PART I

SYNTHESIS

of

3-ARYL-2-METHYL-QUINAZOL-4-ONES
PART I
THEORETICAL SYNTHESIS OF 2-METHYL-3-ARYL-QUINAZOL-4-ONES

Various methods for synthesis of quinazol-4-one derivatives and their reactions are described in the General Introduction. Among these methods, one developed by Grimmel, Guenther and Morgan (J. Am. Chem. Soc., 1946, 68, 542) is an elegant one and has been applied in the present work. It consists in heating an N-acyl- or N-arylanthranilic acid or its derivative with a primary amine in toluene or any other suitable solvent in presence of phosphorus trichloride. Kacker and Zaheer (Jour. Indian Chem. Soc., 1951, 28, 344), Narang and co-workers (ibid., 1953, 30, 331, 401), Shah and co-workers (ibid., 1955, 32, 199, 483; 1956, 32, 140), Subbar am (Proc. Indian Acad. Sci., 1954, 40A, 22) and very recently Joshi and Giri (Jour. Indian Chem. Soc., 1962, 39, 188) have used this method for preparing quinazol-4-one derivatives.

The methyl substituted N-acetylanthranilic acids required for the present work were prepared by the oxidation of the corresponding methyl isatins and the subsequent acetylation of the anthranilic acids thus obtained. This is briefly considered below.

The substituted isatins have been prepared by a process originally developed by Sandmeyer (Helv. Chim. Acta, 1919, 2, 234; Sumpter, "Chemistry of Isatins", Chem. Revs. (U.S.A.), 1944, 34, 393) which centres around the formation of an isonitrosoacetanilide and ring closure of

\[
\begin{align*}
\text{PhNH}_2 + \text{CCl}_3\cdot\text{CH(OH)}_2 & + \text{NH}_2\text{OH} \\
\xrightarrow{\text{H}^+} \\
\text{PhNH} - \text{C-CH:NOH} & + \text{NOH} \\
\xrightarrow{\text{H}^+} \\
\text{PhNH} - \text{C:O} & + \text{NH}_2\text{OH}
\end{align*}
\]

(III) (I)

\[
\begin{align*}
\text{PhNH}_2 + \text{CCl}_3 & \\
\xrightarrow{\text{Conc. H}_2\text{SO}_4} \\
\text{PhNH} - \text{C:O} & + \text{NH}_2\text{OH}
\end{align*}
\]

(II) Isatin
Simple meta-substituted arylamines on similar treatment usually lead to two isomeric products having the expected structures: e.g., m-toluidine gives both 4-methyl- and 6-methyl isatins (Meyer, and Schulze, Ber., 1925, 58, 1465; Sadler, J. Org. Chem., 1956, 21, 169; Narang et al., J. Sci. Industr. Res. India, 1960, 19B, 217). There are on record several instances of the failure of this 'Sandmeyer Synthesis' to yield the desired isatin. Nitranilines react with chloral hydrate to form the corresponding isonitrosoacetanilide derivatives; however, these intermediates failed to undergo ring closure (Borsche, Fritzche and Weusmann, Ber., 1924, 57, 1149; Rupe and Kersten, Helv. Chim. Acta., 1926, 9, 578). According to Halberkann (Ber., 1921, 54, 3079), p-anisidine and p-phenetidine cannot be converted into the corresponding isatins by this method.

5-Methyl- and 7-methyl isatins required for this work have been prepared by the Sandmeyer method referred to above. p-Toluidine in acid solution with chloral hydrate and hydroxylamine gives only isonitroso-p-methylacetanilide which is cyclised to 5-methyl isatin by the action of concentrated sulphuric acid (Marvel and Hiers, loc.cit.) and o-toluidine on similar treatment gives isonitroso-o-methylacetanilide which is similarly cyclised to 7-methyl isatin (Sandmeyer, loc.cit.).

\[
\begin{align*}
(I) & \quad p-\text{CH}_3 \\
(II) & \quad o-\text{CH}_3
\end{align*}
\]

