685. *Derivatives of Benzo*-1 : 4-*dioxan. Part IV.**

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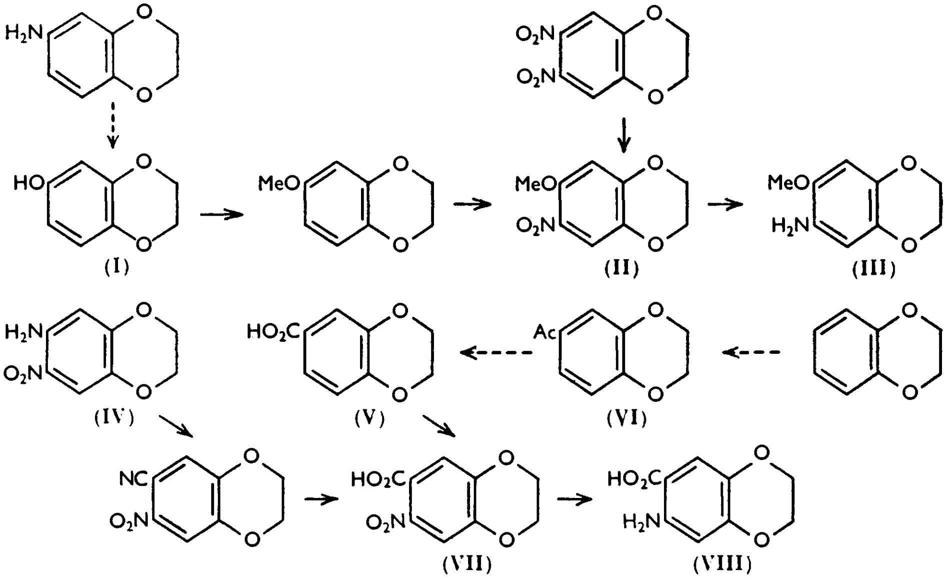
Preparation and orientation of some derivatives of 6-hydroxybenzo-1 : 4-dioxan and benzo-1 : 4-dioxan-6-carboxylic acid are reported.

The reactions described in this paper are represented in the annexed chart; those marked with a broken arrow have been recorded elsewhere. The reactions have been carried out with conventional methods. The preparation of 6-hydroxybenzo-1 : 4-dioxan (I) is given below in detail, since the published procedure [1] gave a different yield. For the preparation of 6-acetylbenzo-1 : 4-dioxan [2] (VI) and benzo-1 : 4-dioxan-6-carboxylic acid (V) [2] no experimental details have hitherto been given.



The structure of the mononitro-derivative (II) of 6-methoxybenzo-1 : 4-dioxan was

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* Parts I—III, *J.*, 1954, 18, 1868; 1955, 1313.

[1] I. G. Farbenind. A.-G., B.P. 458,573/1936; J. R. Geigy, B.P. 566,732/1945.

[2] J. R. Geigy, U.S.P. 2,383,874/1945.

established by the formation of this compound on treatment of 6 : 7-dinitrobenzo-1 : 4-dioxan with sodium methoxide in methanol. That of the mononitro-derivative (VII) of benzo-1 : 4-dioxan-6-carboxylic acid was proved by showing it to be identical with 7-nitrobenzo-1 : 4-dioxan-6-carboxylic acid obtained by converting 6-amino-7-nitrobenzo-1 : 4-dioxan (IV) into 6-cyano-7-nitrobenzo-1 : 4-dioxan, followed by hydrolysis of the cyano-group.

Nitration of benzo-1 : 4-dioxan-6-carboxylic acid gives 7-nitrobenzo-1 : 4-dioxan-6-carboxylic acid as the main product, although the reaction mixture also contains a second, unidentified mononitro-compound. 7-Nitrobenzo-1 : 4-dioxan-6-carboxylic acid can be decarboxylated partly, *e.g.*, when heated in glacial acetic acid; 6-nitrobenzo-1 : 4-dioxan was isolated from its crystallisation product; thus purification of crude 7-nitrobenzo-1 : 4-dioxan-6-carboxylic acid may present difficulties.

