XXIII.—*Chloro-derivatives of* m-*Hydroxybenzaldehyde.*

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THE literature of this subject describes only 6-chloro- (no m. p. recorded) and 4 : 6-dichloro-3-hydroxybenzaldehydes (Friedländer and Schenck, *Ber.*, 1914, **47**, 3044), 2 : 4 : 6-trichloro-3-hydroxybenzaldehyde (Krause, *Ber.*, 1899, **32**, 123), and the conversion of *m*-hydroxybenzaldehyde into aldehydotrichloroquino-dichloride by the action of chlorine in dilute acetic acid solution (Biltz and Kammann, *Ber.*, 1901, **34**, 4118).

The chlorination and the bromination (J., 1925, **127**, 876) of *m*-hydroxybenzaldehyde proceed in general on similar lines. A noteworthy difference is the production of 2-chloro-3-hydroxybenzaldehyde and but little of the 6-chloro-isomeride by direct monochlorination, bromination under similar conditions yielding 6-bromo-3-hydroxybenzaldehyde. The proportion of the 6-chloro-isomeride increases at high temperatures. The presence of water promotes trichlorination and renders regulated chlorination very difficult.

4-Chloro-3-hydroxybenzaldehyde was obtained in good yield from the corresponding 4-nitro-compound, but, as in the case of 6-bromo-3-hydroxybenzaldehyde (*loc. cit.*, p. 878), only poor yields of 6-chloro-3-hydroxybenzaldehyde were produced by a like procedure. This compound, however, was obtained in excellent yield by converting 2-chlorobenzaldehyde quantitatively into 2-chloro-5-nitrobenzaldehyde, reducing the oxime of this, diazotising the resulting 2-chloro-5-aminobenzaldoxime, and decomposing the product.

2 : 6- and 2 : 4-Dichloro-3-hydroxybenzaldehydes were obtained by direct chlorination of 2- and 4-chloro-3-hydroxybenzaldehydes, respectively, in glacial acetic acid solution, but 6-chloro-3-hydroxybenzaldehyde yielded a mixture of dichloro-compounds from which only the 2 : 6-isomeride could be isolated. In the direct dichlorination of *m*-hydroxybenzaldehyde the main product was the 2 : 6-dichloro-compound, Friedländer and Schenck's 4 : 6-dichloro-3-hydroxybenzaldehyde (*loc. cit.*) being isolated only in small quantity. The formation of the 2 : 6-dichloro-compound from both 2- and 6-chloro-3-hydroxybenzaldehyde proves the constitution assigned to it. The presence of the 4 : 6-dichloro-compound in the product of direct dichlorination of *m*-hydroxybenzaldehyde points to chlorination of the 6-monochloro-compound partially in the 4-position. Chlorination, however, takes place preferentially in position 2, and this preference is strong support for the constitution assigned to the 2 : 4-dichloro-compound obtained quantitatively from 4-chloro-3-hydroxybenzaldehyde.

The chloro-3-hydroxybenzaldehydes all have very pronounced sternutatory properties, which are most marked in the 2 : 6-, and but slightly less so in the 2 : 4 : 6-compound. For the monochloro-3-hydroxybenzaldehydes the order is 6-, 2-, and 4-. The property is comparatively feeble in the last compound, and thus is indicated its dependence on ortho-substitution. The property vanishes on methylation, but the methoxy-compounds have now acquired a hawthorn-like odour which in turn vanishes when these are oxidised to the benzoic acids. All these compounds attack the moistened skin, producing painful blisters.

The colours produced by the action of alcoholic potash on the *p*-nitrophenylhydrazones are all claret and conform to Chattaway and Clemo's generalisation (J., 1923, **123**, 3041).

The melting points of the ethers are considerably lower than those of the hydroxy-compounds, as in the case of the bromo-compounds (*loc. cit.*, pp. 878, 879), while those of their *p*-bromophenylhydrazones exhibit noteworthy diversity.

EXPERIMENTAL.

Monochloro-3-hydroxybenzaldehydes.

