# 849. *Syntheses in the Quinazolone Series. Part IV.* The Conversion of N-Aroylorthanilamides into 2-Arylquinazol-4-ones.*

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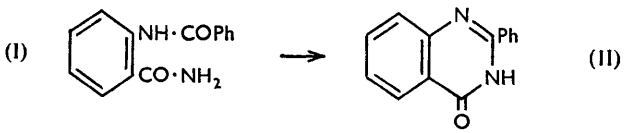
*N*-Aroylorthanilamides are rapidly converted by aqueous sodium hydroxide into the corresponding 2-arylquinazolones (cf. Körner [1]). An alternative synthesis involves the condensation of *N*-α-chlorobenzylidenetoluene-*p*-sulphonamide with methyl anthranilate and subsequent hydrolysis.



Körner [1] first prepared 2-phenyl-4-quinazolone (II) by the action of aqueous potassium hydroxide on *N*-benzoylorthanilamide (I), and the reaction has now been extended to the synthesis of a number of 2-aryl-4-quinazolones of type (II). Amides of type (I) are obtained from the corresponding methyl *N*-aroylorthanilates, which are readily obtained by aroylation of methyl anthranilate. The conversion of the esters into amides by the action of ammonia at room temperature requires from 14 to 30 days to give good yields. In some instances the amides were partially converted into the corresponding quinazolones by the action of ammonia. The amides are completely converted into quinazolones by heating them with 5% aqueous sodium hydroxide for 15 min. Attempts to reduce the time for the formation of the amides by heating the esters with ammonia resulted in hydrolysis and poor yields of amides.




$$p\text{-}C_6H_4Me\cdot SO_2\cdot N{:}CPh\cdot NH\cdot C_6H_4\cdot CO_2Me + NH_3 + H_2O \longrightarrow (II) + p\text{-}C_6H_4Me\cdot SO_2\cdot NH_2 + MeOH$$

(III)

In preliminary experiments attempts were made to prepare the quinazolones by heating methyl *N*-benzoylanthranilate with ammonium carbonate, but the yield was negligible. A small yield was obtained by heating *N*-benzoylanthranilic acid with ammonium carbonate. A more promising synthesis was the condensation of *N*-α-chlorobenzylidenetoluene-*p*-sulphonamide [2] with methyl anthranilate to give *N*-(*o*-methoxycarbonylphenyl)-*N'*-(toluene-*p*-sulphonyl)benzamidine (III), which on hydrolysis in presence of ammonia gave 2-phenyl-4-quinazolone (92%): this synthesis was not investigated further.

## Experimental

*Preparation of Methyl* N-*Aroylanthranilates.*—Most of the *esters* in Table 1 were prepared from the acid chloride and methyl anthranilate in presence of sodium acetate in aqueous ethanol (method 1),[3] and the others by aroylation in pyridine (method 2).[4] All the esters formed needles from ethanol.

*Preparation of* N-*Aroylorthanilamides.*—The following illustrates the preparation of the *amides* in Table 2. Methyl benzoylorthanilate (44·4 g.) in ethanol (2 l.) was saturated with ammonia at 0°, and then kept at room temperature in a stoppered bottle for 14—30 days. Removal of ethanol gave *N*-benzoylanthranilamide (95%) which crystallised from ethanol in needles, m. p. 218°. The esters (nos. 2—5, 7, 8, 10), on treatment with ammonia, gave mixtures of amides and the corresponding quinazolones and no attempt was made to separate them. Amides in Table 2 and the mixtures were converted into the corresponding quinazolones by boiling them for ½ hr. with 5% aqueous sodium hydroxide. The alkaline solution was filtered into dilute hydrochloric acid, then decolorised (charcoal), and the quinazolone was precipitated on addition of ammonia. All the *quinazolones* in Table 3 crystallised in needles from ethanol or ethanol–acetic acid.

* Part III, *J.*, 1956, 4178.

[1] Körner, *J. prakt. Chem.*, 1887, **36**, 155.
[2] Kemp and Stephen, *J.*, 1948, 110.
[3] Reverdin, *Ber.*, 1909, **42**, 1524.
[4] Dehn and Ball, *J. Amer. Chem. Soc.*, 1914, **36**, 2091.

