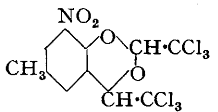
86. *The Action of Alkalis upon Substituted Benzdioxins.*

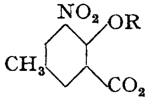
By H. Irving and (in part) E. G. Curtis.

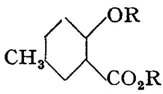
Chloral has been condensed with 2- and with 3-nitro-*p*-cresol. The action of alcoholic potash upon the 7- and the *8-nitro-6-methyl-2 : 4-bistrichloromethyl-1 : 3-benzdioxin* (IV and I) so formed, upon the corresponding amines, and upon other representatives of this heterocyclic system has been examined and found to confirm the reaction mechanisms previously put forward.

In a previous paper (J., 1934, 325) it was shown that the action of alcoholic potash in opening the hetero-ring of various derivatives of 1 : 3-benzdioxin (as I) was initiated by an attack by an ethoxyl ion at the 9-carbon atom, provided that this had been rendered sufficiently kationoid by the presence of enough, and suitably oriented, electron-attracting substituents (*e.g.*, CCl_3 groups) in positions 2 and 4 of the hetero-ring and others (*e.g.*, NO_2, CO_2H) in the 6- and/or 8-positions of the benzene ring.

8-Nitro-6-methyl-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (I) is now found to resemble the isomeric 6-nitro-7-methyl-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (Chattaway and Calvet, J., 1928, 1089), for when it was boiled with alcoholic potash the intrusion of an ethoxyl group opened the hetero-ring and *5-nitro-4-ethoxy-*m*-toluic acid* (II; R = Et, R′ = H) was obtained, whose structure was confirmed by synthesis from 4-hydroxy-*m*-toluic acid (III; R,R′ = H) through ethyl 4-ethoxy-*m*-toluate (III; R,R′ = Et) and *4-ethoxy-*m*-toluic acid* (III; R = Et, R′ = H).


(I.)

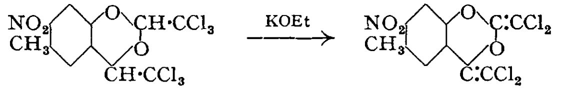

(II.)


(III.)

An unsuccessful attempt was made to synthesise the acid (II; R = Et, R′ = H) by another route in which the nitration of 4-hydroxy-*m*-toluic acid constituted the first stage. The mononitrated acid, hitherto unoriented, was shown to be 5-nitro-4-hydroxy-*m*-toluic acid (II; R,R′ = H) by decarboxylation to 3-nitro-*p*-cresol.

All the benzdioxins hitherto prepared whose hetero-rings have proved susceptible to alkaline fission have contained electron-attracting substituents in positions 6 and/or 8. In *7-nitro-6-methyl-2 : 4-bistrichloromethyl-1 : 3-benzdioxin* (IV), however, the nitro-group is situated meta to the 9-carbon atom, whence its electron-attracting effect cannot now be relayed tautomerically. It was expected that its general effect in making this 9-carbon atom feebly kationoid would be too slight to promote attack by anionoid reagents and consequent ring fission, and, in fact, when (IV) was boiled with alcoholic potash, the hetero-ring remained unbroken and *7-nitro-6-methyl-2 : 4-bisdichloromethylene-1 : 3-benzdioxin* (V) was formed.

(IV.)



(V.)

The stability conferred on the hetero-ring by an amino-group in the benzene ring (Chattaway and Calvet, *loc. cit.*) is further illustrated by the action of alcoholic potash upon *8-amino-6-methyl-2 : 4-bistrichloromethyl-1 : 3-benzdioxin* (as I), which yields *8-amino-6-methyl-2 : 3-bisdichloromethylene-1 : 3-benzdioxin* (as V). A methoxyl group is equally effective, for, when treated with alcoholic potash, the hetero-ring of *5 : 7-dichloro-6-methoxy-2 : 4-bistrichloromethyl-1 : 3-benzdioxin* remains intact, loss of two molecules of hydrogen chloride yielding 5 : 7-*dichloro*-6-*methoxy*-2 : 4-*bisdichloromethylene*-1 : 3-*benzdioxin*, which was also obtained by methylating the unsaturated dioxin previously described (Chattaway and Calvet, *loc. cit.*). Similar stability is conferred by an azo-group, for 6-*p*-tolueneazo-2 : 4-bistrichloromethyl-1 : 3-benzdioxin yields 6-p-*tolueneazo*-2 : 4-*bisdichloromethylene*-1 : 3-*benzdioxin* when treated with alcoholic potash.

