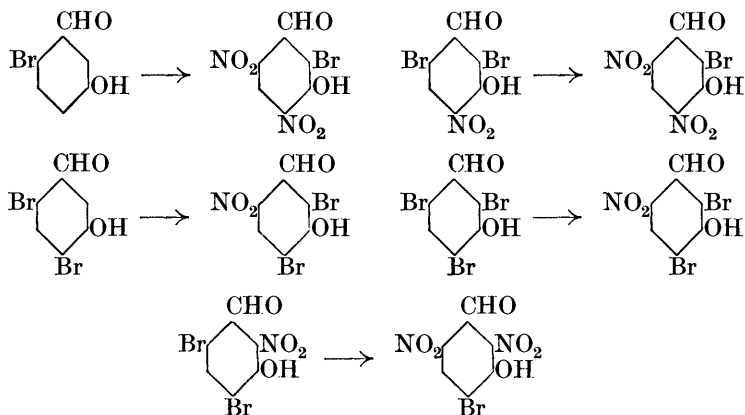


CCV.—*The Nitration of Brominated 3-Hydroxybenzaldehydes and the Bromination of Nitrated 3-Hydroxybenzaldehydes, with Cases of Group Migration.*

By HERBERT HENRY HODGSON and ERNEST WALTER SMITH.

Only a single reference to 2:4-dibromo-6-nitro-3-hydroxybenzaldehyde (Henry and Sharp, J., 1924, **125**, 1049) appears to constitute the literature of this subject. The present investigation relates to the mono- and di-nitration of the 2-, 4-, and 6-bromo-, the nitration of 4:6-dibromo- and 2:4:6-tribromo-, and the bromination of the 2-, 4-, and 6-nitro- and of the 2:6- and 4:6-dinitro-3-hydroxybenzaldehydes.

In all cases when concentrated nitric acid reacts at the ordinary temperature with compounds containing a substituent in position 4 and bromine in position 6, the bromine is displaced by the nitro-group and migrates to position 2, should that be unoccupied; thus it is impossible to dinitrate 6-bromo-3-hydroxybenzaldehyde except at very low temperatures. The following scheme depicts the results obtained:



From electronic considerations (Allan, Oxford, Robinson, and Smith, J., 1926, 401) it would appear that since the reactants with kationoid nitric acid are all highly ionised molecules, positions 2, 4, and 6 will all be activated but the 6-position more frequently than 2- and 4- (Lapworth and Robinson, *Mem. Manchester Phil. Soc.*, 1928, **72**, 47). That such is the case during the mononitration of *m*-hydroxybenzaldehyde itself follows from the results of Hodgson and Beard (J., 1925, **127**, 877), where the 6-, 4- and 2-nitro-3-

hydroxybenzaldehydes produced are in the ratio 48:32:5 respectively. Consequently, in the examples cited, kationoid attack (if any) will be preferentially at position 6 with electron-release from the bromine atom and formation of hypobromous acid, a product actually observed in all cases where displacement of bromine occurs. The kationoid hypobromous acid then attacks the much less activated 2-position, if this is free. The reactions, however, take place slowly, and appear to be dependent on temperature, since it has been possible at low temperatures to dinitrate 6-bromo-3-hydroxybenzaldehyde without displacement of bromine, although 4:6-dibromo-3-hydroxybenzaldehyde is always nitrated in position 6 whatever the temperature, a fact which may be due to the much greater activation of the 6-position in this more highly ionised molecule.

Conversely, during bromination, with great excess of bromine, the nitro-group is displaced from 2-bromo-4-nitro-3-hydroxybenzaldehyde and migrates to give 2:4-dibromo-6-nitro-3-hydroxybenzaldehyde, again showing the preference of the nitro-group for the 6-position. In this case a probable mechanism would be an initial tribromination in positions 2, 4, and 6 with production of the powerful kationoid reagent nitroxyl bromide,  $\text{NO}_2^+\text{Br}^-$ , which would then seek the more strongly anionoid 6-carbon atom. This reaction explains the truly remarkable results of Henry and Sharp (*loc. cit.*), who obtained always the 2:4-dibromo-6-nitro-3-hydroxybenzaldehyde whichever of the dimercuri-compounds from the 2-, 4-, and 6-nitro-3-hydroxybenzaldehydes was treated with bromine.

