

CLXXXV.—*The Monochloro-derivatives of m-Cresol.*

By GEORGE PHILIP GIBSON.

EXCEPT in the case of 6-chloro-*m*-cresol (Kalle and Co., D.R.-PP. 90,847 and 93,694; Friedländer's "Fortschritte," Vol. IV, 94) and 6-chloro-*m*-methoxybenzoic acid (Peratoner and Condorelli, *Gazzetta*, 1898, **28**, i, 214), little information is given in the literature regarding the monochloro-derivatives of *m*-cresol (Mazzura, *Gazzetta*, 1899, **29**, i, 380; 1900, **30**, ii, 84; Friedländer and Schenk, *Ber.*, 1914, **47**, 3040; Raschig, D.R.-P. 232,071, 1909; Biechele, *Annalen*, 1869, **151**, 115).

The author has studied the monochlorination of *m*-cresol, isolated the 2-, 4-, and 6-chloro-*m*-cresols (the first with difficulty), and converted them into the corresponding chloro-*m*-methoxybenzoic acids. The constitutions of these were determined by preparing the respective compounds from the corresponding 2-, 4-, and 6-nitro-*m*-cresols (Gibson, J., 1923, **123**, 1267) by successive methylation, reduction, substitution of chlorine for the amino-group, and oxidation of the resulting chloro-*m*-tolyl methyl ethers.

The reduction of 2-nitro-*m*-tolyl methyl ether by tin and hydrochloric acid produces an oily mixture of bases instead of the pure 3-methoxy-*o*-toluidine which is formed when iron and dilute acetic acid are used (Gibson, *loc. cit.*). The least volatile constituent of this mixture is a chloro-base, m. p. 47°. This is probably 5-chloro-3-methoxy-*o*-toluidine, since an isomeric base, m. p. 50°, was obtained by reducing 6-chloro-2-nitro-*m*-tolyl methyl ether.

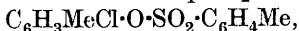
EXPERIMENTAL.

Chlorination of m-Cresol.—A saturated solution of chlorine (1.1 mols.) in carbon tetrachloride (7.5 g. in 100 c.c.) was added gradually to a mechanically stirred solution of *m*-cresol in carbon tetrachloride. The solvent was then evaporated and the residue fractionally distilled. After five operations, 37% of the product boiled at 196–197° and 47% at 231–233°.

The fraction, b. p. 196–197°, was seeded at 0° with a crystal of 4-chloro-*m*-cresol obtained by the hydrolysis of 4-chloro-*m*-tolyl toluene-*p*-sulphonate. The crystals thus produced were separated from the residual oil, washed quickly with ice-cold light petroleum, and recrystallised from that solvent. The crystals obtained by seeding the residual oil, diluted with an equal volume of light petroleum (b. p. 50–60°), at –15° were similarly treated.

4-*Chloro-m-cresol* was thus obtained (29% of the fraction) in large, colourless prisms, m. p. 46°, b. p. 196° (Found: Cl, 24.8.

C_7H_7OCl requires Cl, 24.8%). The *methyl ether* is a colourless, pleasant-smelling liquid, b. p. 212.5°. The *acetate* has b. p. 122—123°/11 mm. The *benzoate* separates from alcohol in massive tablets containing alcohol, m. p. 31°, and from light petroleum in crystals, m. p. 40°. The *toluene-p-sulphonate*,



crystallises from alcohol or acetone in large, six-sided prisms, m. p. 96°. It is sparingly soluble in alcohol or light petroleum.

The mixture of chloro-*m*-cresols obtained from the final petroleum mother-liquor (p. 1424) was converted almost quantitatively by treatment with sodium hydroxide solution and methyl sulphate into a mixture of ethers, b. p. 218—219°, which on oxidation with boiling dilute permanganate solution gave a theoretical yield of a mixture, m. p. 185—196°, of chloromethoxybenzoic acids. This mixture, systematically crystallised from chloroform, gave 42% of 4-chloro-*m*-methoxybenzoic acid, m. p. 211°. The final mother-liquors yielded a glue-like mass, which was dissolved in ether and fractionally extracted with 1% aqueous sodium hydroxide; the ethereal solution of the acid from each of these fractions was again extracted with an aqueous solution of the sodium salt of the next fraction. By repeated treatment of this kind, the mixture was completely separated into 2-chloro- and 4-chloro-*m*-methoxybenzoic acids.