2-*Chloro*-3-*hydroxybenzaldehyde*.—(a) *Preparation by direct chlorination.* Through a solution of *m*-hydroxybenzaldehyde (50 g.) in glacial acetic acid (160 g.) at 15°, chlorine was bubbled (rate about 3 g. per hour) until the increase in weight was 29 g. After 12 hours, the colourless crystals of 2-*chloro*-3-*hydroxybenzaldehyde* were filtered off (22 g.) and recrystallised from dilute acetic acid; m. p. 139·5° (Found: Cl, 22·5. $C_7H_5O_2Cl$ requires Cl, 22·6%). The crystals become pale pink on prolonged exposure to air. On removal of 80 c.c. by distillation from the filtrate, a further crop (11 g.) was obtained, m. p. 138—140° after one recrystallisation. The solvent was then completely evaporated, and the dark residue (28 g.), m. p. 80—90°, resolved into two products by partial dissolution in hot aqueous sodium carbonate (10 g. of residue, 2 g. of Na_2CO_3, 50 c.c. of H_2O) and extraction from the cold solution with ether. The compound thus removed (3—4 g.), after two crystallisations from dilute acetic acid, had m. p. 110° and was identified as 6-chloro-3-hydroxybenzaldehyde by comparison with the synthetic product from 6-nitro-3-hydroxybenzaldehyde (see later) and with the de-alkylated product from 6-chloro-3-methoxybenzaldehyde. On acidification of the sodium carbonate solution after ether extraction, 2-chloro-3-hydroxybenzaldehyde was precipitated; this melted at 139·5° after crystallisation from dilute acetic acid.

The quantity of sodium carbonate to be used varies slightly with each chlorination experiment, the above being a good average and arrived at by trial, *viz.*, a sequence of additions, ether extractions, etc., until only 6-chloro-3-hydroxybenzaldehyde is extracted, this being much less acidic than the 2-chloro-isomeride.

Catalysts such as ferric chloride, quinoline, quinoline sulphate, and iodine have no effect on the chlorination, which proceeds equally well in carbon disulphide, chloroform, or carbon tetrachloride, apart from difficulties arising through the volatility of the solvent. Chlorine in solution is less efficient than flowing chlorine.

The above process was repeated, a stream of bromine being substituted for the stream of chlorine. 6-Bromo-3-hydroxybenzaldehyde was produced as in the regulated bromination previously described (*loc. cit.*, p. 876), but in improved yield.

(b) *Preparation from 2-nitro-3-hydroxybenzaldehyde.* The nitro-compound was reduced with sodium hyposulphite (*loc. cit.*), the mixture just acidified at 0° (Congo-paper) with hydrochloric acid, and sodium nitrite and hydrochloric acid were then added alternately with stirring until diazotisation was complete. The diazo-solution was decomposed with cuprous chloride in the usual way, and the product distilled with steam. The large distillate was concentrated to small bulk after addition of sodium carbonate, and acidified. The product extracted therefrom with ether had m. p. 139·5° after recrystallisation from dilute acetic acid and also when mixed with 2-chloro-3-hydroxybenzaldehyde prepared by method (a) (Found : Cl, 22·55. Calc., Cl, 22·6%).

Evidence for its constitution. Two g. of the presumed 2-chloro-3-hydroxybenzaldehyde obtained in (a) were treated in aqueous 20% sodium hydroxide with methyl sulphate, and the methyl ether was removed in steam and crystallised from dilute alcohol. It melted at 57°, was identical with the methyl ether of the product obtained in (b), and depressed the m. p. (52°) of 4-chloro-3-methoxybenzaldehyde. On oxidation with alkaline permanganate (*loc. cit.*, p. 880), it yielded 2-chloro-3-methoxybenzoic acid, stout, colourless rectangles, m. p. 160° (Found : Cl, 18·8. $C_8H_7O_3Cl$ requires Cl, 19·0%). 4-Chloro-3-methoxybenzoic acid forms needles, m. p. 215—216° (Found : Cl, 18·9%).

The *acetyl* derivative, m. p. 62° (Found : Cl, 18·0. $C_9H_7O_3Cl$ requires Cl, 17·9%), and the *benzoyl* derivative, m. p. 88° (Found : Cl, 13·5. $C_{14}H_9O_3Cl$ requires Cl, 13·6%), both separate from alcohol in stout, rhombic crystals. The *oxime* forms colourless needles, m. p. 149°, from diluted alcohol (Found : Cl, 20·8. $C_7H_6O_2NCl$ requires Cl, 20·7%).

