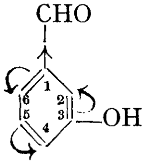
17. *The Iodination of 3-Hydroxy- and of Nitrated 3-Hydroxybenzaldehydes, and the Nitration of Certain Iodo-3-hydroxybenzaldehydes.*

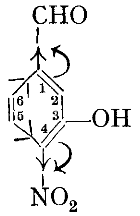
By Herbert H. Hodgson and Ernest W. Smith.

Henry and Sharp (J., 1922, **121**, 1059; 1924, **125**, 1049) found that, whereas *o*- and *p*-hydroxybenzaldehydes were dimercurated readily, the mercuration of *m*-hydroxybenzaldehyde occurred at position 2 only. Similarly Hodgson and Beard (J., 1926, 147; Hodgson, E.P. 258,060) found that chlorination took place initially at position 2, but subsequent reaction occurred mainly at position 6 with, however, some reactivity at position 4. On the other hand regulated bromination was found by Hodgson and Beard (J., 1925, **127**, 876) to proceed in the positional sequence 6, 4, 2, thereby following the order of nitration (Pschorr, *Annalen*, 1912, **391**, 33). The main nitration of 3-methoxybenzaldehyde, however, takes place at position 2 with but little nitration at position 6 and none at position 4. Further, it was found (Hodgson and Beard, J., 1927, 2375) that, whereas the continued nitration of 6-nitro-3-hydroxybenzaldehyde gave a mixture of 2 : 6- and 4 : 6-dinitro-3-hydroxybenzaldehydes, the 2-nitro- and 4-nitro-3-hydroxybenzaldehydes were nitrated the second time at position 6 only.

It would be anticipated, therefore, that for the feebly kationoid reagent iodine, mono-iodination of *m*-hydroxybenzaldehyde in sodium acetate solution might occur exclusively at either the 2- or the 6- position, and probably at the latter position by analogy with the behaviour of bromine. The Kekulé formula being assumed for 3-hydroxybenzaldehyde, the above reactions all indicate a configuration (I), *i.e.*, one showing preferential reactivity for mono-substitution in the sequence 2, 6, 4. It was found that, accompanied by a very small amount of tri-iodination (cf. exclusive trichlorination and tribromination of *m*-hydroxybenzaldehyde in aqueous media; Hodgson and Beard, *loc. cit.*), mono-iodination occurred exclusively in position 6, and that di-iodination subsequently ensued at position 2. The constitution of the 6-*iodo*-3-*hydroxybenzaldehyde* was confirmed by its oxidation to 6-iodo-3-hydroxybenzoic acid (Limpricht, *Annalen*, 1891, **263**, 234), and that of the 2 : 6-*di-iodo*-3-*hydroxybenzaldehyde* by its nitration, under conditions designed to prevent migrations, to 2 : 6-di-iodo-4-nitro-3-hydroxybenzaldehyde (Henry and Sharp, *loc. cit.*).

(I.)





(II.)

4-Nitro-3-hydroxybenzaldehyde resisted iodination under the simple conditions employed for the 6- and the 2-nitro-isomeride, which were di-iodinated to give 2 : 4-di-iodo-6-nitro- and 4 : 6-di-iodo-2-nitro-3-hydroxybenzaldehyde respectively; it was established, however, that 4-nitro-3-hydroxybenzaldehyde was oxidised and not iodinated by iodine to give 4-nitro-3-hydroxybenzoic acid. This anomalous behaviour of 4-nitro-3-hydroxybenzaldehyde is explicable, however, on the assumption that owing to the influence of the 4-nitro-group the Kekulé formula (II) for 4-nitro-3-hydroxybenzaldehyde indicates that position 2 is no longer activated by the phenolic group, while position 6 has its anionoid activity very considerably reduced by the superposed effects of the kationoid aldehyde and nitro-groups.

When 4 : 6-di-iodo-2-nitro-3-hydroxybenzaldehyde is nitrated, it is the 4-iodine which is displaced by the nitro-group to give 6-iodo-2 : 4-dinitro-3-hydroxybenzaldehyde, whereas the analogous nitration of 4 : 6-dibromo-2-nitro-3-hydroxybenzaldehyde afforded 4-bromo-2 : 6-dinitro-3-hydroxybenzaldehyde (Hodgson and Smith, J., 1931, 1500). This apparently anomalous reaction must be ascribed to the relatively feeble negative ($-I$) inductive effect and pronounced electromeric ($+T$) effect of the iodine atom; in consequence, the di-iodo-compound will be less ionised than its dibromo-analogue, and this fact has apparently resulted in an insufficient anionoid activity of the 6-carbon atom for reaction to be directed there; nitric acid therefore attacks the more intensely but less frequently activated 4-position.

