

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

A New Preparation and Some Reactions of Di-(β -chloroethyl) Sulfate

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Only a few alkyl sulfates have been prepared by the action of sulfur trioxide upon the corresponding ethers. Methyl ether is converted into the sulfate by passing it into oleum¹ or by reaction with sulfur trioxide² in methyl sulfate solution. Chloromethyl methyl ether³ and di-(chloromethyl) ether⁴ have been converted into the sulfates in about 30% yields. Ethyl ether reacts with sulfur trioxide at a low temperature⁵ but oxidation and sulfonation products predominate.

Di-(β -chloroethyl) sulfate has been obtained previously by the action of sulfuryl chloride with β -chloroethyl alcohol⁶ or with β -chloroethyl nitrite⁷; it results in good yields from the action of β -chloroethyl chlorosulfonate upon di-(β -chloroethyl) sulfite.⁸

Unlike ethyl ether, di-(β -chloroethyl) ether is not charred by treatment with sulfur trioxide at room temperature. After investigating the products obtained by heating the chloro ether with 30% oleum, chlorosulfonic acid and sulfur trioxide at various temperatures it was found that if a mixture containing equimolecular amounts of sulfur trioxide and the ether were distilled at a low pressure a high yield of nearly pure di-(β -chloroethyl) sulfate was obtained. If the reaction mixture was washed with water after heating to 150° and then distilled the yield was reduced to about 30%. It is necessary to distil the reaction mixture within a few hours after adding the sulfur trioxide to the ether or decomposition is extensive and the yield low.

The most obvious explanation for the conversion of an ether into an alkyl sulfate by the action of sulfur trioxide is to assume the intermediate formation of an addition product,⁹ R₂OSO₃, in which an unshared electron pair of the ether oxygen completes the octet for the sulfur atom. Migration of an alkyl group to another oxygen would then give rise to the alkyl sulfate. A high

yield of the ester can be obtained only when the alkyl group is resistant to the sulfonating and oxidizing action of the sulfur trioxide at the temperature necessary for the transfer of the alkyl from one oxygen to another. So far only ethers in which each carbon is attached to an oxygen or chlorine have shown this resistance to decomposition to any great extent. Di-(β -bromoethyl) ether gave a low yield of the sulfate when treated with sulfur trioxide and distilled. Attempts to obtain sulfates from di-*n*-propyl ether and di-(γ -chloropropyl) ether gave tarry reaction mixtures which could not be distilled even in a high vacuum.

Refluxing a mixture of di-(β -chloroethyl) sulfate and water gives ethylene chlorohydrin, hydrolysis of the chlorine being slight. With concentrated hydrochloric acid ethylene chloride is produced but dry hydrogen chloride does not react appreciably at any temperature up to the decomposition point of the sulfate. The yields of chlorohydrin and ethylene chloride indicate that only one alkyl group reacts.

The reaction of the sulfate with *n*-butyl alcohol is complex; the only products isolated were small amounts of ethylene chlorohydrin and di-(β -chloroethyl) ether. No appreciable quantity of β -chloroethyl *n*-butyl ether was obtained when the reaction was run in the presence of aqueous sodium hydroxide or when the sulfate was added to a solution of sodium butylate in *n*-butyl alcohol.

The sulfate reacts slowly with acetic acid. After fifteen hours at 100° a 30% yield of β -chloroethyl acetate was isolated. Refluxing equimolecular amounts of the sulfate and sodium acetate in glacial acetic acid for one hour gave a 96% yield of the ester. When the sulfate is refluxed with aqueous sodium benzoate the amount of ester formed is small but heating with the dry salt at 170° for two hours produced a 62% yield of β -chloroethyl benzoate. Following the procedure of Hansen and Fosdick¹⁰ for preparing β -chloroethyl *p*-nitrothiobenzoate except for the substitution of the sulfate for ethylene chloriodide gave a 61% yield of the thio ester, m. p. 90–91.5°.

(10) Hansen and Fosdick, *THIS JOURNAL*, **55**, 2872 (1933). We wish to thank Dr. Harold L. Hansen, Northwestern Dental School, for the *p*-nitrothiobenzoic acid used in this reaction.

(1) Guyot and Simon, *Compt. rend.*, **169**, 655, 795 (1919).
 (2) Haworth and Irvine, British Patent 122,498; *C. A.*, **13**, 1716 (1919).

