<td>H</td>
<td>HCl</td>
<td>C₆H₅NO₂H-HCl</td>
<td>9.74</td>
<td>9.65</td>
<td>369.91</td>
<td>180-182.5</td>
</tr>
<tr>
<td>C₂H₅</td>
<td>cy-C₆H₅</td>
<td>H</td>
<td>HCl</td>
<td>C₂H₅NO₂H-HCl</td>
<td>8.94</td>
<td>8.95</td>
<td>429.39</td>
<td>151-155</td>
</tr>
</tbody>
</table>

In evaluating the compounds of the present invention pharmacologically the following experimental testing procedure was utilized.

**ISOLATED GUINEA PIG ILEUM STUDIES**

Guinea pigs were killed by a blow on the head. The ileum was removed and terminal segments were suspended in a 100 ml. smooth muscle bath containing Tyrode's solution which was maintained at 37° C. The bath was aerated by bubbling a continuous stream of oxygen through it. Intestinal activity was recorded by a balanced ink-writing lever yielding five-fold magnification on a Gorrell and Gorrell kymograph operated at speed P.

Aqueous solutions of all materials were employed in these studies. Essentially, the method consisted of initially standardizing submaximal contractions of the isolated ileum to acetylcholine chloride, histamine phosphate, serotonin creatinine sulfate and barium chloride. The test material was then introduced into the bath and at two minutes later the ileum was again challenged with the various spasmogens. Tests were made at various concentrations of the compounds in the bath until it was possible to differentiate their relative activity as antagonists of the spasmogens.
The results of the pharmacological testing indicate that the compounds are predominantly acetylcholine antagonists and are effective in inhibiting gastrointestinal motility in vivo and in vitro. In general, the compounds compared favorably in potency with Methanetheline bromide under the conditions of these tests.

Various modifications may be made in the compounds of the present invention without departing from the spirit and scope thereof, and it is to be understood that the invention is limited only by the scope of the appended claims.

I claim:

1. A compound selected from the group consisting of esters of 3-pyrrolidinols having the structural formula

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wherein R is a hydrocarbon radical selected from the group consisting of lower alkyl, phenylalkyl containing up to nine carbon atoms inclusive, and cycloalkyl containing five to eight carbon atoms inclusive and having five to seven carbon atoms inclusive in the ring.

R' is a cycloalkyl hydrocarbon radical containing five to eight carbon atoms inclusive and having five to seven carbon atoms inclusive in the ring, and

R'' is a radical selected from the group consisting of hydrogen and hydroxyl, and nontoxic acid addition and lower-alkyl and benzyl quaternary ammonium salts thereof.

2. 1-methyl - 3 - pyrrolidyl alpha - cyclopentylmandelate methobromide.
3. 1-methyl - 3 - pyrrolidyl alpha - cyclopentylmandelate hydrochloride.
4. 1-ethyl - 3 - pyrrolidyl alpha - cyclopentylphenylacetate methobromide.
5. 1-methyl - 3 - pyrrolidyl alpha - cyclohexylphenylacetate methiodide.
6. 1-methyl - 3 - pyrrolidyl alpha - cyclohexylphenylacetate hydrochloride.
7. 1-ethyl - 3 - pyrrolidyl alpha - cyclohexylphenylacetate methiodide.
8. 1-benzyl-3-pyrrolidyl alpha-cyclohexylphenylacetate methobromide.
9. 1-lower-alkyl-3-pyrrolidyl cycloalkylmandelate having the structural formula:

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O
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|---|--
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wherein the cycloalkyl radical contains five to eight carbon atoms, inclusive, and has five to seven carbon atoms, inclusive, in the ring.
12. 1-methyl - 3-pyrrolidyl alpha-cyclopentylmandelate.

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