In more complex derivatives of benzdioxin the critical rôle of the 9-carbon atom in determining the stability of the hetero-ring is illustrated by the action of alcoholic potash of various strengths upon *cis*- and *trans*-di-(2 : 4-bistrichloromethyl-1 : 3-benzdioxinyl)-6 : 6′-sulphone, where sulphonyl and trichloromethyl are the activating groups (Chattaway and Bell, J., 1934, 45). Similarly it is now found that, though di-(6-nitrobenzdioxinyl)-8 : 8′-methane (Chattaway and Goepp, J., 1933, 699) resembles 6-nitrobenzdioxin itself in its stability towards alkali (Chattaway and Irving, *loc. cit.*), the combined effect of nitro- and carbonyl groups in di-(6-nitrobenzdioxinyl)-8 : 8′ ketone renders the hetero-ring so prone to fission that with boiling 5% aqueous caustic soda it yields formaldehyde and 5 : 5′-*dinitro*-2 : 2′-*dihydroxy*-3 : 3′-*bishydroxymethylbenzophenone*, characterised by a *phenylhydrazone*.

EXPERIMENTAL.

8-*Nitro*-6-*methyl*-2 : 4-*bistrichloromethyl*-1 : 3-*benzdioxin* (I).—3-Nitro-*p*-cresol (10 g.; 1 mol.) and chloral hydrate (21·6 g.; 2 mols.) were dissolved in concentrated sulphuric acid (100 c.c.) and shaken vigorously at intervals for 18 hours. The product was poured on ice and washed with water and then with dilute aqueous ammonia, to remove unchanged material. After drying at 100°, the benzdioxin was recrystallised several times from boiling alcohol (solubility, about 20 g./l.) and then from glacial acetic acid, from which 8-*nitro*-6-*methyl*-2 : 4-*bistrichloromethyl*-1 : 3-*benzdioxin* (I) separated (21·5 g.; 75%) in short, colourless prisms, m. p. 175—176° (Found : Cl, 49·4. $C_{11}H_7O_4NCl_6$ requires Cl, 49·5%).

Action of alkali. (*a*) The benzdioxin (I) was unaffected by refluxing for 6 hours with excess of 2·5% alcoholic potassium acetate.

(*b*) Potassium hydroxide (10 g.; 8 mols.) in ethyl alcohol (25 c.c.) was added to a solution of the dioxin (10 g.; 1 mol.) in 100 c.c. of alcohol, whereupon a red colour developed and chloroform was liberated. The reaction was completed by gentle heating on the water-bath for 5 minutes; boiling water (200 c.c.) was then added, the solution made slightly acid with hydrochloric acid, and the alcohol removed in a rapid current of steam. From the cooled red solution so obtained, ether extracted a viscous mass of brown crystals, which were purified by solution in very dilute, hot aqueous alkali and, after boiling with animal charcoal, reprecipitated by strong acidification with hydrochloric acid. Repetition of this process several times gave 5-*nitro*-4-*ethoxy*-m-*toluic acid* (II; R = Et, R′ = H), m. p. 142°. After repeated crystallisation from light petroleum (b. p. 100—120°), in which it was sparingly soluble, it separated in slender needles, m. p. 148—149° (Found : C, 53·4; H, 4·6; N, 6·25. $C_{10}H_{11}O_5N$ requires C, 53·3; H, 4·9; N, 6·2%), which slowly developed a yellow colour on exposure to the air but gave no colour reaction with ferric chloride.

