

[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE]

**SOME MONO AND DIBROMO DERIVATIVES OF META-CRESOL**

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The literature gives very little information concerning the bromine derivatives of *m*-cresol. Descriptions of the mono and dibromo derivatives are meager and often contradictory. In some cases definite proof of structure is entirely lacking. Because a more definite knowledge of these seemed desirable and because a knowledge of the structure of some of them was essential in determining the configuration of certain benzylated derivatives of *m*-cresol, the present study was undertaken.

**Monobromo-*m*-Cresols<sup>1</sup>**

**Direct Bromination.**—One hundred and eight grams of purified *m*-cresol was dissolved in 200 cc. of chloroform, cooled to  $-10^{\circ}$ , and stirred continuously while 160 g. of bromine in 100 cc. of chloroform was added at such a rate that the temperature did not at any time exceed  $-5^{\circ}$ . After all of the bromine had been added the stirring was continued for thirty minutes and the mixture was allowed to stand overnight. After several distillations, 26 g. came over at  $120-130^{\circ}$ , and 155 g. at  $130-140^{\circ}$  (16 mm.).

When repeatedly distilled at atmospheric pressure (731 mm.), the  $120-130^{\circ}$  fraction came over at  $205-208^{\circ}$ . A sample dissolved in chloroform and treated with one molecular equivalent of bromine gave an excellent yield of 4,6-dibromo-3-methylphenol, which melted at  $65-66^{\circ}$  and gave a benzoyl derivative melting at  $84-85^{\circ}$  (see below).

*Anal.* Calcd. for  $C_7H_7OBr$ : Br, 42.78. Found: Br, 42.29.

The  $130-140^{\circ}$  fraction solidified and was repeatedly crystallized from petroleum ether. It came down in long colorless silky needles which tended to mat together and melted at  $56-57^{\circ}$ . In some cases it was crystallized from water.

*Anal.* Calcd. for  $C_7H_7OBr$ : Br, 42.78. Found: Br, 42.59, 42.65.

**Preparation of 6-Bromo-3-methylphenol from 4-Bromo-3-aminotoluene.**—Acet-*p*-toluidide was nitrated<sup>2</sup> and the acyl group removed by means of alcoholic potash. The amino group was replaced by bromine through the diazonium perbromide<sup>3</sup> and the nitro group reduced by means of tin and hydrochloric acid to form 6-bromo-*m*-toluidine<sup>4</sup> melting at  $32-33^{\circ}$  and boiling at  $115-118^{\circ}$  (16 mm.).

The 6-bromo-*m*-toluidine was dissolved by boiling with dilute hydrochloric acid. When cooled the hydrochloride separated out. The mixture was cooled to  $0^{\circ}$ , and the calculated amount of sodium nitrite in water solution was added with constant stirring. After two hours the diazonium salt was decomposed by heating on the water-bath. Steam distillation gave a reddish-yellow oil. This was salted out and extracted with ether. After removal of the solvent the residue was treated with dilute sodium hydroxide and filtered. The filtrate was acidified with dilute hydrochloric acid, salted out and

<sup>1</sup> Neville and Winther, *Ber.*, **15**, 2991 (1882); Walther and Zipper, *J. prakt. Chem.*, [2] **91**, 376 (1915); Hodgson and Moore, *J. Chem. Soc.*, 2038 (1926); Hodgson and Beard, *ibid.*, 498 (1926); Darzens and Levy, *Compt. rend.*, **193**, 292 (1931).

<sup>2</sup> Gattermann, *Ber.*, **18**, 1483 (1885).

<sup>3</sup> Bulow and Schmactenberg, *ibid.*, **41**, 2609 (1908).

<sup>4</sup> Neville and Winther, *ibid.*, **13**, 972 (1880); cf. Wroblewsky, *Ann.*, **168**, 177 (1873).

extracted with ether. The 6-bromo-3-methylphenol obtained by distillation of the ether extract was proved by boiling point (206–208° at 731 mm.), analysis, and bromination to 4,6-dibromo-3-methylphenol to be identical with the liquid monobromo-*m*-cresol obtained by direct bromination.

**Preparation of 4-Bromo-3-methylphenol from 2-Bromo-5-aminotoluene.**—Acet-*m*-toluidine was brominated in acetic acid. The acyl group was removed and the 4-bromo-*m*-toluidine crystallized from alcohol to a constant melting point of 79–80°. The purified amine was dissolved in much dilute hydrochloric acid, cooled to 0° and diazotized with the calculated amount of sodium nitrite. After two hours the diazonium salt was decomposed by heating on the water-bath, and steam distilled. The resulting yellow oil was salted out and extracted with ether. After purification of the crude phenol by dissolving in alkali, filtering and reprecipitating with acid, it was extracted with ether, and recrystallized from petroleum ether. It was identical in crystal form and melting point with the solid monobromo-*m*-cresol obtained by direct bromination. The yield was approximately 25%.

*Anal.* Calcd. for C<sub>7</sub>H<sub>7</sub>OBr: Br, 42.78. Found: Br, 42.72.

