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

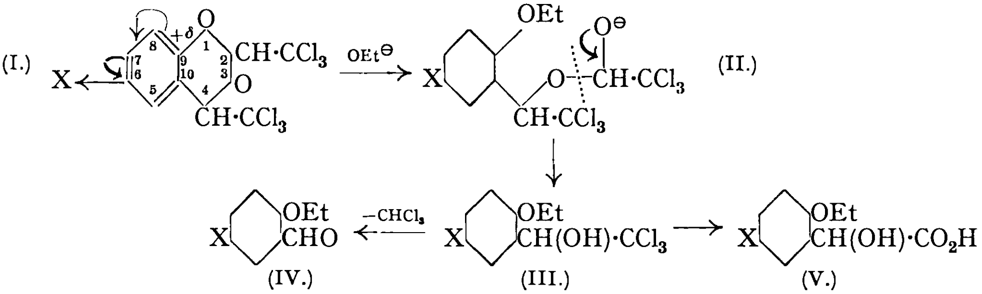
By F. D. Chattaway and H. Irving.

Many *p*-substituted phenols condense readily with formaldehyde, dichloroacetaldehyde, and trichloroacetaldehyde, producing derivatives of 1 : 3-benzdioxin.

The 6-substituted 2 : 4-bistrichloromethyl-1 : 3-benzdioxins (as I) formed by the condensation of *p*-substituted phenols with chloral are all readily attacked by alcoholic potash, the reactions being of two distinct types: (1) the heterocyclic ring is opened and a derivative of phenetole is produced; (2) hydrogen chloride is eliminated from one or both of the $:CH\cdot CCl_3$ groups, and corresponding unsaturated derivatives of benzdioxin containing one or two dichloromethylene groups are produced.

The course of the reaction in any particular case depends mainly upon the nature of the substituent in the homocyclic ring, but is influenced also by the nature of the groups attached to the 2- and 4-carbon atoms of the heterocyclic ring. When the homocyclic ring contains an electron-attracting group (*e.g.*, NO_2, CO_2H, SO_3H), the carbon atom para to this group, the 9-carbon atom, owing to a local recession of electrons, becomes strongly kationoid and consequently vulnerable towards anionic attack. The intrusion of a negative ethoxyl ion ($OEt^{\ominus}$) at this point is therefore facilitated and the heterocyclic ring is ruptured between the 9-carbon atom and the adjoining oxygen atom (compare Chattaway, J., 1926, 2720; Chattaway and Calvet, J., 1928, 1089, 689; Chattaway and Bell, this vol., p. 43).

The further action of alkali upon the product (II) initially formed causes a chloral group to be eliminated as chloroform and formate with the formation of a 5-substituted 2-ethoxy-1-βββ-trichloro-α-hydroxyethylbenzene (III) which, under the existing alkaline conditions, breaks down in two ways and yields either a substituted benzaldehyde (IV) (which is usually oxidised to some extent by the oxygen of the air to the corresponding benzoic acid) by loss of chloroform, or a substituted mandelic acid (V) by hydrolysis of the trichloromethyl group to carboxyl (compare Savarian, *Compt. rend.*, 1908, **146**, 297; Herbert, *Bull. Soc. chim.*, 1920, **27**, 45).

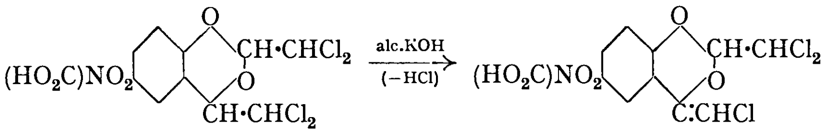


6-Nitro-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (I, $X = NO_2$) behaves typically in this manner, for, when it is heated with an excess of a 20% solution of potassium hydroxide in ethyl alcohol, chloroform and ethyl orthoformate are liberated and 5-nitro-2-ethoxymandelic acid (V, $X = NO_2$) and a small amount of 5-nitro-2-ethoxybenzoic acid are formed (Chattaway, *loc. cit.*).

The influence of the groups in the heterocyclic ring on its stability is shown when

6-nitro- or 6-carboxy-bisdichloromethyl-1 : 3-benzdioxin (VI) is heated to 50—60° with a large excess of 12% alcoholic potash: the ring is not ruptured, though in each case hydrogen chloride is removed from the :CH·$CHCl_2$ group in the 4-position with the formation of 6-nitro- or 6-carboxy-2-dichloromethyl-4-chloromethylene-1 : 3-benzdioxin (VII) (compare Chattaway and Morris, J., 1928, 3243; Chattaway and Farinholt, J., 1931, 1739).