The p-*nitrophenylhydrazone* crystallises in orange-red, microcrystalline needles, m. p. 244—245°, from hot alcohol (Found : N, 14·7; Cl, 12·0. $C_{13}H_{10}O_3N_3Cl$ requires N, 14·4; Cl, 12·2%).

The *semicarbazone* forms pale yellow needles, m. p. 236—237° (Found : Cl, 16·5. $C_8H_8O_2N_3Cl$ requires Cl, 16·6%).

4-*Chloro-3-hydroxybenzaldehyde.*—This compound was prepared from 4-nitro-3-hydroxybenzaldehyde by method (b) above and obtained in colourless needles, m. p. 121° (Found : Cl, 22·55. $C_7H_5O_2Cl$ requires Cl, 22·6%).

The *oxime* separates from dilute alcohol in colourless needles containing water of crystallisation. These decompose at 106—110°.

The anhydrous needles melt at 126° (Found : Cl, 20·6. $C_7H_6O_2NCl$ requires Cl, 20·7%). The p-*nitrophenylhydrazone* separates from dilute alcohol in violet-red needles, m. p. 226—227° (Found : Cl, 11·9. $C_{13}H_{10}O_3N_3Cl$ requires Cl, 12·2%), and the *semicarbazone* crystallises in pale yellow needles, m. p. 238—239° (Found : N, 20·0. $C_8H_8O_2N_3Cl$ requires N, 19·7%).

6-*Chloro*-3-*hydroxybenzaldehyde*.—(a) *Preparation from* 6-*nitro*-3-*hydroxybenzaldehyde*. This was carried out by process (b) above. The yield was very poor. The compound crystallised from dilute acetic acid in colourless needles, m. p. 111° (Found : Cl, 22·4. $C_7H_5O_2Cl$ requires Cl, 22·6%).

(b) *Preparation from* 2-*chlorobenzaldehyde*. *Nitration*. The chloroaldehyde (16·5 g.) was added at 0—5° during 1 hour to a solution of sodium nitrate (11 g.) in 98% sulphuric acid (200 g.). After 30 minutes, the mixture was poured on to ice, and the solid product filtered off, washed with warm dilute sodium carbonate (yield 21 g.), and recrystallised from dilute acetic acid; m. p. 78—79° (Erdmann, *Annalen*, 1893, **272**, 153, gives m. p. 80°). (On oxidation with alkaline permanganate it gives 2-chloro-5-nitrobenzoic acid, m. p. 165°.) *Reduction*. This proceeds normally with sodium hyposulphite, but the resulting 2-chloro-5-aminobenzaldehyde gave only a trace of 6-chloro-3-hydroxybenzaldehyde on decomposition by the usual diazotisation-steam distillation process. The chloronitrobenzaldehyde was therefore converted into its oxime, m. p. 143°, and a solution of this (5·5 g.) in 20 c.c. of aqueous sodium hydroxide (20%) and 100 c.c. of water was added gradually to a mixture of crystallised ferrous sulphate (50 g.), 20% sodium hydroxide (70 c.c.), and water (200 c.c.). After being stirred for 1 hour, the mixture was warmed to 30—40°, filtered, and the filtrate just acidified; 2-*chloro*-5-*aminobenzaldoxime* was then precipitated. This crystallised from alcohol in colourless plates, m. p. 159—160°, which turned brown in the air (Found : Cl, 20·7. $C_7H_7ON_2Cl$ requires Cl, 20·8%). *Diazotisation and decomposition*. The aldoxime was redissolved by the addition of concentrated hydrochloric acid (20 c.c.), diazotised at 0° (sodium nitrite, 1·75 g.), and the solution decomposed by pouring it into boiling dilute sulphuric acid (20%). The 6-chloro-3-hydroxybenzaldehyde thus formed could be removed (very slowly) in steam, but was best extracted with ether. Yield, 3 g.

