A MILD, SELECTIVE REDUCTION OF ALKOXYSULFONIUM SALTS: REDUCTIONS
OF SULFOXIDES USING SODIUM CYANOHYDRIDOBORATE AND CROWN ETHERS

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The work of Johnson and Phillips[1] showed that alkoxysulfonium fluoroborate salts could be reduced to their corresponding sulfide using sodium borohydride as the reducing agent.   Yields of sulfide using this procedure range from 27-90% with most compounds being reduced in the 75-90% yield range.   The alkoxysulfonium salts were prepared by O-alkylation of the corresponding sulfoxides with trimethyloxonium fluoroborate.[1]   This procedure is simple and rapid but the use of the strong reducing agent sodium borohydride precludes the existance of other sensitive groups[2] elsewhere in the molecule.   Chasar[3] reported that sulfides may be prepared by the reduction of sulfoxides in the presence of a cobalt chloride/sodium borohydride reagent.   Yields were usually high in this procedure, but again the very strong reducing conditions[4] precluded this reagent's use where other reactive groups were present.   We wish to report a reduction method which is not affected by the above disadvantages.

The selectivity of sodium cyanohydridoborate has been studied in recent years.[5]   We have found that this selectivity may be extended to the reduction of alkoxysulfonium salts.   The reaction conditions are mild, clean and essentially quantitative based on recovered starting material.   Isolated yields of sulfide range from 55-91%.   Table I tabulates our results on a few model sulfoxides.

We also find that our method allows the reduction of sulfoxides in the presence of other functional groups.   For example, when the alkylation of a sulfoxide is performed with methyl fluorsulfonate[6] at 0° in methylene chloride with a ketone function present, only alkylation of the sulfoxide is observed,[7] which is then reduced to the corresponding sulfide when sodium cyanohydridoborate in methanol is added.   If this procedure is performed at room temperature,

extensive degradation is observed.[8] We observed that, in general, sulfoxides were alkylated at 0° with methyl fluorosulfonate while ketones showed no reaction at all. Since the reduction proceeds well at 0°, keto sulfoxides may be reduced to the corresponding keto sulfides very efficiently.

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TABLE I

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Sulfoxide	Yield of Sulfide[a,b]
dibutylsulfoxide	85%
diphenylsulfoxide	77%
dibenzylsulfoxide	91%
tetramethylenesulfoxide	87%

[a] isolated yield after workup

[b] all sulfide yields were essentially quantitative based on recovery of starting material. No other products besides sulfide and sulfoxide were observed when the crude reaction products were examined by thin layer chromatography or gas chromatography.

In our initial studies we formed the alkoxysulfonium salt in methylene chloride at 0°, removed the solvent at 0° after alkylation of the sulfoxide, then reduced the residual salt at 0° using $NaBH_3CN$ in methanol (or ethanol). We looked for a procedure which would allow us to perform the reduction of the alkoxysulfonium salt without removal of the methylene chloride. We found that the attempted reduction of the alkoxysulfonium salt in methylene chloride with $NaBH_3CN$ gave essentially no reduction (<5%). The recent observations of Liotta[9] on the reactivity of potassium salts in the presence of 1,4,7,10,13,16-hexaoxa-cyclooctadecane (18-crown-6)[10] led us to examine whether this crown ether would efficiently complex sodium cyanohydridoborate in methylene chloride. A catalytic amount of 18-crown-6 was added to the alkoxysulfonium salt in methylene chloride and a solution of sodium cyanohydridoborate in methanol was added at 0°. The yield of sulfide was increased from 2.7% to 58.3% with the only other product being starting sulfoxide. The yield of sulfide was quantitative based on recovered starting material.

Two representative procedures are as follows: A) Dibenzylsulfoxide (700 mg, 3 mM) was dissolved in 15 ml methylene chloride and cooled to 0°. To this cold solution was added methyl fluorosulfonate (Magic Methyl, Aldrich Chemical Co.,

342 mg, 3 mM) dropwise over several minutes. The mixture was then stirred for 1 hour at 0°C. The solvent was evaporated under vacuum at 0°, and to the residue was added sodium cyanohydridoborate (200 mg, 3.17 mM) in 15 ml ethanol at 0°. The mixture was then stirred for several hours, the ethanol removed under vacuum, and the residue partitioned between water and methylene chloride. Removal of the methylene chloride gave only dibenzylsulfide along with a small amount of starting sulfoxide. The yield was quantitative based on recovery of starting material, 92% based on isolated dibenzylsulfide. B) Diphenylsulfoxide (600 mg, 3 mM) was alkylated with methyl fulorosulfonate (342 mg, 3 mM) in 15 ml methylene chloride for 3 hours at 0°. To the cold solution was added 18-crown-6 (130 mg, 0.5 mM), followed by sodium cyanohydridoborate (200 mg, 3.17 mM) in 15 ml methanol. The solution was stirred at 0° for several hours and worked up as above to give 58.3% diphenylsulfide along with 40% diphenylsulfoxide. When the reaction was run without the inclusion of 18-crown-6 only 2.7% diphenylsulfide was obtained.

In conclusion, we think that this procedure offers a very mild, high yielding reduction of sulfoxides to sulfides. The reaction may be used in the presence of aldehydes and ketones to give only sulfoxide reduction.[7] Incorporation of crown ethers into this reaction sequence allows one to run the reaction in solvents not usually associated with cyanohydridoborate anion reductions. Work is continuing to extend these observations into other areas of anion reactivity.

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