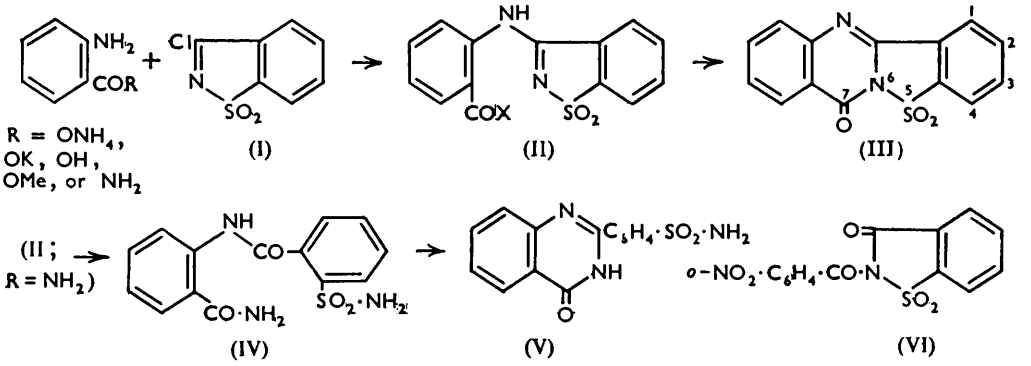
89. *Syntheses in the Quinazolone Series. Part V.* Synthesis of 7-Oxobenzo*[d]*quinazo*[3 : 2-b]*thiazole* 5 : 5-*Dioxide, and of* 2-o-*Sulphamylphenyl*-3H-*quinazol*-4-*one.*

By Edith Stephen and Henry Stephen.

3-*o*-Carboxyanilino- 3-(*o*-methoxycarbonylanilino)-, and 3-*o*-carbamoylanilino-4 : 5-benzo-1 : 2-thiazole 1 : 1-dioxide have been prepared by condensing 3-chloro-4 : 5-benzo-1 : 2-thiazole 1 : 1-dioxide respectively with ammonium or potassium anthranilate, methyl anthranilate, and anthranilamide. With acetic anhydride all three condensation products gave 7-oxobenzo[*d*]quinazo[3 : 2-*b*]thiazole 5 : 5-dioxide. Treatment of 3-*o*-carbamoylanilino-4 : 5-benzo-1 : 2-thiazole 1 : 1-dioxide with dilute alkali gave 2-*o*-sulphamylphenyl-3*H*-quinazol-4-one.

ψ-Saccharin chloride (3-chloro-4 : 5-benzo-1 : 2-thiazole 1 : 1-dioxide) [1] (I), which may be regarded as a cyclic imidoyl chloride, has been condensed with ammonium or potassium anthranilate, methyl anthranilate,[2] and anthranilamide to give respectively 3-*o*-carboxyanilino- (II; X = OH), 3-(*o*-methoxycarbonylanilino)- (II; X = OMe), and 3-*o*-carbamoylanilino-4 : 5-benzo-1 : 2-thiazole 1 : 1-dioxide (II; X = NH_2). Hydrolysis of the ester



yields the acid (II; X = OH). Treatment of the acid, ester, or amide with acetic anhydride brings about ring closure in each case, forming 7-oxobenzo[*d*]quinazo[3 : 2-*b*]-thiazole 5 : 5-dioxide (III). The tetracyclic compound was also obtained during the

* Part IV, *J.*, 1956, 4420.

[1] Jesurun, *Ber.*, 1893, **26**, 2287; Walker and Smith, *J.*, 1906, **89**, 350; Meadoe and Reid, *J. Amer. Chem. Soc.*, 1943, **65**, 457.

[2] Levy and Stephen, *J.*, 1956, 985.

condensation of ammonium or potassium anthranilate with ψ-saccharin chloride, the chlorine atom of which must have reacted with the NH_4 or K to give an intermediate product which would then undergo the Mumm and Hesse rearrangement [3] to give the quinazolone (III). The amide (II; X = NH_2) is converted by dilute sodium hydroxide solution into 2-*o*-sulphamylphenyl-3*H*-quinazol-4-one (V), which involves opening the thiazoline ring to give the diamide (IV), but this was not isolated since it was readily cyclised with elimination of a molecule of water.[4]

2-*o*-Nitrobenzoyl-3-oxo-4 : 5-benzo-1 : 2-thiazoline 1 : 1-dioxide (VI) was synthesised by condensing (i) *o*-nitrobenzoyl chloride with the sodium salt of saccharin, (ii) sodium *o*-nitrobenzoate with ψ-saccharin chloride (involving a Mumm and Hesse rearrangement). All attempts to reduce the nitro-group in the product (VI) to give the amino-compound which could undergo ring closure to (III) were unsuccessful, since the *o*-nitrobenzoyl group was removed by hydrolysis in acid or alkaline solution.