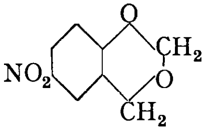
(VI.)



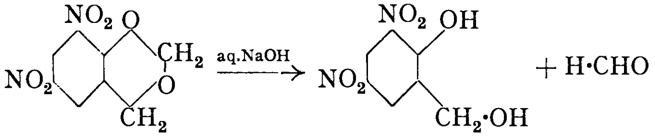
(VII.)

The general electron-attraction effect of the nitro- or the carboxyl group being less strongly reinforced by the $-CHCl_2$ group than by the more powerfully electron-attracting $-CCl_3$ group (compare Sutton, *Proc. Roy. Soc.*, 1931, *A*, **133**, 668), the hetero-ring in the former compounds (VI, VII) is stable.

The resistance of the heterocyclic ring in a benzdioxin to rupture by alkalis unless the 9-carbon atom is rendered sufficiently kationoid by an electron-attracting group in the 6-position, reinforced by sufficiently electron-attracting groups in the 2- and 4-positions, or by a second electron-attracting substituent in the 8-position of the homocyclic ring, is strikingly illustrated by the complete indifference of 6-nitro-1 : 3-benzdioxin (VIII) towards boiling 25% aqueous potash and towards boiling alcoholic potassium ethoxide, whilst the heterocyclic ring in 6 : 8-dinitro-1 : 3-benzdioxin (IX) is opened even by boiling 1% aqueous potash, formaldehyde and 3 : 5-*dinitrosaligenin* (X) being formed:



(VIII.)

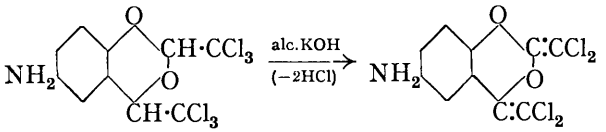


(IX.) (X.)

When the 9-carbon atom is activated by two nitro-groups appropriately situated in the homocyclic ring, as well as by two trichloromethyl groups in the heterocyclic ring, rupture of the latter is still more easy; *e.g.*, the hetero-ring in 6 : 8-dinitro-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (XIX) is opened smoothly and quantitatively by alcoholic potash even at 0°, ωω-dichloro-3 : 5-dinitro-2-ethoxyacetophenone (XXI) being formed (compare Chattaway and Morris, J., 1927, 2016).

Whilst it is thus clear that the presence of an electron-attracting group in the 6- or the 8-position of a substituted benzdioxin makes the 9-carbon atom kationoid and facilitates ring fission, the presence of an electron-donating group ($-NH_2$, $-OH$, $-O^{\ominus}$) renders the 9-carbon atom anionoid and the heterocyclic ring resistant towards anionic attack.* For example, when boiled with excess of 20% alcoholic potash, 6-amino-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (XI) yields 6-amino-2 : 4-bisdichloromethylene-1 : 3-benzdioxin (XII), and 5 : 7-dichloro-6-hydroxy-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (as XI)

(XI.)



(XII.)

similarly yields 5 : 7-dichloro-6-hydroxy-2 : 4-bisdichloromethylene-1 : 3-benzdioxin (as XII). In each case, the heterocyclic ring remains unbroken, the activating effect of the two $-CCl_3$ groups being insufficient to overcome the more powerfully deactivating effect of the electron-donating amino- or hydroxyl group.