\[
\begin{align*}
(I) & \quad 5-\text{CH}_3 \\
(II) & \quad 7-\text{CH}_3
\end{align*}
\]
The oxidation of isatins with alkaline hydrogen peroxide gives the anthranilic acid derivatives (Kolbe, *J. prakt. Chem.*, 1884,30(ii), 84; Kalb and Berrer, *Ber.*, 1924,57,2105; Sumpter and co-workers, *J. Am. Chem. Soc.*, 1932,54,1917; 1941,63,2027; 1943,65,1802). Thus, 5-methyl isatin was oxidised to 5-methylanthranilic acid, which is identical with the product obtained by Ehrlich (*Ber.*, 1901,34,3375) and Findeklee (*Ber.*, 1905,38,3553) by the reduction of 2-nitro-5-methylbenzoic acid. 7-Methyl isatin on similar treatment gave 3-methylanthranilic acid identical with the product obtained by Jacobson (*Ber.*, 1881,14,2354) and Findeklee (*Ber.*, 1905,38,3555) by reduction of 2-nitro-3-methylbenzoic acid. \( N \)-acetylation of these acids with one mole of acetic anhydride in dry benzene gave 5-methyl-\( N \)-acetylanthranilic acid (I) and 3-methyl-\( N \)-acetylanthranilic acid (II) respectively. The former shows all the properties identical with the products obtained by Miller and Ohler (*Ber.*, 1891,24,1910)

\[\begin{align*}
I & : 5-\text{CH}_3 \\
\text{II} & : 7-\text{CH}_3
\end{align*}\]

on oxidation of 2:3:6-trimethylquinoline in neutral potassium permanganate solution and by Hayashi, Tsuruoka and Morikawa (*Bull. Chem. Soc., Japan*, 1936,11,184) by \( N \)-acetylation of the acid with excess of acetic anhydride; while, the latter is identical with the acid obtained by Miller and Meyer (*Ber.*, 1891,24,1909) by
the permanganate oxidation of 2:8-dimethylquinoline in neutral solution.

5-Methyl- as well as 3-methyl-N-acetylanthranilic acids when condensed with suitable primary aryl amines, formed quinazol-4-ones reported in this part of the thesis. The method followed is the one developed by Grimmel, Guenther and Morgan (J.Am.Chem.Soc., loc.cit.), which consists in heating the N-acyl- or N-arylanthranilic acids with primary amines in presence of phosphorus trichloride in toluene or any other suitable non-hydroxy dry inert solvent at its reflux temperature with mechanical stirring. When toluene is used as solvent, the reaction mixture is generally maintained at 130-35°C for a period of about two hours to complete the reaction. The solid cake obtained is treated with sodium carbonate solution to remove unreacted anthranilic acid, if any, and toluene removed by steam distillation. The quinazol-4-one derivative is crystallised from either ethanol or acetone and then petroleum ether (80 -100°). The details of the method are given in the experimental.

\[
\begin{align*}
\text{(A)} & : 3\text{-Methyl-N-acytlyl-anthranilic acid.} \\
\text{(B)} & : 5\text{-Methyl-N-acytlyl-anthranilic acid.}
\end{align*}
\]

\[
\begin{align*}
\text{R : Phenyl;} & \\
& o-,m-,p-Tolyl; \\
& o-,p-Anisyl; \\
& o-,m-,p-Chloro-phenyl.
\end{align*}
\]

\[
\begin{align*}
\text{(A)} & : 2:8\text{-Dimethyl-3-aryl-quinazol-4-one.} \\
\text{(B)} & : 2:6\text{-Dimethyl-3-aryl-quinazol-4-one.}
\end{align*}
\]
It may be noted that this method of synthesis of 2-methyl-quinazol-4-ones from N-acetylanthranilic acids and primary amines is of wide applicability. It can be used successfully to synthesize quinazolone derivatives from aliphatic amines and aryl hydrazines. Nuclear substituted N-acetylanthranilic acids can also be used. The method, however, cannot be applied to 1-naphthylamine, allylamine, 2-aminopyridine and 2-amino-6-ethylbenzothiazole, the N-acetylanthranilic acid being recovered almost quantitatively.

It has been also possible to carry out the reaction using phosphorus oxichloride, although the purity of the product suffers somewhat. Very recently, Klosa (J.prakt.Chem., 1961,14,84; Chem. Abstr., 1962,56,2449) has synthesized a number of 2:3-disubstituted quinazol-4-one derivatives in fairly good yield by heating a mixture N-acetylanthranilic acid and primary amine in toluene using phosphorus oxichloride as the condensing agent.