**Esters of 4-Bromo-3-methylphenol.**—Benzoic, benzenesulfonic and *p*-toluenesulfonic esters were prepared from 4-bromo-3-methylphenol obtained both by direct bromination and by diazotization of 4-bromo-*m*-toluidine. The pyridine method was used.<sup>6</sup>

	Crystal form (from alcohol)	M. p., °C.	Bromine, %	
			Calcd.	Found
Benzoic ester	Fine white fluffy needles	82.5–83	27.32	27.5
Benzenesulfonic ester	Long white needles	79–80	24.46	24.19
<i>p</i> -Toluenesulfonic ester	Small lustrous plates	84–85	23.46	23.25

#### Dibromo-*m*-Cresols<sup>7</sup>

**Direct Bromination.**—One hundred and eight grams of *m*-cresol was brominated with 320 g. of bromine under the same experimental conditions as were used in the preparation of the monobromo-*m*-cresols. Upon distillation practically all of the product came over at 130–140° (16 mm.) and solidified. Recrystallization from petroleum ether gave flat needles melting at 64–65°. Evaporation of the mother liquor gave an oil which did not solidify at room temperature, and distilled at 132–135° (16 mm.). The crystalline compound was shown by analysis to be a dibromo-*m*-cresol.

*Anal.* Calcd. for C<sub>7</sub>H<sub>6</sub>OBr<sub>2</sub>: Br, 60.15. Found: Br, 59.93.

Its sodium salt reacted with benzyl chloride in toluene to give an *ortho* benzyl derivative.<sup>8</sup> The benzoyl derivative, prepared by the pyridine method, crystallized from alcohol in mats of very fine needles melting at 80–81°.

*Anal.* Calcd. for C<sub>14</sub>H<sub>10</sub>O<sub>2</sub>Br<sub>2</sub>: Br, 43.2. Found: Br, 42.35.

Since this phenol has an unsubstituted ortho position, it must be either 2,4-dibromo-3-methylphenol or 4,6-dibromo-3-methylphenol.

The oil (b. p. 132–135°) obtained from the filtrates was seeded with a crystal of 4,6-dibromo-3-methylphenol prepared from the amine (see below). It solidified. After chilling it was pressed between pads of filter paper to remove oily impurities, and recrystallized from petroleum ether. Analysis, melting point (65–66°) and melting point of the benzoyl derivative (84–85°) proved it to be 4,6-dibromo-3-methylphenol.

<sup>6</sup> Neville and Winther, *Ber.*, **13**, 963 (1880).

<sup>8</sup> Einhorn and Holland, *Ann.*, **301**, 95 (1898).

<sup>7</sup> Gibbs and Robertson, *J. Chem. Soc.*, **105**, 1891 (1914); *ibid.*, **105**, 1888 (1914).

<sup>8</sup> Huston and Houk, *THIS JOURNAL*, **54**, 1506 (1932).

*Anal.* Calcd. for  $C_7H_5OBr_2$ : Br, 60.15. Found: Br, 60.01.

The less soluble phenol formed with it is therefore the 2,4-dibromo-3-methylphenol.

**Preparation of 4,6-Dibromo-3-methylphenol from 3-Amino-4,6-dibromotoluene.**—Pure *m*-toluidine was acylated and treated in cold acetic acid solution with two molecular equivalents of bromine. The acyl group was removed by means of alcoholic potash, and the 4,6-dibromo-*m*-toluidine was recrystallized from alcohol to a constant melting point of 75–76°. The purified amine was dissolved in hot, dilute hydrochloric acid, filtered and cooled to 0°. The calculated quantity of sodium nitrite was slowly added and the mixture was stirred until solution was complete. After two hours the diazonium salt was decomposed by heating on the water-bath and the dark colored mixture was steam distilled. The distillate was salted out and extracted with ether. After evaporation of the solvent the phenol was separated from the quinone by dissolving in dilute sodium hydroxide, reprecipitating with hydrochloric acid, and extracting with ether. The purified 4,6-dibromo-3-methylphenol crystallized from petroleum ether in fine flat crystals which cling to the sides of the beaker. The melting point (65–66°) is ten degrees higher than that given by Gibbs and Robertson.<sup>7</sup> The benzoyl derivative came down from alcohol in fine needles melting at 84–85°.

*Anal.* Calcd. for  $C_{14}H_{10}O_2Br_2$ : Br, 43.2. Found: Br, 43.78.

### Summary

Bromination of *m*-cresol in the cold with one molecular equivalent of bromine gave a mixture of 4-bromo-3-methylphenol and 6-bromo-3-methylphenol.

Bromination of *m*-cresol with two molecular equivalents of bromine gave a mixture of 2,4-dibromo-3-methylphenol and 4,6-dibromo-3-methylphenol.

<sup>9</sup> Neville and Winther, *Ber.*, 13, 971 (1880).

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## ACTION OF AROMATIC ALCOHOLS ON AROMATIC COMPOUNDS IN THE PRESENCE OF ALUMINUM CHLORIDE. VIII. BENZYLATION OF META-CRESOL

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This completes a series of three articles from this Laboratory on the benzylation of the cresols.<sup>1</sup>

*m*-Cresol treated with benzyl alcohol and aluminum chloride in petroleum ether gave two monobenzyl cresols and one dibenzyl cresol: 3-methyl-4-benzylphenol,<sup>2</sup> 3-methyl-6-benzylphenol and 3-methyl-4,6-dibenzylphenol. When treated with sodium and benzyl chloride in toluene (Claisen reaction)<sup>3</sup> it gave also two monobenzyl cresols and one dibenzyl cresol: 3-methyl-2-benzylphenol, 3-methyl-6-benzylphenol and 3-methyl-2,6-dibenzyl-

<sup>1</sup> Huston and others, *THIS JOURNAL*, 52, 4484 (1930); 53, 2379 (1931).

<sup>2</sup> Venturi, *Gazz. chim. ital.*, 31, I, 472 (1901).

<sup>3</sup> Claisen, *Ann.*, 442, 221 (1924).