Derivatives of Benzo-1 : 4-*dioxan. Part I. Some Halogenated Benzo*-1 : 4-*dioxans and Amino- and Nitro-derivatives thereof.*

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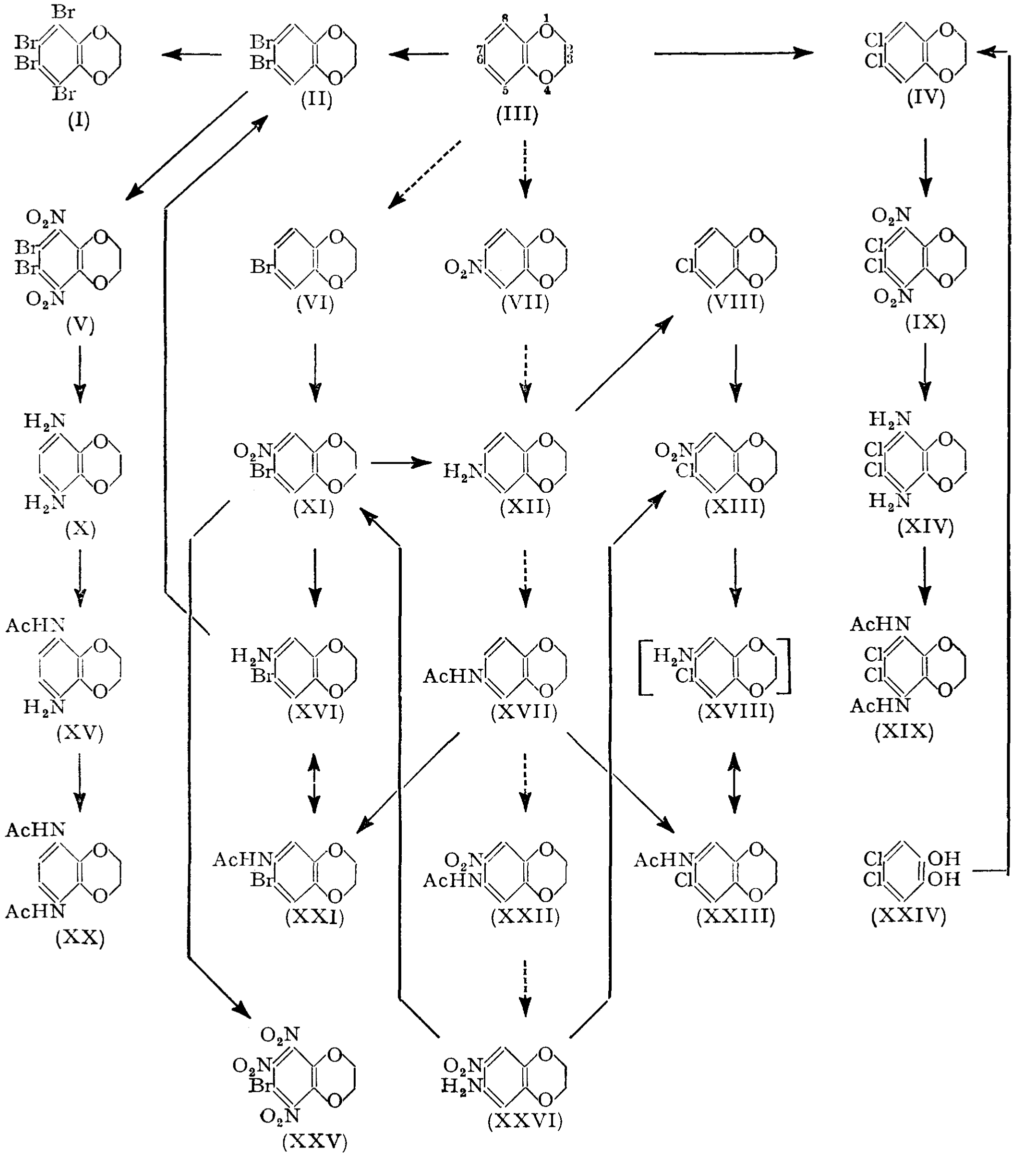
Standard methods are used to prepare and orientate 6-chloro-, 6-bromo-, 6 : 7-dichloro-, and 6 : 7-dibromo-benzo-1 : 4-dioxan and some nitro- and amino-derivatives thereof.

