52. *Halogenation of* m-5- *and* m-2-*Xylenol. Mixed Chlorobromo-derivatives.*

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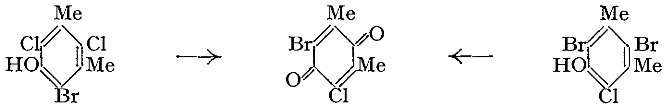
For the purpose of comparison with the degradation products of certain polyhalogeno-*m*-xylenols, eight new mixed *chlorobromo*-m-*xylenols* are prepared. 4-*Chloro*-6-*bromo*-m-*xyloquinone* is characterised.

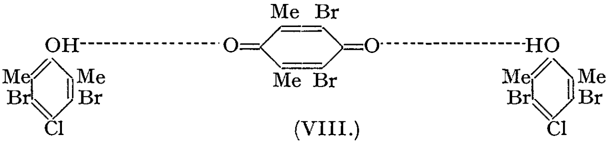
The only mixed halogeno-*m*-xylenol described in the literature is 2-chloro-4 : 6-dibromo-*m*-5-xylenol (Lesser and Gad, *Ber.*, 1923, **56**, 963), prepared by dibrominating 2-chloro-*m*-5-xylenol. The quick monobromination method, using chloroform as solvent and aluminium bromide as catalyst, and used to prepare 2-bromo-4-nitroaniline (*J.*, 1935, 1135), was applied successfully to the preparation in almost theoretical yield of 2-*chloro*-4-*bromo*-m-5-*xylenol* (I) from 2-chloro-*m*-5-xylenol. The usual methods of bromination gave mixtures of 2-chloro- and 2-chloro-4 : 6-dibromo-derivatives. A similar monochlorination, using iodine as catalyst, of 2-bromo-*m*-5-xylenol, gave 4-*chloro*-2-*bromo*-m-5-*xylenol* (II). 2-Chloro-4 : 6-dibromo-*m*-5-xylenol was obtained by further bromination of (I), and the 4 : 6-*dichloro*-2-*bromo*-derivative was prepared by chlorination in chloroform of (II), or by dichlorinating 2-bromo-*m*-5-xylenol in acetic acid. 2 : 6-*Dichloro*-4-*bromo*-m-5-*xylenol* (III) was prepared readily by monobrominating 2 : 4-dichloro-*m*-5-xylenol, or by the monochlorination of (I), whilst bromination of (II) gave 4-*chloro*-2 : 6-*dibromo*-m-5-*xylenol* (IV). Each of the two last-named mixed trihalogeno-derivatives is oxidised by nitric acid to 4-*chloro*-6-*bromo*-m-*xyloquinone* (V) :



(III.) (V.) (IV.)

It is noteworthy that 2 : 4 : 6-tribromo-, m. p. 165—166°, 2-chloro-4 : 6-dibromo-, m. p. 164°, and 2 : 6-dichloro-4-bromo-*m*-5-xylenol, m. p. 165—166°, do not depress the m. p. of one another.

5-*Chloro*-4-*bromo*-m-2-*xylenol* (VI) was prepared in almost theoretical yield from 5-chloro-*m*-2-xylenol by the quick monobromination method; on adding (VI) to excess of liquid bromine, 5-*chloro*-4 : 6-*dibromo*-m-2-*xylenol* (VII), m. p. 188—189°, was formed, which was also obtained by a similar bromination of 5-chloro-*m*-2-xylenol. On adding aqueous bromine to compound (VII) at room temperature, 4 : 6-dibromo-*m*-xyloquinone was obtained, together with a scarlet adduct (VIII) of the quinhydrone type, formed from 1 mol. of the above quinone and 2 mols. of compound (VII). The constitution of this product was confirmed by synthesis.



(VIII.)

