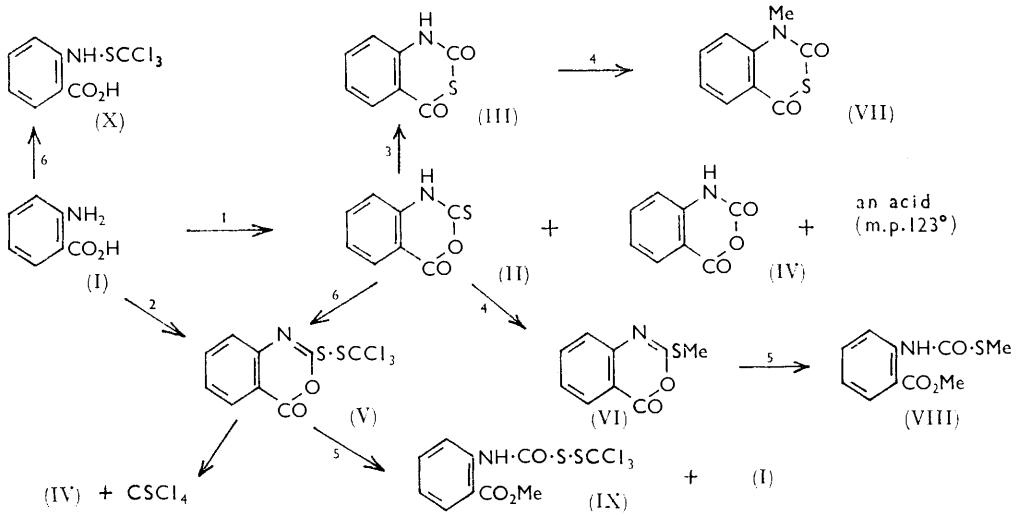
171. *Some Benzoxazines and Benzthiazines derived from Anthranilic Acid.*

By J. R. MARSHALL.

The action of thiophosgene on anthranilic acid led to 1,2-dihydro-2-thiono-3,1-benoxazin-4-one which was isomerised by heat to 3,1-benzothiazine-2(1*H*),4-dione. Derivatives of both compounds are described.

BROWNE and DYSON [1] and other workers have described the preparation of *m*- and *p*-isothiocyanatobenzoic acid by the action of thiophosgene on the corresponding aminobenzoic acid; but there is no record of an attempt to prepare *o*-isothiocyanatobenzoic acid. When thiophosgene and anthranilic acid were allowed to interact, a compound $C_8H_5NO_2S$ was obtained together with isatoic anhydride (IV) and an acid, m. p. 123°, as by-products. The compound $C_8H_5NO_2S$ was not an acid and did not show infrared absorption characteristic of the isothiocyanato or carboxyl groups. Accordingly the structure (II) is assigned to the compound by analogy with the formation of isatoic anhydride [2] from anthranilic



1, $CSCl_2$; 2, $CSCl_2$–$CSCl_4$; 3, $C_6H_3Cl_3$ at 210°; 4, K_2CO_3, MeI, and acetone; 5, MeOH; 6, $CSCl_4$.

acid and phosgene. Further confirmation of the structure comes from the reactions of compound (II). Methylation gave the *S*-methyl derivative (VI) and reaction with trichloromethanesulphenyl chloride gave the trichloromethyldithio-derivative (V) which was also obtained direct from anthranilic acid by the action of thiophosgene and trichloromethanesulphenyl chloride. Compound (V) was unstable and yielded isatoic anhydride and trichloromethanesulphenyl chloride on exposure to air; the action of methanol gave a poor yield of the thiolocarbamate (IX) together with some anthranilic acid. The action of methanol on compound (VI) brought about ring opening to give the thiolocarbamate (VIII). The benzoxazinone (II) isomerised in boiling 1,2,4-trichlorobenzene to the benzothiazinedione (III) which gave the *N*-methyl derivative (VII) on methylation. This isomerisation is characteristic of all double-bonded sulphur compounds which can rearrange to a single bonded form. For instance, Schönberg and Vargha [3] describe the isomerisation of diphenyl thionocarbonate to the thiolocarbonate at 280°,

[1] Browne and Dyson, *J.*, 1934, 178.
[2] Wagner and Fegley, *Org. Synth.*, Coll. Vol. III, 488.
[3] Schönberg and Vargha, *Ber.*, 1930, **63**, 178.

while Elderfield and Short [4] discuss the rearrangement of thionocarbamates to thiolocarbamates. The action of trichloromethanesulphenyl chloride on anthranilic acid yielded *N*-*o*-carboxyphenyltrichloromethanesulphenamide (X).