Analogous with the above migration is the nitration of *p*-iodoanisole to give *o*-iodo-*p*-nitroanisole (Robinson, J., 1916, 109, 1078), where the more frequently activated 4-position is occupied by the iodine atom, which readily releases an electron on demand and so is displaced by the nitro-group with probable formation of hypoiodous acid, this subsequently attacking the 2-position.

4-Nitro-3-hydroxybenzaldehyde cannot be directly monobrominated but is always dibrominated, and 4-bromo-3-hydroxybenzaldehyde is dinitrated most readily under conditions which produce only mononitrated derivatives from the 6- and 2-bromo-3-hydroxybenzaldehydes respectively, whereas dilute nitric acid mononitrates 4-bromo-3-hydroxybenzaldehyde with ease, but does not react with either of the isomerides. The explanation would appear to be as follows: 4-Bromo-3-hydroxybenzaldehyde is the most ionisable of the three isomerides, as shown by the fact that it is the only one which dissolves in aqueous sodium carbonate (the others require caustic alkalis), and therefore will have its 2- and

6-positions much more activated than in the other two cases, and the molecule will be still further ionised when position 6 becomes substituted, with resultant increased activation of position 2. The same explanation holds for the facts that *m*-hydroxybenzaldehyde and phenol are always tribrominated in aqueous solution (compare Hodgson and Beard, J., 1925, **127**, 875).

2 : 4-Dibromo-6-nitro-3-hydroxybenzaldehyde crystallises from aqueous alcohol or chloroform in stout colourless rhombs or needles which melt at 148° with immediate decomposition, whereas prolonged boiling (3 hours) of the substance in xylene solution produces an isomeride (elongated needles) which melts at 152·5° and decomposes at 163°. After recrystallisation from chloroform the isomeride still melts at 152·5°, but now decomposes immediately afterwards. Recrystallisation of both forms from aqueous alcohol reproduces the substance of m. p. 148°. Distillation in steam, in which they are almost non-volatile, slowly transforms them likewise : after passage of steam for an hour, the more stable substance of m. p. 152·5° changes into the less stable product of the same m. p., but further boiling for two hours completes the transformation to the 148° product. It would appear that 3 isomeric forms are capable of existence, connected possibly with the two available cases of co-ordination between the bromo-hydroxy- and the nitro-aldehydo-groups (compare Tanasescu, *Bull. Soc. chim.*, 1927, **41**, 1497) and the third case of absence of co-ordination. 2 : 4-Dibromo-6-nitro-3-methoxybenzaldehyde remains unchanged after 5 hours' boiling in xylene solution.

6-Bromo-2 : 4-dinitro-3-hydroxybenzaldehyde-*p*-nitrophenylhydrazone on treatment with aqueous sodium hydroxide develops a greenish-blue colour (compare the less green royal-blue of the 6-chloro-analogue; Hodgson and Beard, J., 1926, 2031), whereas 2-bromo-4 : 6-dinitro-3-hydroxybenzaldehyde-*p*-nitrophenylhydrazone gives a red colour (compare the absence of colour in the cold, and claret-red colour only on warming, in the case of the 2-chloro-analogue; H. and B., *loc. cit.*). In both cases, the more powerful electron attraction of chlorine in comparison with bromine is shown by this hypsochromic and inhibition effect respectively.

#### EXPERIMENTAL.

The initial materials were prepared by the methods of Hodgson and Beard (J., 1925, **127**, 875) in all cases except where stated otherwise.

The characteristic colours produced by addition of alcoholic potassium hydroxide to an alcoholic solution of the *p*-nitrophenylhydrazone and by the action of concentrated sulphuric acid on the

powdered solid are given in this order in consecutive parentheses after the m. p.

*Nitration of the Bromo-3-hydroxybenzaldehydes.*

(a) *2-Bromo-3-hydroxybenzaldehyde*.—A more convenient method of preparation than that of Hodgson and Beard, which required the difficulty accessible 2-nitro-3-hydroxybenzaldehyde, is the following: A cold solution of 2-mercuriacetato-3-hydroxybenzaldehyde (Henry and Sharp, J., 1922, **121**, 1059) (8 g.) in acetic anhydride (23 c.c.) was treated with bromine (1 c.c.) in acetic anhydride (5 c.c.), poured on ice after 1 hour, and left over-night. The product was collected and hydrolysed with boiling concentrated hydrochloric acid; the 2-bromo-3-hydroxybenzaldehyde obtained crystallised from 50% aqueous alcohol in colourless rhombs, m. p. 148° (Hodgson and Beard give m. p. 141—142°) (Found: Br, 39.6. Calc.: Br, 39.8%).