Intense blue colours are given with alcoholic potassium hydroxide by the *p*-nitrophenylhydrazones of the aldehydes in which a nitro-group occupies the para-position in the aldehyde nucleus, the generalisation of Chattaway and Clemo (J., 1923, **123**, 3043) being thereby supported and a double quinonoid structure indicated (cf. Hodgson and Beard, J., 1927, 2375). All the *p*-nitrophenylhydrazones described below give yellow or orange colours with concentrated sulphuric acid.

EXPERIMENTAL.

Mono-iodination of m-*Hydroxybenzaldehyde.*—The aldehyde (5 g.), dissolved in hot water (500 c.c.), was treated successively with iodine (10 g.) and sodium acetate (15 g.); the mixture was heated on the water-bath until the iodine had disappeared, and then boiled. The crystalline precipitate obtained from the filtered cooled liquid was fractionally recrystallised from hot water; the first small fraction and the final fractions were the tri-iodinated compound and unchanged *m*-hydroxybenzaldehyde respectively; the middle fractions were 6-*iodo*-3-*hydroxybenzaldehyde*, which crystallised from water in colourless needles, m. p. 130° (Found: I, 51·0. $C_7H_5O_2I$ requires I, 51·2%), and was oxidised by cold alkaline potassium permanganate to 6-iodo-3-hydroxybenzoic acid, m. p. 196° (Found: I, 47·9. Calc. for $C_7H_5O_3I$: I, 48·1%). The aldehyde formed a p-*nitrophenylhydrazone*, which crystallised from glacial acetic acid in orange needles, m. p. 215° (Found: N, 11·2; I, 33·0. $C_{13}H_{10}O_3N_3I$ requires N, 11·0; I, 33·2%).

Di-iodination of m-*Hydroxybenzaldehyde.*—A well-stirred solution of the aldehyde (2 g.) in water (100 c.c.) to which saturated aqueous sodium carbonate (30 c.c.) had been added was gradually treated with iodine (7 g.) during 30 minutes. When the iodine had disappeared, solid anhydrous sodium carbonate was stirred into the solution until precipitation ceased; the mixture of sodium salts which separated was then dissolved in water and treated with carbon dioxide. The precipitated 2 : 4 : 6-tri-iodo-3-hydroxybenzaldehyde (see below) was removed; the filtrate on acidification with hydrochloric acid gave 2 : 6-*di-iodo*-3-*hydroxybenzaldehyde*, m. p. 144° (Found: I, 67·8. $C_7H_4O_2I_2$ requires I, 67·9%). Treatment with methyl sulphate in 10% aqueous sodium hydroxide gave 2 : 6-*di-iodo*-3-*methoxybenzaldehyde*, m. p. 81° (Found: I, 65·2. $C_8H_6O_2I_2$ requires I, 65·4%). Both compounds crystallised from 80% aqueous alcohol in iridescent white needles.

Tri-iodination of m-*Hydroxybenzaldehyde.*—A well-stirred solution of the aldehyde (1 g.) in water (100 c.c.) and saturated aqueous sodium carbonate (30 c.c.) was treated with iodine (7 g.) and kept agitated until the iodine had disappeared. The white *sodium* salt of 2 : 4 : 6-tri-iodo-3-hydroxybenzaldehyde which separated (Found: Na, 4·4. $C_7H_2O_2I_3Na$ requires Na, 4·4%) was filtered off and redissolved in water, and 2 : 4 : 6-*tri-iodo*-3-*hydroxybenzaldehyde* (3·5 g.) precipitated by carbon dioxide. It crystallised from alcohol in stellate clusters of pale cream needles, m. p. 146° (Found: I, 76·0. $C_7H_3O_2I_3$ requires I, 76·2%), identical with the tri-iodo-compounds mentioned above. Methylation afforded 2 : 4 : 6-*tri-iodo*-3-*methoxybenzaldehyde*, which crystallised from alcohol in iridescent white needles, m. p. 162° (Found: I, 74·0. $C_8H_5O_2I_3$ requires I, 74·1%). The p-*nitrophenylhydrazone* of the tri-iodohydroxybenzaldehyde crystallised from glacial acetic acid in pale orange needles, m. p. 237° (decomp.) (Found: I, 59·8. $C_{13}H_8O_3N_3I_3$ requires I, 60·0%).