Experimental

1,2-*Dihydro*-2-*thiono*-3,1-*benzoxazin*-4-*one* (II).—Trichloromethanesulphenyl chloride (72 ml.) was added to a stirred mixture of stannous chloride dihydrate (180·8 g.) and concentrated hydrochloric acid (40 ml.) in water and chloroform (total volume 1600 ml.). After 1 hr. anthranilic acid (54·8 g.) was added and the mixture stirred for 2 hr. After a further 2 hr. the product was filtered off. Purification from ethyl acetate and from acetone gave the *benzoxazinone* (29 g.), m. p. 230—235° with hydrogen sulphide evolution after isomerisation at 200° (Found: C, 53·7; H, 2·7. $C_8H_5NO_2S$ requires C, 53·6; H, 2·8%), ν (C=O) 1785 cm.$^{-1}$ (in KBr). A black precipitate is slowly formed on boiling with aqueous lead acetate.

The filtrate later contained plates of isatoic anhydride (24 g.) which was identified by its behaviour on melting. Extraction of the chloroform with sodium hydrogen carbonate yielded a sulphur-free acid (3 g.), m. p. 123° (from light petroleum and from carbon tetrachloride). The m. p. was depressed when the acid was mixed with anthranilic acid.

2-*Trichloromethyldithio*-4H-3,1-*benzoxazin*-4-*one* (V).—(*a*) 1,2-Dihydro-2-thiono-3,1-benzoxazin-4-one (1·79 g.) in chloroform and water was stirred for 1 hr. with concentrated hydrochloric acid (1 ml.) and trichloromethanesulphenyl chloride (1·5 ml.). After a further 10 min. the chloroform was separated, dried and evaporated without heating giving prisms of 2-*trichloromethyldithio*-3,1-*benzoxazin*-4-*one*, m. p. 74—75° (Found: C, 33·0; H, 1·3; N, 4·55. $C_9H_4Cl_3NO_2S_2$ requires C, 32·9; H, 1·2; N, 4·3%). (*b*) Trichloromethanesulphenyl chloride (48·5 ml.) was added to a stirred mixture of anthranilic acid (27·4 g.), stannous chloride dihydrate (49·7 ml.), and concentrated hydrochloric acid (20 ml.) in water and chloroform. The temperature rose to 50° during the 2½ hr. stirring. After a further 1 hr. the chloroform was separated, dried, and evaporated with slight heating giving the benzoxazinone (55 g.) which was purified from light petroleum (b. p. 80—100°).

A solution of this benzoxazinone in carbon tetrachloride soon developed the odour of trichloromethanesulphenyl chloride, and deposited crystals of isatoic anhydride. A solid specimen of the benzoxazinone underwent a similar decomposition during 11 days. On pyrolysis, the benzoxazinone gave trichloromethanesulphenyl chloride.

Trichloromethylthio N-o-*Methoxycarbonylphenylthiolcarbamate* (IX).—2-Trichloromethyldithio-3,1-benzoxazin-4-one (23 g.) was added gradually to methanol (150 ml.) at <30°. The mixture was stirred until the precipitation of yellow plastic material had ceased. The clear decanted solution slowly deposited crystals (1·61 g.) which were chromatographed in methanol (400 ml.) on charcoal (5 g.; Sutcliffe and Speakman N.Y.3) and Celite 545 (15 g.). The first portion (150 ml.) of eluate gave no crystals, but a subsequent portion (600 ml.), on concentration, gave *trichloromethylthio* N-o-*methoxycarbonylphenylthiolocarbamate* (0·54 g.), m. p. 106—107° (Found: C, 33·3; H, 1·95; N, 4·2. $C_{10}H_8Cl_3NO_3S_2$ requires C, 33·3; H, 2·2; N, 3·9%).