*Mononitration.* This was effected by adding 2-bromo-3-hydroxybenzaldehyde (1 g.) to well-stirred nitric acid (12 c.c.; *d* 1.42) at 16—17°. After an hour, the reaction mixture was diluted with water, and the solid product steam-distilled after filtration. The volatile product, *2-bromo-4-nitro-3-hydroxybenzaldehyde*, crystallised from alcohol in pale yellow, feathery needles, m. p. 176° (Found: Br, 32.4.  $C_7H_4O_4NBr$  requires Br, 32.5%); the *p-nitrophenylhydrazone* crystallised from glacial acetic acid in red-orange needles, m. p. 265° (blue-violet) (orange) (Found: Br, 20.8.  $C_{13}H_9O_5N_4Br$  requires Br, 21.0%). The non-volatile product, *2-bromo-6-nitro-3-hydroxybenzaldehyde*, crystallised from water in fine buff needles, m. p. 174° (Found: Br, 32.3%); the *p-nitrophenylhydrazone* crystallised from glacial acetic acid in orange needles, m. p. 230° (pale red) (no colour) (Found: Br, 20.9%).

2-Bromo-4-nitro- and 2-bromo-6-nitro-3-hydroxybenzaldehyde on further treatment with bromine in alcoholic solution both gave 2:4-*dibromo-6-nitro-3-hydroxybenzaldehyde*, which crystallised from 50% aqueous alcohol in colourless rhombs or stout needles, m. p. and mixed m. p. together and with an authentic specimen, 148° (decomp.) (Henry and Sharp, *loc. cit.*, give m. p. 152.5°; see introduction) (Found: Br, 49.3, 49.2. Calc.: Br, 49.2%); the *p-nitrophenylhydrazone* crystallised from glacial acetic acid in orange-yellow needles, m. p. 249° (decomp.) (red) (amber) (Found: Br, 34.7.  $C_{13}H_8O_5N_4Br_2$  requires Br, 34.8%).

2:4-*Dibromo-6-nitro-3-methoxybenzaldehyde* crystallised from alcohol in fine colourless needles, m. p. 119° (Found: Br, 47.0.  $C_8H_5O_4NBr_2$  requires Br, 47.2%).

*Dinitration.* 2-Bromo-3-hydroxybenzaldehyde (2 g.) was added

to nitric acid (9 c.c.;  $d$  1.5) at 5—7° during 1 hour, and the mixture kept for 2 hours at the same temperature and then poured on ice. The precipitated 2-bromo-4 : 6-dinitro-3-hydroxybenzaldehyde crystallised from 10% aqueous alcohol in yellow iridescent prisms, m. p. 131° (Found: N, 9.8; Br, 27.4.  $C_7H_3O_6N_2Br$  requires N, 9.6; Br, 27.5%); the *p*-nitrophenylhydrazone crystallised from glacial acetic acid in scarlet needles, m. p. 242° (decomp.) (blue-violet) (pale yellow) (Found: Br, 18.7.  $C_{13}H_8O_7N_5Br$  requires Br, 18.8%).

(b) 4-Bromo-3-hydroxybenzaldehyde.—*Mononitration*. The aldehyde (1.5 g.) was added to 10 c.c. of a mixture of nitric acid (7 c.c.;  $d$  1.42) and water (3 c.c.) at 20—23° during 1 hour with stirring. After another hour, the mixture was diluted with water (30 c.c.) and the resinous solid which separated was distilled in superheated steam. The volatile product crystallised from aqueous alcohol in pale yellow needles, m. p. 167° (Found: Br, 32.4%) and proved to be identical with the product obtained by the monobromination of 2-nitro-3-hydroxybenzaldehyde (f), *viz.*, 4-bromo-2-nitro-3-hydroxybenzaldehyde, a conclusion supported by the identity of the *p*-nitrophenylhydrazones, orange needles, m. p. and mixed m. p. 205° (purple) (yellow-brown) (Found: Br, 20.8.  $C_{13}H_9O_5N_4Br$  requires Br, 20.9%).

