CHAPTER II

N-ARALKYLANTHRANILIC ACIDS. I
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N-ARALKYLANTHRANILIC ACIDS. I

As stated in the introduction, it was considered of interest to synthesise and test the compounds represented by the general structure (I), for their physiological action in experimental animals.

\[
\begin{align*}
&\text{R} - \text{COOH} \\
&\text{NH} - \text{X} - \text{Z}
\end{align*}
\]

where R = H, 4-Cl, 4-NO₂, 4-CH₃, 5-Cl, and 5-NO₂

\[
\begin{align*}
\text{X} &= \text{CH}_2 -, \text{CH} -, \text{CH} -, \text{CH} -, \text{CH} - , \\
&\text{CH}_3, \text{C}_2\text{H}_5, \text{nC}_3\text{H}_7, \text{C}_8\text{H}_5
\end{align*}
\]

and Z = phenyl

substituted phenyl carrying groups such as chloro, methyl, methoxy, dichloro, dimethoxy

thienyl

furyl

cyclohexyl

benzimidazolyl

naphthyl
These compounds were prepared by the three routes outlined below. The methods of preparation of relevant N-phenyl- and N-benzyl-anthranilic acid derivatives reported in literature, are given in the appendix.

**Route I**

(a) A majority of these compounds was prepared by the Ullmann reaction by condensing a 2-halobenzoic acid with an aralkylamine.

\[
\begin{align*}
& \text{COOH} \\
& \text{Hal} \\
& \text{R} \\
& + \text{H}_2\text{N}-\text{X-Z} \rightarrow \text{R} \\
& \text{COOH} \\
& \text{NH-}\text{X-Z}
\end{align*}
\]

Thus, 2-chloro-; 2,4-dichloro-; 2,5-dichloro-; 2-chloro-4-nitro-; 2-chloro-5-nitro- and 2-bromo-4-methylbenzoic acids were condensed with various aralkylamines in the presence of anhydrous potassium carbonate and catalytic amount of copper oxide. In a number of cases, isoamyl alcohol was used as solvent to bring the reactants together and to keep the mixture fluid.

(b) The alternative route, i.e. the condensation of an aralkyl-halide with anthranilic acid in the presence of copper oxide, potassium carbonate and amyl alcohol, was also tried, but the yields were poorer by this method as compared to the yields obtained by the first method.

\[
\begin{align*}
& \text{COOH} \\
& \text{R} \\
& + \text{Hal-X-Z} \rightarrow \text{R} \\
& \text{COOH} \\
& \text{NH-}\text{X-Z}
\end{align*}
\]
Thus, anthranilic and 4-chloroanthranilic acids were condensed with benzylchloride, 4-chlorobenzyl chloride, 4-nitrobenzyl bromide and 2-chloromethylbenzimidazole.

**Route II**

This involved the reaction of substituted benzylchlorides with anthranilic acid in the presence of aqueous potassium carbonate (Houben & Brassert\(^1\)). Thus the following benzylchlorides were condensed with anthranilic acid.

Benzylchloride, 4-chlorobenzylchloride, 2,4-dichlorobenzylchloride and 3,4-dichlorobenzylchloride.

**Route III**

This consisted of the preparation of \(N\)-benzylideneanthranilic acids (Schiff bases), by reacting suitably substituted benzaldehydes with substituted anthranilic acids, which were then reduced to the corresponding \(N\)-benzylantranilic acid derivatives with sodium borohydride in dry methanol.

\[
\begin{align*}
\text{R-COOH} + \text{ArCHO} & \rightarrow \text{R-CN=CHAr} \\
\text{R-CN=CHAr} & \xrightarrow{\text{NaBH}_4} \text{R-COOH} \\
\text{R-COOH} + \text{ArCH}_{2}\text{NH} & \rightarrow \text{R-COOH}
\end{align*}
\]
It was found that the reduction was smooth and in some cases quantitative. Some of the compounds which were obtained by this method were also prepared by method I as described above. The mixed melting points of the compounds so obtained were undepressed and their IR spectra superimposable.

The use of sodium borohydride in reducing N-benzylidene anthranilic acids appears to be new, as sodium borohydride has not been employed till now for reducing Schiff bases carrying an ortho carboxyl group.

The compounds synthesised by the above methods are listed in Tables I–VI.

Two more compounds (where –X–Z– was different from the groups mentioned on p. 16), i.e., N-4-(2-methylthiachromanyl)–, and N-1-(1,2,3,4-tetrahydronaphthyl)–anthranilic acids (Table VI) were also synthesised during the present work.

The IR spectra of this family of anthranilic acid derivatives consistently showed a bonded carboxyl carbonyl band at 1668 cm⁻¹ and an NH band at 3370 cm⁻¹.

Preparation of the starting materials

The o-halobenzoic acids, anthranilic acids, aralkylamines, and aralkyl halides needed in the preparation of the above N-aralkylanthranilic acids were generally commercially available. Such of these as were not commercially available were prepared by known methods as described in the Experimental section.
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| 40   | 5-Cl | $3,4,5-(\text{CH}_3)_3$        | 181-182 |           |
| 41   | 4-Cl | $3,4,5-(\text{CH}_3)_3$        | 224-225 |           |

* Compounds previously described in literature; other compounds are new.
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Table III
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Two new morphanthridine derivatives, i.e., 5,6-dihydro-8-methoxy-11-morphanthridone (IIIA) and 5,6-dihydro-3-chloro-8-methoxymorphanthridone (IIIB) were also prepared in the course of the present work. These compounds were prepared by the cyclodehydration of N-(3-methoxybenzyl)-, and 4-chloro-N-(3-methoxybenzyl)anthranilic acids (IIA, b) respectively, with polyphosphoric acid.

Werner et al tried the ring closure of the tosylate of N-benzyl-anthranilic acid chloride with aluminium chloride, but they got only tarry products.

Drukker and coworkers were, however, able to synthesise 5,6-dihydro-11-morphanthridone, though by a different route. They prepared the compound by the oxidation of 11-position methylene of 5-acetyl-5,6-dihydromorphanthridine with chromium trioxide. Subsequent hydrolytic cleavage of
the acyl group afforded the required compound.

![Reaction Diagram]

The new route reported here for the synthesis of morphanthridine ring system might be useful for the preparation of substituted morphanthridines.

N-Benzylantranilic acid itself did not undergo ring closure with PPA even though the mixture was heated to 170-180°C for 1 hr. Cyclisation could be made possible only by activating the 2'-position in ring B of N-(3-methoxybenzyl)anthranilic acid (II) with a substituent, like methoxyl, placed para (5'-position, ring B) to the 2'-position. The cyclication could take place at 2'-position or at 6' and the morphanthridone could, therefore, have structures III or IV.

The fact that the cyclisation has taken place at 2'-position and not at 6', is borne out by the NMR spectrum (Fig I) of the compound (IIIA) which is discussed below.

The NMR spectrum of the morphanthridone shows a sharp singlet at 3.86 (integrating for three protons), thereby indicating the presence of a -OCH₃ group. Another singlet is present at 4.25 corresponding to the two
methylene protons adjacent to the nitrogen atom. The -NH proton appears between 4.83 and 5.38 as a broad band which disappears on deuterium exchange. Five aromatic protons appear as a multiplet between 6.70 and 7.48. These chemical shifts are, however, not of any diagnostic value to decide between structures III and IV. This leaves two aromatic protons to account for.

It can be seen from structure III that two down field aromatic protons peri to the carbonyl group can be expected at \( C_1 \) and \( C_{10} \), whereas in structure IV there would be only one down field proton at \( C_1 \); the other peri position at \( C_{10} \) being occupied by the methoxyl group.

The PMR spectrum clearly shows two down field protons; a doublet centred at 7.86 for an ortho-coupled proton (\( J = 8.5 \) cps), which could only arise from the \( C_{10} \) proton (\( C_8 \) position carries a methoxyl, and no meta coupling is thus possible; para coupling seldom shows up as \( J \) for para-coupled aromatic proton is less than 1 cps).

The other down field proton shows up as a quartet centred at 8.30 (\( J_1 = 8.5 \) cps; \( J_2 = 2 \) cps). This can be assigned to the \( C_1 \) proton which is ortho-coupled to the \( C_2 \) position and meta-coupled to the \( C_3 \) position.

The IR spectrum (Fig II) of III(a) shows a band at 1590 \( \text{cm}^{-1} \) (CO) and another band at 3360 \( \text{cm}^{-1} \) (-NH).
EXPERIMENTAL

Starting materials and intermediates

(a) ACIDS

2-Amino-, 2-amino-4-chloro-, 2-amino-5-chloro-, 2-chloro-, 2,4-dichloro-, and 2-chloro-4-nitrobenzoic acids were commercial samples. 2-Chloro-5-nitro-, and 2-bromo-4-methylbenzoic acids were prepared by the literature methods. 2,5-Dichlorobenzoic acid was prepared by the following sequence of reactions:

\[
\begin{align*}
\text{Cl} & \quad \text{CHCOCI} & \quad \text{Cl} \\
\text{Cl} & \quad \text{AlCl}_3 & \quad \text{Cl} \\
\text{Cl} & \quad \text{COCH}_3 & \quad \text{COOH} \\
\end{align*}
\]

(i) Preparation of 2,5-dichloroacetophenone\(^9\). A mixture of p-dichlorobenzene (44.1 g; 0.3 mole) and acetyl chloride (39.2 g; 0.5 mole) was taken in a 1-l round-bottomed flask equipped with a reflux condenser carrying a calcium chloride guard tube. To this mixture anhydrous aluminium chloride (80 g) was added in small lots. When the addition of aluminium chloride was over, the reaction mixture was heated on a water bath for 5 hr. It was then cooled and decomposed by the addition of ice and hydrochloric acid followed by steam-distillation. The condensate was filtered and the filtrate extracted with ether. The ethereal solution was dried over anhydrous calcium chloride and the residual ketone, obtained after removing the solvent, was distilled.