Synthesis of 4-*Ethoxy*-m-*toluic Acid* (III; R = Et, R′ = H).—Ethyl 4-ethoxy-*m*-toluate (III; R,R′ = Et), prepared by Auwers's method (*J. pr. Chem.*, 1924, **107**, 355) from ethyl 4-hydroxy-*m*-toluate, ethyl bromide, and sodium ethoxide, or by refluxing for 10 hours a suspension of 4-hydroxy-*m*-toluic acid (10 g.), ethyl sulphate (30 g.), potassium carbonate (20 g.), and dry acetone (50 c.c.), had b. p. 144—145°/10 mm. Saponification with a slight excess of boiling aqueous alcoholic potash (2 hours) gave 4-*ethoxy*-m-*toluic acid* (III; R = Et, R′ = H) in almost colourless needles, m. p. 76—78° after crystallisation from aqueous alcohol or benzene. It gave no marked colour with ferric chloride (Found : C, 66·4; H, 6·6. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

Nitration was effected by dropwise addition of nitric acid (3·3 g., *d* 1·40) to a solution of the ethoxy-acid (5 g.) in acetic acid (15 c.c.) below 5° (1 hour). 5-Nitro-4-ethoxy-*m*-toluic acid, which separated when the mixture was poured on ice, was purified as described above, forming slender needles, m. p. 148—149° alone or mixed with the specimen described above.

Decarboxylation of 5-*Nitro*-4-*hydroxy*-m-*toluic Acid* (II; R = R′ = H).—The nitro-acid, prepared by the controlled nitration of 4-hydroxy-*m*-toluic acid (Einhorn and Pfyl, *Annalen*, 1900, **311**, 51), separated from boiling benzene–acetone in colourless, friable prisms, m. p. 176—177° (Kostanecki and Niementowski, *Ber.*, 1885, **18**, 254, give m. p. 172°). The position of the nitro-group was established by refluxing the acid (3·5 g.) with quinoline (20 c.c.) for 5 hours. From the cold reaction mixture, aqueous potash extracted 3-nitro-*p*-cresol, m. p. and mixed m. p. 35—36°. Further confirmation of the position of the nitro-group is afforded by the observation that 3 : 5-dinitro-*p*-cresol is the principal product obtained when 4-hydroxy-*m*-toluic acid is rapidly treated with concentrated nitric acid at or above room temperature.

7-*Nitro*-6-*methyl*-2 : 4-*bistrichloromethyl*-1 : 3-*benzdioxin* (IV).—This was prepared from 2-nitro-*p*-cresol (63 g.; 1 mol.), chloral hydrate (140·5 g.; 2 mols.), and 850 c.c. of concentrated sulphuric acid. After 14 days the *benzdioxin*, isolated and purified as in the case of (I), was obtained in friable, colourless prisms, m. p. 143° (Found : Cl, 49·5%).

Action of alcoholic potash. A solution of the benzdioxin (IV) (1·4 g., 1 mol.) in alcohol (75 c.c.) was mixed with a solution of potassium hydroxide (3 g.; 16·5 mols.) in alcohol (40 c.c.) and boiled for ½ hour; potassium chloride separated. After filtration, addition of water yielded 7-*nitro*-6-*methyl*-2 : 4-*bisdichloromethylene*-1 : 3-*benzdioxin* (V), which crystallised from alcohol, in which it was very soluble, in colourless needles, m. p. 101°, which gradually turned red and decomposed in the air (Found : Cl, 39·5. $C_{11}H_5O_4NCl_4$ requires Cl, 39·7%).

8-*Amino*-6-*methyl*-2 : 4-*bistrichloromethyl*-1 : 3-*benzdioxin* (as I).—The nitro-compound (I) (10·3 g.) was warmed on the water-bath (½ hour) with stannous chloride (55 g.) in acetic acid (250 c.c.) and acetic anhydride (50 g.) saturated with hydrogen chloride (cf. Albert and Linnell, J., 1936, 1615). After cooling and filtration, addition of water gave 8-*amino*-6-*methyl*-2 : 4-*bistrichloromethyl*-1 : 3-*benzdioxin* as a flocculent white precipitate (7·8 g., 80%), which, after being collected and dried, crystallised from alcohol, in which it was readily soluble, in compact colourless prisms, m. p. 140° (Found : Cl, 53·7. $C_{11}H_9O_2NCl_6$ requires Cl, 53·2%). The *acetyl* derivative crystallised from alcohol, in which it was very soluble, in highly refracting, colourless prisms, m. p. 171·5° (Found : Cl, 48·3. $C_{13}H_{11}O_3NCl_6$ requires Cl, 48·2%).