The *oxime* separates from dilute alcohol in colourless needles containing $1H_2O$ (Found : H_2O, 10·0. $C_7H_6O_2NCl,H_2O$ requires H_2O, 9·5%), and from absolute alcohol in anhydrous needles, m. p. 146—147° (Found : Cl, 20·6. $C_7H_6O_2NCl$ requires Cl, 20·7%). The p-*nitrophenylhydrazone* crystallises from dilute alcohol in red needles, m. p. 250—251° (Found : Cl, 12·0. $C_{13}H_{10}O_3N_3Cl$ requires Cl, 12·2%).

The *semicarbazone* forms pale yellow needles, m. p. 236° (Found : N, 19·9. $C_8H_8O_2N_3Cl$ requires N, 19·7%).

Dichloro-3-*hydroxybenzaldehydes*.

2 : 6-*Dichloro*-3-*hydroxybenzaldehyde*.—(a) *Preparation by chlorination of* 2-*chloro*-3-*hydroxybenzaldehyde*. A solution of 5 g. of the aldehyde in glacial acetic acid (50 c.c.) was treated at room temperature (15°) with chlorine until the weight had increased by 2·5 g. (50 minutes). The white solid that separated crystallised from water in colourless needles, m. p. 140°. These melted at 116° when mixed with 2-chloro-3-hydroxybenzaldehyde (m. p. 139·5°) (Found : Cl, 36·8. $C_7H_4O_2Cl_2$ requires Cl, 37·1%). On concentrating the solution to 20 c.c. the bulk of the product separated. It melted at 115—118°, and at 140° after two crystallisations from water (yield 6 g.). There were no coloured by-products such as were formed during monochlorination.

(b) *Preparation from* m-*hydroxybenzaldehyde*. Through a solution of 20 g. of the aldehyde in glacial acetic acid (90 c.c.), chlorine was passed until the increase in weight was 22 g. After an interval the rate of absorption slackened, presumably when monochlorination had taken place. The product (15 g.) was collected after 12 hours and fractionally crystallised from water. The more sparingly soluble 2 : 6-dichloro-3-hydroxybenzaldehyde separated in stout, white, rhombic crystals (yield 12 g.), m. p. 140°, identical with those obtained in (a) (Found : Cl, 36·9%). From the concentrated mother-liquor 1·5 g. of a homogeneous substance separated in needles, m. p. 129°. This was identified with the 4 : 6-dichloro-3-hydroxybenzaldehyde of Friedländer and Schenck (*loc. cit.*) and was evidently formed from the 6-chloro-3-hydroxybenzaldehyde produced in the initial monochlorination (see above).

(c) *Preparation from* 6-*chloro*-3-*hydroxybenzaldehyde*. A solution of 2 g. of the aldehyde in glacial acetic acid (15 g.) was chlorinated for 18 minutes. Crystals (0·5 g.) of 2 : 6-dichloro-3-hydroxybenzaldehyde separated (m. p. 140° ; mixed m. p. 140°). On evaporating the filtrate, a mixture of dichloro-compounds (1·5 g.), m. p. 120°, was obtained which has defied resolution (Found : Cl, 36·8. Calc., Cl, 37·1%). It is probably a mixture of the 2 : 6- and 4 : 6-isomerides. The *p*-nitrophenylhydrazone prepared from it melts at a lower temperature than that of either of these two compounds.

The *oxime* of 2 : 6-dichloro-3-hydroxybenzaldehyde crystallises from dilute alcohol in clusters of felted needles, m. p. 174—175° (Found : Cl, 34·2. $C_7H_5O_2NCl_2$ requires Cl, 34·5%) and the p-*nitrophenylhydrazone* in deep orange-red needles, m. p. 205—206° (Found : Cl, 21·6. $C_{13}H_9O_3N_3Cl_2$ requires Cl, 21·8%).

2 : 4-*Dichloro*-3-*hydroxybenzaldehyde*.—The crystals obtained quantitatively by the direct chlorination of 4-chloro-3-hydroxybenzaldehyde as in (c) above melted at 136—140°, and at 141° after crystallisation from dilute acetic acid. Mixed with 2 : 6-dichloro-3-hydroxybenzaldehyde (m. p. 140°), they melted at 111° (Found : Cl, 36·9. $C_7H_4O_2Cl_2$ requires Cl, 37·1%).