B.P. 246-251°C Yield 28.3 g.
(ii) Oxidation of 2,5-dichloroacetophenone with potassium permanganate. In a three-necked flask equipped with a mechanical stirrer and a reflux condenser, were taken 2,5-dichloroacetophenone (30 g), water (400 ml), and sodium hydroxide solution (10%; 20 ml) and the mixture was heated on a water bath. Potassium permanganate (45 g) was added in small lots, with stirring, over a period of 3 hr. Heating was continued for 2 hr more. Unoxidised dichloroacetophenone was removed by steam-distillation. The mixture was then filtered and the filtrate concentrated to about half the original volume. Acidification of the solution with hydrochloric acid gave 2,5-dichlorobenzoic acid as colourless solid, which was sufficiently pure to be used in the next step.

M.P. 155°C
Yield 15 g.

(b) AMINES

Benzy1-, o-chlorobenzyl-, p-chlorobenzyl-, p-methylbenzyl-, p-methoxybenzyl-, piperonyl-, veratryl-, furfuryl-, α-methylbenzyl and benzhydryl amines were commercial samples. Hexahydrobenzylamine was prepared from cyclohexylacetic acid by the Hofmann reaction employing sodium azide and sulphuric acid as reported by Smith et al. m-Methoxybenzylamine was prepared from p-hydroxybenzaldehyde as follows:

\[
\begin{align*}
\text{CHO} & \quad \xrightarrow{(CH_3)_2SO_4} \quad \xrightarrow{\text{NH}_2\text{OH}} \quad \xrightarrow{\text{Na}/\text{H}_2/\text{AcOH}} \\
\text{HO} & \quad \text{H}_3\text{CO} & \quad \text{CHO} & \quad \text{H}_3\text{CO} & \quad \text{CH}=\text{NOH} \\
\end{align*}
\]
(i) m-Hydroxybenzaldehyde was converted to m-methoxybenzaldehyde by dimethylsulphate and alkali in 96% yield (B.P. 104°/2.5 mm)\(^\text{12}\).

(ii) Oximation of m-methoxybenzaldehyde\(^\text{13}\). m-Methoxybenzaldehyde (40.8 g; 0.3 mole) was dissolved in alcohol and to it were added hydroxylamine hydrochloride (1.25 equivalents; 26 g) and sodium hydroxide (2 equivalents; 24 g); each dissolved in a small quantity of water. The mixture was left for 24 hr, then diluted with water, and the oil which separated was extracted with ether. After removing the ether, the oil was left overnight on ice, when it solidified to a crystalline mass. This was collected and recrystallised from benzene and petroleum-ether (40-60°). m-Methoxybenzaldehyde formed colourless crystals, melting at 39-40°. Yield 82%.

(iii) m-Methoxybenzylamine\(^\text{14}\). m-Methoxybenzaldehyde (15.1 g; 0.1 mole) was dissolved in ethanol (150 ml) and acetic acid (30 g) was added to the ethanolic solution. Sodium amalgam (2.5%; 300 g) was added in small lots over a period of 2 hr with mechanical stirring. After the addition, the reaction mixture was stirred for 1 hr more. The solution was then diluted with water and extracted with ether to remove unreacted oxime. The amine was then liberated from the aqueous solution with alkali and extracted with ether. The ethereal extract was dried, ether removed and the residual amine distilled under reduced pressure.

\[
\text{B.P. 100-101°/4 mm} \quad \text{Yield 10.5 g.}
\]

Other amines required were synthesised from the corresponding ketones by the Leuckart reaction using ammonium carbonate and formic acid according to the general procedure given below.

**General procedure for the preparation of aralkylamines by the Leuckart reaction\(^\text{15}\)**

Ammonium carbonate (215 g; 4 moles) was placed in a 1-1 three-necked
round-bottomed flask fitted with a thermometer, a dropping funnel and a bent tube attached for distillation to a short condenser. Formic acid (215-230 g) was taken in the dropping funnel and added dropwise. When the reaction subsided, the mixture was heated slowly until the temperature rose to about 165°. The ketone (1 mole) was added in one lot and the temperature slowly raised to 180-185°. Water, ammonia, carbon dioxide and some of the ketone distilled over, the distilled ketone was separated and returned to the reaction mixture. The mixture, which gradually became homogeneous was maintained at 180-185° for 4-5 hr. When the reaction was complete, the mixture was cooled and stirred thoroughly with twice its volume of water. The aqueous layer was separated, and the formyl derivative of the amine so obtained was refluxed with 100-150 ml of conc. hydrochloric acid for 2-3 hr. After the hydrolysis, the reaction mixture was cooled and extracted with ether to remove any unreacted ketone. The aqueous solution was made strongly alkaline with 30% sodium hydroxide solution and the separated amine was extracted with ether. The ethereal extract was dried over anhydrous sodium sulphate, and after removal of the solvent the product distilled under reduced pressure.

The aralkylamines thus obtained are listed in Table VII.
Table VII.

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Ketone used</th>
<th>Amine obtained</th>
<th>B.P. °C/mm</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>p-Chloroacetophenone</td>
<td>dl-α-Methyl-p-chlorobenzylamine</td>
<td>96-98/8</td>
<td>16, 17, 18</td>
</tr>
<tr>
<td>2.</td>
<td>p-Methylacetophenone</td>
<td>dl-α, p-Dimethylbenzylamine</td>
<td>90-92/2</td>
<td>16, 17, 18</td>
</tr>
<tr>
<td>3.</td>
<td>p-Methoxyacetophenone</td>
<td>dl-α-Methyl-p-methoxybenzylamine</td>
<td>98-101/3.5</td>
<td>16, 18</td>
</tr>
<tr>
<td>4.</td>
<td>3,4-Dichloroacetophenone</td>
<td>dl-α-Methyl-3,4-dichlorobenzylamine</td>
<td>118/5.5</td>
<td>19</td>
</tr>
<tr>
<td>5.</td>
<td>3,4-Dimethylacetophenone</td>
<td>dl-α,3,4-Trimethylbenzylamine</td>
<td>92-96/4.5</td>
<td>19</td>
</tr>
<tr>
<td>6.</td>
<td>Propiophenone</td>
<td>dl-α-Ethylbenzylamine</td>
<td>78-82/5</td>
<td>18, 20</td>
</tr>
<tr>
<td>7.</td>
<td>p-Chloropropiophenone</td>
<td>dl-α-Ethyl-p-chlorobenzylamine</td>
<td>92-94/3.5</td>
<td>18</td>
</tr>
<tr>
<td>8.</td>
<td>Butyrophenone</td>
<td>dl-α-Propylbenzylamine</td>
<td>94-96/5</td>
<td>18</td>
</tr>
<tr>
<td>9.</td>
<td>o-Methoxyacetophenone</td>
<td>dl-α-Methyl-o-methoxybenzylamine</td>
<td>110-112/3</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>2-Acetylfuran</td>
<td>dl-α-Methylfurfurylamine</td>
<td>46-48/3</td>
<td>21</td>
</tr>
<tr>
<td>11.</td>
<td>2-Acetylthiophene</td>
<td>dl-α-Methylthiophenylamine</td>
<td>68-70/6</td>
<td>23</td>
</tr>
<tr>
<td>12.</td>
<td>2-Naphthylmethylketone</td>
<td>dl-α-(2-naphthyl)ethylamine</td>
<td>138-142/2</td>
<td>17</td>
</tr>
<tr>
<td>13.</td>
<td>p-Thiophenacetophenone</td>
<td>dl-α-Methyl-p-thiophenylbenzylamine</td>
<td>142-144/8</td>
<td>24</td>
</tr>
<tr>
<td>14.</td>
<td>α-Tetralone</td>
<td>1,2,3,4-Tetrahydro-α-naphthylamine</td>
<td>112-114/3</td>
<td>25</td>
</tr>
<tr>
<td>15.</td>
<td>2-Methylthiachroman-4-one</td>
<td>2-Methyl-4-amino thiachroman</td>
<td>58/3</td>
<td></td>
</tr>
</tbody>
</table>
Preparation of N-substituted anthranilic acids

Route I (a): General procedure

In a 250 ml, three-necked round-bottomed flask fitted with a reflux condenser and mechanical stirrer, was placed an intimate mixture of appropriately substituted 2-halobenzoic acid (0.02 mole), potassium carbonate (0.02 mole) and copper oxide (0.2 g). Substituted aralkylamine (0.03 mole) was then added and the mixture was heated on an oil bath maintained at 160-170° for 2-3 hr. At the end of the reaction, the contents of the flask were allowed to cool and hot water (ca 25 ml) was added. Excess of amine was removed by steam-distillation. The aqueous solution was boiled with decolourising carbon (Norit) for 10 min. and then filtered. On acidifying the filtrate with conc. hydrochloric acid and adjusting the pH to 5, the required N-aralkylanthranilic acid was precipitated. The precipitate was collected, washed with water and then further boiled with water for 10 min. to remove unreacted 2-halobenzoic acid and was again collected by filtration. Recrystallisation from aqueous ethanol yielded the desired product.

The above condensations were also carried out in presence of isoamyl alcohol (3-5 ml) and the reaction mixture was worked up as described above.

