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Preparation of Methanesulfonyl Chloride-d_3 from Dimethyl Sulfoxide-d_6

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A convenient method for the preparation of methanesulfonyl chloride-d_3 is described. The procedure consists of the anhydrous chlorination of dimethyl sulfoxide-d_6 with chlorine and the aqueous chlorination. Methanesulfonyl chloride-d_3 was obtained in a 52% yield, and a small amount of dimethyl sulfone-d_6 was also isolated. Trichloromethyl methyl sulfide (-d_3) was found to be one of the intermediates in this reaction.

Keywords——chlorination; DMSO; deuterated DMSO; sulfonyl chloride; deuterated sulfonyl chloride; sulfone; deuterated sulfone; chlorinated sulfide

In the course of an investigation of the vibrational spectra of methanesulfonyl chloride[2a] and methanesulfonamide,[2b] it became desirable to obtain the spectra of their C-deuterated compounds in order to ascertain the vibrational assignments. Several methods can be used for the preparation of methanesulfonyl chloride-d_3, namely, by the action of phosphorus trichloride or phosphorus pentachloride on sodium methanesulfonate,[3] by the action of phosphorus trichloride or thionyl chloride on methanesulfonic acid,[4] and by the aqueous chlorination of S-methylisothiourea salt,[5a] sodium methyl thiosulfate,[5b] methyl thiocyanate,[5c] dimethyl disulfide[5d] or dimethyl sulfide.[6] Bürger, *et al.*[7a] and Tóth, *et al.*[7b] obtained methanesulfonyl chloride-d_3 according to Douglass and Johnson's method[5b] by the chlorination of sodium methyl thiosulfate-d_3 which was prepared from dimethyl sulfate-d_6 or methyl iodide-d_3 and sodium thiosulfate. However, we obtained this compound by a simpler method described below.

Among the above methods we noted the last one, since dimethyl sulfoxide, whose deuterated compound is commercially available and inexpensive, is involved in the reaction: Bennett, *et al.*[6] have reported that the aqueous chlorination of dimethyl sulfide with chlorine proceeds *via* the formation of dimethyl sulfoxide to give methanesulfonyl chloride. In the literature[8a] methanesulfonyl chloride is known to be formed from dimethyl sulfoxide by the aqueous chlorination, but no detailed reaction conditions have been reported. The formation of ethanesulfonyl chloride and butanesulfonyl chloride from diethyl sulfoxide and dibutyl sulfoxide, respectively, by the aqueous chlorination has also been reported in the literature.[8b,8c] Thus, the optimum conditions for the preparation of methanesulfonyl chloride from dimethyl sulfoxide were first determined.

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In the reaction of dimethyl sulfide with chlorine,[6] the presence of a large amount of water leads almost exclusively to the formation of dimethyl sulfone, but the yield of methanesulfonyl chloride is increased by the chlorination of the sulfide to at least monochloro level before introduction of water. Therefore, dimethyl sulfoxide was chlorinated in the two steps, the first step in the absence of water and the second step in the presence of water, as described below.

Dimethyl sulfoxide was allowed to react with chlorine under various conditions (mole ratios and temperatures). The pure methanesulfonyl chloride was obtained in 57—60% yield when 0.2 mole of chlorine in the first step and 0.8 mole in the second step was introduced into 0.1 mole of the sulfoxide at 15—20°. A small amount of dimethyl sulfone was also isolated as one of the products. When water was added in the first step, the yield of dimethyl sulfone increased, but that of methanesulfonyl chloride decreased. Methanesulfonyl chloride-d_3 was obtained in a 52% yield under the same conditions.

In order to elucidate the reaction mechanism, the products formed in the first step were analyzed, and it was found that trichloromethyl methyl sulfide was one of the main products and that methanesulfonyl chloride (about 0.02 mole) and dimethyl sulfone (about 0.01 mole) were formed in this step. Although the details of the mechanism have not been revealed yet, the formation of these compounds are presumed to be due to a complicated mechanism as in the reaction of dimethyl sulfoxide with bromine.[9]

Experimental

Methanesulfonyl Chloride——A 50-ml cylindrical flask was equipped with a magnetic stirrer, a thermometer, a gas inlet tube extending as deep as possible into the flask, and a vent for exit gas. In the flask was placed 0.1 mole (7.81 g) of dimethyl sulfoxide, which was purified by the crystallization-distillation method,[10] and 0.2 mole of dry chlorine gas was introduced at 15—20°. Water (5 ml) was then added dropwise at 15—20°, and the chlorination was continued at this temperature until 0.8 mole of chlorine was introduced. The aqueous layer was shaken with a small amount of $CHCl_3$. The extracts were combined with the lower layer and washed with ice-cold water. The washings were combined with the aqueous layer of the reaction mixture. Evaporation of water under reduced pressure gave 0.33 g of dimethyl sulfone, which was crystallized from EtOH to give the needles of mp 109.5° (uncorr.). The $CHCl_3$ solution was then washed with a chilled 5% aqueous solution of $NaHSO_3$ and again with ice-cold water, and dried over Na_2SO_4. After removal of the solvent, the residual oil was distilled under reduced pressure to give 6.60 g of methanesulfonyl chloride, bp 65° (26—26.5 mmHg). The infrared spectrum[1a] of the chloride obtained was identical with that of an authentic sample. Furthermore, it was converted by the ammonolysis to the crystalline methanesulfonamide, $CH_3SO_2NH_2$, mp 91.5° (uncorr.), which was identified by elemental analysis. The distillation residue solidified and gave 0.10 g of dimethyl sulfone. In this reaction the total yield of the sulfone was 0.43 g.

Methanesulfonyl Chloride-d_3——Under the same conditions as described above 0.1 mole (8.42 g) of dimethyl sulfoxide-d_6 (E. Merck Ag., an isotopic purity of 99.5%) was chlorinated. Before introduction of 0.8 mole of chlorine, heavy water (5 ml) was added in the place of ordinary water. The reaction mixture was treated in the same manner. Distillation gave 6.14 g of methanesulfonyl chloride-d_3, bp 65.5° (24.5—25.5 mmHg). Its infrared spectrum[1a] was consistent with the structure of CD_3SO_2Cl. Dimethyl sulfone-d_6 (1.56 g), mp 111°, was also obtained from the washings of the reaction mixture and the distillation residue.

Trichloromethyl Methyl Sulfide——The mixture obtained by the anhydrous chlorination was distilled (0.7 g of dimethyl sulfone from the residue), and the distillate was submitted to gas chromatography (Shimadzu GC-3BF Gas Chromatograph, column: stainless steel, 150×0.3 cm I.D., packed with 7% PEGS; column temperature: 80°) and fractionated. A droplet of colourless liquid was obtained as the main fraction and identified as trichloromethyl methyl sulfide by comparing its infrared spectrum with that of the authentic sample prepared according to the method of Richtzenhain and Alfredsson.[11]

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