(3) Houben and Arnold, *Ber.*, **40**, 4306 (1907).

(4) Grignard, Toussaint and Cazin, *Bull. soc. chim.*, **43**, 537 (1928).

(5) Hübner, *Ann.*, **223**, 198 (1884).

(6) Nekrasov and Komisarov, *J. prakt. Chem.*, **123**, 160 (1929).

(7) Levaillant, *Compt. rend.*, **187**, 730 (1928).

(8) Levaillant, *ibid.*, **189**, 465 (1929); **190**, 54 (1930).

(9) It is shown in the following paper that dioxane forms such a compound.

The reaction of di-(β -chloroethyl) sulfate with the Grignard reagent is comparable to that of ethyl sulfate. Refluxing an ether solution of phenylmagnesium bromide with a 50% excess of the chlorosulfate for three hours gave a 25% yield of β -phenylethyl chloride and an equivalent amount of ethylene chlorobromide. The reaction with benzylmagnesium chloride proceeds more rapidly; the yield of γ -phenyl-*n*-propyl chloride was 66% based upon the benzyl chloride employed in preparing the Grignard reagent.

Clemo and Perkin¹¹ reported the preparation of β -chlorophenetole from refluxing β -chloroethyl *p*-toluenesulfonate with aqueous sodium phenoxide. The sulfate gives a good yield of the ether under similar conditions, only one alkyl group reacting. Attempts to introduce the β -chloroethyl group into ethyl malonate were not successful. Similar difficulties have been reported in using β -chloroethyl *p*-toluenesulfonate in this alkylation.¹² Reaction occurred readily but attempts to isolate pure compounds from the resulting mixture failed, regardless of whether the sulfate or the ethyl sodiomalonate was kept in excess during the reaction.

Experimental

Preparation of Di-(β -chloroethyl) Sulfate.—To 100 g. of di-(β -chloroethyl) ether there was added slowly 48.4 g. (theoretical 56 g.) of sulfur trioxide. The mixture was then distilled from an all-glass apparatus at 2–3 mm. After a second fractionation there were obtained 28 g. of unchanged ether and 102 g. of sulfate, b. p. 126–129° (3 mm.).⁷ Based upon the unrecovered ether the yield was 91%. The material obtained in this way darkens upon

(11) Clemo and Perkin, *J. Chem. Soc.*, **121**, 642 (1922).

(12) Clemo and Tenniswood, *ibid.*, 2549 (1931).

standing but if the crude mixture is stirred with warm dilute alkali before the second fractionation the ester remains water-white indefinitely.

β -Chloroethyl Acetate.—A mixture of 20 g. (0.09 mole) of di-(β -chloroethyl) sulfate, 7.5 g. (0.09 mole) of sodium acetate and 15 cc. of glacial acetic acid was refluxed for one hour. Pouring the reaction mixture into water, neutralizing with sodium carbonate and extracting with ether gave 10.5 g. of β -chloroethyl acetate, b. p. 145°. The yield was 95.5%.

β -Chloroethyl Benzoate.—A flask containing 5.6 g. (0.039 mole) of sodium benzoate and 8.7 g. (0.039 mole) of di-(β -chloroethyl) sulfate was heated at 170° for two hours with occasional stirring. Extraction with ether gave 4.4 g. (61.5% yield) of the ester, b. p. 125–130 (14 mm.). In aqueous or alcoholic solution the yield was small.

γ -Phenylpropyl Chloride.—To a solution of benzylmagnesium chloride in ether prepared from 9.5 g. (0.075 mole) of benzyl chloride there was added dropwise 25 g. (0.112 mole) of di-(β -chloroethyl) sulfate. The reaction was vigorous. The mixture was then heated and stirred for two hours, hydrolyzed with dilute sulfuric acid and the ether layer dried and distilled. There were obtained 1.7 g. of ethylene chloride, b. p. 83–84°, and 7.6 g. (66% yield based on the benzyl chloride) of γ -phenylpropyl chloride, b. p. 93.5–95° (11 mm.).

In contrast to the benzyl compound phenylmagnesium bromide reacted slowly with the sulfate. By refluxing the reaction mixture for three hours a 25% yield of β -phenylethyl chloride was obtained.

Summary

1. Distillation of a mixture containing di-(β -chloroethyl) ether and sulfur trioxide under reduced pressure produces a good yield of the corresponding sulfate.
2. Several alkylation reactions of this ester have been investigated.

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