(b) Equimolar quantities of anthranilic acid and suitable aralkylhalide were condensed in the presence of potassium carbonate, copper oxide and amyl alcohol. The reaction mixture was worked up as in I (a).
Route II: General procedure

Anthranilic acid (0.1 mole) and benzyl- or substituted benzyl-chloride (0.1 mole) were added to a solution of potassium carbonate (7.0 g) in water (210 ml) and the mixture was refluxed for 3-6 hr. N-benzyl- or N-substituted benzylanthalranilic acid which separated as solid was collected by filtration. The product obtained was recrystallized twice from ethanol.

Route III: General procedure

(i) Preparation of N-benzylideneanthranilic acids. These compounds were prepared by mixing ethanolic solutions of equimolar quantities of a suitably substituted anthranilic acid and an aromatic aldehyde and refluxing for 1-1½ hr on a water bath. After the heating was over, the alcoholic solution was poured on crushed ice and the separated solid was recrystallised from ethanol.

The compounds so obtained are listed in Table VIII.

(ii) Reduction of N-benzylideneanthranilic acids with sodium borohydride. A solution of N-substituted benzylidene anthranilic acid (0.014 mole) in absolute methanol (75 ml) was placed in a three-necked flask-fitted with a mechanical stirrer and a condenser. Sodium borohydride (0.028 mole) was added in small lots to the refluxing methanolic solution. When the addition of sodium borohydride was over, the reaction solution was refluxed an additional 30 min. and then the solvent removed under reduced pressure. Water (25 ml) was added to the residue and the aqueous solution, after filtration was acidified with hydrochloric acid. The solid which separated was collected, washed with water and recrystallised from ethanol.
### TABLE VIII

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>S.No.</th>
<th>R¹</th>
<th>R²</th>
<th>M.P. °C</th>
<th>Formula</th>
<th>Analysis</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>H</td>
<td>126</td>
<td>C₁₄H₁₁NO₂</td>
<td></td>
<td>27</td>
</tr>
<tr>
<td>2</td>
<td>H</td>
<td>4-CH₃</td>
<td>154</td>
<td>C₁₆H₁₃NO₂</td>
<td></td>
<td>28</td>
</tr>
<tr>
<td>3</td>
<td>4-Cl</td>
<td>4-CH₃</td>
<td>216-217</td>
<td>C₁₆H₁₂ClNO₂</td>
<td>5.11</td>
<td>5.03</td>
</tr>
<tr>
<td>4</td>
<td>H</td>
<td>3-0CH₃</td>
<td>123-124</td>
<td>C₁₅H₁₃NO₃</td>
<td>5.49</td>
<td>5.16</td>
</tr>
<tr>
<td>5</td>
<td>4-Cl</td>
<td>3,4-Cl₂</td>
<td>237-238</td>
<td>C₁₄H₈Cl₃NO₂</td>
<td>4.26</td>
<td>4.01</td>
</tr>
<tr>
<td>6</td>
<td>5-Cl</td>
<td>3,4-Cl₂</td>
<td>214</td>
<td>C₁₄H₈Cl₃NO₂</td>
<td>4.26</td>
<td>4.00</td>
</tr>
<tr>
<td>S.No.</td>
<td>R^1</td>
<td>R^2</td>
<td>M.P. °C</td>
<td>Formula</td>
<td>Analysis</td>
<td>Reference</td>
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<tr>
<td>-------</td>
<td>-----</td>
<td>-----------</td>
<td>---------</td>
<td>------------------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3,4-(OCH₃)₂</td>
<td>169</td>
<td>C₁₆H₁₅NO₄</td>
<td></td>
<td>29</td>
</tr>
<tr>
<td>8</td>
<td>H</td>
<td>3,4-(O₂H₅)₂</td>
<td>118-119</td>
<td>C₁₈H₁₉NO₄</td>
<td>4.47</td>
<td>4.26</td>
</tr>
<tr>
<td>9</td>
<td>4-Cl</td>
<td>3,4-(O₂H₅)₂</td>
<td>207-208</td>
<td>C₁₈H₁₈ClNO₄</td>
<td>4.02</td>
<td>3.86</td>
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<tr>
<td>10</td>
<td>5-Cl</td>
<td>3,4-(O₂H₅)₂</td>
<td>202-203</td>
<td>C₁₈H₁₈ClNO₄</td>
<td>4.02</td>
<td>3.92</td>
</tr>
<tr>
<td>11</td>
<td>4-Cl</td>
<td>3,4,5-(OCH₃)₃</td>
<td>231-232</td>
<td>C₁₇H₁₇ClNO₅</td>
<td>3.99</td>
<td>4.03</td>
</tr>
<tr>
<td>12</td>
<td>5-Cl</td>
<td>3,4,5-(OCH₃)₃</td>
<td>191-192</td>
<td>C₁₇H₁₇ClNO₅</td>
<td>3.99</td>
<td>3.83</td>
</tr>
</tbody>
</table>
1. **N-Benzylantranilic acid**

(a) Starting materials (route I b): anthranilic acid, 2.7 g (0.02 mole); benzylchloride, 2.5 g (0.02 mole); potassium carbonate, 2.7 g (0.02 mole); copper oxide, 0.2 g; isoamyl alcohol, 3 ml.

Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 1.8 g; 40%

(b) Starting materials (route II): anthranilic acid, 14.0 g; benzylchloride, 12.6 g; potassium carbonate, 7.0 g; water, 210 ml.

Duration of reaction 4 hr
Yield 16.0 g; 70%

(c) Starting materials (route III): benzylideneanthranilic acid, 3.1 g; sodium borohydride, 1.0 g; absolute methanol, 75 ml.

Duration of reaction 1.5 hr
Yield 2.7 g; 87%

N-Benzylantranilic acid, m.p. 174-175°C.

Lit. m.p. 173°C.

Anal. calcd. for C_{14}H_{13}NO_{2} (227.3): C, 73.99; H, 5.77; N, 6.16%

Found: C, 73.62; H, 5.44; N, 5.83%

2. **5-Chloro-N-benzylantranilic acid (route I)**

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; benzylamine, 3.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amyl alcohol, 3 ml.

Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 3.0 g; 70%

5-Chloro-N-benzylantranilic acid, m.p. 147-148°C.

Anal. calcd. for C_{14}H_{12}ClNO_{2} (261.75): C, 64.25; H, 4.62; N, 5.35%

Found: C, 63.92; H, 4.33; N, 5.08%
3. **4-Chloro-N-benzylanthranilic acid**

(a) Starting materials (route Ia): 2,4-dichlorobenzoic acid, 3.8 g; benzylamine, 3.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amyl alcohol, 3 ml.

<table>
<thead>
<tr>
<th>Temperature of reaction</th>
<th>160-170°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of reaction</td>
<td>2.5 hr</td>
</tr>
<tr>
<td>Yield</td>
<td>3.7 g; 71%</td>
</tr>
</tbody>
</table>

(b) Starting materials (route Ib): 4-chloroanthranilic acid, 3.5 g (0.02 mole); benzyl chloride, 2.5 g (0.02 mole); potassium carbonate, 2.7 g (0.02 mole); copper oxide, 0.2 g; amyl alcohol, 3 ml.

<table>
<thead>
<tr>
<th>Temperature of reaction</th>
<th>160-170°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of reaction</td>
<td>2.5 hr</td>
</tr>
<tr>
<td>Yield</td>
<td>2.0 g; 40%</td>
</tr>
</tbody>
</table>

**4-Chloro-N-benzylanthranilic acid, m.p. 171-172°C**

Lit² m.p. 171°C

Anal. calcd. for \( \text{C}_{14}\text{H}_{12}\text{ClN}_2 \) (261.75): C, 64.25; H, 4.62; N, 5.35%

Found: C, 64.01; H, 4.43; N, 5.16%

4. **5-Nitro-N-benzylanthranilic acid (route I)**

Starting materials: 2-chloro-5-nitrobenzoic acid, 4.0 g; benzylamine, 3.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amyl alcohol, 3 ml.

<table>
<thead>
<tr>
<th>Temperature of reaction</th>
<th>160-170°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of reaction</td>
<td>2.5 hr</td>
</tr>
<tr>
<td>Yield</td>
<td>3.6 g; 66%</td>
</tr>
</tbody>
</table>

**5-Nitro-N-benzylanthranilic acid, m.p. 195-196°C**

Anal. calcd. for \( \text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_4 \) (272.3): C, 61.76; H, 4.44; N, 10.29%

Found: C, 61.55; H, 4.29; N, 10.08%
5. N-(4-Nitrobenzyl)anthranilic acid (route I)

Starting materials: anthranilic acid, 2.7 g; 4-nitrobenzylbromide, 4.3 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 5 ml.