N-(o-*Methoxycarbonylphenyl*)-N'-(*toluene*-p-*sulphonyl*)*benzamidine* (III).—*N*-Chlorobenzylidenetoluene-*p*-sulphonamide (10·5 g.) in dry acetone (50 c.c.) was added to methylanthranilate (13·5 g.) in dry acetone (50 c.c.). There was a slight rise of temperature and methyl anthranilate hydrochloride was deposited during ½ hr. and then removed. The acetone filtrate was

TABLE 1. *Methyl* N-*aroylorthanilates.*

| No. | Ar | Method | Yield (%) | M. p. | Found (%) C | Found (%) H | Formula | Required (%) C | Required (%) H |
|---|---|---|---|---|---|---|---|---|---|
| 1 | PhO·$CH_2$ | 1, 2 | 82 | 87° | 67·3 | 5·4 | $C_{16}H_{15}O_4N$ | 67·3 | 5·3 |
| 2 | o-$C_6H_4$Me·O·$CH_2$ | 2 | 84 | 85 | 68·2 | 6·0 | $C_{17}H_{17}O_4N$ | 68·2 | 5·7 |
| 3 | m-$C_6H_4$Me·O·$CH_2$ | 2 | 96 | 88 | 68·1 | 5·8 | | | |
| 4 | p-$C_6H_4$Me·O·$CH_2$ | 2 | 90 | 95 | 68·1 | 5·9 | | | |
| 5 | Ph·$CH_2$ | 1, 2 | 55 | 58 | 71·35 | 5·8 | $C_{16}H_{15}O_3N$ | 71·36 | 5·62 |
| 6 | p-$C_6H_4$·OMe | 1 | 80 | 113 | 67·2 | 5·3 | $C_{16}H_{15}O_4N$ | 67·36 | 5·3 |
| 7 | 3 : 4-$C_6H_3(OMe)_2$ | 1 | 60 | 108 | 64·9 | 5·25 | $C_{17}H_{17}O_5N$ | 64·95 | 5·13 |
| 8 | 3 : 4 : 5-$C_6H_2(OMe)_3$ | 1 | 60 | 138 | 62·54 | 5·6 | $C_{18}H_{19}O_6N$ | 62·6 | 5·55 |
| 9 | o-$C_6H_4$Me | 1 | 83 | 114 | 71·45 | 5·83 | $C_{16}H_{15}O_3N$ | 71·36 | 5·62 |
| 10 | m-$C_6H_4$Me | 1 | 71 | 74 | 71·45 | 5·59 | | | |
| 11 | p-$C_6H_4$Me | 1 | 40 | 100 | 71·35 | 5·64 | | | |
| 12 | Ph·CH:CH | 1 | 73 | 99 | 72·5 | 5·51 | $C_{17}H_{15}O_3N$ | 72·58 | 5·38 |

TABLE 2. N-*Aroylorthanilamides.*

| Ar | Yield (%) | Time (days) | M. p. | Found (%) C | Found (%) H | Formula | Required (%) C | Required (%) H |
|---|---|---|---|---|---|---|---|---|
| Ph | 95 | 30 | 218° | — | — | — | — | — |
| PhO·$CH_2$ | 80 | 30 | 234 | 66·5 | 5·17 | $C_{15}H_{14}O_3N_2$ | 66·65 | 5·22 |
| p-$C_6H_4$·OMe | 25 | 30 | 209 | 66·86 | 5·25 | $C_{15}H_{14}O_3N_2$ | 66·65 | 5·22 |
| o-$C_6H_4$Me | 20 | 30 | 185 | 71·12 | 5·6 | $C_{15}H_{14}O_2N_2$ | 70·85 | 5·5 |
| p-$C_6H_4$Me | 15 | 30 | 218 | 71·1 | 5·6 | $C_{15}H_{14}O_2N_2$ | 70·85 | 5·5 |
| Ph·CH:CH | 15 | 14 | 237 | 72·14 | 5·37 | $C_{16}H_{14}O_2N_2$ | 72·16 | 5·3 |

