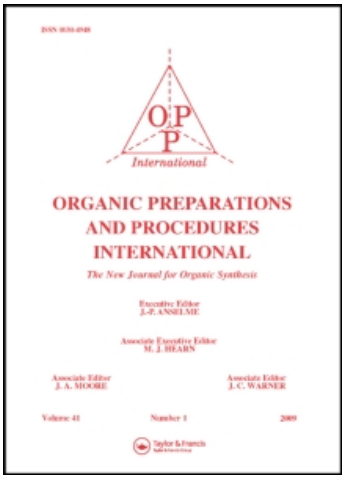

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CHLOROMETHYL METHYL SULFONE BY OXIDATION OF CHLOROMETHYL METHYL SULFIDE

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CHLOROMETHYL METHYL SULFONE BY OXIDATION OF CHLOROMETHYL METHYL SULFIDE

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For studies of the Ramberg-Bäcklund rearrangement and other reactions of carbanions of α-chloromethyl sulfones,[1] multigram quantities of the simplest representative of these compounds, namely chloromethyl methyl sulfone (**1**) were required. Surprisingly, the reported syntheses of this sulfone are far from satisfactory. The simplest path to **1** would seem to be the oxidation of chloromethyl methyl sulfide **2**. While the Pummerer reaction of dimethyl sulfoxide with thionyl chloride gave **2** in excellent yield,[2] its oxidation described in a few papers[3-7] was not satisfactory in our hands. Due to their facile hydrolysis, α-chloromethylsulfides cannot be efficiently oxidized to sulfones in aqueous solution[3] and thus many of the common oxidizing agents cannot be used. Perbenzoic acid,[4] perphtalic acid,[3, 5] peracetic acid,[6] and chromic anhydride in glacial acetic acid[7] have been previously used for the oxidation of α-chlorosulfides to sulfones.

We tested a few other oxidation procedures with rather disappointing results. Only when dimethyldioxirane in acetone[8] was used as the oxidant was the desired sulfone **1** obtained in good yield (84%). However, this procedure was impractical for the synthesis of large quantities of **1**. Further experimentation showed that the oxidation of **2** with a solution of H_2O_2 in diethyl ether also gave good results (*Table 1*). The hydrogen peroxide-ether solution is prepared by simple extraction of H_2O_2 from 30% aqueous hydrogen peroxide with diethyl ether.[9] As it has been shown previously, this solution is reasonably stable and can be handled without difficulty. Efficient oxidation of **2** to **1** requires the addition of acetic acid as a catalyst and anhydrous $MgSO_4$ in order to remove the water generated.

In the earlier paper on use of H_2O_2/diethyl ether,[9] no incidents were reported and we have also observed none. Nevertheless, for safety reasons all operations should be carried out with maximum care. The oxidation can also be carried out with H_2O_2 extracted to *t*-butylmethyl ether but results are not as good.

EXPERIMENTAL SECTION

Melting point is uncorrected. ^{1}H NMR spectrum was recorded on a Varian Gemini 200 (200 MHz spectrometer). Chemical shifts are reported in δ relative to TMS as internal standard. Aqueous hydrogen peroxide (30%), diethyl ether and Na_2SO_3 were reagent grade purchased from POCh. Starting α-chloromethyl methyl sulfide was prepared according to the described procedure.[2]

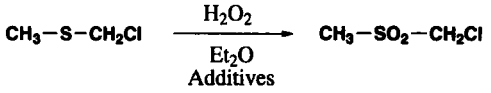

Table 1. Oxidation of **2** with Hydrogen Peroxide under Different Conditions

Entry	Additives	Eq. of H_2O_2	Time (hrs)	Temp.	Yield (%)
1	None	5	30	r.t.	50
2	V_2O_5	10	48	r.t.	33
3	Mo_2O_5	10	48	r.t.	55
4	$NaHCO_3$ (0.5 eq)	6	30	r.t.	53
5	$NaHCO_3$ (5 eq)	10	48	r.t.	0[a]
6	AcOH 1 mL	5	30	Reflux, r.t.	57
7	AcOH 1 mL, $MgSO_4$ excess	5	30	Reflux, r.t.	89

a) Reaction stopped at the sulfoxide stage.

Oxidation of α-Chloromethyl Methyl Sulfide.- One hundred milliliters of 30% aqueous hydrogen peroxide (CAUTION) was extracted with diethyl ether (8 x 30 mL). The combined etheral extracts were dried over $MgSO_4$ for 3 hrs. Assay of the solution by iodometric titration was found to be ca. 2 M.

To a stirred solution of AcOH (1 mL) and the ethereal solution of H_2O_2 (210 mL, 0.515 mole) was added $MgSO_4$ (25 g) and followed by the addition of α-chloromethyl methyl sulfide (10 g, 0.104 mole) in diethyl ether (10 mL) at such rate that the solution was maintained at gentle reflux. After addition was completed, the mixture was refluxed for 10 h and then stirred for additional 20 h. The solid was filtered off and washed with diethyl ether (100 mL). To the organic solution was added water (5 mL) and slowly Na_2SO_3 (10 g) in order to destroy peroxides and excess hydrogen peroxide, then the mixture was stirred overnight. The etheral layer was separated and the solvent evaporated to give white crystals which were triturated with hexane-diethyl ether (5:1) and recrystallized from EtOH to give 11.9 g (89%) of white needles, mp. 56-57°C, *lit.*[7b] 57-58°C.

^{1}H NMR (200 MHz, $CDCl_3$): δ 4.66 (s, 2H), 3.06 (s, 3H).

Anal. Calcd for $C_2H_5ClSO_2$: C, 18.68; H, 3.92; Cl, 27.57. Found: C, 18.41; H, 4.18; Cl, 27.85

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SIMPLE METHODOLOGY FOR THE PURIFICATION OF AMINO ACIDS

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Amino acids are among the most important substances for life and are present in all living organisms. They are the basic constituents of proteins, which participate in a large number of biochemical processes. Indeed, with the completion of the human genome sequence, the next major scientific goal is the determination of the structure and function of all proteins of biological relevance.[1] This effort requires, among others things, the specific preparation of both natural and unnatural amino acids, as well as their coupling in the synthesis of model peptides and proteins and remarkable activity is presently under way in this area.[2-4] In this context, the synthesis and purification of amino acids continues to present a significant challenge to synthetic chemists. While ionic exchange resins are still one of the most reliable techniques especially for large-scale preparations,[5] on occasion polar contaminants in reaction mixtures may cause interference that complicates the detection and purification (impurities may go unnoticed). Indeed,