As stated in the General Introduction, the quinazolone derivatives are pharmacologically important compounds. More recently, it has been observed by Zaheer, Sidhu and Kacker (Jour.Indian Chem. Soc., 1961,38,621) that 2-methyl-3-(o-tolyl)-quinazol-4-one is the most potent hypnotic and has no adverse side effects (see also: Ravina, Brit.Med.Jour., 1959,1619). In the present work, the author has synthesized the corresponding 6- and 8-methyl derivatives. The pharmacological testing of these compounds will be taken up in future. In view of the above work, they may turn out pharmacologically active.
PART I

EXPERIMENTAL

(A): SYNTHESIS OF 2,8-DIMETHYL-3-ARYL-QUINAZOL-4-ONES

3-Methyl-N-acetylanthranilic acid required for this work was prepared by the following sequence of reactions:

(i) Isonitroso-o-methylacetanilide: In a two-litre flask was placed a solution of chloral hydrate (30 g; 0.18 mol) in water (400 ml). To this solution was added anhydrous sodium sulphate (200 g in 230 ml of water), o-toluidine (18 g; 0.17 mol) dissolved in water (100 ml) containing concentrated hydrochloric acid (15 ml; 0.18 mol; d 1.19) and finally, a solution of hydroxylamine hydrochloride (37 g; 0.53 mol) in water (170 ml). The mixture was then heated on wire-gauze so that vigorous boiling started within about 25-30 minutes and then cooled under running water-tap, when isonitroso-o-methylacetanilide crystallised out. It was recrystallised from hot water, pale yellow flocculent crystals, m.p. 121°. Sandmeyer (Helv. Chim. Acta., 1919, 2, 234; Brit. Abstr., 1919, 318) records the same melting point. (Yield; 13 g.).

(ii) 7-Methyl isatin: In a half-litre three-necked flask, fitted with a mechanical stirrer and a thermometer and placed in water-bath, was taken concentrated sulphuric acid (120 g or 65 ml; d 1.84). It was then heated to 50°. Well powdered isonitroso-o-methylacetanilide (15 g) was added to this warm acid in small lots at a time carefully maintaining the temperature of the reaction mixture between 60-70°. After the addition was over, the temperature
was raised to $80^\circ$ and the reaction mixture was kept at this temperature for further ten minutes with continuous stirring to complete the reaction. It was then cooled to room temperature and poured over cracked ice (about 1 kg.). After standing for an hour, the red solid that settled down was filtered, washed with cold water till free from acid and finally crystallised from glacial acetic acid (30 ml), scarlet red glistening plates, $m.p. 266^\circ$. Bouer (Ber., 1907, 40, 2656) records the same melting point. (Yield : 9 g.).

(iii) : 3-Methyl anthranilic acid : 3-Methyl isatin (8 g.) was dissolved in sodium hydroxide solution (150 ml; 10%) in a half-litre three-necked flask equipped with a mechanical stirrer and a tap-funnel. Hydrogen peroxide (150 ml; 3%) was then added dropwise at room temperature in about half an hour with continuous stirring. After the addition was over, the mixture was stirred for fifteen minutes more. It was then evaporated to one-half of its original bulk, cooled externally by ice and carefully acidified, first with cold hydrochloric acid and then with acetic acid, when 3-methylanthranilic acid separated. It was filtered and crystallised from dilute acetic acid, white needles, $m.p. 174^\circ$. Findeklee (Ber., 1905, 38, 3555), who prepared it by reduction of 2-nitro-3-methylbenzoic acid, records $m.p. 172^\circ$. (Yield : 3.5 g.).

(iv) : 3-Methyl-N-acetylanthranilic acid : To a hot solution of 3-methylanthranilic acid (1.8 g.) in minimum quantity of dry benzene (30 ml) acetic anhydride (1.2 ml) was added dropwise with continuous shaking. A crystalline solid that separated on cooling was collected, washed with petroleum ether ($b.p. 60-80^\circ$; 10 ml) and crystallised
from dilute acetic acid, small pinkish cubes, m.p.196°. Miller and Meyer (Ber., 1891,24,1909) who prepared it by the neutral permanganate oxidation of 2:8-dimethylquinoline, record m.p.194°. (Yield:1.1g.).

(I) : 2:8-DIMETHYL-3-PHENYL-QUINAZOL-4-ONE : 3-Methyl-N-acetyl-anthranilic acid (1.0 g.) and aniline (0.5 g.) were mixed in dry toluene (30 ml) in a 250-ml three-necked flask equipped with a mechanical stirrer, a reflux condenser and a dropping funnel. A solution of phosphorus trichloride in dry toluene (5.0 ml, 10%; 0.34 mol.) was added dropwise with continuous stirring when a thick white solid separated. The resulting mixture was then refluxed at 130-35° on an oil-bath for two hours with continued stirring. On cooling, the yellow pasty mass that separated was treated with sodium carbonate solution (100 ml; 10%) when it became almost white and solidified. Toluene was then steam-distilled off and the residual mass was collected and crystallised from ethanol (50%). It was then crystallised from petroleum ether (b.p. 80-100°), colourless rhombic crystals, m.p.148°. (Yield : 0.8 g.).