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 2.7 g; 50%

N-(4-Nitrobenzyl)anthranilic acid, m.p. 208-210°C

Lit³ m.p. 208-210°C

Anal. calcd. for \( \text{C}_{14}\text{H}_{12}\text{N}_4 \) (272.3): C, 61.76; H, 4.44; N, 10.29%

Found: C, 61.61; H, 4.19; N, 9.92%

6. N-(2-Chlorobenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; 2-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.7 g; 71%

N-(2-Chlorobenzyl)anthranilic acid, m.p. 184-185°C

Lit⁴ m.p. 185-185.5°C

Anal. calcd. for \( \text{C}_{14}\text{H}_{12}\text{ClNO}_2 \) (261.75): C, 64.25; H, 4.62; N, 5.35%

Found: C, 63.88; H, 4.46; N, 5.12%

7. 5-Chloro-N-(2-chlorobenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; 2-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 4.1 g; 70%

5-Chloro-N-(2-chlorobenzyl)anthranilic acid, m.p. 216-217°C
8. **4-Chloro-N-(2-chlorobenzyl)anthranilic acid (route I)**

Starting materials: 2,4-dichlorobenzonic acid, 3.8 g; 2-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.8 g; 64%

4-Chloro-N-(2-chlorobenzyl)anthranilic acid, m.p. 211-212°C

Anal. calcd. for \( \text{C}_{14} \text{H}_{11} \text{Cl}_2 \text{N}_2 \text{O}_2 \) (296.17): C, 56.78; H, 3.74; N, 4.73%

Found: C, 56.59; H, 3.64; N, 4.67%

9. **5-Nitro-N-(2-chlorobenzyl)anthranilic acid (route I)**

Starting materials: 2-chloro-5-nitrobenzoic acid, 4.0 g; 2-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.8 g; 62%

5-Nitro-N-(2-chlorobenzyl)anthranilic acid, m.p. 224-225°C

Anal. calcd. for \( \text{C}_{14} \text{H}_{11} \text{Cl}_1 \text{N}_2 \text{O}_4 \) (306.71): C, 54.81; H, 3.61; N, 9.13%

Found: C, 54.58; H, 3.40; N, 9.05%

10. **4-Nitro-N-(2-chlorobenzyl)anthranilic acid (route I)**

Starting materials: 2-chloro-4-nitrobenzoic acid, 4.0 g; 2-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.6 g; 60%

4-Nitro-N-(2-chlorobenzyl)anthranilic acid, m.p. 201-202°C
11. \textit{N-(4-Chlorobenzyl)anthranilic acid}

(a) Starting materials (route Ia): 2-chlorobenzoic acid, 3.1 g; 4-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 2.6 g; 50%

(b) Starting materials (route II): anthranilic acid, 14.0 g; 4-chlorobenzylchloride, 16.1 g; potassium carbonate, 7.0 g; water, 210 ml.

Duration of reaction 4 hr

Yield 15.6 g; 60%

\textit{N-(4-Chlorobenzyl)anthranilic acid}, m.p. 140°C.

Lit \textsuperscript{5} m.p. 146°C.

Anal. calcd. for C\textsubscript{14}H\textsubscript{12}ClNO\textsubscript{2} (261.75): C, 64.25; H, 4.62; N, 5.35%

Found: C, 64.02; H, 4.51; N, 5.29%

12. \textit{5-Chloro-N-(4-chlorobenzyl)anthranilic acid (route I)}

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; 4-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.1 g; 52%

\textit{5-Chloro-N-(4-chlorobenzyl)anthranilic acid}, m.p. 190-191°C

Lit \textsuperscript{6} m.p. 193-195°C

Anal. calcd. for C\textsubscript{14}H\textsubscript{11}ClNO\textsubscript{2} (296.17): C, 56.78; H, 3.74; N, 4.73%

Found: C, 56.58; H, 3.60; N, 4.72%
13. 4-Chloro-N-(4-chlorobenzyl)anthranilic acid

(a) Starting materials (route Ia): 2,4-dichlorobenzoic acid, 3.8 g; 4-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

- Temperature of reaction: 160-170°C
- Duration of reaction: 2 hr
- Yield: 3.5 g; 60%

(b) Starting materials (route Ib): 4-chloroanthranilic acid, 3.5 g; 4-chlorobenzylchloride, 3.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml.

- Temperature of reaction: 160-170°C
- Duration of reaction: 2.5 hr
- Yield: 2.6 g; 44%

4-Chloro-N-(4-chlorobenzyl)anthranilic acid, m.p. 197-198°C

Anal. calcd. for C_{14}H_{11}Cl_{2}NO_{2} (296.17): C, 56.78; H, 3.74; N, 4.73%

Found: C, 56.70; H, 3.69; N, 4.71%

14. 4-Methyl-N-(4-chlorobenzyl)anthranilic acid (route I)

Starting materials: 2-bromo-4-methylbenzoic acid, 4.3 g; 4-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

- Temperature of reaction: 160-170°C
- Duration of reaction: 2.5 hr
- Yield: 4.0 g; 72%

4-Methyl-N-(4-chlorobenzyl)anthranilic acid, m.p. 159-160°C

Anal. calcd. for C_{15}H_{14}ClNO_{2} (275.74): C, 56.33; H, 5.11; N, 5.08%

Found: C, 56.11; H, 4.86; N, 4.78%

15. 4-Nitro-N-(4-chlorobenzyl)anthranilic acid (route I)

Starting materials: 2-chloro-4-nitrobenzoic acid, 3.8 g; 4-chlorobenzylamine, 4.2 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml.
Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 3.6 g; 60%

4-Nitro-N-(4-chlorobenzyl)anthranilic acid, m.p. 209-210°C
Anal. calcd. for C_{14}H_{11}ClN_{2}O (306.71): C, 54.81; H, 3.61; N, 9.13%
Found: C, 54.66; H, 3.56; N, 8.83%

16. N-(4-Methylbenzyl)anthranilic acid
(a) Starting materials (route I): 2-chlorobenzoic acid, 3.1 g; 4-methylbenzylamine, 3.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.0 g; 62%

(b) Starting materials (route III): 4-methylbenzylidene-anthranilic acid, 3.3 g; sodiumborohydride, 1.0 g; methanol, 75 ml
Duration of reaction 1.5 hr
Yield 2.5 g; 76%

N-(4-Methylbenzyl)anthranilic acid, m.p. 147-148°C
Anal. calcd. for C_{15}H_{15}NO_{2} (241.3): C, 74.67; H, 6.27; N, 5.80%
Found: C, 74.43; H, 6.08; N, 5.69%

17. 5-Chloro-N-(4-methylbenzyl)anthranilic acid (route I)
Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; 4-methylbenzylamine, 3.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 4.5 g; 60%

5-Chloro-N-(4-methylbenzyl)anthranilic acid, m.p. 198-199°C
18. 4-Chloro-N-(4-methylbenzyl)anthranilic acid

(a) Starting materials (route I): 2,4-dichlorobenzoic acid, 3.8 g; 4-methylbenzylamine, 3.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction: 160-170°C
Duration of reaction: 2.5 hr
Yield: 4.5 g; 60%

(b) Starting materials (route III): 4-chloro-N-(4-methylbenzylidene)-anthranilic acid, 3.8 g; sodium borohydride, 1.0 g; methanol, 75 ml.

Duration of reaction: 1.5 hr
Yield: 3.8 g; 66%

4-Chloro-N-(4-methylbenzyl)anthranilic acid, m.p. 194°C

Anal. calcd. for C_{15}H_{14}ClNO_{2} (375.75): C, 47.94; H, 3.75; N, 3.72%
Found: C, 47.63; H, 3.45; N, 3.62%

19. N-(3-Methoxybenzyl)anthranilic acid

(a) Starting materials (route I): 2-chlorobenzoic acid, 3.1 g; 3-methoxybenzylamine, 4.1 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction: 160-170°C
Duration of reaction: 2 hr
Yield: 2.8 g; 66%

(b) Starting materials (route III): N-(3-methoxybenzylidene)-anthranilic acid, 3.5 g; sodium borohydride, 1.0 g; methanol, 75 ml

Anal. calcd. for C_{15}H_{14}ClNO_{2} (375.75): C, 47.94; H, 3.75; N, 3.72%
Found: C, 47.71; H, 3.58; N, 3.67%
Duration of reaction 1.5 hr
Yield 3.0 g; 83%
N-(3-Methoxybenzyl)anthranilic acid, m.p. 158-159°C
Anal. calcd. for $C_{15}H_{15}NO_3$ (257.3): C, 70.02; H, 5.88; N, 5.44%
Found: C, 69.81; H, 5.75; N, 5.19%

20. 4-Chloro-N-(3-methoxybenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; 3-methoxybenzylamine, 4.1 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g
Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 4.0 g; 70%
4-Chloro-N-(3-methoxybenzyl)anthranilic acid, m.p. 167-168°C
Anal. calcd. for $C_{15}H_{14}ClNO_3$ (291.75): C, 61.75; H, 4.83; N, 4.80%
Found: C, 61.69; H, 4.66; N, 4.73%

21. N-(4-Methoxybenzyl)anthranilic acid (route I)

Starting materials (route Ia): 2-chlorobenzoic acid, 3.1 g; 4-methoxybenzylamine, 4.1 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.
Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.4 g; 66%
N-(4-Methoxybenzyl)anthranilic acid, m.p. 156-157°C
Lit m.p. 159-160°C
Anal. calcd. for $C_{15}H_{15}NO_3$ (257.3): C, 70.02; H, 5.88; N, 5.44%
Found: C, 69.82; H, 5.67; N, 5.32%
22. 5-Chloro-N-(4-methoxybenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; 4-methoxybenzylamine, 4.1 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml.

Temperature of reaction 160-170°C
Duration of reaction 3.5 hr
Yield 3.4 g; 60%

5-Chloro-N-(4-methoxybenzyl)anthranilic acid, m.p. 181-182°C
Anal. calcd. for C_{16}H_{14}ClNO_{3} (291.75): C, 61.75; H, 4.83; N, 4.80%
Found: C, 61.66; H, 4.58; N, 4.75%

23. 4-Chloro-N-(4-methoxybenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; 4-methoxybenzylamine, 4.1 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml.

Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 3.2 g; 55%

4-Chloro-N-(4-methoxybenzyl)anthranilic acid, m.p. 192°C
Anal. calcd. for C_{16}H_{14}ClNO_{3} (291.75): C, 61.75; H, 4.83; N, 4.80%
Found: C, 61.56; H, 4.72; N, 4.68%

24. 4-Nitro-N-(4-methoxybenzyl)anthranilic acid (route I)

Starting materials: 2-chloro-4-nitrobenzoic acid, 4.0 g; 4-methoxybenzylamine, 4.1 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml.

Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 2.6 g; 42%

4-Nitro-N-(4-methoxybenzyl)anthranilic acid, m.p. 159-160°C
Anal. calcd. for C_{16}H_{14}N_{2}O_{5} (302.3): C, 59.60; H, 4.67; N, 9.27%
Found: C, 59.42; H, 4.38; N, 9.30%
25. **N-(2,4-Dichlorobenzyl)anthranilic acid (route II)**

Starting materials: anthranilic acid, 14.0 g; 2,4-dichlorobenzylchloride, 19.5 g; potassium carbonate, 7.0 g; water, 210 ml

Duration of reaction 5 hr

Yield 14.2 g; 41%

**N-(2,4-Dichlorobenzyl)anthranilic acid**, m.p. 184-185°C

Anal. calcd. for C_{14}H_{11}Cl_{2}NO_{2} (296.17): C, 56.78; H, 3.74; N, 4.73%

Found: C, 56.49; H, 3.51; N, 4.63%

26. **5-Chloro-N-(2,4-dichlorobenzyl)anthranilic acid (route Ib)**

Starting materials: 5-chloroanthranilic acid, 3.5 g; 2,4-dichlorobenzylchloride, 3.9 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 4 ml

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 3.3 g; 50%

**5-Chloro-N-(2,4-dichlorobenzyl)anthranilic acid**, m.p. 104-105°C

Anal. calcd. for C_{14}H_{10}Cl_{3}NO_{2} (330.61): C, 50.86; H, 3.04; N, 4.23%

Found: C, 50.75; H, 2.88; N, 4.03%

27. **N-(3,4-Dichlorobenzyl)anthranilic acid (route II)**

Starting materials: anthranilic acid, 14.0 g; 3,4-dichlorobenzylchloride, 19.5 g; potassium carbonate, 7.0 g; water, 210 ml.

Duration of reaction 5 hr

Yield 15.0 g; 50%

**N-(3,4-Dichlorobenzyl)anthranilic acid**, m.p. 159-160°C

Anal. calcd. for C_{14}H_{11}Cl_{2}NO_{2} (296.17): C, 56.78; H, 3.74; N, 4.73%

Found: C, 56.60; H, 3.58; N, 4.63%
28. 5-Chloro-N-(3,4-dichlorobenzyl)anthranilic acid (route III)

Starting materials: 5-chloro-N-(3,4-dichlorobenzylidene)-anthranilic acid, 4.5 g; sodium borohydride, 1.0 g; methanol, 75 ml.

Duration of reaction 1.5 hr
Yield 3.0 g; 60%

5-Chloro-N-(3,4-dichlorobenzyl)anthranilic acid, m.p. 214-215°C
Anal. calcd. for C_{14}H_{10}Cl_{3}NO_{2} (330.61): C, 50.86; H, 3.04; N, 4.23%
Found : C, 50.65; H, 2.87; N, 4.12%

29. 4-Chloro-N-(3,4-dichlorobenzyl)anthranilic acid (route III)

Starting materials: 4-chloro-N-(3,4-dichlorobenzylidene)anthranilic acid, 4.5 g; sodium borohydride, 1.0 g; methanol, 75 ml.

Duration of reaction 1.5 hr
Yield 2.3 g; 50%

4-Chloro-N-(3,4-dichlorobenzyl)anthranilic acid, m.p. 186-187°C
Anal. calcd. for C_{14}H_{10}Cl_{3}NO_{2} (330.61): C, 50.86; H, 3.04; N, 4.23%
Found : C, 50.71; H, 3.01; N, 4.19%

30. N-(3,4-Dimethoxybenzyl)anthranilic acid

(a) Starting materials (route Ia): 2-chlorobenzoic acid, 3.1 g; 3,4-dimethoxybenzylamine, 5.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr
Yield 3.8 g; 66%

(b) Starting materials (route III): N-(3,4-dimethoxybenzylidene)-anthranilic acid, 3.6 g; sodium borohydride, 1.0 g; methanol, 75 ml.

Duration of reaction 1.5 hr
Yield 3.2 g; 80%

N-(3,4-Dimethoxybenzyl)anthranilic acid, m.p. 90-91°C
Anal. calcd. for C_{16}H_{17}N_{4}O (287.3): C, 66.89; H, 5.96; N, 4.87%
Found : C, 66.78; H, 5.82; N, 4.83%
31. **5-Chloro-N-(3,4-dimethoxybenzyl)anthranilic acid (route I)**

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; 3,4-dimethoxybenzylamine, 5.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction: 160-170°C

Duration of reaction: 2 hr

Yield: 3.2 g; 50%

5-Chloro-N-(3,4-dimethoxybenzyl)anthranilic acid, m.p. 150-151°C

Anal. calcd. for C_{16}H_{16}ClNO_{4} (321.77): C, 59.71; H, 5.01; N, 4.35%

Found: C, 59.64; H, 4.87; N, 4.16%

32. **4-Chloro-N-(3,4-dimethoxybenzyl)anthranilic acid (route I)**

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; 3,4-dimethoxybenzylamine, 5.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction: 160-170°C

Duration of reaction: 2 hr

Yield: 4.0 g; 60%

4-Chloro-N-(3,4-dimethoxybenzyl)anthranilic acid, m.p. 193-194°C

Anal. calcd. for C_{16}H_{16}ClNO_{4} (321.77): C, 59.71; H, 5.01; N, 4.35%

Found: C, 59.61; H, 4.96; N, 4.22%

33. **N-(3,4-Methylenedioxybenzyl)anthranilic acid (route I)**

Starting materials: 2-chlorobenzoic acid, 3.1 g; piperonylamine, 4.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction: 160-170°C

Duration of reaction: 2 hr

Yield: 4.2 g; 75%

N-(3,4-Methylenedioxybenzyl)anthranilic acid, m.p. 164-165°C

Anal. calcd. for C_{15}H_{13}NO_{4} (271.3): C, 66.41; H, 4.83; N, 5.16%

Found: C, 66.36; H, 4.68; N, 5.00%
34. 5-Chloro-N-(3,4-methylenedioxybenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; piperonylamine, 4.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.8 g; 62%

5-Chloro-N-(3,4-methylenedioxybenzyl)anthranilic acid, m.p. 153-154°C

Anal. calcd. for C_{15}H_{12}ClNO_4 (305.73): C, 58.91; H, 3.95; N, 4.58%

Found: C, 58.85; H, 3.81; N, 4.4%

35. 4-Chloro-N-(3,4-methylenedioxybenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; piperonylamine, 4.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 4.5 g; 73%

4-Chloro-N-(3,4-methylenedioxybenzyl)anthranilic acid, m.p. 194-195°C

Anal. calcd. for C_{15}H_{12}ClNO_4 (305.73): C, 58.91; H, 3.95; N, 4.58%

Found: C, 58.76; H, 3.79; N, 4.40%

36. 4-Nitro-N-(3,4-methylenedioxybenzyl)anthranilic acid (route I)

Starting materials: 2-chloro-4-nitrobenzoic acid, 4.0 g; piperonylamine, 5.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.6 g; 57%

4-Nitro-N-(3,4-methylenedioxybenzyl)anthranilic acid, m.p. 196-197°C

Anal. calcd. for C_{15}H_{12}N_2O_6 (316.3): C, 56.97; H, 3.82; N, 8.86%

Found: C, 56.72; H, 3.65; N, 8.81%
37. **N-(3,4-Diethoxybenzyl)anthranilic acid (route III)**

Starting materials: N-(3,4-diethoxybenzylidene)anthranilic acid, 4.3 g; sodium borohydride, 1.0 g; methanol, 75 ml.

Duration of reaction: 1.5 hr
Yield: 3.3 g; 75%

N-(3,4-Diethoxybenzyl)anthranilic acid, m.p. 164-165°C
Anal. calcd. for C_{18}H_{21}NO_{4} (315.4): C, 68.55; H, 6.71; N, 4.44%
Found: C, 68.36; H, 6.55; N, 4.26%

38. **5-Chloro-N-(3,4-diethoxybenzyl)anthranilic acid (route III)**

Starting materials: 5-chloro-N-(3,4-diethoxybenzylidene)anthranilic acid, 4.8 g; sodium borohydride, 1.0 g; methanol, 75 ml

Duration of reaction: 1.5 hr
Yield: 3.6 g; 75%

5-Chloro-N-(3,4-diethoxybenzyl)anthranilic acid, m.p. 192-193°C
Anal. calcd. for C_{18}H_{20}ClNO_{4} (349.8): C, 61.81; H, 5.76; N, 4.00%
Found: C, 61.66; H, 5.57; N, 3.84%

39. **4-Chloro-N-(3,4-diethoxybenzyl)anthranilic acid (route III)**

Starting materials: 4-chloro-N-(3,4-diethoxybenzylidene)anthranilic acid, 4.8 g; sodium borohydride, 1.0 g; methanol, 75 ml

Duration of reaction: 1.5 hr
Yield: 3.2 g; 66%

4-Chloro-N-(3,4-diethoxybenzyl)anthranilic acid, m.p. 219-220°C
Anal. calcd. for C_{18}H_{20}ClNO_{4} (349.8): C, 61.81; H, 5.76; N, 4.00%
Found: C, 61.73; H, 5.64; N, 3.81%
40. 5-Chloro-N-(3,4,5-trimethoxybenzyl)anthranilic acid (route III)

Starting materials: 5-chloro-N-(3,4,5-trimethoxybenzylidene)-
anthranilic acid, 4.8 g; sodium borohydride, 1.0 g; methanol, 75 ml

Duration of reaction 1.5 hr
Yield 2.8 g; 57%

5-Chloro-N-(3,4,5-trimethoxybenzyl)anthranilic acid, m.p. 181-182°C
Anal. calcd. for C_{17}H_{18}ClNO_{5} (351.79): C, 58.02; H, 5.15; N, 3.98%
Found: C, 57.65; H, 4.78; N, 3.78%