The *oxime* crystallises from dilute alcohol in fine needles, m. p. 188° (Found : Cl, 34·3. $C_7H_5O_2NCl_2$ requires Cl, 34·5%), and the p-*nitrophenylhydrazone* in orange-red needles, m. p. 277—278° (decomp.) (Found : N, 13·2; Cl, 21·6. $C_{13}H_9O_3N_3Cl_2$ requires N, 12·9; Cl, 21·8%).

2 : 4 : 6-*Trichloro*-3-*hydroxybenzaldehyde*.

This is obtained normally by trichlorination in glacial acetic acid solution. The crystals separate with acetic acid of crystallisation and immediately effloresce when exposed to air. They melt at 114°, and at the same temperature after they have been crystallised from dilute acetic acid (Krause, *loc. cit.*, gives m. p. 116°).

The *sodium* salt crystallises in pure yellow needles, which are sparingly soluble in water. The *oxime* separates from dilute alcohol in needles, m. p. 174° (Krause, *loc. cit.*, gives m. p. 170°) (Found : Cl, 44·1. Calc., Cl, 44·3%).

The p-*nitrophenylhydrazone* was prepared by mixing alcoholic solutions of the components at 70° and then adding one drop of water to the cooled mixture. Crystallisation was spontaneous and the product was then almost insoluble in alcohol. It crystallises in yellow-orange, microcrystalline needles, m. p. 272—273° (decomp.) (Found : Cl, 28·9. $C_{13}H_8O_3N_3Cl_3$ requires Cl, 29·5%).

Methyl Ethers of the Chloro-3-*hydroxybenzaldehydes*.

These were prepared from the corresponding chloro-3-hydroxy- or nitro-3-methoxy-benzaldehydes by the methods used in the case of the bromo-compounds (Hodgson and Beard, *loc. cit.*, p. 878).

The following details of the methylation are reported because their adoption greatly improves the yield : a solution of 6-nitro- or 4-nitro-3-hydroxybenzaldehyde (20 g.) in water (100 c.c.) containing sodium bicarbonate (25 g.) is boiled and methyl sulphate (25 c.c.) gradually added with vigorous shaking. The mixture is heated under reflux for 15 minutes (not longer, else the yield is diminished), and the product filtered off on cooling (yield 18·5 g.).

6-*Nitro*-3-*methoxybenzoic acid*, prepared by alkaline oxidation of the aldehyde, has m. p. 255° (Rieche, *Ber.*, 1889, **22**, 2347, gives

m. p. 132—133°). It crystallises in thick, colourless prisms (Found : N, 7·0. Calc., N, 7·1%). The *silver* salt is a white, crystalline solid (Found : Ag, 35·2. Calc., Ag, 35·5%).

Nitration of 3-Methoxybenzaldehyde.—Friedländer's method (*loc. cit.*) of adding the nitric acid "*auf einmal*" proved impracticable owing to the explosive violence of the reaction.

3-Methoxybenzaldehyde (20 g.) was added drop by drop during 2 hours to a mixture of 88·1% nitric acid (94 c.c.) and water (6 c.c.) maintained below 5°. The crude product (26·5 g.) obtained on pouring the mixture on to ice was washed, dried, and dissolved in hot benzene (80 c.c.). On cooling, 2-nitro-3-methoxybenzaldehyde (12 g.) separated in crystals, m. p. 98°, and more (3 g.) was obtained on concentrating the mother-liquor. Recrystallised several times from acetic acid, it melted at 102°. The material remaining in the benzene solution, consisting mainly of 6-nitro- mixed with a little 2-nitro-3-methoxybenzaldehyde, was distilled with steam and the 6-nitro-isomeride, which is the more volatile, was thus isolated. No 4-nitro-3-methoxybenzaldehyde was detected in the mixture, for on oxidation with alkaline permanganate this yielded an acid of m. p. 250° (6-nitro-, 2-nitro-, and 4-nitro-3-methoxybenzoic acids have m. p. 255°, 251°, and 208°, respectively).