Analysis : 0.0832 g. substance on Kjeldahl determination required 11.1 ml of 0.0609 N sulphuric acid.

\[
\text{Found: } N, \ 11.37 \ \text{per cent} \\
\text{C}_{16}\text{H}_{14}\text{ON}_{2} \ \text{requires } N, \ 11.20 \ \text{per cent}
\]

HYPDROCHLORIDE : To a hot ethanolic solution of the above quinazolone (0.2 g. in 10 ml) was added a drop of concentrated hydrochloric acid. The hydrochloride that separated as a colourless crystalline product after keeping the reaction mixture at room temperature for about an hour was filtered and washed with little (2 ml) alcohol, colourless long needles, m.p.212°.
Analysis: 0.0388 g. substance required 2.2 ml of 0.0614 N alkali.
Found: Equiv. wt., 280.9
\[ C_{16}H_{14}ON_2 \cdot HCl \] requires: Equiv. wt., 286.5

(II): 2,8-DIMETHYL-3-(o-TOLYL)-QUINAZOL-4-ONE: 3-Methyl-N-acetylanthranilic acid (1.0 g) and o-toluidine (0.52 g) in dry toluene (30 ml) was slowly added phosphorus trichloride in dry toluene (5 ml; 10%) with stirring. A light yellow pasty mass that separated on working up the reaction mixture as above was solidified on treatment of sodium carbonate solution (100 ml; 10%) and toluene removed by steam distillation. The residue that left over was collected and crystallised first from ethanol and then from petroleum ether (80-100°), colourless short needles, m.p. 140°. (Yield: 0.65 g).

Analysis: 0.0812 g. substance on Kjeldahl determination required 12.9 ml of 0.04816 N sulphuric acid.
Found: N, 10.71 per cent
\[ C_{17}H_{16}ON_2 \] requires N, 10.60 per cent

(III): 2,8-DIMETHYL-3-(m-TOLYL)-QUINAZOL-4-ONE: 3-Methyl-N-acetylanthranilic acid (1.0 g) was condensed with m-toluidine (0.52 g) as above. On working up the reaction mixture as before, the product obtained was crystallised from ethanol, colourless short needles, m.p. 103°. (Yield: 0.5 g).

Analysis: 0.0468 g. substance on Kjeldahl determination required 7.3 ml of 0.04816 N sulphuric acid.
Found: N, 10.52 per cent
\[ C_{17}H_{16}ON_2 \] requires N, 10.60 per cent

(IV): 2,8-DIMETHYL-3-(p-TOLYL)-QUINAZOL-4-ONE: 3-Methyl-N-acetylanthranilic acid (1.0 g) was similarly condensed with p-toluidine (0.52 g). The quinazolone isolated as before was
crystallised from alcohol (50 %), colourless feathery plates, m.p. 140°. (Yield : 0.7 g).

**Analysis**: 0.0782 g. substance on Kjeldahl determination required 12.5 ml of 0.04816 N sulphuric acid.

    Found : N, 10.77 per cent

\( \text{C}_{17}\text{H}_{16}\text{O}_2\text{N}_2 \text{ requires } \text{N, 10.60 per cent} \)

**HYDROCHLORIDE** : It was prepared by adding a drop of concentrated hydrochloric acid into hot alcoholic solution of the above base. Colourless long needles, m.p.218°.

**Analysis**: 0.0932 g. substance required 4.6 ml of 0.0683 N alkali.

    Found : Equiv. wt., 296.6

\( \text{C}_{17}\text{H}_{16}\text{O}_2\text{N}_2\text{HCl requires Equiv. wt.}, 300.5 \)

(\( \text{V} \)) : 2-8-DIMETHYL-3-(o-ANISYL)-QUINAZOL-4-ONE : 3-Methyl-N-acetylanthranilic acid (1.0 g) and o-anisidine (0.62 g) suspended in dry toluene (30 ml) were treated with phosphorus trichloride in toluene (5 ml; 10 %) as before. A light yellow pasty mass that separated on working up the reaction mixture was solidified on treatment with sodium carbonate solution (100 ml; 10 %). The residue obtained after removing toluene was collected and crystallised from ethanol. It was recrystallised from petroleum ether into colourless plates, m.p.168°. (Yield : 0.7 g).