IN an investigation of dyes, particularly azo-dyes, derived from benzo-1 : 4-dioxan (III), several simple derivatives were required. The present paper records the preparation of the derivatives mentioned in the Summary; the dyes will be described later.

The reactions realised are shown in the annexed chart; those marked with broken arrows have already been recorded elsewhere. The methods used were halogenation in acetic acid, nitration (usually with nitric acid alone), reduction of nitro- to amino-groups (usually with stannous chloride), and diazo-reactions.

The orientations of the 6-nitro-, 6-amino-, and 6-amino-7-nitro-compounds being known, those of the others follow from the interconversions effected, except that for (I) and (XXV) the 5 : 8-substitution is not rigidly proved.

The following points merit mention. 6-Bromo-7-nitrobenzo-1 : 4-dioxan (XI) is unaffected by iron or tin in dilute hydrochloric acid; stannous chloride in aqueous-ethanolic hydrochloric acid reduces the nitro-groups but also removes the bromine; the amino-bromo-compound (XVI) is obtained by cathodic reduction, but in only 24% yield, and is best prepared from 6-acetamidobenzo-1 : 4-dioxan (XVII) by bromination and subsequent hydrolysis. Stannous chloride also removed the bromine from (V), and this is the best method for preparation of the 5 : 8-diamine since the 5 : 8-dinitro-compound can be obtained only indirectly and in poor yield (unpublished work). On the other hand, the chlorine in 6 : 7-dichloro-5 : 8-dinitrobenzo-1 : 4-dioxan (IX) was removed by stannous



chloride in only one experiment, the product in all the others being the 5 : 8-diamino-6 : 7-dichloro-compound (XIV). 5-Acetamido-8-aminobenzo-1 : 4-dioxan (XV) yields azo-dyes giving bright fast colours.

EXPERIMENTAL

6-*Bromobenzo*-1 : 4-*dioxan* (VI).—This, b. p. 153—154°/23 mm., was obtained in 60% yield as described by Ghosh (*J.*, 1915, **107**, 1592) who gave b. p. 275—276°/754 mm. but did not orientate the compound.

6-*Bromo*-7-*nitrobenzo*-1 : 4-*dioxan* (XI).—(*a*) To a stirred mixture of 6-bromobenzo-1 : 4-dioxan (18·35 g.) in water (25 ml.) at 60° nitric acid (*d* 1·52; 5·5 ml.) was added dropwise. The precipitated *nitro*-compound crystallised from ethanol and then acetic acid as faintly yellow needles (60%), m. p. 171·9—172·1° (Found: N, 5·4, 5·3. $C_8H_6O_4NBr$ requires N, 5·4%).

(*b*) 6-Amino-7-nitrobenzo-1 : 4-dioxan (XXVI) (5 g.) in a mixture of concentrated sulphuric acid (10 ml.) and water (25 ml.) was diazotised at 20° with a solution of sodium nitrite (1·75 g.) in water (3 ml.) and then poured into a boiling cuprous bromide solution prepared by boiling copper sulphate (1·6 g.), copper turnings (0·5 g.), sodium bromide dihydrate (4 g.), concentrated sulphuric acid (2 ml.), and water (25 ml.) under reflux for 3 hr. The yellow precipitate (60% yield) had m. p. and mixed m. p. 170·1—171·1° after repeated crystallisation from ethanol.

6-*Bromo*-5 : (?)7 : (?)8-*trinitrobenzo*-1 : 4-*dioxan* (XXV).—6-Bromo-7-nitrobenzo-1 : 4-dioxan (2·85 g.) was dissolved in nitric acid (*d* 1·52; 12 ml.) at 0°, kept for 2 hr. at room temperature, and then poured into ice-water (80 ml.). The precipitated *trinitro*-compound (3·0 g., 80%) crystallised from 1 : 1 ethanol–acetic acid and then *iso*butanol, yielding faintly yellow needles, m. p. 248·2—248·6° (Found: N, 11·8, 11·9. $C_8H_4O_8N_3Br$ requires N, 12·0%).