41. 4-Chloro-N-(3,4,5-trimethoxybenzyl)anthranilic acid (route III)

Starting materials: 4-chloro-N-(3,4,5-trimethoxybenzylidene)-
anthranilic acid, 4.8 g; sodium borohydride, 1.0 g; methanol, 75 ml

Duration of reaction 1.5 hr
Yield 3.5 g; 70%

4-Chloro-N-(3,4,5-trimethoxybenzyl)anthranilic acid, m.p. 224-225°C
Anal. calcd. for C_{17}H_{18}ClNO_{5} (351.79): C, 58.02; H, 5.15; N, 3.98%
Found: C, 57.73; H, 4.86; N, 4.01%

42. N-(α-Methylbenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; α-Methyl-
benzylamine, 3.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 2.0 g; 41%

N-(α-Methylbenzyl)anthranilic acid, m.p. 155-158°C
Anal. calcd. for C_{10}H_{15}NO_{2} (241.3): C, 74.67; H, 6.27; N, 5.80%
Found: C, 74.36; H, 6.08; N, 5.72%
43. 5-Chloro-N-(α-methylbenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α-methylbenzylamine, 3.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 2.2 g; 40%

5-Chloro-N-(α-methylbenzyl)anthranilic acid, m.p. 145-146°C

Anal. calcd. for $C_{15}H_{14}ClNO_2$ (275.75): C, 65.33; H, 5.11; N, 5.08%

Found: C, 64.94; H, 4.87; N, 4.96%

44. 4-Chloro-N-(α-methylbenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; α-methylbenzylamine, 3.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 2.5 g; 42%

4-Chloro-N-(α-methylbenzyl)anthranilic acid, m.p. 117-118°C

Anal. calcd. for $C_{15}H_{14}ClNO_2$ (275.75): C, 65.33; H, 5.11; N, 5.08%

Found: C, 65.10; H, 4.88; N, 4.85%

45. 5-Nitro-N-(α-methylbenzyl)anthranilic acid (route I)

Starting materials: 2-chloro-5-nitrobenzoic acid, 4.0 g; α-methylbenzylamine, 3.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml.

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 3.6 g; 63%

5-Nitro-N-(α-methylbenzyl)anthranilic acid, m.p. 178-179°C

Anal. calcd. for $C_{15}H_{14}N_2O_4$ (286.31): C, 62.93; H, 4.93; N, 9.78%

Found: C, 62.65; H, 4.71; N, 9.73%
46. 4-Nitro-N-(α-methylbenzyl)anthranilic acid (route I)

Starting materials: 2-chloro-4-nitrobenzoic acid, 4.0 g; α-methylbenzylamine, 3.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 3.9 g; 68%

4-Nitro-N-(α-methylbenzyl)anthranilic acid, m.p. 174-175°C
Anal. calcd. for C_{15}H_{14}N_2O_4 (286.31): C, 62.93; H, 4.93; N, 9.78%
Found: C, 62.82; H, 4.79; N, 9.66%

47. N-(α-Methyl-4-chlorobenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; α-methyl-4-chlorobenzylamine, 4.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.3 g; 60%

N-(α-Methyl-4-chlorobenzyl)anthranilic acid, m.p. 162-163°C
Anal. calcd. for C_{15}H_{14}ClNO_2 (275.75): C, 65.33; H, 5.11; N, 5.08%
Found: C, 65.03; H, 4.87; N, 4.86%

48. 5-Chloro-N-(α-methyl-4-chlorobenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α-methyl-4-chlorobenzylamine, 4.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 3.3 g; 53%

5-Chloro-N-(α-methyl-4-chlorobenzyl)anthranilic acid, m.p. 151-152°C
Anal. calcd. for C_{15}H_{13}Cl_2NO_2 (310.2): C, 58.08; H, 4.22; N, 4.51%
Found: C, 57.87; H, 4.02; N, 4.37%
49. 4-Chloro-N-(α-methyl-4-chlorobenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; α-methyl-4-chlorobenzylamine, 4.6 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction: 160-170°C

Duration of reaction: 2.5 hr

Yield: 3.1 g; 50%

4-Chloro-N-(α-methyl-4-chlorobenzyl)anthranilic acid, m.p. 163-164°C

Anal. calcd. for C_{15}H_{12}Cl_{2}NO_{2} (310.2): C, 58.08; H, 4.22; N, 4.51%

Found: C, 57.85; H, 3.98; N, 4.49%

50. N-(α,4-Dimethylbenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; α,4-dimethylbenzylamine, 4.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction: 160-170°C

Duration of reaction: 2 hr

Yield: 2.4 g; 47%

N-(α,4-Dimethylbenzyl)anthranilic acid, m.p. 139-140°C

Anal. calcd. for C_{16}H_{17}NO_{2} (255.3): C, 75.27; H, 6.71; N, 5.49%

Found: C, 75.13; H, 6.66; N, 5.35%

51. 5-Chloro-N-(α,4-dimethylbenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α,4-dimethylbenzylamine, 4.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction: 160-170°C

Duration of reaction: 2.5 hr

Yield: 3.0 g; 52%

5-Chloro-N-(α,4-dimethylbenzyl)anthranilic acid, m.p. 157-158°C

Anal. calcd. for C_{16}H_{16}ClNO_{2} (289.76): C, 66.30; H, 5.56; N, 4.83%

Found: C, 66.19; H, 5.48; N, 4.77%
52. 4-Chloro-N-(\(\alpha\),4-dimethylbenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; \(\alpha\),4-dimethylbenzylamine, 4.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 2.9 g; 50%

4-Chloro-N-(\(\alpha\),4-dimethylbenzyl)anthranilic acid, m.p. 151-152°C

Anal. calcd. for C\(_{16}\)H\(_{16}\)ClNO\(_2\) (289.76): C, 66.30; H, 5.56; N, 4.83%

Found: C, 64.93; H, 5.22; N, 4.58%

53. N-(\(\alpha\)-Methyl-2-methoxybenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; \(\alpha\)-methyl-2-methoxybenzylamine, 4.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.9 g; 72%

N-(\(\alpha\)-Methyl-2-methoxybenzyl)anthranilic acid, m.p. 155-156°C

Anal. calcd. for C\(_{16}\)H\(_{17}\)NO\(_3\) (271.3): C, 70.83; H, 6.32; N, 5.16%

Found: C, 70.55; H, 6.11; N, 5.03%

54. N-(\(\alpha\)-Methyl-4-methoxybenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; \(\alpha\)-methyl-4-methoxybenzylamine, 4.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.6 g; 66%

N-(\(\alpha\)-Methyl-4-methoxybenzyl)anthranilic acid, m.p. 147-148°C

Anal. calcd. for C\(_{16}\)H\(_{17}\)NO\(_3\) (271.3): C, 70.83; H, 6.32; N, 5.16%

Found: C, 70.74; H, 6.16; N, 5.02%
55. **5-Chloro-N-(α-methyl-4-methoxybenzyl)anthranilic acid (route I)**

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α-methyl-4-methoxybenzylamine, 4.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction: 160-170°C

Duration of reaction: 2.5 hr

Yield: 4.0 g; 65%

5-Chloro-N-(α-methyl-4-methoxybenzyl)anthranilic acid, m.p. 152-153°C

Anal. calcd. for C_{16}H_{16}ClNO_{3} (305.75): C, 62.84; H, 5.27; N, 4.58%

Found: C, 62.66; H, 5.13; N, 4.47%

56. **4-Methyl-N-(α-methyl-4-methoxybenzyl)anthranilic acid (route I)**

Starting materials: 2-bromo-4-methylbenzoic acid, 4.3 g; α-methyl-4-methoxybenzylamine, 4.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amyl alcohol, 3 ml.

Temperature of reaction: 160-170°C

Duration of reaction: 2.5 hr

Yield: 3.0 g; 52%

4-Methyl-N-(α-methyl-4-methoxybenzyl)anthranilic acid, m.p. 173-174°C

Anal. calcd. for C_{17}H_{19}NO_{3} (285.3): C, 71.56; H, 6.71; N, 4.91%

Found: C, 71.33; H, 6.62; N, 4.85%

57. **N-(α-Methyl-3,4-dichlorobenzyl)anthranilic acid (route I)**

Starting materials: 2-chlorobenzoic acid, 3.1 g; α-methyl-3,4-dichlorobenzylamine, 5.7 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction: 160-170°C

Duration of reaction: 2 hr

Yield: 3.1 g; 50%

N-(α-Methyl-3,4-dichlorobenzyl)anthranilic acid, m.p. 175-176°C

Anal. calcd. for C_{15}H_{13}Cl_{2}NO_{2} (310.2): C, 58.05; H, 4.22; N, 4.51%

Found: C, 57.83; H, 4.06; N, 4.33%
58. 5-Chloro-N-(α-methyl-3,4-dichlorobenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α-methyl-3,4-dichlorobenzylamine, 5.7 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction: 160-170°C

Duration of reaction: 2 hr

Yield: 3.0 g; 44%

5-Chloro-N-(α-methyl-3,4-dichlorobenzyl)anthranilic acid, m.p. 138-139°C

Anal. calcd. for C_{15}H_{12}Cl_{3}NO_{2} (344.64): C, 52.25; H, 3.51; N, 4.06%

Found: C, 52.11; H, 3.26; N, 4.02%

59. 4-Chloro-N-(α-methyl-3,4-dichlorobenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; α-methyl-3,4-dichlorobenzylamine, 5.7 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction: 160-170°C

Duration of reaction: 2 hr

Yield: 3.2 g; 47%

4-Chloro-N-(α-methyl-3,4-dichlorobenzyl)anthranilic acid, m.p. 180-181°C

Anal. calcd. for C_{15}H_{12}Cl_{3}NO_{2} (344.64): C, 52.25; H, 3.51; N, 4.06%

Found: C, 51.88; H, 3.22; N, 3.89%

60. N-(α,3,4-Trimethylbenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; α,3,4-trimethylbenzylamine, 4.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction: 160-170°C

Duration of reaction: 2 hr

Yield: 3.0 g; 56%

N-(α,3,4-Trimethylbenzyl)anthranilic acid, m.p. 208-209°C

Anal. calcd. for C_{17}H_{19}NO_{2} (269.3): C, 75.81; H, 7.11; N, 5.20%

Found: C, 75.77; H, 6.88; N, 5.15%
61. **5-Chloro-N-(α,3,4-trimethylbenzyl)anthranilic acid (route I)**

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α,3,4-trimethylbenzylamine, 4.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml.

