[Contribution from the Chemistry Laboratory of Mount Holyoke College]

THE CHLORINATION OF DIETHYL ETHER AT LOW TEMPERATURES[1, 2]

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A study of the properties, especially the ultraviolet absorption spectra, of nitrogen and oxygen compounds due to the unshared pair of electrons on the nitrogen or oxygen atom is being conducted in this laboratory. Unsaturated ethers of the type RCH=CHOCH=CHR are of interest in view of the conjugation of the two olefinic bonds with the oxygen electron-pairs. A possible general synthesis of these unsaturated ethers would be the dehydrohalogenation of α,α'-dihalo derivatives of aliphatic ethers or oxygen-containing heterocycles. This type of synthesis has been reported by Smedley (1) for the preparation of dioxadiene from 2,5-dichloro-1,4-dioxane.

This paper is a report of the initial investigation of a new preparation of the required α,α'-dihalo ethers. The only previously reported method for the preparation of these dihalo ethers is the treatment of an aldehyde with hydrogen chloride in the cold (2).

$$2\,RCHO + 2\,HCl \rightarrow RCHClOCHClR + H_2O$$

This method is limited to the availability of the aldehyde. It does not seem practical to attempt the preparation of the dichlorides of unsymmetrical ethers by this method, nor has the method been shown to be applicable to the preparation of dichloro cyclic ethers.

In the search for a more general method of preparation of α,α'-dichloro ethers, the mechanism proposed by Summerbell and Bauer (3) to account for the predominant formation of 2,3-dichloro-1,4-dioxane in the chlorination of 1,4-dioxane at room temperature or above suggested that low-temperature chlorination might be a feasible means of approach. They suggest that the unstable monochlorodioxane first formed loses a molecule of hydrogen chloride to form 1,4-dioxene, which then adds a molecule of chlorine to give 2,3-dichloro-1,4-dioxane. The present investigators consider this sequence to be applicable also to the chlorination of diethyl ether. At ordinary temperatures the products formed by successive substitution of four chlorine atoms (4, 5) are α-chloroethyl, α,β-dichloroethyl, α,β,β-trichloroethyl, and α,β,β,β-tetrachloroethyl ethyl ether. The introduction of the chlorine atoms in the β-position may be formulated as occurring by the repeated loss of hydrogen chloride and addition of chlorine to the resultant double bond, the chlorine of the hydrogen chloride coming in each case from the labile α-position. The lability of a chlorine atom in the α-position of an ether and the olefin-like behavior of such an ether is emphasized by the work of Shostakovskiĭ and Bogdanova (6).

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[1] Abstracted from the Master's thesis of Florence M. Ubertini, Mount Holyoke College, June 1949.

[2] This work was carried out under contract with the Office of Naval Research.

Chlorination of chloromethyl ethyl ether gives α-chloroethyl chloromethyl ether (7), indicating that an entering chlorine atom will attack a new α-position in preference to an α-position already substituted. This suggests that if the loss of hydrogen chloride from α-chloro ethers could be avoided, as by operating at a low temperature, the second atom of chlorine would enter the second alkyl group to form, in the case of diethyl ether, α,α′-dichlorodiethyl ether. In agreement with this postulate, Smedley (1) has obtained 2,5-dichloro-1,4-dioxane by chlorinating dioxane at low temperatures. Pendleton (8) in this laboratory has been able to confirm this reaction and to increase the yields with decreased reaction time by irradiating the reaction mixture with light of short wave length.

In this investigation it has been found that α,α′-dichlorodiethyl ether could be prepared without difficulty by the chlorination of either diethyl ether or α-chloroethyl ethyl ether at −20° or lower. It is essential to conduct the reaction at a low temperature to avoid the formation of β-chloro products. In contrast to the 57% yield of α,α′-dichlorodiethyl ether at −20° to −30°, a chlorination at +5° to −5° gave a mixture of approximately equal parts of α-chloroethyl ethyl ether, α,β-dichloroethyl ethyl ether, and α,α′-dichlorodiethyl ether. While these results are in agreement with the reaction route suggested above, no attempt has been made to study the electronic mechanism of the chlorination.