4 : 5-*Dichloro*-6-*bromo*-m-2-*xylenol* (IX), m. p. 186—188°, was prepared by adding molten 4 : 5-dichloro-*m*-2-xylenol to excess of liquid bromine, but no mixed nuclear halogeno-*m*-2-xylenol was isolable by attempted chlorination of 5-bromo-*m*-2-xylenol. In chloroform at 5—15°, only an intractable oil was obtained, whilst more vigorous chlorination of 5-bromo-*m*-2-xylenol caused some displacement of bromine.

Improved methods were devised for the preparation of 5-bromo-, 4 : 5-dibromo-, and 4 : 5 : 6-tribromo-*m*-2-xylenol (X) (cf. Auwers and Markovitz, *Ber.*, 1908, **41**, 2336) by the direct bromination of *m*-2-xylenol. In contrast to the halogeno-*m*-5-xylenols, the third bromine atom is difficult to introduce, compound (X) being obtained by adding *m*-2-xylenol to a large excess of bromine.

In view of the similarities in m. p. and the tendency to show no depression on admixture of mixed halogeno-derivatives, it was imperative to control constitution by full analysis, and as far as possible by using only the requisite molecular proportion of halogen; *e.g.*, in preparing 2 : 6-dichloro-4-bromo-*m*-5-xylenol from 2 : 6-dichloro-*m*-5-xylenol, only 1 mol. of bromine was used, and the resulting product was shown to contain three halogen atoms. Replacements of one halogen by another were thus carefully controlled.

EXPERIMENTAL.

2-*Chloro*-4-*bromo*-m-5-*xylenol* (I).—Bromine (20·5 g.; 1 mol.) in dry chloroform (100 c.c.) was added rapidly to a stirred mixture of 2-chloro-*m*-5-xylenol (20 g.; 1 mol.), dry chloroform (200 c.c.), and a little anhydrous aluminium bromide. A vigorous reaction was complete in a few seconds, and, after removal of solvent, 2-*chloro*-4-*bromo*-m-5-*xylenol* was crystallised from light petroleum; it formed colourless needles, m. p. 68° (yield, 29 g.; 96·3%) (Found : C, 41·3; H, 3·5; 0·2715 g. gave 0·3829 g. of AgCl + AgBr. C_8H_8OClBr requires C, 40·8; H, 3·4%; AgCl + AgBr, 0·3822 g.). Its constitution was further established by bromination to 2-chloro-4 : 6-dibromo-*m*--5-xylenol.

4-*Chloro*-2-*bromo*-m-5-*xylenol* (II).—Solutions of 2-bromo-*m*-5-xylenol (20 g.; 1 mol.) in dry chloroform containing a few crystals of iodine, and chlorine (7·1 g.; 1 mol.) in the same solvent (100 c.c.), were mixed rapidly. 4-*Chloro*-2-*bromo*-m-5-*xylenol* separated from light petroleum in colourless needles, m. p. 90—110°, softening at 83° (yield, 18·2 g.; 77·4%) (Found : C, 40·85; H, 3·5; total halogen, 49·7. C_8H_8OClBr requires C, 40·8; H, 3·4; total halogen, 49·05%).

2-*Chloro*-4 : 6-*dibromo*-m-5-*xylenol*.—Bromine (103 g.; 2 mols.) in acetic acid (200 c.c.) was added to a solution of 2-chloro-*m*-5-xylenol (50 g.; 1 mol.) in the same solvent (600 c.c.) during 3 hours, with stirring. After addition to water, the precipitate was collected; it crystallised from light petroleum in long, colourless needles, m. p. 164° (yield, 88 g.; 87·5%) (Found : C, 32·0; H, 2·4; 0·1135 g. gave 0·1886 g. of AgCl + AgBr. Calc. for $C_8H_7OClBr_2$: C, 30·5; H, 2·2%; AgCl + AgBr, 0·1875 g.) (cf. Lesser and Gad, *loc. cit.*). It was oxidised by nitric acid (*d* 1·42) at 100° for 10 minutes to 4 : 6-dibromo-

m-xyloquinone, golden-yellow plates, m. p. 172° (Kohn and Feldmann, *Monatsh.*, 1928, **49**, 169, record m. p. 169°).