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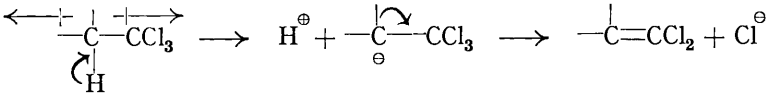
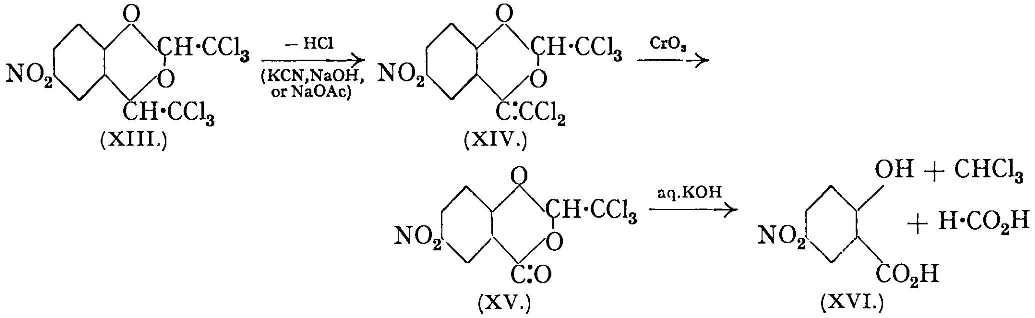
* The resistance of 4 : 5-dibromocatechol methylene ether to sodium alkoxide, which opens the heterocyclic ring in 4 : 5-dinitrocatechol methylene ether (Parijs, *Rec. trav. chim.*, 1930, **49**, 40) and in 4-nitrocatechol methylene ether (G. M. and R. Robinson, J., 1917, **111**, 929), is a similar case. In the latter reaction, as would be expected, the alkoxy-group is introduced para to the nitro-group.

An electron-attracting group in the 6-position of a 2 : 4-bistrichloromethyl-1 : 3-benzdioxin (as I) not only renders the heterocyclic ring susceptible to rupture by alkalis, but also enhances the positive character and reactivity of the hydrogen atoms in the groups :CH·CCl$_3$ attached in the 2- and 4-positions. Elimination of hydrogen chloride from such groups can therefore be effected with unusual ease as follows,



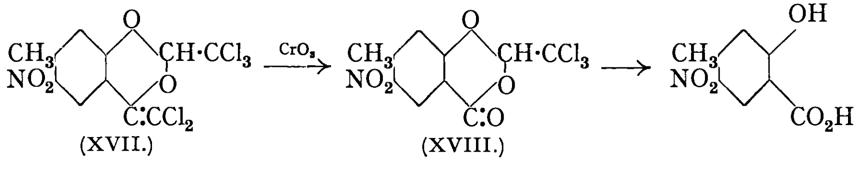
even when such mild alkaline conditions are employed that the heterocyclic ring itself remains unbroken. For example, a very dilute boiling alcoholic solution of potassium cyanide (Chattaway and Irving, J., 1929, 1041) or of caustic soda (Lapworth, Peters, and Cocker, J., 1931, 1388) or even of anhydrous sodium acetate will remove one molecule, and one molecule only, of hydrogen chloride from 6-nitro-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (XIII), yielding 6-nitro-2-trichloromethyl-4-dichloromethylene-1 : 3-benzdioxin (XIV).

Since, however, in this compound (XIII) the effect of the nitro-group can be transmitted to neither of the :CH·CCl$_3$ groups through a conjugate series of bonds, only its "field" effect can be in question, and a preferential activation of the hydrogen atom attached to the nearest carbon atom, the 4-carbon atom, appears most probable. That elimination of hydrogen chloride actually occurs at this point * is shown by oxidising the unsaturated compound (XIV) with chromic acid: the :CCl$_2$ group is replaced by an atom of oxygen and *6-nitro-4-keto-2-trichloromethyl-1 : 3-benzdioxin* (XV) is formed, which yields chloroform and 5-nitrosalicylic acid (XVI) when warmed with dilute aqueous alkali.



(XIII.) (XIV.) (XV.) (XVI.)

Similarly, when refluxed with potassium cyanide in alcoholic solution, 6-nitro-2 : 4-bistrichloromethyl-7-methyl-1 : 3-benzdioxin (as I) yields *6-nitro-2-trichloromethyl-4-dichloromethylene-7-methyl-1 : 3-benzdioxin* (XVII). This is oxidised by chromic acid † to *6-nitro-4-keto-2-trichloromethyl-7-methyl-1 : 3-benzdioxin* (XVIII), which yields 5-nitro-2-hydroxy-4-methylbenzoic acid and chloroform on warming with aqueous alkalis.



(XVII.) (XVIII.)