**Analysis**: 0.0828 g. substance on Kjeldahl determination required 9.5 ml of 0.0609 N sulphuric acid.

    Found : N, 9.78 per cent

\( \text{C}_{17}\text{H}_{16}\text{O}_2\text{N}_2 \text{ requires N, 10.00 per cent} \)

**HYDROCHLORIDE** : To a hot alcoholic solution of the above base was passed dry hydrochloric acid gas for about two minutes. The hydrochloride crystallised out on keeping the mixture at room temperature.
for some time, colourless short needles, m.p. 229°.

Analysis: 0.0918 g. substance required 4.7 ml 0.0614 N alkali.

Found: Equiv. wt., 318.1

\[ C_{17}H_{16}O_2N_2 \cdot HCl \text{ requires Equiv. wt., 316.6} \]

**(VI)**: 2:8-DIMETHYL-3-(p-ANISYL)-QUINAZOL-4-ONE: 3-Methyl-N-acetylanthranilic acid (1.0 g) on treatment with p-anisidine (0.62 g) as above gave the product which was crystallised from alcohol followed by recrystallisation from petroleum ether, colourless rhombic crystals, m.p. 135°. (Yield: 0.78 g).

Analysis: 0.0772 g. substance on Kjeldahl determination required 9.2 ml of 0.0609 N sulphuric acid.

Found: N, 10.16 per cent

\[ C_{17}H_{16}O_2N_2 \text{ requires N, 10.00 per cent} \]

HYDROCHLORIDE: It was prepared by adding a drop of concentrated hydrochloric acid into hot alcoholic solution of the above base, colourless long glistening needles, m.p. 220°.

Analysis: 0.1188 g. substance required 6.2 ml of 0.0614 N alkali.

Found: Equiv. wt., 312.1

\[ C_{17}H_{16}O_2N_2 \cdot HCl \text{ requires Equiv. wt., 316.5} \]

**(VII)**: 2:8-DIMETHYL-3-(o-CHLOROPHENYL)-QUINAZOL-4-ONE: 3-Methyl-N-acetylanthranilic acid (1.0 g) and o-chloroaniline (0.65 g) were suspended in dry toluene (30 ml) and phosphorus trichloride in toluene (5.0 ml; 10%) was gradually added to it. The solid that separated on working up the reaction mixture as before was collected and crystallised from alcohol, colourless prismatic needles, m.p. 150°. (Yield: 0.7 g).
Analysis: (a) 0.0592 g. substance on Kjeldahl determination required 7.0 ml of 0.0609 N sulphuric acid.

Found: N, 10.08 per cent

\( C_{16}H_{13}ON_2Cl \) requires N, 9.84 per cent

(b) 0.0638 g. substance gave 0.0330 g. AgCl.

Found: Cl, 12.79 per cent

\( C_{16}H_{13}ON_2Cl \) requires Cl, 12.51 per cent

(VIII): 2,8-DIMETHYL-3-(m-CHLOROPHENYL)-QUINAZOL-4-ONE:

3-Methyl-N-acetylanthranilic acid (1.0 g) was condensed with m-chloroaniline (0.65 g) as above. The quinazolone isolated similarly was crystallised first from alcohol and then from petroleum ether, colourless small prisms, m.p. 188°. (Yield: 0.5 g).

Analysis: (a) 0.0684 g. substance on Kjeldahl determination required 9.8 ml of 0.04816 N sulphuric acid.

Found: N, 9.67 per cent

\( C_{16}H_{13}ON_2Cl \) requires N, 9.84 per cent

(b) 0.0532 g. substance gave 0.0272 g. AgCl.

Found: Cl, 12.65 per cent

\( C_{16}H_{13}ON_2Cl \) requires Cl, 12.51 per cent

(IX): 2,8-DIMETHYL-3-(p-CHLOROPHENYL)-QUINAZOL-4-ONE:

3-Methyl-N-acetylanthranilic acid (1.0 g) was similarly condensed with p-chloroaniline (0.65 g.). The quinazolone isolated as before was crystallised from alcohol and then from petroleum ether, colourless thick plates, m.p. 151°. (Yield: 0.75 g).

Analysis: (a) 0.0488 g. substance on Kjeldahl determination required 5.6 ml of 0.0609 N sulphuric acid.

Found: N, 9.78 per cent

\( C_{16}H_{13}ON_2Cl \) requires N, 9.84 per cent

(b) 0.0586 g. substance gave 0.0302 g. AgCl.

Found: Cl, 12.75 per cent

\( C_{16}H_{13}ON_2Cl \) requires Cl, 12.51 per cent
5-Methyl-N-acetylanthranilic acid required for the synthesis of 2:6-dimethyl-3-aryl-quinazol-4-ones was prepared by a similar method described for the preparation of isomeric 3-methyl derivative.