6-*Amino*-7-*bromobenzo*-1 : 4-*dioxan* (XVI).—(*a*) Cathodic reduction of 6-bromo-7-nitrobenzo-1 : 4-dioxan was effected (see Heertjes and Dahmen, *Rec. Trav. chim.*, 1943, **62**, 620) in a copper vessel as cathode, with a lead anode. The catholyte consisted of the nitro-compound (5 g.) in ethanol (150 ml.) containing concentrated hydrochloric acid (20 ml.) and stannous chloride dihydrate (1·5 g.), and the anolyte was aqueous sulphuric acid (1 : 4). A current of 2 amp., at a density of 3—7 amp./100 cm.^{2}, was passed through the solution at 25—30° for 2½ hr. Unchanged nitro-compound was filtered off from the cathode liquid, the filtrate basified with sodium hydroxide solution, and the amine extracted with ether. Passage of hydrogen chloride through the extract precipitated the hydrochloride (1·25 g., 24%). To a solution of this in the minimum amount of water, sodium acetate (2 g.) and then acetic anhydride (2 ml.) were added. After the mixture had been kept for 15 min., with occasional shaking, the excess of anhydride was destroyed by boiling. 6-*Acetamido*-7-*bromobenzo*-1 : 4-*dioxan* (XXI) (1·02 g., 80%) separated from the solution on cooling and, when recrystallised from water, had m. p. 179·1—179·4° (Found: N, 5·2, 5·2. $C_{10}H_{10}O_3NBr$ requires N, 5·15%).

(*b*) Bromine (9·73 g.) in acetic acid (10 ml.) was added, dropwise with stirring at room temperature, to 6-acetamidobenzo-1 : 4-dioxan (11·2 g.) in acetic acid (40 ml.) and water (10 ml.). After a further 10 min.' stirring, pouring into water (300 ml.) precipitated the bromo-amide (14·0 g., 89%) which, recrystallised from dilute acetic acid, had m. p. 178·7—179·0°, not depressed on admixture with the compound prepared as in (*a*).

The amide (10 g.) was boiled under reflux for 15 min. with concentrated hydrochloric acid (20 ml.) and ethanol (20 ml.). The cooled solution was diluted, made alkaline with sodium hydroxide, and extracted with benzene. Passage of hydrogen chloride through the dried benzene extract precipitated the amine hydrochloride (6·4 g., 70%).

6 : 7-*Dibromobenzo*-1 : 4-*dioxan* (II).—(*a*) Treatment of benzo-1 : 4-dioxan (300 g.) in acetic acid (500 ml.) at 30° with bromine (730 g.) in acetic acid (500 ml.) and storage overnight gave a precipitate of the 6 : 7-dibromo-compound (518 g., 80%), which formed colourless needles, m. p. 139·6—140·0° (from ethanol). Ghosh (*loc. cit.*) reports m. p. 138°.

(*b*) Diazotisation of 6-amino-7-bromobenzo-1 : 4-dioxan hydrochloride (5 g.) in water (20 ml.) and concentrated sulphuric acid (4 ml.) with sodium nitrite (1·4 g.) in water (2·5 ml.) at 10°, and pouring of the solution into boiling cuprous bromide solution (from 1·26 g. of cupric sulphate as before) gave crude dibromo-compound (3·5 g., 63%) which on repeated crystallisation from dilute acetic acid and from ethanol had m. p. 137·0—139·2°, not depressed on admixture with material prepared as in (*a*) but still having a green colour.

(?)5 : 6 : 7 : (?)8-*Tetrabromobenzo*-1 : 4-*dioxan* (I).—The mother-liquor after separation of the dibromo-compound as in (*a*) above was evaporated on the water-bath. Repeated crystallisation of the residue (10 g.) from ethanol yielded the tetrabromo-compound as colourless needles, m. p. 212·8—213·4° (Found: Br, 71·3, 71·6. Calc. for $C_8H_4O_2Br_4$: Br, 70·8%). Horner and Merz (*Annalen*, 1950, **570**, 89) report a product of m. p. 210°.

6 : 7-*Dibromo*-5 : 8-*dinitrobenzo*-1 : 4-*dioxan* (V).—6 : 7-Dibromobenzo-1 : 4-dioxan (297 g.) was added gradually, with stirring, to nitric acid (*d* 1·52; 100 ml.), cooled in ice–salt so that the temperature did not exceed 5°. After a further 1·5 hr.' stirring the mixture was poured into ice-water. Repeated crystallisation of the crude product (361 g., 93%) from 1 : 5 ethanol–acetic acid gave 6 : 7-*dibromo*-5 : 8-*dinitrobenzo*-1 : 4-*dioxan* as faintly yellow needles, m. p. 318—319° (decomp.) (Found: N, 7·5, 7·6. $C_8H_4O_6N_2Br_2$ requires N, 7·7%).