Action of alcoholic potash. The amino-compound (3 g.) in alcohol (30 c.c.) was boiled with caustic potash (3 g.; 7 mols.) in alcohol (50 c.c.); potassium chloride separated. After ½ hour, when much water was added to the cold filtrate, 8-*amino*-6-*methyl*-2 : 4-*bisdichloromethylene*-1 : 3-*benzdioxin* separated. It crystallised from alcohol as a felt of colourless needles, m. p. 121° (Found : Cl, 44·0. $C_{11}H_7O_2NCl_4$ requires Cl, 43·4%). The *acetyl* derivative crystallised from alcohol in fine, long, colourless needles, m. p. 201° (Found : Cl, 38·3. $C_{13}H_9O_3NCl_4$ requires Cl, 38·4%).

Methylation of 5 : 7-*Dichloro*-6-*hydroxy*-2 : 4-*bistrichloromethyl*-1 : 3-*benzdioxin*.—The benzdioxin (15·2 g.; 1 mol.) was shaken with water (10 c.c.) and methyl sulphate (10 c.c.; 2½ mols.), and dilute aqueous potash, added in portions. 5 : 7-*Dichloro*-6-*methoxy*-2 : 4-*bistrichloromethyl*-1 : 3-*benzdioxin* separated as a dirty white, granular material (15 g.). After being dried, it crystallised from boiling acetic acid, in which it was moderately easily soluble, in clusters of fine colourless rhombs, m. p. 189—190° (Found : Cl, 60·7. $C_{11}H_6O_3Cl_8$ requires Cl, 60·4%).

5 : 7-*Dichloro*-6-*methoxy*-2 : 4-*bisdichloromethylene*-1 : 3-*benzdioxin*, similarly obtained from 5 : 7-dichloro-6-hydroxy-

2 : 4-bisdichloromethylene-1 : 3-benzdioxin (Chattaway and Calvet, J., 1928, 2913), was very soluble in acetic acid and separated thence or from boiling alcohol, in which it was much less soluble, in colourless prisms, m. p. 114·5—115° (Found : Cl, 54·0. $C_{11}H_4O_3Cl_6$ requires Cl, 53·8%). The same compound was obtained when the preceding methoxy-benzdioxin (11·3 g.; 1 mol.) was boiled for 15 minutes with a solution of caustic potash (12·2 g.; 9 mols.) in alcohol (120 c.c.).

Action of Alcoholic Potash upon 6-p-*Tolueneazo*-2 : 4-*bistrichloromethyl*-1 : 3-*benzdioxin.*—The azo-compound (4 g.; 1 mol.) (Chattaway and Calvet, *loc. cit.*) was refluxed (½ hour) with caustic potash (4·5 g.; 9 mols.) in alcohol (50 c.c.). A rapid current of steam removed the alcohol and precipitated 6-p-*tolueneazo*-2 : 4-*bisdichloromethylene*-1 : 3-*benzdioxin* (2·8 g.). This, crystallised from alcohol, in which it was moderately easily soluble, and then from acetic acid, in which it was readily soluble, formed clumps of very small, compact, orange prisms, m. p. 147—148° (Found : Cl, 34·0. $C_{17}H_{10}O_2N_2Cl_4$ requires Cl, 34·1%).

Hydrolysis of Di-(6-*nitrobenzdioxinyl*)-8 : 8′ *Ketone.*—The ketone (5 g.) was boiled with 50 c.c. of 5% caustic soda solution for 1 hour; formaldehyde was evolved. After cooling and filtration, the red solution deposited 5 : 5′-*dinitro*-2 : 2′-*dihydroxy*-3 : 3′-*bishydroxymethylbenzophenone*, which separated from dilute aqueous alcohol as a felt of tiny, colourless needles, m. p. 260° (Found : N, 7·9. $C_{15}H_{12}O_9N_2$ requires N, 7·7%). The *phenylhydrazone* separated from alcohol, in which it was very sparingly soluble, in compact, deep red rhombs, m. p. 226—227° (Found : N, 12·2. $C_{21}H_{18}O_8N_4$ requires N, 12·3%).

THE INORGANIC LABORATORIES, OXFORD UNIVERSITY. [*Received, January* 16*th*, 1943.]