toluenes were unavailing, due in part to the formation of bromopicrin.

Preparation of *p*-Nitrobenzotribromide (II).—A mixture of 10 g. of pulverized *p*-nitrobenzal bromide (Eastman Kodak Company) and hypobromite (300 cc. of water, 30 g. of sodium hydroxide and 10 cc. of bromine) was agitated for four days. The mixture was filtered and washed with water; after two crystallizations from methanol the residue was nearly colorless leaflets melting at 86–87°. The yield was 10 g. (78%).

Anal. Calcd. for $C_7H_4O_2NBr_3$: C, 22.5; H, 1.1. Found: C, 22.8; H, 1.3.

Reactions of *p*-Nitrobenzotribromide.—(a) The tribromo compound (2 g.) was refluxed for seven hours with 10 g. of sodium carbonate and 60 cc. of water. The solid obtained after filtration and acidification weighed 0.8 g. (88%), and melted at 235–237°. After crystallization it was shown to be *p*-nitrobenzoic acid by the mixed m. p. method. (b) Two grams of *p*-nitrobenzotribromide was refluxed for nine hours with 50 cc. of water. The amount of *p*-nitrobenzoic acid isolated was 0.85 g. (95%); the m. p. was 235–237°. (c) Phenol (0.28 g.) and 1.12 g. of the tribromide were heated at 135–145° for three hours. The reaction mixture was then extracted with alkali, and the residue was crystallized from methanol. The melting point of the product (79–81°) was depressed when taken with the starting material, but not when taken with *p*-nitrobenzal bromide. (d) The tribromo compound (0.559 g., 0.0015 mole) and 10 cc. of alcohol were placed in the reaction chamber of a modified Zerewitinoff machine, and 5 cc. of a hydrazine solution (4 cc. of hydrazine in 35 cc. of alcohol) was added. The amount of gas liberated during twenty-four hours was 11 cc. (corrected); during the first ten minutes 9 cc. was liberated. The reaction mixture was added to water, and the precipitate which appeared was filtered; the m. p. was 80–190°. No pure product was isolated.

Summary

A good method of preparing *p*-nitrobenzotribromide has been developed, and a study of the behavior of this compound toward several typical dehalogenating agents has been made.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Preparation and Germicidal Properties of 2-Methyl-4-hydroxyphenyl Alkyl Sulfides

BY C. M. SUTER AND JAMES P. MCKENZIE

Since it has been found[1] that hydroxyphenyl alkyl sulfides have considerable germicidal activity, a further investigation of this type of compound seemed desirable. The present communication describes the study of a series of alkyl sulfides derived from *m*-cresol in which the alkyl group varies from methyl to *n*-amyl.

The method of preparation employed may be outlined as

$$CH_3C_6H_4OCH_3 \longrightarrow CH_3C_6H_3(OCH_3)SO_3Na \longrightarrow$$
$$CH_3C_6H_3(OCH_3)SO_2Cl \longrightarrow CH_3C_6H_3(OCH_3)SH \longrightarrow$$
$$CH_3C_6H_3(OCH_3)SR \longrightarrow CH_3C_6H_3(OH)SR$$

The yield in each step was good except for the demethylation. The hydrobromic acid–acetic acid mixture employed in this reaction acted as a reducing agent toward the sulfide linkage producing a considerable quantity of *m*-cresol. The other products of this reaction were not identified. Hydrobromic acid also converts 2-methyl-4-methoxythiophenol into *m*-cresol with rapid evolution of hydrogen sulfide. It will be of interest to study this reaction further.

It has been found previously[1a] that the presence of a methoxy group in an aryl alkyl sulfide causes a considerable exaltation in the molecular refraction of the compound. This exaltation, although still appreciable, is much less for the 2-methyl-4-methoxyphenyl alkyl sulfides than for the compounds which do not contain the 2-methyl group. The values for the former compounds are given in Table I.

TABLE I

2-METHYL-4-METHOXYPHENYL ALKYL SULFIDES

Alkyl group	d_4^{25}	n_D^{25}	MR Found	MR Calcd.	E.M.$_D$
Methyl	1.0867	1.5712	50.86	50.48	0.38
Ethyl	1.0554	1.5576	55.62	55.08	.54
n-Propyl	1.0362	1.5496	60.25	59.70	.55
n-Butyl	1.0182	1.5436	65.13	64.32	.81
n-Amyl	1.0086	1.5399	70.10	68.94	1 16

The atomic refraction used for sulfur (7.97) was that of Price and Twiss.[2] The germicidal properties[3] of 2-methyl-4-hydroxyphenyl alkyl sulfides

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(1) (a) Suter and Hansen, THIS JOURNAL, **54**, 4100 (1932); (b) Miller and Read, *ibid.*, **55**, 1244 (1933).

(2) Price and Twiss, *J. Chem. Soc.*, **101**, 1263 (1912).

(3) We are very much indebted to Dr. Oliver Kamm, Scientific Director, and Mr. W. C. Hamilton, Pharmacologist, of Parke, Davis and Company for permission to include a report of the germicidal properties determined by them.

are at a maximum toward *B. typhosus* with the *n*-propyl compound. The *n*-amyl compound is the most effective toward *Staph. aureus* and *Strep. hemolyticus*. The phenol coefficients are given in Table II.