TABLE 3. 2-*Substituted quinazolones.*

| Ar | Yield (%) | M. p. | Found (%) C | Found (%) H | Formula | Required (%) C | Required (%) H |
|---|---|---|---|---|---|---|---|
| Ph [a] | 90 | 236° | — | — | — | — | — |
| PhO·$CH_2$ | 91 | 209 | 71·56 | 5·05 | $C_{15}H_{12}O_2N_2$ | 71·4 | 4·8 |
| o-$C_6H_4$Me·O·$CH_2$ | 80 | 185 | 72·27 | 5·4 | $C_{16}H_{14}O_2N_2$ | 72·16 | 5·3 |
| m-$C_6H_4$Me·O·$CH_2$ | 90 | 233 | 72·19 | 5·4 | | | |
| p-$C_6H_4$Me·O·$CH_2$ | 70 | 235 | 72·02 | 5·46 | | | |
| Ph·$CH_2$ [b] | 75 | 256 | 76·28 | 5·35 | $C_{15}H_{12}ON_2$ | 76·25 | 5·12 |
| p-$C_6H_4$·OMe | 98 | 247 | 71·34 | 4·9 | $C_{15}H_{12}O_2N_2$ | 71·41 | 4·8 |
| 3 : 4-$C_6H_3(OMe)_2$ | 90 | 246 | 68·21 | 5·13 | $C_{16}H_{14}O_3N_2$ | 68·06 | 5·0 |
| 3 : 4 : 5-$C_6H_2(OMe)_3$ | 56 | 255 | 65·27 | 5·31 | $C_{17}H_{16}O_4N_2$ | 65·38 | 5·16 |
| Ph·CH:CH [c] | 90 | 246 | 77·28 | 4·88 | $C_{16}H_{12}ON_2$ | 77·4 | 4·87 |
| o-$C_6H_4$Me | 89 | 236 | 76·2 | 5·2 | $C_{15}H_{12}ON_2$ | 76·25 | 5·12 |
| m-$C_6H_4$Me | 63 | 212 | 76·13 | 5·28 | | | |
| p-$C_6H_4$Me | 80 | 241 | 76·23 | 5·19 | | | |

[a] Bogert, Gortner, and Amend (*J. Amer. Chem. Soc.*, 1911, **33**, 949) give m. p. 234° (corr.). [b] König (*J. prakt. Chem.*, 1904, **69**, 20) gives m. p. 242° and Aggarawal and Ray (*J. Indian Chem. Soc.*, 1929, **6**, 288) give m. p. 247°. [c] Bogert, Beal, and Amend (*J. Amer. Chem. Soc.*, 1910, **32**, 1657) give m. p. 252° (corr.).

steam-distilled to remove unchanged methyl anthranilate, and the residue made alkaline with ammonia, giving needles (13·7 g., 94%), which after recrystallisation from ethanol melted at 146·5° (Found: C, 64·7; H, 5·1. $C_{22}H_{20}O_4N_2S$ requires C, 64·7; H, 4·9%). For conversion into 2-phenyl-4-quinazolone, the amidine (III) (3 g.) was dissolved in ethanol, saturated with ammonia, allowed to remain at room temperature overnight, and poured into water (50 c.c.). 2-Phenyl-4-quinazolone (1·5 g., 92%), m. p. 235°, was obtained (Found: C, 75·6; H, 4·5. Calc. for $C_{14}H_{10}ON_2$: C, 75·7; H, 4·5%). The quinazolone was also obtained by heating an intimate mixture of *N*-benzoylanthranilic acid (5 g.) with ammonium carbonate (5 g.) at 250° for 45 min., and adding small amounts of ammonium carbonate from time to time. The fused mass was cooled, macerated with dilute hydrochloric acid, and filtered. The insoluble portion was *N*-benzoylanthranilic acid, m. p. 178°, which was removed, and the acidic filtrate on addition of ammonia gave 2-phenyl-4-quinazolone, m. p. 235° (2·0 g., 44%).

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