Temperature of reaction: 160-170°C

Duration of reaction: 2.5 hr

Yield: 3.2 g; 53%

5-Chloro-N-(α,3,4-trimethylbenzyl)anthranilic acid, m.p. 177-178°C

Anal. calcd. for $C_{17}H_{18}ClN_2O_2$ (303.79): C, 67.20; H, 5.97; N, 4.61%

Found: C, 66.85; H, 5.74; N, 4.51%

62. **4-Chloro-N-(α,3,4-trimethylbenzyl)anthranilic acid (route I)**

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; α,3,4-trimethylbenzylamine, 4.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction: 160-170°C

Duration of reaction: 2.5 hr

Yield: 3.2 g; 53%

4-Chloro-N-(α,3,4-trimethylbenzyl)anthranilic acid, m.p. 178-179°C

Anal. calcd. for $C_{17}H_{18}ClN_2O_2$ (303.79): C, 67.20; H, 5.97; N, 4.61%

Found: C, 66.88; H, 5.82; N, 4.49%

63. **N-(α-Methyl-4-thiomethylbenzyl)anthranilic acid (route I)**

Starting materials: 2-chlorobenzoic acid, 3.1 g; α-methyl-4-thiomethylbenzylamine, 5.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction: 160-170°C

Duration of reaction: 2 hr

Yield: 3.5 g; 61%

N-(α-Methyl-4-thiomethylbenzyl)anthranilic acid, m.p. 141-142°C

Anal. calcd. for $C_{16}H_{17}NO_2S$ (287.3): C, 66.89; H, 5.96; N, 4.87%

Found: C, 66.73; H, 5.81; N, 4.68%
64. **N-(α-Ethylbenzyl)anthranilic acid (route I)**

Starting materials: 2-chlorobenzoic acid, 3.1 g; α-ethylbenzylamine, 4.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g;

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 2.0 g; 40%

**N-(α-Ethylbenzyl)anthranilic acid, m.p. 141-142°C**

Anal. calcd. for C<sub>16</sub>H<sub>17</sub>NO<sub>2</sub> (255.3); C, 75.27; H, 6.71; N, 5.49%

Found: C, 75.06; H, 6.68; N, 5.38%

65. **5-Chloro-N-(α-ethylbenzyl)anthranilic acid (route I)**

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α-ethylbenzylamine, 4.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.4 g; 60%

**5-Chloro-N-(α-ethylbenzyl)anthranilic acid, m.p. 138-139°C**

Anal. calcd. for C<sub>16</sub>H<sub>16</sub>ClNO<sub>2</sub> (289.76); C, 66.30; H, 5.56; N, 4.83%

Found: C, 66.15; H, 5.42; N, 4.76%

66. **4-Chloro-N-(α-ethylbenzyl)anthranilic acid (route I)**

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; α-ethylbenzylamine, 4.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.4 g; 60%

**4-Chloro-N-(α-ethylbenzyl)anthranilic acid, m.p. 136-137°C**

Anal. calcd. for C<sub>16</sub>H<sub>16</sub>ClNO<sub>2</sub> (289.76); C, 66.30; H, 5.56; N, 4.83%

Found: C, 66.12; H, 5.46; N, 4.81%
67. 4-Methyl-N-(α-ethylbenzyl)anthranilic acid (route I)

Starting materials: 2-bromo-4-methylbenzoic acid, 4.3 g; α-ethylbenzylamine, 4.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g.

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 4.0 g; 75%

4-Methyl-N-(α-ethylbenzyl)anthranilic acid, m.p. 181-182°C
Anal. calcd. for C_{17}H_{19}NO_{2} (269.3): C, 75.81; H, 7.11; N, 5.20%
Found: C, 75.68; H, 6.91; N, 5.25%

68. N-(α-Ethyl-4-chlorobenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; α-ethyl-4-chlorobenzylamine, 5.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.8 g; 66%

N-(α-Ethyl-4-chlorobenzyl)anthranilic acid, m.p. 147-148°C
Anal. calcd. for C_{16}H_{16}ClNO_{2} (289.76): C, 66.30; H, 5.56; N, 4.83%
Found: C, 66.21; H, 5.52; N, 4.80%

69. 5-Chloro-N-(α-ethyl-4-chlorobenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α-ethyl-4-chlorobenzylamine, 5.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.6 g; 56%

5-Chloro-N-(α-ethyl-4-chlorobenzyl)anthranilic acid, m.p. 164-165°C
Anal. calcd. for C_{16}H_{15}Cl_{2}NO_{2} (324.22): C, 59.26; H, 4.66; N, 4.32%
Found: C, 59.18; H, 4.53; N, 4.33%
70. 4-Chloro-N-(\(\alpha\)-ethyl-4-chlorobenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; \(\alpha\)-ethyl-4-chlorobenzylamine, 5.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.7 g; 57%

4-Chloro-N-(\(\alpha\)-ethyl-4-chlorobenzyl)anthranilic acid, m.p. 130-131°C

Anal. calcd. for C\(_{16}\)H\(_{15}\)Cl\(_2\)N\(_2\)O\(_2\) (324.22): C, 59.26; H, 4.66; N, 4.32%

Found: C, 59.08; H, 4.51; N, 4.13%

71. N-(\(\alpha\)-Propylbenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; \(\alpha\)-propylbenzylamine, 4.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 2.5 g; 47%

N-(\(\alpha\)-Propylbenzyl)anthranilic acid, m.p. 107-108°C

Anal. calcd. for C\(_{17}\)H\(_{19}\)N\(_2\)O\(_2\) (269.3): C, 75.81; H, 7.11; N, 5.20%

Found: C, 75.77; H, 6.85; N, 5.16%

72. 5-Chloro-N-(\(\alpha\)-propylbenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; \(\alpha\)-propylbenzylamine, 4.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.5 g; 58%

5-Chloro-N-(\(\alpha\)-propylbenzyl)anthranilic acid, m.p. 103-104°C

Anal. calcd. for C\(_{17}\)H\(_{18}\)ClN\(_2\)O\(_2\) (303.79): C, 67.20; H, 5.97; N, 4.61%

Found: C, 67.14; H, 5.83; N, 4.59%
73. 4-Chloro-N-(α-propylbenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; α-propylbenzylamine, 4.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.3 g; 55%

4-Chloro-N-(α-propylbenzyl)anthranilic acid, m.p. 182-183°C

Anal. calcd. for C17H18ClNO2 (303.79): C, 67.20; H, 5.97; N, 4.61%

Found: C, 66.99; H, 5.86; N, 4.57%

74. N-(α-Phenylbenzyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; benzhydrylamine, 5.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 2.5 g; 41%

N-(α-Phenylbenzyl)anthranilic acid, m.p. 229-230°C

Anal. calcd. for C20H17NO2 (303.4): C, 79.19; H, 5.65; N, 4.62%

Found: C, 78.96; H, 5.57; N, 4.62%

75. 5-Chloro-N-(α-phenylbenzyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; benzhydrylamine, 5.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 3.0 g; 44%

5-Chloro-N-(α-phenylbenzyl)anthranilic acid, m.p. 158-159°C

Anal. calcd. for C20H16ClNO2 (337.8): C, 71.12; H, 4.77; N, 4.14%

Found: C, 70.90; H, 4.69; N, 4.03%
76. 4-Chloro-N-(α-phenylbenzyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.1 g; benzhydrylamine, 5.5 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 2.8 g; 41%

4-Chloro-N-(α-phenylbenzyl)anthranilic acid, m.p. 143-144°C

Anal. calcd. for C_{20}H_{16}ClNO_2 (337.8): C, 71.12; H, 4.77; N, 4.14%

Found: C, 70.98; H, 4.72; N, 4.11%

77. N-Hexahydrobenzylanthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; hexahydrobenzylamine, 3.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 4.0 g; 87%

N-Hexahydrobenzylanthranilic acid, m.p. 119-120°C

Anal. calcd. for C_{14}H_{18}NO_2 (233.3): C, 72.07; H, 8.21; N, 6.00%

Found: C, 71.86; H, 8.15; N, 5.93%

78. 5-Chloro-N-hexahydrobenzylanthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; hexahydrobenzylamine, 3.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 3.5 g; 66%

5-Chloro-N-hexahydrobenzylanthranilic acid, m.p. 160-161°C

Anal. calcd. for C_{14}H_{18}ClNO_2 (267.76): C, 62.81; H, 6.77; N, 5.23%

Found: C, 62.75; H, 6.73; N, 5.21%
79. **4-Chloro-N-hexahydrobenzylanthranilic acid (route I)**

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; hexahydrobenzylamine, 3.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 3.2 g; 60%