TABLE II

Alkyl group	*B. typhosus* (a)	*B. typhosus* (b)	*Staph. aureus* (a)	*Staph. aureus* (b)	*Strep. hemolyticus* (a)	*Strep. hemolyticus* (b)
Methyl	1800	13	1200	12	1500	10
Ethyl	3000	20	5000	50	6000	40
n-Propyl	3000	23	8000	80	12000	80
n-Butyl	2000	14	10000	100	12000	80
n-Amyl	1000	8	25000	250	30000	200

Column (a) in each case gives the highest dilutions effective in five minutes while column (b) gives the phenol coefficients. The figures for *B. typhosus* were obtained by the F. D. A. method at 37°, while those for *Staph. aureus* and *Strep. hemolyticus* were determined at 37° by a method quite similar to that described by Reddish.[4]

Experimental

2-Methyl-4-methoxybenzenesulfonic Acid.—Sulfonation of *m*-cresol methyl ether with an equimolecular quantity of concentrated sulfuric acid at room temperature for twelve hours and pouring the reaction mixture into saturated sodium chloride solution gave a 55% yield of sodium 2-methyl-4-methoxybenzenesulfonate. With two moles of acid the yield increased to 74–86% of the theoretical amount. Haworth and Lapworth[5] have prepared the same compound by sulfonation of *m*-cresol methyl ether with chlorosulfonic acid in carbon bisulfide at a low temperature. The *p*-toluidine salt melted at 204–205° (corr.).

Anal. Calcd. for $C_{15}H_{19}O_4NS$: N, 4.53. Found: N, 4.37.

2-Methyl-4-methoxybenzenesulfonyl Chloride.—This was obtained from the sodium sulfonate and phosphorus oxychloride. It distilled at 173–175° (17 mm.); d_4^{25} 1.321, n_D^{25} 1.5685. The amide melted at 128–129° (corr.). Haworth and Lapworth[5] report the acid chloride as a solid, m. p. 23°, whose amide melted at 129–130°.

3-Methyl-4-methoxythiophenol.—This was prepared according to the method of Adams[6] in 75–83% yields. It was obtained as a colorless liquid, b. p. 130–132° (22 mm.); d_4^{25} 1.173, n_D^{25} 1.5760. This was recently[7] reported as an oil of b. p. 253–254° but no analysis was given.

Anal. Calcd. for $C_8H_{10}OS$: S, 20.6. Found: S, 20.2.

The benzoyl derivative melted at 78–79° while 84° was given by Shah and co-workers.[7]

Reaction of the sodium thiophenolate with sodium chloroacetate gave the thioglycolic acid derivative. The acid when recrystallized from water melted at 72–73°.

Anal. Calcd. for $C_{10}H_{12}O_3S$: neutral equiv., 212. Found: neutral equiv., 213.

2-Methyl-4-methoxyphenyl Alkyl Sulfides.—These were prepared according to methods already reported.[8] In Table III are listed the yields, boiling points and analyses. Other properties have been given in Table I.

TABLE III

2-METHYL-4-METHOXYPHENYL *n*-ALKYL SULFIDES

Alkyl group	Yield, %	B. p., °C.	Pressure, mm.	Sulfur, % Found	Sulfur, % Calcd.
Methyl	86	145–147	26	18.8	19.0
Ethyl	85	150–151	23	17.8	17.6
n-Propyl	82	162–163	22	16.3	16.3
n-Butyl	81	173–175	23	15.2	15.2
n-Amyl	75	165–167	15	14.0	14.3

2-Methyl-4-hydroxyphenyl Alkyl Sulfides.—The methoxy compounds were all demethylated according to the procedure described by Suter and Hansen.[1a] The results are summarized in Table IV. The approximate solubility of each phenol in 20% alcohol at 25° is given in the last column.

TABLE IV

2-METHYL-4-HYDROXYPHENYL ALKYL SULFIDES

Alkyl group	Yield, %	B. p., °C.	*p*, mm.	Sulfur, % Found	Sulfur, % Calcd.	Soly. in 20% alc., g./100 cc.
Methyl	33	148–151	15	20.3	20.8	0.34
Ethyl	30	159–163	20	17.9	19.0	.11
n-Propyl	43	165–170	20	17.6	17.8	.06
n-Butyl	43	180–186	27	16.3	16.3	.04
n-Amyl	21	193–197	24	15.1	15.2	.04

Summary

A series of *n*-alkyl sulfides has been prepared from 2-methyl-4-methoxythiophenol. These compounds upon demethylation give fair yields of the corresponding phenols. The germicidal properties of these phenolic compounds are tabulated.

EVANSTON, ILLINOIS RECEIVED AUGUST 9, 1934

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[4] Reddish, *J. Lab. Clin. Med.*, **14**, 649 (1929).

[5] Haworth and Lapworth, *J. Chem. Soc.*, **125**, 1299 (1925).

[6] Adams, "Organic Syntheses," Vol. I, John Wiley and Sons, New York, 1921, p. 71.

[7] Shah, Bhott and Kanga, *J. Chem. Soc.*, 1375 (1933).

[8] Gilman and Beaber, THIS JOURNAL, **47**, 1449 (1925); Suter and Hansen, *ibid.*, **54**, 4100 (1932).