2-Chloro-m-cresol, the presence of which in the crude chlorination product was thus established, was obtained by boiling its methyl ether (below) with hydriodic acid for 6 hours. The product was freed from the unchanged methyl ether with the aid of sodium hydroxide and distilled (b. p. about 194°); it then crystallised from light petroleum in massive, ill-defined, transparent crystals, m. p. 55—56°, having a pronounced phenolic odour and being very sparingly soluble in cold water. The *methyl ether*, prepared from 2-nitro-*m*-tolyl methyl ether (p. 1426), crystallised from light petroleum in massive prisms, m. p. 24.2°, b. p. 218.5° (Found: Cl, 22.7. C_8H_9OCl requires Cl, 22.7%).

6-Chloro-m-cresol.—A portion (49%) of the fraction of the crude chlorination product, b. p. 231—233°, solidified, and recrystallisation from light petroleum gave pure 6-chloro-*m*-cresol, m. p. 57° (Kalle and Co., *loc. cit.*, give 66°), b. p. 234° (Found: Cl, 24.9. Calc.: Cl, 24.8%).

The *methyl ether* boils at 213.5° and the *acetate* at 123—124° 11 mm. The *benzoate*, m. p. 86°, crystallises in thin, rectangular plates from alcohol, carbon tetrachloride, or light petroleum, and is not freely soluble in the latter two (Found: C, 68.1; H, 4.5. $C_{14}H_{11}O_2Cl$ requires C, 68.2; H, 4.4%). The *toluene-p-sulphonate*,

m. p. 98°, crystallises from alcohol and light petroleum, in both of which it is only slightly soluble, in plates and needles respectively.

The mother-liquors from the 6-chloro-*m*-cresol (p. 1425) gave, on evaporation, a solid of low melting point, which was treated with methyl sulphate and alkali; the resulting mixture of methyl ethers * gave, after repeated fractional distillation, 35% of 6-chloro-*m*-tolyl methyl ether (b. p. 213.5°) and about 21% of a liquid, b. p. 248—249°, which was probably a mixture of 2 : 6- and 4 : 6-dichloro-*m*-tolyl methyl ethers.

Reduction of 2-Nitro-m-tolyl Methyl Ether (compare Gibson, J., 1923, **123**, 1267; Hodgson and Beard, J., 1925, **127**, 498).—By the action of tin and hydrochloric acid on this ether a mixture (m. p. 27°) of 3-methoxy-*o*-toluidine and 5-chloro-3-methoxy-*o*-toluidine (about 10% of the product) is produced. The former is removed by fractional distillation in steam, and the residue, after being freed from a red impurity by distillation in a vacuum, separates from light petroleum in slender needles of 5-chloro-3-methoxy-*o*-toluidine, m. p. 47°, b. p. 140—142°/11.5 mm., which are slightly soluble in light petroleum (Found: N, 8.1. C₈H₁₀ONCl requires N, 8.2%).

The *acetyl* derivative, obtained by means of acetic anhydride containing a trace of sulphuric acid (Smith and Orton, J., 1908, **93**, 1250), crystallises from alcohol, acetone, or benzene in colourless needles, m. p. 170°. It is sparingly soluble in water, light petroleum, carbon tetrachloride, or benzene (Found: N, 6.5. C₁₀H₁₂O₂NCl requires N, 6.6%).

2-Chloro-m-tolyl Methyl Ether.—The more volatile portion of the steam distillate (see above), consisting of 3-methoxy-*o*-toluidine with a small proportion of the chloro-base just described, is transformed into a mixture of chloro- and dichloro-*m*-tolyl methyl ethers by the Sandmeyer method. This product is distilled in steam, extracted from the distillate with ether, freed from any phenolic compounds by shaking with dilute aqueous alkali hydroxide, and repeatedly fractionally distilled. 2-Chloro-*m*-tolyl methyl ether (p. 1425) is thus obtained in a pure state (yield 54%, calculated on the nitro-compound used). The fractions of high boiling point, after distillation in a vacuum and recrystallisation from light petroleum, give 2 : 5-dichloro-*m*-tolyl methyl ether (yield 8.7%), which crystallises from light petroleum in slender

* Methylation in this type of compound overcomes the lowering of the boiling point due to the ortho Cl : OH grouping and the effect of a second chlorine atom in the molecule is then appreciable: 6-chloro-*m*-tolyl methyl ether boils at 213.5° and 4 : 6-dichloro-*m*-tolyl methyl ether at 249°, whereas the corresponding cresols boil at 234° and 232°, respectively.

prisms, m. p. 52°, b. p. 119—120°/12.5 mm., having the pleasant odour characteristic of these chloro-ethers (Found : OMe, 16.2; Cl, 37.0. $C_8H_8OCl_2$ requires OMe, 16.2; Cl, 37.1%).