Monochlorination at low temperatures is also a convenient method of preparation of α-chloroethyl ethyl ether. The more common method, originated by Henry (9), is the reaction of acetaldehyde, ethanol, and hydrogen chloride. This method suffers from the disadvantage that water is one of the products and α-chloro ethers are sensitive to hydrolysis. If the direct chlorination of diethyl ether at low temperatures is stopped when the gain in weight is equivalent to a one-mole portion of chlorine, the monochloro ether is the chief product. The separation of α-chloroethyl ethyl ether prepared by chlorination from the more highly chlorinated products in the reaction mixture is easier, because of the greater difference in boiling points, than is the separation of the chloro ether from the by-products, such as acetal, formed in Henry's method.

An attempt to substitute a third chlorine atom at low temperatures was unsuccessful. In one experiment the passage of chlorine into the reaction mixture at −20° to −30° was continued for eight hours after the mixture had gained the weight calculated for the substitution of two chlorine atoms. A loss of weight occurred during this period, indicating that the chlorine was acting merely as an inert gas to flush hydrogen chloride out of the solution. No trichloro ether could be isolated.

It has been essential in this work to determine the identity of the various chlorination products. There is a paucity of reports of derivatives of the chloro ethers suitable for their characterization (17). No solid derivative of α-chloroethyl ethyl ether has been reported. In view of Houben's (10) identification of α,β-dichloroethyl ethyl ether by its reaction with urethane in the presence of water to form β-chloroethylidene diurethane, a similar method was applied to α-chloroethyl ethyl ether to give ethylidene diurethane. However, this reaction would give the same product from α,α′-dichlorodiethyl ether as from the mono α-chloro ether. For a specific, although non-solid, derivative of the monochloro compound, it was treated with sodium ethoxide to give diethyl acetal.

Geuther (11) has reported a solid formed on treatment of α,α′-dichlorodiethyl ether with sodium benzoate but gave no melting point. The use of this procedure by the present investigators gave only benzoic acid. Treatment of the dichloro ether with phenyl- or α-naphthyl-magnesium bromide gave oils which could not be crystallized. An attempt to prepare the S-alkylisothiourea picrate (12) was unsuccessful. However, treatment of the dichloro ether with potassium phthalimide did give a nicely crystalline derivative.

The extension of this reaction to other ethers and an investigation of the use of α,α′-dichloro ethers in synthesis is in progress.

EXPERIMENTAL [3, 4]

Chlorination procedure. The general method of chlorination was to pass dry chlorine into the ether contained in a 500-ml. three-neck flask equipped with an alcohol thermometer and a mechanical stirrer and protected by a drying-tube. The flask used in all cases except the chlorination of α-chloroethyl ethyl ether was of Vycor brand no. 791 glass. This high silica content glass has a guaranteed transmission of 70% at 254 mμ for a thickness of 2 mm. (13). The reaction flask was cooled in a Dry Ice-acetone bath and irradiated with light from a carbon arc.

In the early runs the addition of the chlorine was interrupted whenever the solution became deep yellow and was not resumed until it had again become nearly colorless. This was done because it was feared, in view of the experience of early investigators (14, 15) at higher temperatures, that the reaction might become violent if the chlorine concentration became too great. In later runs the chlorine was added continuously with a corresponding decrease in the time necessary to accomplish the chlorination. No difficulty was encountered if, after the chlorine addition had been stopped, the irradiation was continued until the remaining chlorine had reacted. Otherwise, as the reaction mixture warmed up the excess chlorine reacted vigorously and exothermically forming β-chloro products. Pendleton (8) noted the same effect in the low-temperature chlorination of 1,4-dioxane in carbon tetrachloride, the reaction being sufficiently violent in larger runs to eject a large part of the liquid from the flask.