After filtration of the resinous solid above, 4-bromo-6-nitro-3-hydroxybenzaldehyde was salted out from the filtrate by means of sodium nitrate; it crystallised from water in cream-coloured plates, m. p. 72° (Found: Br, 32.3.  $C_7H_4O_4NBr$  requires Br, 32.5%); on treatment with bromine in alcoholic solution, 2 : 4-dibromo-6-nitro-3-hydroxybenzaldehyde was obtained, which crystallised from aqueous alcohol in colourless rhombs, m. p. and mixed m. p. with authentic specimen (see later), 148° (Found: Br, 49.1%). The *p*-nitrophenylhydrazone of 4-bromo-6-nitro-3-hydroxybenzaldehyde crystallised from glacial acetic acid in red needles, m. p. 271° (purple) (amber) (Found: Br, 20.7.  $C_{13}H_9O_5N_4Br$  requires Br, 20.9%).

*Dinitration*. 4-Bromo-3-hydroxybenzaldehyde (2 g.) was added with stirring to nitric acid (10 c.c.;  $d$  1.42) at 17—19° during 1 hour; the mixture was kept for 2 hours at room temperature and diluted with ice-water. The 4-bromo-2 : 6-dinitro-3-hydroxybenzaldehyde obtained crystallised from 10% aqueous alcohol in iridescent, pale yellow plates, m. p. 128° and mixed m. p. with the bromination product of 2 : 6-dinitro-3-hydroxybenzaldehyde, 128°. The *p*-nitrophenylhydrazone crystallised from glacial acetic acid in bright red needles, m. p. 226° (decomp.) (violet) (amber) (Found: Br, 18.6.  $C_{13}H_8O_7N_5Br$  requires Br, 18.8%).

(c) *6-Bromo-3-hydroxybenzaldehyde*.—*Mononitration*. The aldehyde (4.5 g.) was added to nitric acid (20 c.c.;  $d$  1.42) at 20—23° with stirring during 1 hour, the mixture kept for another hour and diluted with water, and the precipitate of *6-bromo-4-nitro-3-hydroxybenzaldehyde* recrystallised twice from 50% aqueous acetic acid, giving fine, deep yellow needles, m. p. 118° (Found: Br, 32.4.  $C_7H_4O_4NBr$  requires Br, 32.5%). The *p-nitrophenylhydrazone* crystallised from glacial acetic acid in stout, deep red needles, m. p. 236° (blue) (red) (Found: Br, 20.8.  $C_{13}H_9O_5N_4Br$  requires Br, 21.0%). On treatment with excess of bromine in alcoholic solution, the above aldehyde gave 2:6-dibromo-4-nitro-3-hydroxybenzaldehyde identical with the product of the dibromination of 4-nitro-3-hydroxybenzaldehyde (see later).

*Dinitration*. By the method described under 2-bromo-3-hydroxybenzaldehyde, *6-bromo-2:4-dinitro-3-hydroxybenzaldehyde* was obtained; it crystallised from water in yellow prisms, m. p. 129° (Found: Br, 27.3.  $C_7H_3O_6N_2Br$  requires Br, 27.5%), and depressed the m. p. of the 4-bromo-2:6-dinitro-isomeride and of 4:6-dinitro-3-hydroxybenzaldehyde. The *p-nitrophenylhydrazone* crystallised from glacial acetic acid in bright red needles, m. p. 256° (greenish-blue) (red) (Found: Br, 18.7.  $C_{13}H_8O_7N_5Br$  requires Br, 18.8%).

When 6-bromo-4-nitro-3-hydroxybenzaldehyde is heated with dilute nitric acid, it is converted into 2-bromo-4:6-dinitro-3-hydroxybenzaldehyde, m. p. and mixed m. p. with authentic specimens prepared by brominating 4:6-dinitro-3-hydroxybenzaldehyde and by the action of nitric acid on 2:6-dibromo-4-nitro-3-hydroxybenzaldehyde (see later), 131° (Found: N, 9.9; Br, 27.4%).

(d) *4:6-Dibromo-3-hydroxybenzaldehyde*.—The aldehyde (3 g.) was added to nitric acid (15 c.c.;  $d$  1.42) at room temperature during 1 hour, an odour resembling that of hypobromous acid being perceived as dissolution took place. On dilution, 2:4-dibromo-6-nitro-3-hydroxybenzaldehyde was precipitated, which crystallised from aqueous alcohol in buff rhombs, m. p. and mixed m. p. with authentic specimen, 148° (Found: Br, 49.5%); the *p*-nitrophenylhydrazone crystallised from glacial acetic acid in orange-yellow needles, m. p. and mixed m. p. with authentic specimen, 249° (decomp.) (red) (amber) (Found: Br, 34.7%).