(i) Isonitroso-p-methylacetanilide: It was prepared by condensing p-toluidine (18 g; 0.17 mol) with hydroxylamine hydrochloride (37 g; 0.53 mol) and chloral hydrate (30 g; 0.18 mol) by a method similar to that described for the isomeric o-methyl derivative. The product obtained was crystallised from hot water, pale yellow flocculent crystals, m.p.168°. Marvel and Hiers (Blatt (Ed.), "Organic Syntheses", Coll.Vol.I, 1941, p.330) record m.p.162°. (Yield: 13.2 g).

(ii) 5-Methyl isatin: Dry isonitroso-p-methylacetanilide (15 g; 0.09 mol) was treated with concentrated sulphuric acid (120 g or 65 ml; d 1.84; 1.2 mol) as described in the preparation of 7-methyl isatin, when 5-methyl isatin was obtained. It was crystallised from glacial acetic acid, scarlet red glistening plates, m.p.186°. Meyer (Ber., 1883,16,2265) records m.p.184°, while Panaotovic (Ber., 1908,41,3034) as well as Marvel and Hiers (loc.cit.) report m.p.187°. (Yield: 10 g).

(iii) 5-Methyl anthranilic acid: 5-Methyl isatin (8.0 g) was oxidised in alkaline hydrogen peroxide as before. 5-Methyl anthranilic acid was separated on careful acidification of the reaction mixture. The acid thus obtained was filtered and crystallised from dilute acetic acid, pale yellow needles, m.p.175°. Findeklee (Ber., 1905,32, 3553), who prepared it by reduction of 2-nitro-5-methylbenzoic acid records the same melting point. (Yield: 3.5 g).
(iv) : 5-Methyl-N-acetylanthranilic acid : The hot solution of 5-methylanthranilic acid (1.8 g) in dry benzene (25 ml) was treated with acetic anhydride (1.2 ml). A crystalline solid that separated on cooling was filtered and recrystallised from dilute acetic acid, fibrous long white silky needles, m.p.188-89°. Miller and Ohler, (Ber., 1891,24,1910), who prepared it by oxidation of 2:3:6-trimethyl-quinoline, record m.p.193-94°; while Hayashi, Tsuruoka and Morikawa, (Bull.Chem.Soc.,Japan, 1936,11,184; Chem.Abstr., 1956,30,5965), who obtained it by treating 5-methylanthranilic acid with excess of acetic anhydride record m.p.189-90°. (Yield : 1.2 g).

(I) : 2:6-DIMETHYL-3-PHENYL-QUINAZOL-4-ONE : 5-Methyl-N-acetylanthranilic acid (1.0 g) and aniline (0.5 g) suspended in dry toluene (30 ml) were treated with phosphorus trichloride in toluene (5.0 ml; 10 %) as already described. A light yellow pasty product that separated on working up the reaction mixture was solidified on treatment with sodium carbonate solution (100 ml; 10 %). The residue obtained after removing toluene by steam distillation was collected and crystallised from ethanol (50 %). It was recrystallised from petroleum ether (b.p. 80-100°), colourless rhombic crystals, m.p.124°. (Yield : 0.6 g).

Analysis : 0.1424 g. substance on Kjeldahl determination required 18.2 ml of 0.0609 N sulphuric acid.

Found : N, 10.9 per cent

\[ C_{16}H_{14}ON_2 \] requires N, 11.2 per cent

HYDROCHLORIDE : It was prepared by adding a drop of concentrated hydrochloric acid to the hot alcoholic solution of the above base (0.2 g in 10 ml). Colourless short needles obtained after keeping
the reaction mixture at room temperature for about an hour were
filtered and washed with little alcohol (2.0 ml), m.p. 272°.

**Analysis**: 0.0516 g. substance required 2.7 ml of 0.0683 N alkali.

*Found*: Equiv. wt., 279.8

\[C_{16}H_{14}ON_2 \cdot HCl\] requires Equiv. wt., 286.5

(II): **2:6-DIMETHYL-3-(o-TOLYL)-QUINAZOL-4-ONE**: 5-Methyl-N-acetylanthranilic acid (1.0 g) and o-toluidine (0.52 g) were suspended in dry toluene (30 ml) and phosphorus trichloride in toluene (5.0 ml; 10%) was added to it as above. The product obtained on working up the reaction mixture as before, was crystallised from alcohol, followed by recrystallisation from petroleum ether, colourless long needles, m.p. 166°. Subbaram (Proc. Ind. Acad. Sci., 1954, 40, 22) records m.p. 159-61°. (Yield : 0.7 g).