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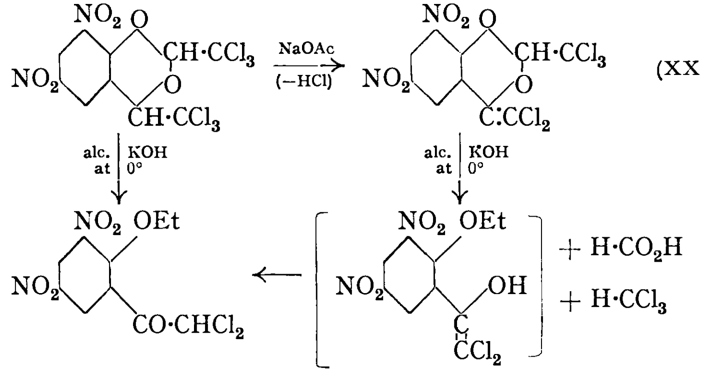
* 6-Carboxy(or carbethoxy)-2-dichloromethyl-4-chloromethylene-1 : 3-benzdioxin (as VI), which is obtained by the action of potassium hydroxide (but not potassium cyanide) upon an alcoholic solution of 6-carboxy(or carbethoxy)-2 : 4-bisdichloromethyl-1 : 3-benzdioxin (as VII), has already been shown to have its double bond in the 4-position by independent reasoning (compare Chattaway and Farinholt, J., 1931, 1737).

† When the simple benzdioxins derived from formaldehyde are oxidised by chromic acid, the 4-position only is attacked: *e.g.*, 6 : 8-dinitro-1 : 3-benzdioxin yields 6 : 8-dinitro-4-keto-1 : 3-benzdioxin (Chattaway and Irving, J., 1931, 2492).

In the case of 6 : 8-dinitro-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (XIX), where the heterocyclic ring is even more sensitive to anionic attack than that in the mononitro-compound (XIII), when exceptionally mild alkaline conditions are employed, such as refluxing the compound with alcoholic sodium acetate, it is possible to remove one molecule only of hydrogen chloride, 6 : 8-dinitro-2-trichloromethyl-4-dichloromethylene-1 : 3-benzdioxin (XX) being produced. Although this compound is destructively oxidised by chromic acid, and therefore it has not been possible to prepare the corresponding 4-keto-derivative, the existence of the dichloromethylene group in the 4-position is proved by the action of cold alcoholic potash, whereby chloroform and ωω-dichloro-3 : 5-dinitro-2-ethoxy-acetophenone (XXI) are produced. The latter compound is also formed quantitatively by the action at 0° of alcoholic potash upon the original benzdioxin (XIX) itself.

(XIX.) (XX.) (XXI.)



It is not possible to remove a second molecule of hydrogen chloride from the 2-position in 6-nitro(or 6 : 8-dinitro)-2-trichloromethyl-4-dichloromethylene-1 : 3-benzdioxin (XIV or XX), since, the 2-hydrogen atom not being sufficiently activated,* the heterocyclic ring, which has been rendered very susceptible to anionic attack by the electron-attracting substituents in the 6- (or 6 : 8-)position of the homocyclic ring, would be preferentially attacked under such strongly alkaline conditions as would be necessary.

Whilst electron-attracting substituents in the 6-position of a substituted 2 : 4-bistrichloromethyl-1 : 3-benzdioxin (as I) activate the hydrogen atom attached to the 4-carbon atom and promote the facile elimination of hydrogen chloride from the $:CH\cdot CCl_3$ group attached at this point, a similarly situated electron-donating group (NH_2, OH), in addition to rendering the heterocyclic ring very stable, should de-activate the 4-hydrogen atom and prevent, or at least markedly hinder, any such loss of hydrogen chloride. Such hindrance is in fact observed, for 6-amino-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (XI) can be recovered quantitatively unchanged after having been refluxed for 3 hours with an excess of an alcoholic solution of anhydrous sodium acetate, or potassium cyanide, that is, under conditions which readily effect the elimination of hydrogen chloride from the corresponding 6-nitro-compound (XIII) (compare p. 327).

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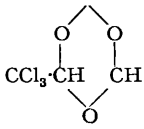
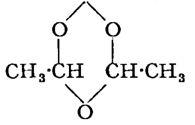
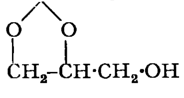
* That the elimination of hydrogen chloride in these reactions does not occur in the 2-position is supported by the fact that in other compounds which contain a $:CH\cdot CCl_3$ group situated between two oxygen atoms, as, *e.g.*, the cyclic acetals para-chloral (XXII) (Chattaway and Kellett, J., 1928, 2709), 2-trichloromethyl-4 : 6-dimethyl-1 : 3 : 5-trioxan (XXIII) (Helferich and Besler, *Ber.*, 1924, **57**, 1278), and chloral glycerol (XXIV) (Hibbert, Morazain, and Paquet, *Canadian J. Research*, 1930, **24**, 21091),



(XXII.)