EXPERIMENTAL

M. p.s are corrected.

6-*Hydroxybenzo*-1 : 4-*dioxan* (I) (cf. Geigy [1]).—6-Aminobenzo-1 : 4-dioxan [3] (180 g.) was diazotised in N-sulphuric acid (1 l.) with sodium nitrite (51 g.) in water (250 ml.). The solution was then added during 2 hr. to a boiling mixture of sulphuric acid (400 ml.; *d* 1·84) and water (400 ml.). The thick red oil formed was decanted and distilled in a vacuum, giving crude 6-*hydroxybenzo*-1 : 4-*dioxan* (108 g., 60%). The pure compound boiled at 170°/12 mm. (Found : C, 63·0; H, 5·4. Calc. for $C_8H_8O_3$: C, 63·1; H, 5·3%).

6-*Methoxybenzo*-1 : 4-*dioxan*.—6-Hydroxybenzo-1 : 4-dioxan (I) (30 g.), dissolved in 2N-potassium hydroxide (100 ml.), was shaken with dimethyl sulphate (27 g.), added in three equal portions during 15 min. The mixture was then refluxed for 30 min. and, after cooling, extracted with ether. After evaporation of the ether the *methyl ether* (30 g., 90%) was distilled in a vacuum (b. p. 110°/10 mm.) (Found : C, 64·9; H, 6·0. $C_9H_{10}O_3$ requires C, 65·1; H, 6·0%).

6-*Acetoxybenzo*-1 : 4-*dioxan*.—Refluxing 6-hydroxybenzo-1 : 4-dioxan (I) (12 g.) with acetic anhydride (10 g.) in benzene (25 ml.) containing a drop of concentrated sulphuric acid for 10 min. gave the *acetoxy-compound* (12·5 g., 80%), b. p. 150—152°/6 mm. (Found : C, 61·8; H, 5·3. $C_{10}H_{10}O_4$ requires C, 61·8; H, 5·2%).

6-*Methoxy*-7-*nitrobenzo*-1 : 4-*dioxan* (II).—(*a*) To 6-methoxybenzo-1 : 4-dioxan (50 g.) in glacial acetic acid (500 ml.) at 25°, nitric acid (*d* 1·4; 25 ml.) in acetic acid (68 ml.) was added during 1½ hr. The precipitated *nitro-compound* was filtered off and washed with 50% acetic acid and then with alcohol (yield, 47 g.). Pouring the filtrate into water gave a further 10 g. (total, 90%). Crystallisation from alcohol raised the m. p. to 144·4—144·8° (Found : N, 6·6, 6·6. $C_9H_9O_5N$ requires N, 6·6%).

(*b*) 6 : 7-Dinitrobenzo-1 : 4-dioxan [4] was refluxed with an excess of 0·1N-methanolic sodium methoxide for 15 min. After repeated crystallisation from alcohol the product had m. p. 143·0—143·6° alone or mixed with the material obtained as in (*a*).

6-*Amino*-7-*methoxybenzo*-1 : 4-*dioxan* (III).—Cast-iron powder (8 g.), water (50 ml.), and hydrochloric acid (*d* 1·19; 0·8 ml.) were refluxed for 5 min. While nitrogen was passed through the flask 6-methoxy-7-nitrobenzo-1 : 4-dioxan (II) (7 g.) was added in portions during 30 min. Refluxing was continued for another 15 min. The mixture was cooled to 70°, made alkaline by sodium hydroxide solution, and filtered. The filtrate and the precipitate were extracted with benzene, the dried extracts were treated with hydrogen chloride, and the 6-amino-7-methoxybenzo-1 : 4-dioxan hydrochloride was filtered off. The free *base* (5·5 g., 90%) was obtained by treating the hydrochloride with aqueous alkali and had m. p. 63·8—64·5° (Found : N, 7·65, 7·7. $C_9H_{11}O_3N$ requires N, 7·7%).

The amine (2 g.) with acetic anhydride (2 ml.) in boiling benzene (10 ml.) gave the *acetyl* derivative (2 g.), m. p. 148·6—148·9° (from 1 : 1 aqueous alcohol) (Found : N, 6·2, 6·2. $C_{11}H_{13}O_4N$ requires N, 6·3%).

6-*Acetylbenzo*-1 : 4-*dioxan* [2] (VI).—To a stirred suspension of aluminium chloride (200 g.) in carbon disulphide (600 g.) at 10—15° a solution of acetyl chloride (118 g.) and benzo-1 : 4-dioxan

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[3] Cf. Heertjes and Dahmen, *Rec. Trav. chim.*, 1943, **62**, 620.