**Analysis**: 0.0664 g. substance on Kjeldahl determination required 10.1 ml of 0.04816 N sulphuric acid.

*Found*: N, 10.25 per cent

\[C_{17}H_{16}O_N_2\] requires N, 10.60 per cent

**HYDROCHLORIDE**: Dry hydrochloric acid gas was passed into the solution of the above base (0.2 g) in acetone (10 ml) for two minutes and the solution was kept at room temperature for half an hour when the hydrochloride crystallised out. It was collected and washed with acetone (2 ml), colourless short needles, m.p. 248°.

**Analysis**: 0.0826 g. substance required 4 ml of 0.0683 N alkali.

*Found*: Equiv. wt., 302.4

\[C_{17}H_{16}O_N_2 \cdot HCl\] requires Equiv. wt., 300.5

(III): **2:6-DIMETHYL-3-(m-TOLYL)-QUINAZOL-4-ONE**: 5-Methyl-N-acetylanthranilic acid (1.0 g) when similarly treated with
m-toluidine (0.52 g) as above gave this quinazolone. It was crystallised first from alcohol and then from petroleum ether, colourless prismatic needles, m.p. 125°. (Yield: 0.45 g).

**Analysis**: 0.0534 g. substance on Kjeldahl determination required 8.2 ml of 0.04816 N sulphuric acid.

Found: N, 10.35 per cent

\[ \text{C}_{17}\text{H}_{16}\text{ON}_2 \] requires N, 10.60 per cent

**HYDROCHLORIDE**: It was prepared as before in acetone medium, colourless short needles, m.p. 252°.

**Analysis**: 0.1148 g. substance required 6.4 ml of 0.0683 N alkali.

Found: Equiv. wt., 296.5

\[ \text{C}_{17}\text{H}_{16}\text{ON}_2\cdot\text{HCl} \] requires Equiv. wt., 300.5

(IV): 2:6-DIMETHYL-3-(p-TOLYL)-QUINAZOL-4-ONE: 5-Methyl-N-acetylanthranilic acid (1.0 g) was condensed with p-toluidine (0.52 g) as above. The product obtained was crystallised from alcohol and then from petroleum ether, colourless thick plates, m.p. 136°. (Yield: 0.5 g).

**Analysis**: 0.0932 g. substance on Kjeldahl determination required 11.2 ml of 0.0609 N sulphuric acid.

Found: N, 10.24 per cent

\[ \text{C}_{17}\text{H}_{16}\text{ON}_2 \] requires N, 10.60 per cent

**HYDROCHLORIDE**: It was prepared by passing dry hydrochloric acid gas through the hot alcoholic solution of the above quinazolone, colourless small rhombic crystals, m.p. 262°.

**Analysis**: 0.0928 g. substance required 5.1 ml of 0.0609 N alkali.

Found: Equiv. wt., 298.7

\[ \text{C}_{17}\text{H}_{16}\text{ON}_2\cdot\text{HCl} \] requires Equiv. wt., 300.5
(V) : 2:6-DIMETHYL-3-(o-ANISYL)-QUINAZOL-4-ONE : 5-Methyl-N-acetylanthranilic acid (1.0 g) was treated with o-anisidine (0.62 g) as above. The reaction mixture, on working up as before, gave the quinazolone. It was crystallised from alcohol and then from petroleum ether, colourless thin plates, m.p. 142°. (Yield : 0.6 g).

Analysis : 0.0844 g. substance on Kjeldahl determination required 9.6 ml of 0.0609 N sulphuric acid.

Found : N, 9.72 per cent
\[ C_{17}H_{16}O_{2}N_{2} \text{ requires } N, 10.00 \text{ per cent} \]

HYDROCHLORIDE : It was prepared in acetone medium as above, colourless short needles, m.p. 272°.

Analysis : 0.0978 g. substance required 5.1 ml of 0.0614 N alkali.

Found : Equiv. wt., 311.7
\[ C_{17}H_{16}O_{2}N_{2}\cdot HCl \text{ requires } \text{Equiv. wt.}, 316.5 \]

(VI) : 2:6-DIMETHYL-3-(p-ANISYL)-QUINAZOL-4-ONE : 5-Methyl-N-acetylanthranilic acid (1.0 g) was condensed with p-anisidine (0.62 g) as above. The product obtained was crystallised from alcohol and then from petroleum ether, colourless rhombic crystals, m.p. 148°. (Yield : 0.65 g).

Analysis : 0.1460 g. substance on Kjeldahl determination required 18.8 ml of 0.0609 N sulphuric acid.