α-Chloroethyl ethyl ether. Chlorine was passed into 150 g. (2.02 moles) of anhydrous diethyl ether at −25° to −30° during 4 hours until the reaction mixture had gained 144 g. (equivalent to 2.01 moles chlorine). The product was distilled through a Vigreux column. The fraction boiling at 98–100° [reported b.p., 93–94° at 735 mm. (16) and 97.5° at 750 mm. (17)] weighed 94.0 g. (42%). The α-chloroethyl ethyl ether reacted vigorously with dry sodium ethoxide to give diethyl acetal, identified by its boiling point and its characteristic odor.

α,α′-Dichlorodiethyl ether. Anhydrous diethyl ether (82 g., 1.1 moles) was placed in the Vycor flask and cooled to −25°. Chlorine was passed into the ether at −20° to −30° during 15 hours. The addition was interrupted whenever the solution became deep yellow and was resumed when the solution had become colorless or nearly so. The reaction mixture gained 85 g., 9% in excess of that calculated for the substitution of two chlorine atoms. Distillation of one-half of the product at 761 mm. gave a dark, tarry residue and the following fractions: 70–111°, 9.3 g.; 111–115°, 44.7 g.; 115–122°, 13.2 g.; 122–132°, 5.5 g. The second fraction represents a 57% yield of α,α′-dichlorodiethyl ether. It is probable that the yield could be increased by better fractionation of the third fraction. Redistillation gave a colorless liquid

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[3] All experimentally determined melting points are corrected for stem exposure.

[4] Analyses by Clark Microanalytical Laboratory, Urbana, Illinois.

with a sharp, irritating odor boiling at 113–114° (corr.), n_D^{24} 1.4183 [reported (18) b.p. 112.5-114°; n_D^{25} 1.4186].

α,α′-Diphthalimidodiethyl ether. Two grams (0.014 mole) of α,α′-dichlorodiethyl ether was refluxed with 5.5 g. (0.029 mole) of dry potassium phthalimide (19) in 100 ml. of dioxane for 1.5 hours. The salts were filtered out and water added to precipitate the phthalimido derivative. The product was crystallized three times from absolute alcohol to constant melting point to give fine, colorless needles; m.p. 270.5–271°. Material prepared from α,α′-dichlorodiethyl ether obtained by chlorination had properties identical with those of a sample prepared from known α,α′-dichlorodiethyl ether obtained by the treatment of acetaldehyde with dry hydrogen chloride (20). A mixed melting point showed no depression.

Anal. Calc'd for $C_{20}H_{16}N_2O_5$: C, 65.93; H, 4.40; N, 7.69.

Found: C, 65.99, 65.71; H, 4.32, 4.46; N, 7.69, 7.63.

Urethane derivatives from α-chloro ethers. A small amount of solid urethane was placed in a beaker moistened with water. Enough α-chloro ether was added to wet the solid. The mixture was stirred vigoruosly until it became thick, at which point water was immediately added to prevent polymerization. The residual solid was recrystallized from water. The results are shown in Table I.

TABLE I

URETHANE DERIVATIVES FROM α-CHLORO ETHERS

ETHER	DERIVATIVE	M.P., °C.	
		Observed	Reported (Ref.)
α-Chloroethyl ethyl	Ethylidene diurethane	125.2–126	126 (21)
α,α′-Dichlorodiethyl	Ethylidene diurethane	124.5–125.6	126 (21)
α,β-Dichloroethyl ethyl	β-Chloroethylidene diurethane	148.5–149	148–149 (10)

SUMMARY

1. Direct chlorination at −20° and below has been employed to prepare α,α′-dichlorodiethyl ether from diethyl ether and from α-chloroethyl ethyl ether and to prepare α-chloroethyl ethyl ether from diethyl ether.

2. Derivatives to characterize these chlorinated ethers are described.

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