Heertjes, Dahmen, and Wierda, *ibid.*, 1941, **60**, 569.

(194 g.) in carbon disulphide (450 g.) was added during 3½ hr. Thereafter the mixture was stirred at room temperature for 3 hr., refluxed for 3 hr., cooled, and poured on ice (2 kg.). The crude white acetyl compound was filtered off, washed with water, and crystallised once from 60% alcohol (yield, 224 g., 88%; m. p. 82—87°). Several crystallisations from dilute alcohol or acetone were necessary to obtain the pure compound, m. p. 86—87·5° (Found: C, 67·3; H, 5·6. Calc. for $C_{10}H_{10}O_3$: C, 67·4; H, 5·6%).

Benzo-1 : 4-*dioxan*-6-*carboxylic Acid*[2] (V).—6-Acetylbenzo-1 : 4-dioxan (VI) (9 g.) was added in portions to a stirred 13% solution of sodium hypochlorite in water (110 ml.). The temperature was kept at 65°, first by the heat of reaction and later by external heat. After stirring of the mixture for 30 min. 25% sodium hydrogen sulphite solution (10 ml.) was added to remove excess of hypochlorite. The mixture was cooled to 25°, filtered, and acidified with hydrochloric acid. The white precipitate of benzo-1 : 4-dioxan-6-carboxylic acid was filtered off, washed with water, and crystallised once from 60% alcohol (yield, 8·5 g., 94%; m. p. 131·5—133°). Further purification was effected by continued crystallisation from dilute alcohol; the m. p. of the pure compound was 137—138° (Found: C, 59·7; H, 4·4. Calc. for $C_9H_8O_4$: C, 60·0; H, 4·4%).

7-*Nitrobenzo*-1 : 4-*dioxan*-6-*carboxylic Acid* (VII).—(*a*) To a stirred solution of benzo-1 : 4-dioxan-6-carboxylic acid (20 g.) in glacial acetic acid (200 ml.) a mixture of nitric acid (*d* 1·52; 5 ml.) and sulphuric acid (*d* 1·84; 35 ml.) was added at room temperature during 30 min. After another 30 minutes' stirring the mixture was poured into water (300 ml.). The precipitated 7-*nitro-acid* was filtered off, washed with acetic acid to remove benzo-1 : 4-dioxan-6-carboxylic acid, and crystallised once from dilute alcohol (yield, 17·5 g., 70%; m. p. 220°). The m. p. of the pure compound, obtained after several crystallisations, was 230—231° (Found: N, 6·2, 6·3. $C_9H_7O_6N$ requires N, 6·2%).

(*b*) 6-Amino-7-nitrobenzo-1 : 4-dioxan[5] was diazotised in 50% sulphuric acid, then added during 2 hr. to sodium cuprocyanide in boiling water. The resulting solution was filtered hot and on cooling deposited yellowish-white 6-cyano-7-nitrobenzo-1 : 4-dioxan. The crude cyanide was refluxed with 50% sulphuric acid for 10 hr., then diluted with an equal amount of water, and sodium nitrite solution was added slowly. The precipitate, when crystallised from dilute alcohol, had m. p. 226·5—227·5°, not depressed on admixture with the product obtained as above.

7-*Aminobenzo*-1 : 4-*dioxan*-6-*carboxylic Acid* (VIII).—7-Nitrobenzo-1 : 4-dioxan-6-carboxylic acid (2·7 g.) in 97·8% alcohol (50 ml.) was hydrogenated in presence of Raney nickel at 25°. The solution was filtered and the filtrate concentrated in a vacuum. The separated 7-*amino-benzo*-1 : 4-*dioxan*-6-*carboxylic acid* was filtered off (1·6 g., 65%). Crystallised from dry methanol, it had m. p. 191—192° (Found: N, 7·2, 7·3. $C_9H_9O_4N$ requires N, 7·2%).

Acetylation as above gave the *acetamido-acid* (98%), m. p. 231—232° (from 60% alcohol) (Found: N, 5·9, 6·0. $C_{11}H_{11}O_5N$ requires N, 5·9%).

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[5] Heertjes and Revallier, *Rec. Trav. chim.*, 1950, **69**, 262.