Anthranilic acid hydrochloride was obtained from the original methanolic mother-liquors. Decomposition of the benzoxazinone in boiling methanol also gave a small yield of the thiolocarbamate, but the reaction with methanol in chloroform led only to anthranilic acid.

2-*Methylthio*-3,1-*benzoxazin*-4-*one* (VI).—1,2-Dihydro-2-thiono-3,1-benzoxazin-4-one (5·4 g.) was refluxed in acetone for 1½ hr. with methyl iodide (3 ml.) and potassium carbonate (3 g.). The solid, precipitated by the addition of water, was recrystallised from ethyl acetate (charcoal) giving needles of 2-*methylthio*-3,1-*benzoxazin*-4-*one* (3·45 g.), m. p. 106·5—108·5° (Found: C, 56·0; H, 3·65. $C_9H_7NO_2S$ requires C, 56·0; H, 3·6%).

Methyl N-o-*Methoxycarbonylphenylthiolocarbamate* (VIII).—1,2-Dihydro-2-thiono-3,1-benzoxazin-4-one (5·4 g.) was methylated as in the above experiment, and the crude product boiled with methanol for ½ hr. When the mixture cooled the *thiolocarbamate* (4 g.) separated in needles, m. p. 86·5—88° (Found: C, 53·5; H, 5·0. $C_{10}H_{11}NO_3S$ requires C, 53·3; H, 4·9%).

3,1-*Benzothiazine*-2(1*H*),4-*dione* (III).—1,2-Dihydro-2-thiono-3,1-benzoxazin-4-one (10 g.) was heated in boiling 1,2,4-trichlorobenzene (50 ml.) for 20 min. The odour of hydrogen sulphide was present and the solution became slightly coloured. After the mixture had cooled,

[4] Elderfield and Short, *J. Org. Chem.*, 1953, **18**, 1092.

the solid was removed and purified from acetone (charcoal) giving prisms of the *benzothiazinedione* (6·1 g.), m. p. 226—235°, to a red liquid with gas evolution (Found: C, 53·5; H, 2·7. $C_8H_5NO_2S$ requires C, 53·6; H, 2·8%).

After 10 minutes' refluxing the isomerisation was incomplete since needles of the benzoxazinone formed on cooling. Attempts to carry out the reaction without solvent led to poor yield. The approximate solubilities of the benzoxazinone and the benzothiazinedione in acetone at room temperature are 1 : 15 and 1 : 80, respectively.

1-*Methyl*-3,1-*benzothiazine*-2(1H),4-*dione* (VII).—The above benzothiazine (0·895 g.) was refluxed in acetone (10 ml.) for 18 hr. with methyl iodide (0·5 ml.) and potassium carbonate (0·5 g.). Water precipitated 1-*methyl*-3,1-*benzothiazine*-2(1*H*),4-*dione* (0·47 g.) as fine prisms from alcohol and from acetone (charcoal), m. p. 170·5—172° (Found: C, 56·1; H, 3·6. $C_9H_7NO_2S$ requires C, 56·0; H, 3·6%).

N-o-*Carboxyphenyltrichloromethanesulphenamide* (X).—Anthranilic acid (13·7 g.) and trichloromethanesulphenyl chloride (15 ml.) were stirred in water (100 ml.) and chloroform (100 ml.) for 20 hr. The solid was removed and washed with dilute hydrochloric acid to free it from anthranilic acid. The *sulphenamide* (22·7 g.), from ethyl acetate, had m. p. 177—178°, and yielded a brown-green liquid with gas evolution (Found: C, 33·6; H, 2·2; N, 4·8. $C_8H_6Cl_3NO_2S$ requires C, 33·6; H, 2·1; N, 4·9%); ν (C=O) 1658 cm.$^{-1}$, (NH) 3312 cm.$^{-1}$, and absorption in the range 2500—3000 cm.$^{-1}$ characteristic of the carboxyl group (in KBr). The acid is insoluble in sodium hydrogen carbonate, but will dissolve on addition of a little ethyl acetate.

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RESEARCH DEPARTMENT, BOOTS PURE DRUG CO. LTD.,
NOTTINGHAM.

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