Experimental

Sulphur analyses were done with a Parr bomb.

ψ-Saccharin chloride was prepared by heating saccharin (1 mol.) with phosphorus pentachloride (1·1 mol.) at 170° for 1½ hr. Phosphorus oxychloride was then removed at 60°/30 mm. and the yellow crystalline residue consisting of ψ-saccharin chloride and *o*-cyanobenzenesulphonyl chloride was treated with ether in which the latter is readily soluble; the sparingly soluble ψ-saccharin chloride was collected and crystallised from ether as white needles (35%), m. p. 143°.

3-o-*Carboxyanilino*-4 : 5-*benzo*-1 : 2-*thiazole* 1 : 1-*Dioxide* (II; X = OH).—(*a*) Potassium anthranilate (1·8 g., 1 mol.) was refluxed with ψ-saccharin chloride (2 g., 1 mol.) in dry acetone (30 c.c.) for ½ hr. After evaporation the residue was treated with hot water to remove potassium chloride and unchanged potassium anthranilate. The residue (2·12 g.) consisting of the quinazolone (III) (0·4 g.) and the acid (II; X = OH) (1·72 g.) was separated by dissolving the acid in dilute ammonia, filtering the mixture, and precipitating the acid with dilute hydrochloric acid as a buff crystalline powder which recrystallised from ethyl methyl ketone in white needles, m. p. 320°.

(*b*) The acid was also obtained by dissolving ammonium anthranilate (1·2 g., 1·2 mol.) in dry acetone (30 c.c.) and adding ψ-saccharin chloride (2·44 g., 1 mol.) in dry acetone (30 c.c.). There was immediate precipitation of ammonium chloride which was filtered off after 15 min. Evaporation gave the product (III) and the acid (II) which were separated as above.

(*c*) The following method gives only the acid (II). Anthranilic acid (1·2 g., 2 mols.) in dry acetone (30 c.c.) was added to ψ-saccharin chloride (1 g., 1 mol.) in dry acetone (25 c.c.). Reaction took place on warming, with separation of a cream-coloured solid which was filtered off and washed with hot water; the residual acid crystallised from ethyl methyl ketone in white needles (1·34 g., 89%), m. p. 320°. The *acid* was also obtained by refluxing the ester (II; X = OMe) with 1% sodium hydroxide solution until completely dissolved, precipitating the acid with dilute acetic acid, and crystallising it from ethyl methyl ketone. It had m. p. and mixed m. p. 320° (Found: N, 9·3; S, 10·9. $C_{14}H_{10}O_4N_2S$ requires N, 9·3; S, 10·6%).

3-(o-*Methoxycarbonylanilino*)-4 : 5-*benzo*-1 : 2-*thiazole* 1 : 1-*Dioxide* (II; X = OMe).—Methyl anthranilate (1·5 c.c., 2 mols.) was added to ψ-saccharin chloride (1 g., 1 mol.) in dry acetone (20 c.c.). The temperature rose 12° and after a few minutes a mixture of methyl anthranilate hydrochloride and the ester was deposited; after 1 hr. at room temperature the solid was filtered off, treated with dilute ammonia solution, and steam-distilled to remove methyl anthranilate. The residue (1·14 g.) crystallised from dilute dioxan in colourless needles, m. p. 252°. The acetone filtrate on evaporation gave 0·06 g. of the ester (total yield = 1·2 g., 76%). A 78% yield was obtained by using chloroform as solvent. ψ-Saccharin chloride (1 g., 1 mol.) and methyl anthranilate (1·5 c.c., 2 mols.) in chloroform (30 c.c.) were refluxed for 1 hr., then poured into water, ammonia was added to alkalinity, and the whole was steam-distilled. The *ester* remaining (1·24 g.) crystallised from dilute dioxan. It is soluble in chloroform, acetone, dioxan, ethanol, and methanol (Found: N, 8·9; 8·9; S, 10·5, 10·6. $C_{15}H_{12}O_4N_2S$ requires N, 8·9; S, 10·1%).