5 : 8-*Diaminobenzo*-1 : 4-*dioxan* (X).—6 : 7-Dibromo-5 : 8-dinitrobenzo-1 : 4-dioxan (80 g.) was heated with stannous chloride dihydrate (600 g.) in concentrated hydrochloric acid (600 ml.) and ethanol (600 ml.) on the water-bath with efficient stirring. At 60° a rapid exothermic reaction occurred. When the temperature was kept at 60—70° reaction was complete in *ca.* 30 min. and a clear brown solution resulted. Most of the ethanol was then removed at

reduced pressure and concentrated potassium hydroxide solution was added until all the tin compounds had redissolved. The remaining precipitate and the solution were extracted separately with benzene, and the diamine hydrochloride (41·5 g., 84%) was precipitated from the extracts by hydrogen chloride. Alternatively, the benzene extracts were concentrated to small volume, whereafter the *diamine*, m. p. 99·1—99·7° (from benzene), crystallised on cooling (Found: N, 16·8, 16·7. $C_8H_{10}O_2N_2$ requires N, 16·9%).

Treatment of the amine in benzene with an excess or 1 mol. of acetic anhydride at room temperature gave a precipitate of, respectively, the *diacetyl* (XX), needles (from ethanol; 64% yield), m. p. 287—289° (Found: N, 11·2, 11·1. $C_{12}H_{14}O_4N_2$ requires N, 11·2%), or the *monoacetyl* derivative (XV), m. p. 141·2—141·9° (from benzene) (Found: N, 13·3, 13·3. $C_{10}H_{12}O_3N_2$ requires N, 13·5%).

6 : 7-*Dichlorobenzo*-1 : 4-*dioxan* (IV).—(*a*) Chlorine was passed into a solution of benzo-1 : 4-dioxan (76 g.) in acetic acid (200 ml.) at 10—20° until a yellow colour persisted. The dichloro-compound (80·7 g., 71%) separated and crystallised from ethanol as colourless needles, m. p. 150·6—151·1°.

(*b*) (Cf. Heertjes, Dahmen, and Wierda, *Rec. Trav. chim.*, 1941, **60**, 569.) To a solution of 4 : 5-dichloropyrocatechol (7·5 g.; m. p. 116—117°; Slooff, *ibid.*, 1935, **54**, 995) and 1 : 2-dibromoethane (75 g.) in ethylene glycol (50 ml.) at 140°, anhydrous potassium carbonate was added gradually, with good stirring, until the mixture no longer gave a blue colour with ferric chloride (3—4 hr.). The mixture was cooled and poured into water (300 ml.). The precipitated 6 : 7-*dichlorobenzo*-1 : 4-*dioxan* (6·8 g., 70%), crystallised as above, had m. p. 151·4—152·1°, or 150·8—152·0° when mixed with the product from (*a*) (Found: Cl, 34·6, 34·5. $C_8H_6O_2Cl_2$ requires Cl, 34·6%).

6 : 7-*Dichloro*-5 : 8-*dinitrobenzo*-1 : 4-*dioxan* (IX).—When nitrated as described for the bromo-analogue, 6 : 7-dichlorobenzo-1 : 4-dioxan gave the *dinitro*-compound (84%), m. p. 287·7—288·6° (from acetic acid or *iso*butanol) (Found: Cl, 24·1, 23·8; N, 9·6. $C_8H_4O_6N_2Cl_2$ requires Cl, 24·0; N, 9·5%).

5 : 8-*Diamino*-6 : 7-*dichlorobenzo*-1 : 4-*dioxan* (XIV).—Reduction of the foregoing compound with stannous chloride and hydrochloric acid in ethanol, as described for the bromo-analogue, and acetylation in benzene at *ca.* 50° (not at room temperature) gave 5 : 8-*bisacetamido*-6 : 7-*dichlorobenzo*-1 : 4-*dioxan* (XIX), needles (from ethanol), m. p. 299·0—300·3° (decomp.) (Found: N, 8·9, 8·85. $C_{12}H_{12}O_4N_2Cl_2$ requires N, 8·8%).