(XXIII.)



(XXIV.)

the removal of hydrogen chloride by alkali does not occur except under conditions which bring about disruption of the heterocyclic ring.

Since, however, an electron-donating group in the 6-position protects the heterocyclic ring from rupture by anionic attack (p. 327), the behaviour of the $\vdots CH\cdot CCl_3$ group in such a compound towards boiling concentrated alkali should resemble that of such a group when attached to an indifferent hydrocarbon, as, *e.g.*, in the diaryltrichloroethanes, $Ar_2CH\cdot CCl_3$, where hydrogen chloride can be removed under sufficiently strongly alkaline conditions, and the corresponding dichloromethylene compounds, $Ar_2C\colon CCl_2$, formed. This is found to be the case, for with excess of boiling 20% alcoholic potash (20 mols.), hydrogen chloride is removed from both the 4- and the 2-position in 6-amino-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (XI), the heterocyclic ring remaining intact (compare p. 326).

EXPERIMENTAL.

Oxidation of 6-*Nitro*-2-*trichloromethyl*-4-*dichloromethylene*-1 : 3-*benzdioxin* (XIV) *to* 6-*Nitro*-4-*keto*-2-*trichloromethyl*-1 : 3-*benzdioxin* (XV).—The unsaturated benzdioxin (XIV), previously prepared (Chattaway and Irving, J., 1929, 1041) by heating 6-nitro-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (XIII) with alcoholic potassium cyanide, is more conveniently prepared by refluxing this substance for 3 hours with an excess of anhydrous sodium acetate in alcoholic suspension.

Chromic anhydride (4 g.; 4 mols.) was added in portions to a slightly warmed solution of 11·5 g. of the unsaturated benzdioxin (XIV) in 50 c.c. of glacial acetic acid, and after a few minutes' boiling the green reaction mixture was poured into 750 c.c. of cold water and kept for 12 hours. 6-*Nitro*-4-*keto*-2-*trichloromethyl*-1 : 3-*benzdioxin* (XV), which separated as a crystalline solid, crystallised from boiling glacial acetic acid, in which it was moderately easily soluble, in fine colourless prisms, m. p. 172·5° (Found : Cl, 34·0. $C_9H_4O_5NCl_3$ requires Cl, 34·1%).

Although this compound may be regarded as the chloralide derived from 5-nitrosalicylic acid, it could not be prepared directly from this acid and chloral: no condensation took place when 5-nitrosalicylic acid and anhydrous chloral were kept in concentrated sulphuric acid at the ordinary temperature, or were refluxed together at the boiling point for 12 hours, or were heated at 150° for 6 hours in a sealed tube.

Action of Alkali upon 6-*Nitro*-4-*keto*-2-*trichloromethyl*-1 : 3-*benzdioxin* (XV).—When the oxidation product (XV) (3·6 g.) was gently warmed with 50 c.c. of 10% aqueous caustic soda and 15 c.c. of alcohol, it dissolved readily and chloroform was liberated. After being boiled for 2 minutes, the solution was cooled and acidified. 5-Nitrosalicylic acid, which separated (2·8 g., m. p. 225°; calc., 3·0 g.), crystallised from alcohol in colourless crystals, m. p. 228°, and did not depress the m. p. of an authentic specimen prepared from salicylic acid (Raiziss and Proskouriakoff, *J. Amer. Chem. Soc.*, 1922, **44**, 791).

Preparation of 6-*Nitro*-2-*trichloromethyl*-4-*dichloromethylene*-7-*methyl*-1 : 3-*benzdioxin* (XVII).—8·0 G. of 6-nitro-2 : 4-bistrichloromethyl-7-methyl-1 : 3-benzdioxin were refluxed for ½ hour with 2·5 g. (3 mols.) of potassium cyanide in 50 c.c. of alcohol. The *product* (XVII), which separated when the reaction mixture was poured into a large volume of water, crystallised from boiling ethyl alcohol, in which it was somewhat sparingly soluble, in colourless rhombic plates, frequently twinned, m. p. 120—121° (Found : Cl, 45·2. $C_{11}H_6O_4NCl_5$ requires Cl, 45·1%).