4 : 6-*Dichloro*-2-*bromo*-m-5-*xylenol*.—Compound (II) was treated with a further mol. of chlorine as above; the *dichlorobromo*-derivative crystallised from light petroleum in long, colourless needles, m. p. 182°, in almost theoretical yield (Found : C, 35·3; H, 2·8; total halogen, 56·2. $C_8H_7OCl_2Br$ requires C, 35·55; H, 2·6; total halogen, 55·9%). Larger amounts were prepared by adding chlorine (37 g.; 2 mols.) in acetic acid (500 c.c.), slowly and with good agitation, to a cooled solution of 2-bromo-*m*-5-xylenol (52 g.; 1 mol.) in acetic acid (500 c.c.), and diluting the mixture (yield, 61 g.; 87%).

2 : 6-*Dichloro*-4-*bromo*-m-5-*xylenol*.—(*a*) Chlorine (4·5 g.; 1 mol.) in acetic acid (150 c.c.) was added slowly to a solution of (I) (15 g.; 1 mol.) in acetic acid (120 c.c.) at $<20°$. After dilution, the precipitate was collected; it crystallised from light petroleum in long, colourless needles, m. p. 165—166° (yield, 16·8 g.; 97·6%) (Found : C, 35·8; H, 2·8; 5·014 mg. gave 8·940 mg. of AgCl + AgBr. $C_8H_7OCl_2Br$ requires C, 35·55; H, 2·6%; AgCl + AgBr, 8·821 mg.). 2 : 6-*Dichloro*-4-*bromo*-m-5-*xylenol* was oxidised by nitric acid (*d* 1·42) at 100° to 4-*chloro*-6-*bromo*-m-*xyloquinone*, which crystallised from light petroleum in large yellow plates, m. p. 170—171° (Found : 4·693 mg. gave 6·215 mg. AgCl + AgBr. $C_8H_6O_2ClBr$ requires AgCl + AgBr, 6·235 mg.).

(*b*) Bromine (10 g.; 1 mol.) in acetic acid (80 c.c.) was added slowly, with stirring, to a solution of 2 : 4-dichloro-*m*-5-xylenol (12 g.; 1 mol.) in acetic acid (120 c.c.) at room temperature. Next day, the mixture was added to water (500 c.c.); yield, 14·4 g. (84·7%).

4-*Chloro*-2 : 6-*dibromo*-m-5-*xylenol*.—Bromine (10 g.; 1 mol.) in acetic acid (100 c.c.) was added slowly to a solution of compound (II) (14·7 g.; 1 mol.) in the same solvent at below 20°. After 1 hour, the mixture was poured on ice-water (600 g.); the *chloro-dibromo*-compound crystallised from light petroleum in long, colourless needles, m. p. 170° (yield, 18 g.; 90%) (Found : C, 30·1; H, 2·4; 4·618 mg. gave 7·515 mg. of AgCl + AgBr. $C_8H_7OClBr_2$ requires C, 30·5; H, 2·2%; AgCl + AgBr, 7·628 mg.). Oxidation as above gave 4-chloro-6-bromo-*m*-xyloquinone.

5-*Chloro*-4-*bromo*-m-2-*xylenol* (VI).—Bromine (16·8 g.; 1 mol.) in dry chloroform (75 c.c.) was added rapidly to 5-chloro-*m*-2-xylenol (15 g.; 1 mol.) in chloroform (150 c.c.), in presence of a little aluminium bromide, and the mixture kept at 50° for 2 hours. The *compound* (VI) formed fine colourless needles, m. p. 86—87°, from light petroleum (yield, 21·8 g.; 96·6%) (Found : 2 mg. gave 2·812 mg. of AgCl + AgBr. C_8H_8OClBr requires 2·815 mg. AgCl + AgBr).