Found : N, 9.81 per cent
\[ C_{17}H_{16}O_{2}N_{2} \text{ requires } N, 10.00 \text{ per cent} \]

HYDROCHLORIDE : It was prepared by the acetone method, colourless short needles, m.p. 246°.
Analysis: 0.1180 g. substance required 6.2 ml of 0.0614 N alkali.

Found: Equiv. wt., 309.9
\[ \text{C}_{17}\text{H}_{16}\text{O}_{2}\text{N}_{2}\cdot\text{HCl} \text{ requires Equiv. wt., 316.5} \]

(VII): 2:6-DIMETHYL-3-(O-CHLOROPHENYL)-QUINAZOL-4-ONE: 5-Methyl-N-acetylanthranilic acid (1.0 g) and o-chloroaniline (0.65 g) were suspended in dry toluene (30 ml) and a solution of phosphorous trichloride in toluene (5.0 ml; 10%) was slowly added at a time. On working up the reaction mixture as before, the solid that separated was collected and crystallised first from alcohol and then from petroleum ether, colourless prismatic needles, m.p. 175°. (Yield: 0.7 g).

Analysis: (a) 0.1568 g. substance on Kjeldahl determination required 9.5 ml of 0.1154 N sulphuric acid.

Found: N, 9.67 per cent
\[ \text{C}_{16}\text{H}_{13}\text{O}_{2}\text{N}_{2}\text{Cl} \text{ requires N, 9.84 per cent} \]

(b) 0.1084 g. substance gave 0.0542 g. AgCl.

Found: Cl, 12.37 per cent
\[ \text{C}_{16}\text{H}_{13}\text{O}_{2}\text{N}_{2}\text{Cl} \text{ requires Cl, 12.51 per cent} \]

HYDROCHLORIDE: It was prepared by the acetone method, colourless small prisms, m.p. 240°.

Analysis: 0.0984 g. substance required 4.5 ml of 0.0683 N alkali.

Found: Equiv.wt., 320.2
\[ \text{C}_{16}\text{H}_{13}\text{O}_{2}\text{N}_{2}\text{Cl} \cdot\text{HCl} \text{ requires Equiv.wt., 321.5} \]

(VIII): 2:6-DIMETHYL-3-(M-CHLOROPHENYL)-QUINAZOL-4-ONE: 5-Methyl-N-acetylanthranilic acid (1.0 g) was similarly treated with m-chloroaniline (0.65 g) as above. The quinazolone obtained was crystallised from alcohol, colourless short needles, m.p. 144°. (Yield: 0.6 g).
Analysis: (a) 0.0432 g. substance on Kjeldahl determination required 6.3 ml of 0.04816 N sulphuric acid.

\[ C_{16}H_{13}ON_2Cl \text{ requires } N, 9.84 \text{ per cent} \]

(b) 0.0938 g. substance gave 0.0454 g. AgCl.

\[ C_{16}H_{13}ON_2Cl \text{ requires } Cl, 12.51 \text{ per cent} \]

HYDROCHLORIDE: It was prepared by adding a drop of concentrated hydrochloric acid into the alcoholic solution of the quinazolone. Colourless short needles, m.p. 255-56°.

Analysis: 0.0836 g. substance required 3.8 ml of 0.0683 N alkali.

\[ C_{16}H_{13}ON_2Cl \cdot \text{HCl requires Equiv. wt., 321.5} \]

(IX): 2:6-DIMETHYL-3-(p-CHLOROPHENYL)-QUINAZOL-4-ONE: 5-Methyl-N-acetylanthranilic acid (1.0 g) and p-chloroaniline (0.65 g) on similar treatment as above gave this quinazolone. It was crystallised from alcohol and then from petroleum ether as colourless plates, m.p. 150°. (Yield: 0.65 g).

Analysis: (a) 0.1228 g. substance on Kjeldahl determination required 7.3 ml of 0.1154 N sulphuric acid.

\[ C_{16}H_{13}ON_2Cl \text{ requires } N, 9.84 \text{ per cent} \]

(b) 0.0948 g. substance gave 0.0492 g. AgCl.

\[ C_{16}H_{13}ON_2Cl \text{ requires } Cl, 12.51 \text{ per cent} \]

HYDROCHLORIDE: It was prepared as above in alcoholic medium. Colourless long needles, m.p. 264-65°.

Analysis: 0.0538 g. substance required 2.4 ml of 0.0683 N alkali.

\[ C_{16}H_{13}ON_2Cl \cdot \text{HCl requires Equiv. wt., 321.5} \]