(e) *2:4:6-Tribromo-3-hydroxybenzaldehyde*.—The aldehyde (3 g.) was added to concentrated nitric acid as under (d); the odour of hypobromous acid was again perceived as the product slowly dissolved to form a deep red solution. On dilution with water, 2:4-dibromo-6-nitro-3-hydroxybenzaldehyde separated; it was identified as above.

*Bromination of the Nitro-3-hydroxybenzaldehydes.*

(f) *2-Nitro-3-hydroxybenzaldehyde*.—*Monobromination*. The aldehyde (1 g.), dissolved in chloroform (30 c.c.), was treated with bromine (1 c.c.), and the mixture boiled under reflux for 12 hours. The resinous solid which remained after removal of the chloroform by distillation was partly recrystallised from hot water, the residual tar being distilled with superheated steam. Only *4-bromo-2-nitro-3-hydroxybenzaldehyde* could be isolated, as pale yellow needles, m. p. and mixed m. p. with the product under (b) 167° (Found : Br, 32.4.  $C_7H_4O_4NBr$  requires Br, 32.5%).

*Dibromination*. *2-Nitro-3-hydroxybenzaldehyde* (1 g.) was dissolved in the minimum quantity of alcohol and excess of bromine added; *4 : 6-dibromo-2-nitro-3-hydroxybenzaldehyde*, obtained in theoretical yield, crystallised from alcohol in yellow-brown prismatic needles, m. p. 140° (decomp.) (Found : Br, 49.0.  $C_7H_3O_4NBr_2$  requires Br, 49.2%). The *p-nitrophenylhydrazone* crystallised from glacial acetic acid in deep orange needles, m. p. 218° (decomp. (purple) (amber) (Found : Br, 34.5.  $C_{13}H_8O_5N_4Br_2$  requires Br, 34.8%).

*Displacement of bromine by the nitro-group*. When *4 : 6-dibromo-2-nitro-3-hydroxybenzaldehyde* was kept in contact with cold nitric acid (*d* 1.42), dissolution occurred and the odour of hypobromous acid became perceptible. The mixture, after dilution with water and saturation with sodium nitrate, deposited *4-bromo-2 : 6-dinitro-3-hydroxybenzaldehyde*, which crystallised like the product under (b) and (i), m. p. and mixed m. p. 128° (Found : Br, 27.4%); the *p-nitrophenylhydrazone* [see (b)] has m. p. and mixed m. p. 226° (decomp.) (violet) (amber) (Found : Br, 18.8%).

(g) *4-Nitro-3-hydroxybenzaldehyde*.—In non-aqueous media this aldehyde resists bromination; in aqueous suspension, dibromination occurs solely, even with a deficiency of bromine, no monobromo-derivative being formed.

The aldehyde (3 g.), suspended in a solution of potassium bromate (2 g.) and potassium bromide (8 g.) in water (50 c.c.), was treated gradually, with vigorous stirring, with concentrated hydrochloric acid (20 c.c.), the reaction being completed by gentle warming on the water-bath for 15 minutes. *2 : 6-Dibromo-4-nitro-3-hydroxybenzaldehyde*, which separated on cooling, crystallised from benzene-light petroleum in bright yellow plates, m. p. 95° (Found : Br, 48.9.  $C_7H_3O_4NBr_2$  requires Br, 49.2%), identical with the product under (c). The *p-nitrophenylhydrazone* crystallised from glacial acetic acid in deep red needles, m. p. 242° (brown-purple) (yellow-brown) (Found : Br, 34.6.  $C_{13}H_8O_5N_4Br_2$  requires Br, 34.8%).

*Displacement of bromine by the nitro-group.* When 2 : 6-dibromo-4-nitro-3-hydroxybenzaldehyde (2 g.) was kept at room temperature with nitric acid (10 c.c.; *d* 1.42) for 5 days, 2-bromo-4 : 6-dinitro-3-hydroxybenzaldehyde crystallised in iridescent yellow prisms, m. p. and mixed m. p. with the product obtained by bromination of 4 : 6-dinitro-3-hydroxybenzaldehyde, 131° (Found : Br, 27.4%).