Improved Preparation of 2-*Nitro*-3-*hydroxybenzaldehyde.*—Pschorr's method of nitrating 100 g. of 3-hydroxybenzaldehyde (*Annalen*, 1912, **391**, 23; see also Friedländer, *Ber.*, 1914, **47**, 3040) as modified by Hodgson and Beard (J., 1925, **127**, 875) afforded only 5 g. of 2-nitro-3-hydroxybenzaldehyde, but the yield and purity of the product have now been improved by adding calcium chloride to the flask liquor after the removal of the readily steam-volatile 4-nitro-3-hydroxybenzaldehyde, and continuing the steam-distillation. The colourless needles of 2-nitro-3-hydroxybenzaldehyde so obtained had m. p. 157° (Friedländer and Schenck, *Ber.*, 1914, **47**, 3043, 3046, give m. p. 152°; Henry and Sharp, *loc. cit.*, give m. p. 157°). The p-*nitrophenylhydrazone* crystallised from aqueous 80% acetic acid in iridescent orange needles, m. p. 250° (decomp.) [Hodgson and Beard, *loc. cit.*, give m. p. 240—250° (decomp.)] (Found: N, 18·7. Calc. for $C_{13}H_{10}O_5N_4$: N, 18·5%).

Iodination of 2-*Nitro*-3-*hydroxybenzaldehyde.*—When a saturated aqueous solution of the aldehyde was vigorously shaken with excess of iodine, 4 : 6-di-iodo-2-nitro-3-hydroxybenzaldehyde separated as a crystalline precipitate. It was freed from admixed iodine, and recrystallised from aqueous 70% alcohol, forming colourless needles, m. p. 158° (Henry and Sharp, *loc. cit.*, give m. p. 154·5°) (Found : I, 60·4. Calc. for $C_7H_3O_4NI_2$: I, 60·6%). The p-*nitrophenylhydrazone* crystallised from aqueous 70% alcohol in orange-yellow needles, m. p. 250° (decomp.) (Found : I, 45·6. $C_{13}H_8O_5N_4I_2$ requires I, 45·8%).

4-Nitro-3-hydroxybenzaldehyde could not be iodinated under similar conditions.

Iodination of 6-*Nitro*-3-*hydroxybenzaldehyde.*—A suspension of the aldehyde (6 g.) and iodine (9·2 g.) in chloroform (80 c.c.) was shaken vigorously for 3 hours with mercuric oxide (10 g.); the solid was then collected and extracted with aqueous 10% sodium carbonate. On acidification of the extract with dilute hydrochloric acid, 2 : 4-di-iodo-6-nitro-3-hydroxybenzaldehyde was precipitated; it crystallised from aqueous 50% alcohol in cream-coloured needles, m. p. 142° (Henry and Sharp, *loc. cit.*, give m. p. 142°). The p-*nitrophenylhydrazone* crystallised from glacial acetic acid in orange-yellow needles, m. p. 244° (decomp.) (Found : N, 10·3. $C_{13}H_8O_5N_4I_2$ requires N, 10·1%).

4-Nitro-3-hydroxybenzaldehyde remained unchanged when subjected to the above procedure.

2 : 4-*Di-iodo*-6-*nitro*-3-*methoxybenzaldehyde* was obtained when the hydroxy-aldehyde (1 g.), ground intimately with moist potassium carbonate (1 g.), was treated with methyl sulphate (3 c.c.), and the mixture heated on the water-bath for 3 hours, stirred into a large excess of saturated aqueous sodium carbonate, and again heated for 2 hours. The insoluble ether was crystallised once from alcohol and once from aqueous 80% acetic acid; it was then obtained in buff needles, m. p. 142°, depressed by admixture with the unmethylated product (m. p. 142°) (Found : I, 58·4. $C_8H_5O_4NI_2$ requires I, 58·6%). The p-*nitrophenylhydrazone* crystallised from glacial acetic acid in deep orange needles, m. p. 220° (decomp.) (Found : N, 10·0. $C_{14}H_{10}O_5N_4I_2$ requires N, 9·8%).