6-*Nitro*-4-*keto*-2-*trichloromethyl*-7-*methyl*-1 : 3-*benzdioxin* (XVIII) was obtained by oxidising a solution of 4·5 g. of the unsaturated benzdioxin (XVII) in 30 c.c. of hot glacial acetic acid with 1·52 g. of chromic anhydride. It separated from boiling acetic acid, in which it was moderately easily soluble, in small colourless prisms, m. p. 149° (Found : Cl, 32·4. $C_{10}H_6O_5NCl_3$ requires Cl, 32·6%).

When warmed with 10% aqueous caustic soda, this lactone gave chloroform and 5-nitro-2-hydroxy-4-methylbenzoic acid. This crystallised from boiling water in almost colourless needles, m. p. 225°, and did not depress the m. p. of an authentic specimen prepared by the nitration of 3-hydroxy-*p*-toluic acid (Chattaway and Calvet, J., 1928, 1094).

Preparation of 6 : 8-*Dinitro*-2-*trichloromethyl*-4-*dichloromethylene*-1 : 3-*benzdioxin* (XX).—23 G. of 6 : 8-dinitro-2 : 4-bistrichloromethyl-1 : 3-benzdioxin (XIX) were dissolved in 150 c.c. of boiling ethyl alcohol and refluxed for 2 hours with 15 g. (excess) of anhydrous sodium acetate. On dilution with cold water, 6 : 8-dinitro-2-trichloromethyl-4-dichloromethylene-1 : 3-benzdioxin (XX) separated as a crystalline solid. Recrystallised from ethyl alcohol, in which it was moderately easily soluble, it formed splendid fern-like growths of colourless prisms, m. p. 148—149° (18 g.; calc., 21 g.).

When 6 : 8-dinitro-2-trichloromethyl-4-dichloromethylene-1 : 3-benzdioxin (XX) (5·5 g.)

was dissolved in 50 c.c. of warm acetic acid, and sufficient chromic acid (1·8 g.) added to convert the $\colon C\colon CCl_2$ group into $\colon C\colon O$, oxidation of a part only occurred, the 4-ketobenzdioxin being more readily oxidised than the unsaturated benzdioxin (XX), which was in great part (3·2 g.) recovered unchanged.

Action of Alcoholic Potash upon 6 : 8-*Dinitro*-2-*trichloromethyl*-4-*dichloromethylene*-1 : 3-*benzdioxin* (XX).—5·0 G. of the unsaturated benzdioxin (XX) (1 mol.) were finely powdered and added in small portions to a solution of 7·0 g. of potassium hydroxide (10 mols.) in 75 c.c. of ethyl alcohol at —5° to —10°. The liquid became purple and chloroform was liberated. After 15 minutes, the liquid was neutralised by hydrochloric acid, and the alcohol distilled in steam; ωω-dichloro-3 : 5-dinitro-2-ethoxyacetophenone (XXI) separated from the residue as a liquid which solidified, on cooling, to a yellow crystalline mass (yield theoretical, 3·8 g.). It crystallised from boiling alcohol in small yellow prisms, m. p. 82—83°, alone or mixed with an authentic specimen (compare Chattaway and Morris, J., 1927, 2026).

Action of Aqueous Alkali upon 6 : 8-*Dinitro*-1 : 3-*benzdioxin* (IX).—3 G. of 6 : 8-dinitro-1 : 3-benzdioxin (IX) were boiled for 3 minutes with 25 c.c. of 1% aqueous caustic soda. Formaldehyde was liberated and the benzdioxin dissolved to give a clear red solution, from which, on acidification with hydrochloric acid, 3 : 5-*dinitrosaligenin* (X) separated. It crystallised from boiling water, in which it was moderately easily soluble, in pale yellow needles, m. p. 104—104·5° (Found : N, 12·95. $C_7H_6O_6N_2$ requires N, 13·1%).

The *diacetate*, prepared by heating it with acetic anhydride and a drop of concentrated sulphuric acid, crystallised from boiling alcohol, in which it was readily soluble, in very slender, colourless prisms, m. p. 81·5—82° (Found : N, 9·5. $C_{11}H_{10}O_8N_2$ requires N, 9·4%).

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