(h) 6-Nitro-3-hydroxybenzaldehyde.—The aldehyde (5 g.) was dissolved in alcohol (40 c.c.) and treated gradually (vigorous stirring) with bromine (6 c.c.). 2 : 4-Dibromo-6-nitro-3-hydroxybenzaldehyde, which separated, crystallised from aqueous alcohol in colourless rhombs, m. p. 148° (decomp.) (Henry and Sharp, J., 1924, **125**, 1054, give m. p. 152.5°) (Found : Br, 49.3. Calc. : Br, 49.2%). Specimens of this product have also been obtained by the bromination of 2-bromo-4-nitro-, 2-bromo-6-nitro-, and 4-bromo-6-nitro-3-hydroxybenzaldehyde and by the action of nitric acid on 4 : 6-dibromo- and 2 : 4 : 6-tribromo-3-hydroxybenzaldehyde, all of which, after recrystallisation from aqueous alcohol, melted at 148°. Henry and Sharp (*loc. cit.*) crystallised their product from chloroform, but our product after crystallisation from chloroform still melted at 148°.

(i) *Bromination of 2 : 6- and 4 : 6-Dinitro-3-hydroxybenzaldehydes.*—According to Hodgson and Beard (J., 1927, 2378), when 6-nitro-3-hydroxybenzaldehyde is nitrated, a mixture of 2 : 6- and 4 : 6-dinitro-isomerides is obtained. Owing to an error in transcription, the former was stated to be the more soluble in water; actually, the 4 : 6-isomeride is much more soluble than the 2 : 6.

The nitration mixture (*loc. cit.*) was diluted with water, and the solution filtered and treated with excess of bromine. The product crystallised from aqueous alcohol in yellow iridescent prisms, m. p. 131° (Found : Br, 27.4%), and was identical (m. p. and mixed m. p.) with the products obtained from the nitration of 2 : 6-dibromo-4-nitro-3-hydroxybenzaldehyde and of 6-bromo-4-nitro-3-hydroxybenzaldehyde, namely, 2-bromo-4 : 6-dinitro-3-hydroxybenzaldehyde. The nitration product more soluble in water must therefore be 4 : 6-dinitro-3-hydroxybenzaldehyde. The less soluble 2 : 6-dinitro-3-hydroxybenzaldehyde was recrystallised several times from water and obtained in long colourless needles, m. p. 106° (Hodgson and Beard, *loc. cit.*, give m. p. 106° for the 4 : 6-isomeride), which, when brominated in alcoholic solution with excess of bromine, yielded 4-bromo-2 : 6-dinitro-3-hydroxybenzaldehyde, which crystallised from 10% aqueous alcohol in iridescent yellow plates, m. p. 128° (Found : Br, 27.3%), identical with the dinitration product from 4-bromo-3-hydroxybenzaldehyde.

The following method for the nitration of 6-nitro-3-hydroxy-



benzaldehyde gives better results than that described previously. The aldehyde (10 g.) was stirred into nitric acid (15 c.c.; *d* 1.42) at room temperature, and the mixture kept over-night; the clear solution obtained solidified when agitated. Treatment with water separated the isomerides.

*Nitration of 4-Nitro-3-hydroxybenzaldehyde.*—The aldehyde (5 g.) was very gradually added with stirring to nitric acid (20 c.c.; 98%) at 5–10°, the temperature rising very rapidly at the outset. As the reaction proceeded, additions could be made in increasingly larger amounts without undue elevation of temperature, but towards the end the temperature was allowed to reach 22° before the mixture was poured on ice. 4:6-Dinitro-3-hydroxybenzaldehyde, obtained in quantitative yield, crystallised from benzene–ligroin in cream-coloured stellate clusters, m. p. 104° (Found: N, 13.4. Calc.: N, 13.2%). The *p*-nitrophenylhydrazone crystallised from glacial acetic acid in scarlet needles, m. p. and mixed m. p. with Hodgson and Beard's specimen from the erroneously named 2:6-dinitro-compound, 240–242° (reddish-blue) (red-orange). M.p. and mixed m. p. of the *p*-nitrophenylhydrazone of the 2:6-dinitro-compound (H. and B.'s 4:6-compound) 282–283° (purple) (amber).

Bromination of a saturated solution of 4:6-dinitro-3-hydroxybenzaldehyde in water gives 2-bromo-4:6-dinitro-3-hydroxybenzaldehyde, m. p. 131°; *p*-nitrophenylhydrazone, m. p. 242° (blue-violet) (pale yellow).

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TECHNICAL COLLEGE, HUDDERSFIELD.

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