BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 688—689 (1973)

On the Cleavage of 2,4-Dibromo-5-methylanisole

Kazuo Adachi
Osaka Institute of Technology, Omiya, Asahi-ku, Osaka

(Received June 13, 1972)

The phenolic hydroxyl group is sensitive to numerous reactions, but it may be protected in the ethers. On the treatment of phenol ethers with hydriodic or hydrobromic acid, the ether bond cleaves to the regenerated original phenols. This important reaction has been employed frequently in synthetic organic chemistry.[1]

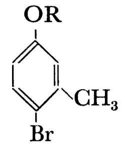
However, the refluxing of 2,4-dibromo-5-methylanisole (**2b**) with hydrobromic acid in acetic acid unexpectedly gave a mixture of 4-bromo-3-methylphenol (**1a**), 2,4-dibromo-5-methylphenol (**2a**), and 2,4,6-tribromo-3-methylphenol (**3a**). These three phenols, **1a**, **2a**, and **3a**, were methylated with dimethyl sulfate to give 4-bromo-3-methylanisole (**1b**), **2b**, and 2,4,6-tribromo-3-methylanisole (**3b**) respectively.

---

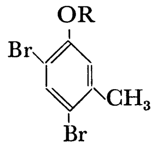
[1] R. B. Wagner and H. D. Zook, "Synthetic Organic Chemistry," John Wiley & Sons, New York, N. Y. (1953), p. 171.

These results show that the cleavage of the methoxyl group of **2b** with hydrobromic acid is accompanied by bromination and debromination of **2a**.

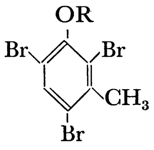
In a recent paper, Kamikawa and his collaborators[2] described that the treatment of 2,4-dibromo-3,5-dimethylanisole with hydriodic acid gave 3,5-dimethylphenol. Similarly, the refluxing of **2b** with hydriodic acid in acetic acid gave *m*-cresol.



(**1a, b**)



(**2a, b**)



(**3a, b**)

a: R=H, **b**: $R=CH_3$

Experimental

*4-Bromo-3-methylanisole (**1b**) and 2,4-Dibromo-5-methylanisole (**2b**).* *m*-Cresol was brominated[3] to give 4-bromo-3-methylphenol (**1a**) containing 2,4-dibromo-5-methylphenol (**2a**).

*4-Bromo-3-methylphenol (**1a**)*: Needles from petroleum ether; mp 59—60°C (lit,[3] mp 56—57°C).

The crude bromo-*m*-cresol was methylated with dimethyl sulfate and then distilled. 4-Bromo-3-methylanisole (**1b**) and 2,4-dibromo-5-methylanisole (**2b**) were thus obtained.

*4-Bromo-3-methylanisole (**1b**)*: bp 91°C/4 mmHg (lit,[4] bp 81—83°C/4 mmHg).

*2,4-Dibromo-5-methylanisole (**2b**)*: Prisms from petroleum ether; mp 73—74°C (lit,[5] mp 73—74°C).

*Treatment of 2,4-Dibromo-5-methylanisole (**2b**) with Hydriodic Acid.* A mixture of **2b** (25.0 g), hydriodic acid (*d*, 1.7; 50 ml), and glacial acetic acid (50 ml) was refluxed with stirring for 4 hr. The reaction mixture was then diluted with water and extracted with benzene. The benzene layer was washed with aq. $NaHSO_3$ and then water, and extracted with aq. NaOH. The oil obtained by the subsequent acidification of the resulting alkaline solution with HCl was extracted with ether. The distillation of the crude product gave an oil boiling at 93—94°C/13 mmHg (5.7 g; 58.7%) which was identical with *m*-cresol (IR spectrum).

The removal of the solvent from the above benzene solution gave the unchanged **2b** (4.1 g).

*Treatment of **2b** with Hydrobromic Acid.* A mixture of **2b** (39.0 g), hydrobromic acid (*d*, 1.48; 280 ml), and glacial acetic acid (280 ml) was refluxed with stirring for 10 hr. The subsequent distillation of the phenolic components in the reaction mixture gave an oily mixture of bromo-*m*-cresols boiling at 83—130°C/6 mmHg (22.0 g; 57.9%) and 2,4,6-tribromo-3-methylphenol (**3a**) boiling at 130—166°C/6 mmHg (12.1 g; 31.9%), which solidified. The higher-boiling distillate was recrystallized to give **3a**.

*2,4,6-Tribromo-3-methylphenol (**3a**)*: Needles from petroleum ether; mp 81.5—82.5°C(lit,[6] mp 80—81°C).

By redistillation, the lower-boiling distillate was divided into three fractions, A, B, and C. The components in each fraction were confirmed by gas chromatography.

Fraction A (2.8 g), boiling at 85—120°C/7 mmHg, was a mixture of 4-bromo-3-methylphenol (**1a**), 2,4-dibromo-5-methylphenol (**2a**), and a trace of *m*-cresol.

From Fraction B (16.6 g), boiling at 120—127°C/7 mmHg, crystals (4.3 g) of **2a** and an oily mixture (11.9 g) of **1a** and **2a** were obtained. The crude crystals of **2a** were filtered and purified by recrystallization to give *2,4-dibromo-5-methylphenol (**2a**)*; needles from petroleum ether; mp 64—64.5°C (lit,[3] mp 65—66°C).

Fraction C (2.0 g), boiling at 127—136°C/7 mmHg, was a mixture of **1a**, **2a**, and **3a**. Fractions B and C contained two more components, which appeared to be isomers of **1a** and **2a** but which were not identified.

The methylation of **2a** and **3a** with dimethyl sulfate gave **2b** and 2,4,6-tribromo-3-methylanisole (**3b**) respectively. The oily mixture of bromo-*m*-cresols, obtained after the removal of **2a** from Fraction B, was methylated with dimethyl sulfate to give a mixture of **1b**, **2b**, and **3b**.

*2,4,6-Tribromo-3-methylanisole (**3b**)*: Microneedles from petroleum ether; mp 75.5—76.5°C. Found: C, 26.55; H, 1.94%. Calcd. for $C_8H_7Br_3O$: C, 26.77; H, 1.97%. IR: 6.89, 7.08, 7.40, 7.91, 9.56, 10.78, 11.58, and 13.00 μ.

*Treatment of **2b** with the Other Acids.* When **2b** (14.0 g) was refluxed with 20% HCl (140 ml) and also with 63% H_2SO_4 (140 ml) in glacial acetic acid (140 ml) with stirring for 10 hr, only a small amount of **2a** was obtained (0.6 g) in either case.

---

2) T. Kamikawa, M. Nakatani, and T. Kubota, *Tetrahedron*, **24**, 2091 (1968).

3) R. C. Huston and J. A. Hutchinson, *J. Amer. Chem. Soc.*, **54**, 1504 (1932).

4) M. S. Carpenter, W. M. Easter, and T. F. Wood, *J. Org. Chem.*, **16**, 586 (1951).

5) W. O. Kermack and T. W. Wight, *J. Chem. Soc.*, **1935**, 1421.

6) R. C. Huston and W. J. Peterson, *J. Amer. Chem. Soc.*, **55**, 3879 (1933).