5-*Chloro*-4 : 6-*dibromo*-m-2-*xylenol* (VII).—(*a*) Molten 5-chloro-4-bromo-*m*-2-xylenol (2·3 g.; 1 mol.) was added in small quantities to liquid bromine (7·4 g.; 4·5 mols.) during 15 minutes at room temperature. Compound (VII) crystallised from chloroform in almost colourless, prismatic needles, m. p. 188—189° (yield, 3·05 g.; 96·9%) (Found : 2 mg. gave 3·21 mg. of AgCl + AgBr. $C_8H_7OClBr_2$ requires AgCl + AgBr, 3·33 mg.). Bromine (2 mols.) in twelve times its weight of water was added to finely-ground 5-*chloro*-4 : 6-*dibromo*-m-2-*xylenol* at room temperature, to give 4 : 6-dibromo-*m*-xyloquinone and an adduct (VIII) of the same quinone (1 mol.) and 5-chloro-4 : 6-dibromo-*m*-2-xylenol (2 mols.), which crystallised from dry chloroform in scarlet, prismatic needles, m. p. 141—142°; its constitution was confirmed by synthesis, by melting the requisite proportions of the two constituents and crystallising.

(*b*) Finely-ground 5-chloro-*m*-2-xylenol (10·5 g.; 1 mol.) was added gradually to liquid bromine (43 g.; 4 mols.) at 20° during 1 hour; yield, 20·7 g. (98·5%).

4 : 5-*Dichloro*-6-*bromo*-m-2-*xylenol* (IX).—Molten 4 : 5-dichloro-*m*-2-xylenol (5·75 g.; 1 mol.) was added gradually to liquid bromine (19·3 g.; 4 mols.) at room temperature. The *compound* (IX) crystallised from chloroform in long, pale yellow, prismatic needles, m. p. 188° (yield, 8 g.; 98·4%) (Found : C, 35·7; H, 2·8; 8·459 mg. gave 14·785 mg. of AgCl + AgBr. $C_8H_7OCl_2Br$ requires C, 35·55; H, 2·6%; AgCl + AgBr, 14·822 mg.).

5-*Bromo*-m-2-*xylenol*.—Bromine (99·4 g.; 1 mol.) and *m*-2-xylenol (75 g.; 1 mol.) in acetic acid (575 c.c.) at 15° gave the bromo-xylenol, which crystallised from light petroleum in long, fine, colourless needles, m. p. 80—81° (Auwers and Markovitz record m. p. 79·5°) (yield, 118·5 g.; 95·9%).

4 : 5-*Dibromo*-m-2-*xylenol*.—Bromine (9 g.; 1·1 mols.) in dry chloroform (20 c.c.) was added quickly to a solution of 5-bromo-*m*-2-xylenol (10 g.; 1 mol.) in chloroform (100 c.c.) and a little aluminium bromide, and the mixture kept at 55° for 30 minutes. After being left overnight at room temperature, the solvent was removed; the residue crystallised from light petroleum in fine, colourless needles, m. p. 86° (yield, 13·2 g.; 94·8%), stable in alcohol solution to sulphur dioxide.

4 : 5 : 6-*Tribromo*-m-2-*xylenol*.—(*a*) Molten *m*-2-xylenol (18·3 g.; 1 mol.) was added to liquid bromine (144 g.; 6 mols.) at 0°, and after 2 hours excess of bromine was removed on the water-bath and the residue extracted with boiling 15% aqueous sodium hydroxide. The tribromo-compound crystallised from chloroform in pink-tinged needles, m. p. 206—207° (Auwers and Markovitz record m. p. 201°) (yield, 49·5 g.; 92·1%) (Found: C, 27·6; H, 2·4; Br, 67·5. Calc. for $C_8H_7OBr_3$: C, 26·7; H, 1·95; Br, 66·85%), stable to sulphur dioxide in alcohol and to boiling aqueous methyl-alcoholic silver nitrate. The use of excess of bromine in acetic acid gives only the 4 : 5-dibromo-derivative.

(*b*) Molten 4 : 5-dibromo-*m*-2-xylenol (2·5 g.; 1 mol.) and liquid bromine (2 g.; 2 mols.) at 0° for 12 hours gave the tribromo-derivative (yield, 2·9 g.; 90·5%).

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