[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Reactive Methyl Group in Toluene Derivatives. II. *p*-Nitrobenzotribromide

BY C. HAROLD FISHER

Since the compounds formed by replacing the hydrogen atoms of active methyl groups by halogen are in many instances halogenating agents,[1] it might be expected that the substances formed by halogenating the active methyl group of the nitrotoluenes would possess similar properties. In examining this possibility, attention was directed toward the α-polybromo derivatives because in general the tendency to halogenate is greater in bromine compounds than in their chlorine analogs.[2] In view of the difficulty experienced in introducing halogen atoms into the methyl group of nitrotoluenes by direct halogenation[3] and the avidity with which hypobromite attacks some active methyl groups, attempts to brominate several nitrotoluenes were made with the latter reagent. Only in the case of *p*-nitrobenzal bromide (I) were these efforts successful; this compound was converted into *p*-nitrobenzotribromide (II) in good yield at room temperature. Hypobromite did not react with *p*-nitrotoluene in two days, and only a small yield of *p*-nitrobenzoic acid, along with starting material, was obtained in eight days. A good yield of *p*-nitrobenzoic acid was obtained from alkaline hypobromite and *p*-nitrobenzyl bromide, presumably after preliminary hydrolysis to *p*-nitrobenzyl alcohol.

The behavior of *p*-nitrobenzotribromide toward several reagents which have been used in a similar study[4] of a tribromomethyl phenyl ketone was examined. The tribromo compound (II) was found to be stable to cold alkali. With hot alkali *p*-nitrobenzoic acid, instead of the dehalogenation product (I), was obtained. Since the yield was high (88%), it is not possible that the product (III) resulted solely from the Cannizzaro reaction involving *p*-nitrobenzaldehyde. It is of interest that the action of alkali did not cause the cleavage (to *p*-nitrophenol and bromoform) which would be expected if *p*-nitrobenzotribromide behaved as does α-tribromoacetophenone.[5] The transformation of II into *p*-nitrobenzoic acid in good yield was accomplished also by long boiling with water. However, the starting material was recovered unchanged after being heated for twenty hours on a steam cone with methanol.

$$\underset{\text{I}}{p\text{-NO}_2\text{C}_6\text{H}_4\text{CHBr}_2} \rightleftharpoons \underset{\text{II}}{p\text{-NO}_2\text{C}_6\text{H}_4\text{CBr}_3} \longrightarrow \underset{\text{III}}{p\text{-NO}_2\text{C}_6\text{H}_4\text{COOH}}$$

Phenol reacted with *p*-nitrobenzotribromide (II) to give a small yield of *p*-nitrobenzal bromide and an alkali-soluble, colored substance. Condensation products predominated also in the reaction of II with dimethylaniline,[6] and it was not found possible to isolate *p*-nitrobenzal bromide. Treatment of the tribromo compound (II) with hydrazine liberated 65% of the theoretical amount of nitrogen, as calculated from the equation[7]

$$2\text{RX} + \text{NH}_2\text{NH}_2 \longrightarrow 2\text{RH} + \text{N}_2 + 2\text{HX}$$

which has been written for the reaction of hydrazine with halogenating compounds. Iodine was liberated instantly from an acetone solution of potassium iodide by the action of *p*-nitrobenzotribromide, but the exact course of the reaction could not be determined because of the difficulty of isolating pure products. Repeated crystallization from water of the reaction product gave *p*-nitrobenzoic acid, but this compound must have been formed during crystallization since extraction of the crude reaction product with alkali showed acidic substances to be absent. It was not found possible to cause dehalogenation of II with boiling acetone, or with acetophenone. The starting material was recovered from acetone and also in the case of acetophenone when the temperature was kept low enough to prevent condensation reactions.

A study could not be made of 2,4-dinitro- and 2,4,6-trinitrobenzotribromide, which should be much more active as brominating agents than the mononitro compound (II). Efforts to prepare these polynitrobenzotribromides by the action of hypobromite on the corresponding polynitro-

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(1) For references see Howk and McElvain, THIS JOURNAL, **55**, 3372 (1933), and Ref. 4.

(2) Gott and Hunter, *J. Chem. Soc.*, **125**, 442 (1924); Zinke and Gerland, *Ber.*, **21**, 2388 (1888).

(3) Ganguly, *ibid.*, **58B**, 708 (1925).

(4) Fisher, THIS JOURNAL, **55**, 5003 (1933).

(5) That nitrotoluene and acetophenone derivatives may be compared in some cases has been pointed out [Borsche, *Ber.*, **42**, 1316 (1909)].

(6) Dimethylaniline has been used to dehalogenate certain α-bromo ketones [K. von Auwers and Lämmerhirt, *ibid.*, **53B**, 428 (1920)].

(7) Cox, Macbeth and Pennycuick, *J. Chem. Soc.*, 1871 (1931).

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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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.