Properties of the Chloro-3-methoxybenzaldehydes.—These all crystallise in colourless needles from dilute alcohol, sublime readily, and are very volatile in steam.

2-*Chloro*-3-*methoxybenzaldehyde* has m. p. 56° (Found : Cl, 21·0. $C_8H_7O_2Cl$ requires Cl, 20·8%).

The *oxime* crystallises from dilute alcohol in stout needles, m. p. 130·5° (Found : Cl, 18·9. $C_8H_8O_2NCl$ requires Cl, 19·1%), the p-*nitrophenylhydrazone* from alcohol in old-gold needles, m. p. 226—227° (Found : N, 14·0; Cl, 11·9. $C_{14}H_{12}O_3N_3Cl$ requires N, 13·7; Cl, 11·6%), and the p-*bromophenylhydrazone* from alcohol in pale yellow plates, m. p. 155—156° (Found : N, 8·3. $C_{14}H_{12}ON_2ClBr$ requires N, 8·2%. 0·1624 G. gave 0·1592 g. of mixed silver halides. Calc., 0·1585 g.).

4-*Chloro*-3-*methoxybenzaldehyde* has m. p. 52° and acquires a beautiful silver-grey colour on keeping (Found : Cl, 20·8%).

The *oxime* crystallises in colourless feathery needles, m. p. 98—99° (Found : Cl, 18·9%), the p-*nitrophenylhydrazone* in old-gold needles, m. p. 251° (Found : N, 14·1%), and the p-*bromophenylhydrazone* in pale pink, feathery crystals, m. p. 134° (Found : N, 8·0%).

6-*Chloro*-3-*methoxybenzaldehyde* has m. p. 62° (Found : Cl, 21·2%) and on oxidation (*loc. cit.*, p. 880) yields 6-chloro-3-methoxybenzoic acid, which crystallises in needles, m. p. 170—171°, from dilute acetic acid (Found : Cl, 18·8. Calc., Cl, 19·0%). Peratoner and Condorell (*Gazzetta*, 1898, **28**, i, 197) give 171° as the m. p. of the acid prepared from 6-chloro-3-methoxytoluene.

The *oxime* forms fine needles, m. p. 101·5° (Found : Cl, 19·0%), the p-*nitrophenylhydrazone* crystallises in old-gold needles, m. p. 229° (Found : N, 14·0%), and the p-*bromophenylhydrazone* in pale yellow plates, m. p. 100° (Found : N, 8·0%).

2 : 6-*Dichloro*-3-*methoxybenzaldehyde* has m. p. 102° (Found : Cl, 34·9. $C_8H_6O_2Cl$ requires Cl, 34·6%) and on oxidation yields 2 : 6-*dichloro*-3-*methoxybenzoic acid*, which crystallises in stout needles, m. p. 149·5°, from dilute alcohol (Found : Cl, 32·0. $C_8H_6O_3Cl_2$ requires Cl, 32·1%).

The p-*nitrophenylhydrazone* forms old-gold needles, m. p. 214—215° (Found : Cl, 20·7. $C_{14}H_{11}O_3N_3Cl_2$ requires Cl, 20·9%).

2 : 4-*Dichloro*-3-*methoxybenzaldehyde* has m. p. 82° (Found : Cl, 35·0%) and on oxidation yields 2 : 4-dichloro-3-methoxybenzoic acid, which crystallises in colourless needles, m. p. 163° (Found : Cl, 32·0%).

The p-*nitrophenylhydrazone* forms old-gold needles, m. p. 258—260° (Found : Cl, 20·7%).

2 : 4 : 6-*Trichloro*-3-*methoxybenzaldehyde* was prepared by methylating the hydroxy-compound. It is only slowly volatile in steam and crystallises from alcohol in stout needles, m. p. 76° (Found : Cl, 44·1. $C_8H_5O_2Cl_3$ requires Cl, 44·4%). By very slow oxidation with alkaline permanganate it is converted into 2 : 4 : 6-trichloro-3-methoxybenzoic acid, which crystallises in needles, m. p. 109° (Found : Cl, 41·6. Calc., Cl, 41·7%). Zincke (*Annalen*, 1891, **261**, 239) gives m. p. 90°.

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