6-Chloro-2-nitro-*m*-tolyl methyl ether is formed when 2-nitro-*m*-tolyl methyl ether is treated with chlorine at 160—170° until the gain in weight corresponds to 1 g.-atom. The dark reddish-brown product is repeatedly distilled (10 mm.) to free it from unchanged 2-nitro-ether (b. p. 120—130°), and the larger fraction (b. p. 140—145°), which solidifies, is fractionally crystallised from alcohol in order to remove some impurity, probably 4-chloro-2-nitro-*m*-tolyl methyl ether, which crystallises from the mother-liquors in tufts of very slender needles.

The 6-chloro-derivative (yield 55%) crystallises readily from alcohol, light petroleum, or carbon tetrachloride in large, pale yellow prisms, m. p. 112°. It is sparingly soluble in hot or cold water, alcohol, light petroleum, or carbon tetrachloride, but is fairly easily soluble in acetone, benzene, or chloroform (Found : Cl, 17.9. $C_8H_8O_3NCl$ requires Cl, 17.65%).

6-Chloro-3-methoxy-*o*-toluidine, prepared by reducing the preceding compound with iron borings and dilute acetic acid (compare p. 1424), crystallises from light petroleum, in which it is fairly easily soluble, in long needles, m. p. 50°, b. p. 145—146°/12 mm. (Found : N, 8.2. $C_8H_{10}ONCl$ requires N, 8.2%).

The *acetyl* derivative, m. p. 154°, crystallises readily from organic solvents, and is sparingly soluble in light petroleum, carbon tetrachloride, or benzene (Found : N, 6.3. $C_{10}H_{12}O_2NCl$ requires N, 6.6%).

When diazotised 6-chloro-3-methoxy-*o*-toluidine is treated with an alkaline solution of sodium stannite, and the resulting 6-chloro-*m*-tolyl methyl ether (b. p. 213—214°) oxidised with boiling dilute permanganate solution, 6-chloro-*m*-methoxybenzoic acid, m. p. 173.5°, is obtained (p. 1428).

Orientation of the 2-, 4-, and 6-Chloro-m-cresols.—The orientation of 2-chloro-*m*-cresol, by the preparation of its methyl ether from 2-nitro-*m*-cresol, has already been described (p. 1426). From the isomeric 4- and 6-nitro-*m*-cresols, the corresponding chloro-*m*-tolyl methyl ethers were prepared in a similar manner and oxidised to the corresponding chloro-*m*-methoxybenzoic acids. These compounds were identical respectively with those prepared by methylating the 4- and 6-chloro-*m*-cresols and oxidising the methyl ethers to the corresponding chloro-acids. These results are confirmed by the observed differences in the rates of oxidation of the methyl ethers to the acids; comparative experiments showed that the times required for the oxidation of equal weights (5 g.) of the

ethers were : 2-chloro-, 7.25 hours; 4-chloro-, 2.7 hours; and 6-chloro-, 6.7 hours.

2-Chloro-m-methoxybenzoic acid,* m. p. 160.5° , is almost insoluble in benzene, chloroform, carbon tetrachloride, or light petroleum (b. p. $60-80^{\circ}$) (Found : equiv., 186.9. Calc. for $C_8H_7O_3Cl$: equiv., 186.5). *4-Chloro-m-methoxybenzoic acid*,* m. p. 211° , crystallises from 50% aqueous alcohol in slender prisms and from chloroform in plates (Found : equiv., 186.5). *6-Chloro-m-methoxybenzoic acid*, m. p. 173.5° (Peratoner and Condorelli, *loc. cit.*, give 171°), is only sparingly soluble in benzene, light petroleum, or carbon tetrachloride, but dissolves freely in alcohol, acetone, or chloroform (Found : equiv., 187.6).

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UNIVERSITY COLLEGE, NOTTINGHAM.

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