Iodination of 2 : 6-*Dinitro*-3-*hydroxybenzaldehyde.*—The aldehyde (1 g.), dissolved in aqueous 10% sodium carbonate (100 c.c.), was stirred with iodine (1·2 g.) during the addition of aqueous 20% sodium hydroxide until the iodine had completely dissolved. After 1 hour, the solution was acidified with hydrochloric acid; the precipitated 4-*iodo*-2 : 6-*dinitro*-3-*hydroxybenzaldehyde* crystallised from water in long buff needles, m. p. 168° (Found : I, 37·5. $C_7H_3O_6N_2I$ requires I, 37·6%). The p-*nitrophenylhydrazone* crystallised from cellusolve in bright red needles, decomp. 310° (Found : I, 26·6. $C_{13}H_8O_7N_5I$ requires I, 26·9%).

Iodination of 4 : 6-*Dinitro*-3-*hydroxybenzaldehyde.*—A solution of 4 : 6-dinitro-3-hydroxybenzaldehyde prepared by the method of Hodgson and Beard (J., 1927, 2378) was poured on ice and, after filtration, shaken with excess of iodine; the pure 2-*iodo*-4 : 6-*dinitro*-3-*hydroxybenzaldehyde* which separated was recrystallised from water, forming long, pale yellow needles, m. p. 106·5° (Found : N, 8·5; I, 37·4. $C_7H_3O_6N_2I$ requires N, 8·3; I, 37·6%). The p-*nitrophenylhydrazone* crystallised from glacial acetic acid in scarlet needles, m. p. 282° (decomp.) (Found : I, 26·8. $C_{13}H_8O_7N_5I$ requires I, 26·9%).

Action of Nitric Acid on 2 : 6-*Di-iodo*-3-*hydroxybenzaldehyde.*—The aldehyde, left in contact with dilute (30%) nitric acid, was gradually converted into 2 : 6-di-iodo-4-nitro-3-hydroxybenzaldehyde, which crystallised from water in yellow needles, m. p. 123° [Henry and Sharp, *loc. cit.*, give m. p. 122° (corr.)] (Found : I, 60·7. Calc. for $C_7H_3O_4NI_2$: I, 60·6%), formed a red *sodium* salt (Found : Na, 5·0. $C_7H_2O_4NI_2Na$ requires Na, 5·2%), and was oxidised by alkaline permanganate to give Henry and Sharp's di-iodo-4-nitro-3-hydroxybenzoic acid. The p-*nitrophenylhydrazone* crystallised from glacial acetic acid in brick-red needles, m. p. 218° (decomp.) (Found : N, 10·2. $C_{13}H_8O_5N_4I_2$ requires N, 10·1%).

Action of Nitric Acid on 4 : 6-*Di-iodo*-2-*nitro*-3-*hydroxybenzaldehyde.*—Although this aldehyde remained unaffected by nitric acid (*d* 1·42), it slowly dissolved in a stronger acid (*d* 1·5), and when the solution was poured on ice and saturated with sodium nitrate, 6-*iodo*-2 : 4-*dinitro*-3-*hydroxybenzaldehyde* separated in yellow needles, which were recrystallised from water; m. p. 160° (Found : I, 37·3. $C_7H_3O_6N_2I$ requires I, 37·6%).

The Action of Iodine on 4-*Nitro*-3-*hydroxybenzaldehyde.*—A solution of the aldehyde (1 g.) in saturated aqueous sodium carbonate was treated with iodine (1·5 g.) dissolved in aqueous potassium iodide (1·5 g.), and kept until the colour of the iodine had disappeared. On acidification with hydrochloric acid, 4-nitro-3-hydroxybenzoic acid separated; it crystallised from aqueous 50% alcohol in yellow needles, m. p. 238° [Henry and Sharp, *loc. cit.*, give m. p. 235° (corr.)] (Found : N, 7·8. Calc. for $C_7H_5O_5N$: N, 7·6%), and did not depress the m. p. of an authentic specimen prepared by the oxidation of 4-nitro-3-hydroxybenzaldehyde with alkaline permanganate.

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