3-o-*Carbamoylanilino*-4 : 5-*benzo*-1 · 2-*thiazole* 1 : 1-*Dioxide* (II; X = NH_2).—ψ-Saccharin chloride (1 g., 1 mol.) in dry chloroform (20 c.c.) was mixed with anthranilamide (1·36 g., 2 mols.)

[3] Mumm and Hesse, *Ber.*, 1910, **43**, 2511.
[4] Körner, *J. prakt. Chem.*, 1887, **36**, 155; Stephen and Wadge, *J.*, 1956, 4420.

in chloroform (50 c.c.), the temperature rising 10° with deposition of a white solid. After 2 days the chloroform was evaporated, and the residue treated with water to remove anthranilamide hydrochloride, giving the *amide* which crystallised in needles (from dioxan), m. p. 265° (89%) (Found : N, 14·1, 14·1; S, 10·9. $C_{14}H_{11}O_3N_3S$ requires N, 14·0; S, 10·6%).

7-*Oxobenzo*[d]*quinazo*[3 : 2-b]*thiazole* 5 : 5-*Dioxide* (III).—The acid (II; X = OH) (1·14 g.), dissolved in acetic anhydride (20 c.c.), was refluxed for 15 min. and, on cooling, the *product* (III) was precipitated by water, and crystallised from dilute dioxan in needles (1 g.), m. p. 276° (Found : N, 10·1; S, 11·7. $C_{14}H_8O_3N_2S$ requires N, 10·0; S, 11·4%). It was also obtained by refluxing the corresponding ester and amide severally with glacial acetic acid, in each case almost quantitatively.

2-o-*Sulphamylphenyl*-3H-*quinazol*-4-*one* (V).—The amide (II; X = NH_2) (1·3 g.) was refluxed with 1% sodium hydroxide solution until dissolved. On cooling and acidification with dilute acetic acid, the *product* (V) was precipitated. It crystallised from dilute dioxan in white needles, m. p. 283° (Found : N, 14·0; S, 10·3. $C_{14}H_{11}O_3N_3S$ requires N, 14·0; S, 10·6%) Its solubility is 25·12 mg./100 ml. in water and 73·5 mg./100 ml. in ethanol, both at 22·5°.

2-o-*Nitrobenzoyl*-3-*oxo*-4 : 5-*benzo*-1 : 2-*thiazoline* 1 : 1-*Dioxide* (VI).—(*a*) Finely powdered sodium saccharin (9·3 g., 1 mol.) was added to *o*-nitrobenzoyl chloride (10 g., 1 mol.) in benzene (10 c.c.) : a vigorous reaction took place. The mixture was refluxed for 2 hr. and the benzene distilled off, leaving the *dioxide* (VI) which after being washed with water and dilute sodium hydrogen carbonate solution crystallised from dilute dioxan in needles, m. p. 208° (Found : N, 8·5; S, 9·2. $C_{14}H_8O_6N_2S$ requires N, 8·4; S, 9·6%). (*b*) ψ-Saccharin chloride (2 g., 1 mol.) was refluxed for ½ hr. in dry acetone (30 c.c.) with sodium *o*-nitrobenzoate (2 g., 1 mol.). The mixture was filtered and on evaporation gave a mixture of the product (VI) and unchanged sodium *o*-nitrobenzoate. The latter was removed by treatment with water, leaving the dioxide (2·26 g.). (*c*) ψ-Saccharin chloride (2 g., 1 mol.) was intimately mixed with sodium *o*-nitrobenzoate (2·5 g., 1·5 mol.) and heated at 150° for ½ hr. The product (1 g.), after purification, melted at 208°. Attempts to reduce it with sodium dithionite (hydrosulphite), tin and hydrochloric acid, aluminium amalgam, Raney nickel, iron and acetic acid, and hydrazine hydrate [5] were unsuccessful owing to the removal of the *o*-nitrobenzoyl group by hydrolysis.

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UNIVERSITY OF THE WITWATERSRAND,
JOHANNESBURG, SOUTH AFRICA.

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[5] Curtius, *J. prakt. Chem.*, 1907, **76**, 281.