4-Chloro-N-hexahydrobenzylanthranilic acid, m.p. 165-166°C

Anal. calcd. for C_{14}H_{18}ClNO_{2} (267.76): C, 62.81; H, 6.77; N, 5.23%

Found: C, 62.79; H, 6.66; N, 5.03%

80. **4-Methyl-N-hexahydrobenzylanthranilic acid (route I)**

Starting materials: 2-bromo-4-methylbenzoic acid, 4.3 g; hexahydrobenzylamine, 3.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 3.5 g; 71%

4-Methyl-N-hexahydrobenzylanthranilic acid, m.p. 147-148°C

Anal. calcd. for C_{15}H_{21}NO_{2} (247.3): C, 72.84; H, 8.56; N, 5.66%

Found: C, 72.74; H, 8.48; N, 5.64%

81. **N-Furfurylanthranilic acid (route I)**

Starting materials: 2-chlorobenzoic acid, 3.1 g; furfurylamine, 3.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C

Duration of reaction 2 hr

Yield 3.1 g; 72%

N-Furfurylanthranilic acid, m.p. 158-159°C

Anal. calcd. for C_{12}H_{11}NO_{3} (217.2): C, 66.35; H, 5.10; N, 6.45%

Found: C, 66.25; H, 4.88; N, 6.42%
82. 5-Chloro-N-furfurylanthranilic acid (route I)
Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; furfurylamine, 3.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 2.7 g; 56%

5-Chloro-N-furfurylanthranilic acid, m.p. 161-162°C
Anal. calcd. for C_{12}H_{10}ClNO_{3} (251.67): C, 57.28; H, 4.00; N, 5.56%
Found: C, 57.18; H, 3.97; N, 5.55%

83. 4-Chloro-N-furfurylanthranilic acid (route I)
Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; furfurylamine, 3.0 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction 160-170°C
Duration of reaction 2.5 hr
Yield 2.5 g; 50%

4-Chloro-N-furfurylanthranilic acid, m.p. 156-157°C
Anal. calcd. for C_{12}H_{10}ClNO_{3} (251.67): C, 57.28; H, 4.00; N, 5.56%
Found: C, 57.20; H, 3.85; N, 5.49%

84. N-(α-Methylfurfuryl)anthranilic acid (route I)
Starting materials: 2-chlorobenzoic acid, 3.1 g; α-methylfurfurylamine, 3.3 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.0 g; 65%

N-(α-Methylfurfuryl)anthranilic acid, m.p. 133-134°C
Anal. calcd. for C_{13}H_{13}NO_{3} (231.3): C, 67.52; H, 5.67; N, 6.06%
Found: C, 67.47; H, 5.63; N, 6.01%
85. 5-Chloro-N-(α-methylfurfuryl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α-methylfurfurylamine, 3.3 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 2.8 g; 52%

5-Chloro-N-(α-methylfurfuryl)anthranilic acid, m.p. 110-111°C

Anal. calcd. for C₁₃H₁₂ClN₂O₃ (265.7): C, 58.75; H, 4.55; N, 5.27%

     Found: C, 58.73; H, 4.52; N, 5.25%

86. 4-Chloro-N-(α-methylfurfuryl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; α-methylfurfurylamine, 3.3 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 2.8 g; 52%

4-Chloro-N-(α-methylfurfuryl)anthranilic acid, m.p. 146-147°C

Anal. calcd. for C₁₃H₁₂ClN₂O₃ (265.7): C, 58.75; H, 4.55; N, 5.27%

     Found: C, 58.66; H, 4.47; N, 5.17%

87. 4-Methyl-N-(α-methylfurfuryl)anthranilic acid (route I)

Starting materials: 2-bromo-4-methylbenzoic acid, 4.3 g; α-methylfurfurylamine, 3.3 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amylalcohol, 3 ml

Temperature of reaction 160-170°C

Duration of reaction 2.5 hr

Yield 3.2 g; 65%

4-Methyl-N-(α-methylfurfuryl)anthranilic acid, m.p. 125-128°C

Anal. calcd. for C₁₄H₁₅N₂O₃ (245.3): C, 68.56; H, 6.16; N, 5.71%

     Found: C, 68.41; H, 5.87; N, 5.66%
88. N-(α-Methylthienyl)anthranilic acid (route I)

Starting materials: 2-chlorobenzoic acid, 3.1 g; α-methylthienylamine, 3.8 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.0 g; 61%

N-(α-Methylthienyl)anthranilic acid, m.p. 143-144°C

Anal. calcd. for C_{13}H_{13}NO_2S (247.3): C, 63.15; H, 5.30; N, 5.66%
Found: C, 62.99; H, 5.24; N, 5.48%

89. 5-Chloro-N-(α-Methylthienyl)anthranilic acid (route I)

Starting materials: 2,5-dichlorobenzoic acid, 3.8 g; α-methylthienylamine, 3.8 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.2 g; 57%

5-Chloro-N-(α-Methylthienyl)anthranilic acid, m.p. 148-149°C

Anal. calcd. for C_{13}H_{12}ClNO_2S (281.75): C, 55.42; H, 4.29; N, 4.97%
Found: C, 55.36; H, 4.18; N, 4.96%

90. 4-Chloro-N-(α-Methylthienyl)anthranilic acid (route I)

Starting materials: 2,4-dichlorobenzoic acid, 3.8 g; α-methylthienylamine, 3.8 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.0 g; 53%

4-Chloro-N-(α-Methylthienyl)anthranilic acid, m.p. 159-160°C

Anal. calcd. for C_{13}H_{12}ClNO_2S (281.75): C, 55.42; H, 4.29; N, 4.97%
Found: C, 55.39; H, 4.21; N, 4.88%
91. N-(2-Benzimidazolyl)methylanthranilic acid, or

2-(o-Carboxyanilino)methylbenzimidazole (route Ib)

Starting materials: anthranilic acid, 2.8 g; 2-chloromethylbenzimidazole, 3.3 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g; amyl alcohol, 5 ml

Temperature of reaction 160-170°C
Duration of reaction 3 hr
Yield 3.5 g; 66%

N-(2-Benzimidazolyl)methylanthranilic acid, m.p. 159-160°C
Anal. calcd. for C_{15}H_{13}N_{3}O_{2} (267.3): C, 67.41; H, 4.90; N, 15.72%
Found: C, 67.28; H, 4.71; N, 15.53%

92. N-\(\alpha\)-(2-Naphthyl)ethyl anthranilic acid (route Ia)

Starting materials: 2-chlorobenzoic acid, 3.1 g; \(\alpha\)-(2-naphthyl)ethylamine, 5.1 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 3.7 g; 63%

N-\(\alpha\)-(2-Naphthyl)ethyl anthranilic acid, m.p. 183-184°C
Anal. calcd. for C_{19}H_{17}N_{2}O_{2} (291.4): C, 78.33; H, 5.88; N, 4.81%
Found: C, 78.16; H, 5.68; N, 4.77%

93. N-(1,2,3,4-Tetrahydro-\(\alpha\)-naphthyl)anthranilic acid (route Ia)

Starting materials: 2-chlorobenzoic acid, 3.1 g; 1,2,3,4-tetrahydro-\(\alpha\)-naphthylamine, 4.4 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction 160-170°C
Duration of reaction 2 hr
Yield 2.9 g; 54%

N-(1,2,3,4-Tetrahydro-\(\alpha\)-naphthyl)anthranilic acid, m.p. 153-154°C
Anal. calcd. for C_{17}H_{17}NO_{2} (267.3): C, 76.38; H, 6.41; N, 5.24%
Found: C, 76.27; H, 6.33; N, 5.17%
94. **N-4-(2-Methylthiachromanyl)anthranilic acid (route Ia)**

Starting materials: 2-chlorobenzoic acid, 3.1 g; 2-methyl-4-aminothiachroman, 5.3 g; potassium carbonate, 2.7 g; copper oxide, 0.2 g

Temperature of reaction: 160-170°C
Duration of reaction: 2 hr
Yield: 3.0 g; 50%

**N-4-(2-Methylthiachromanyl)anthranilic acid, m.p. 188.189°C**

Anal. calcd. for C_{17}H_{17}NO_{2}S (299.3): C, 68.22; H, 5.72; N, 4.68%

Found: C, 68.12; H, 5.57; N, 4.55%

95. **5,6-Dihydro-8-methoxy-11-morphanthridone (IIIa)**

N-(3-Methoxybenzyl)anthranilic acid (1.5 g) and polyphosphoric acid (20 g) were stirred on a water bath for 1 hr, poured onto crushed ice (ca 100 g), and neutralized by the addition of aqueous ammonia. The solid which separated was removed by filtration, washed with water and recrystallized from ethanol yielding the title compound as yellow crystals (0.9 g; 64.2%). m.p. 119-120°C.

Anal. calcd. for C_{15}H_{13}NO_{2} (239.3): C, 75.30; H, 5.48; N, 5.85%

Found: C, 75.06; H, 5.22; N, 5.70%

96. **3-Chloro-5,6-dihydro-8-methoxy-11-morphanthridone (IIlb)**

This compound was prepared as lemon yellow plates from 4-chloro-N-(3-methoxybenzyl)anthranilic acid (1.5 g) and PPA (20 g) in the same manner as compound (IIIa) above was prepared and recrystallized from ethanol.

(yield, 1.0 g; 76%). m.p. 175-176°C

Anal. calcd. for C_{15}H_{12}ClNO_{2} (273.7): C, 65.79; H, 4.42; N, 5.11%

IR absorption

<table>
<thead>
<tr>
<th>$\nu_{\text{KBr}}$ (cm$^{-1}$)</th>
<th>3280 (NH)</th>
<th>1590 (C=O)</th>
</tr>
</thead>
</table>

Found: C, 65.69; H, 4.37; N, 5.06%
References

1. (a) J. Houben and W. Brasser, Ber., 36, 3233-3240 (1906)
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7. H. Rupe, Ber., 30, 1099 (1897).