Alternatively, hydrogen chloride was passed into a mixture of stannous chloride dihydrate (50 g.) in acetic acid (100 ml.) until a clear solution was obtained. 6 : 7-Dichloro-5 : 8-dinitrobenzo-1 : 4-dioxan (5 g.) was then added and the mixture heated. At 60° reaction set in, with rise in temperature to *ca.* 90°. Reaction was complete in about 1 hr., and the crystals were then collected, basified with sodium hydroxide solution, and extracted with ether, from which the *diamine*, decomp. 137—140° (Found: N, 11·9, 11·9. $C_8H_8O_2N_2Cl_2$ requires N, 11·9%) was obtained on evaporation. The base is slowly oxidised in air.

6-*Chlorobenzo*-1 : 4-*dioxan* (VIII).—6-Aminobenzo-1 : 4-dioxan hydrochloride (39 g.) (Heertjes and Revallier, *ibid.*, 1950, **69**, 262) in water (65 ml.) and concentrated hydrochloric acid (65 ml.) was diazotised with aqueous sodium nitrite (18 g. in 40 ml.) at 0° and added slowly to a solution of cuprous chloride (30 g.) in concentrated hydrochloric acid (100 ml.). The mixture was heated at 70° until evolution of nitrogen ceased, then extracted with ether. Drying (Na_2SO_4) and evaporation of the extract, and fractionation of the residue, gave 6-*chlorobenzo*-1 : 4-*dioxan* (26 g., 76%), b. p. 98—100°/3 mm. (Found: Cl, 20·6, 20·8. $C_8H_7O_2Cl$ requires Cl, 20·8%).

6-*Chloro*-7-*nitrobenzo*-1 : 4-*dioxan* (XIII).—(*a*) A mixture of nitric acid (*d* 1·52; 1·4 ml.) and sulphuric acid (*d* 1·84; 10 ml.) was added dropwise to a stirred solution of 6-chlorobenzo-1 : 4-dioxan (5 g.) in acetic acid (50 ml.) at 15°. Pouring the whole into water and crystallisation of the precipitate from 1 : 1 acetone–acetic acid gave the *nitro*-compound (4·5 g., 73%), m. p. 158·5—160·2°, raised to 161·7—162·1° by repeated crystallisation (Found: N, 6·3, 6·5, 6·5. $C_8H_6O_4NCl$ requires N, 6·5%).

(*b*) 6-Amino-7-nitrobenzo-1 : 4-dioxan (6 g.) in concentrated hydrochloric acid (70 ml.) and water (30 ml.) was diazotised with sodium nitrite solution (2·5 g. in 10 ml.) and added to a solution of cuprous chloride (15 g.) in concentrated hydrochloric acid (100 ml.). Decomposition at 70°, dilution with water, and crystallisation as in (*a*) gave the chloro-nitro-compound, m. p. and mixed m. p. 160·2—161·5°.

Derivatives of 6-*Amino*-7-*chlorobenzo*-1 : 4-*dioxan* (XVIII).—(*a*) 6-Acetamidobenzo-1 : 4-dioxan (20·4 g.) in acetic acid (100 ml.) was treated, with cooling, with chlorine (1·9 g.) in acetic acid (50 ml.). Addition of the mixture to water (300 ml.) and crystallisation of the precipitate from 50% aqueous acetone gave 6-acetamido-7-chlorobenzo-1 : 4-dioxan as needles, m. p. 171·7—172·4°.

(*b*) Hydrogenation of 6-chloro-7-nitrobenzo-1 : 4-dioxan (4 g.) in ethanol in presence of Raney nickel at room temperature, filtration, and acidification with hydrochloric acid gave 6-amino-7-chlorobenzo-1 : 4-dioxan hydrochloride (3·5 g.); a further 0·5 g. (total yield, 97%) was obtained on concentration of the mother-liquor. Acetylation, as for the bromo-analogue, gave 6-*acetamido*-7-*chlorobenzo*-1 : 4-*dioxan* (crude yield 86%), prisms, m. p. 172·9—173·5° (from 50% aqueous acetone) (mixed m. p. 171·9—172·6°) (Found: N, 6·0, 6·05. $C_{10}H_{10}O_3NCl$ requires N, 6·15%). This was reconverted into the amine hydrochloride when boiled with 1 : 1 (v/v) ethanol–concentrated hydrochloric acid.

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