

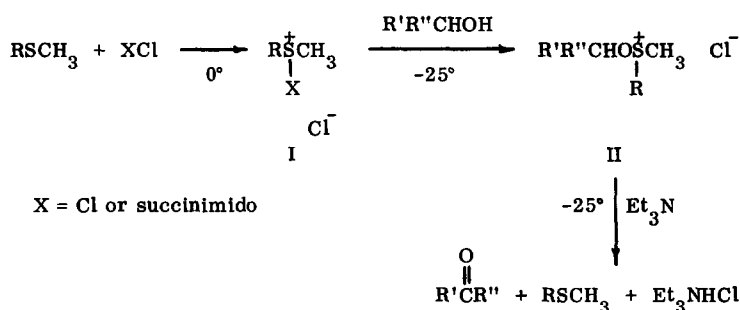
OXIDATION OF PRIMARY AND SECONDARY ALCOHOLS TO CARBONYL COMPOUNDS
USING DIMETHYL SULFOXIDE--CHLORINE COMPLEX AS REAGENT

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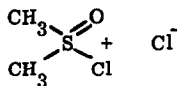
Recent reports from this laboratory have described a new process for alcohol \rightarrow carbonyl conversion which can be represented by Scheme A.^{1,2} This process provides a highly efficient and useful new method



Scheme A

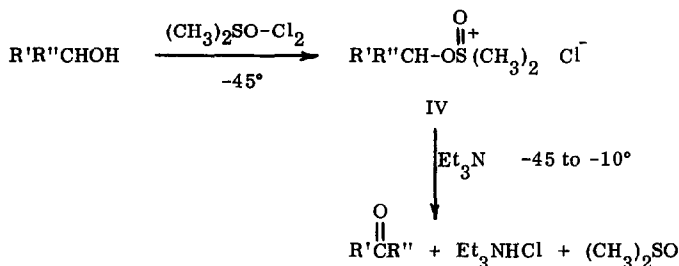
which promises to be highly advantageous, even in comparison to the best of existing procedures, for example, those of Collins,³ Jones,⁴ and Moffatt.⁵ As an extension of our earlier work, it seemed interesting to examine the possibility of substituting dimethyl sulfoxide for the sulfide component of complex I. Observations of complex formation between dimethyl sulfoxide and halogens have previously been recorded,⁶ but detailed information, especially with regard to structure, is lacking.

Addition of 1 equivalent of dimethyl sulfoxide to a solution of chlorine in methylene chloride at -45° produces a colorless precipitate which is stable at that temperature but which decomposes slowly at -20° and rapidly at 0° . Although we have no evidence on the constitution of this complex, the formulation III



III

seems not unreasonable.⁷ Of greatest interest to us with regard to the objective set forth above was the finding that the dimethyl sulfoxide--chlorine complex did serve as a reagent for the oxidation of alcohols to carbonyl compounds by a process analogous to that outlined in Scheme A for sulfide complexes. Best results were obtained in general by using an excess of dimethyl sulfoxide (ca. 5-fold) over chlorine and conducting complex formation at -45° (dry ice--acetonitrile bath, only a few minutes were required for generation of the complex). Reaction of the complex (2 equivalents, 100% excess) with the alcohol for ca. 2.5 hr. at -45° followed by addition of excess triethylamine and gradual warming over a 5-min. period produced the desired carbonyl compound usually in excellent yield. The process is summarized in Scheme B which depicts the presumed precursor IV of the final oxidation product.⁸

Scheme B

The following oxidation processes were demonstrated experimentally (% yield given in parentheses):

- 1-octanol \rightarrow octanal (>95%)
- cyclohexylcarbinol \rightarrow cyclohexylcarboxaldehyde (>94%)
- benzyl alcohol \rightarrow benzaldehyde (>98%)
- 4-t-butylcyclohexanol (mixture cis and trans) \rightarrow 4-t-butylcyclohexanone (>97%)
- benzhydrol \rightarrow benzophenone (>98%)

All reaction products were analyzed by infrared and proton magnetic resonance spectroscopy and vapor phase chromatography and were found to be identical with pure authentic samples. The following experimental procedure is illustrative.

Octanal. --To a cooled (-45°) solution of 284 mg. (4.0 mmol.) of chlorine in 4 ml. of methylene chloride (distilled from phosphorus pentoxide) was added a solution of 1.4 ml. (20 mmol.) of dimethyl sulfoxide (distilled from calcium hydride) in 1 ml. of methylene chloride under argon with good mechanical stirring. A white precipitate appeared during the addition. To this mixture was added a solution of 260 mg. (2.0 mmol.) of 1-octanol in 0.5 ml. of methylene chloride. After stirring for 2.5 hr. at -45° , a solution of 808 mg. (8.0 mmol.) of triethylamine in 0.5 ml. of methylene chloride was added dropwise. The cooling bath was removed and after 5 min., 20 ml. of ether was added. The organic layer was washed with 7 ml. of 1% aqueous hydrochloric acid and three times with 10 ml. of water. Removal of dried (magnesium sulfate) solvents under reduced pressure left 262 mg. (100%) of octanal. Vapor phase chromatographic analysis indicated a yield of >95% (xylene as internal standard with a 10% SE-30, 10-ft. column). The infrared and n. m. r. spectra were identical with those of an authentic sample.

There are significant differences between the dimethyl sulfoxide--chlorine reagent and the sulfide-based reagents of type I. The formation of chloride which is observed in the reaction of the sulfide reagents I and alcohols corresponding to stabilized carbonium ions^{1,2} (e.g., benzhydrol) does not appear to be a serious side reaction when the dimethyl sulfoxide--chlorine reagent is used. On the other hand, the dimethyl sulfoxide--chlorine reagent reacts readily with olefins to form vicinal dichlorides. Thus, cyclooctene is converted cleanly by the chlorine--dimethyl sulfoxide reagent to 1,2-dichlorocyclooctane.⁹ It is not clear whether the chlorination is the result of reaction of molecular chlorine which may be in equilibrium with the complex or a direct reaction of the chlorine--dimethyl sulfoxide complex itself. In any event, this reaction occurs sufficiently rapidly to interfere with the oxidation of unsaturated alcohols such as 2-cyclohexenol, which are found to undergo both addition of chlorine to unsaturated carbon and alcohol oxidation.

Although there are clear limitations on the scope of the oxidation process based on the dimethyl sulfoxide--chlorine complex as described above, the method promises to be economical, convenient, and efficient for a wide variety of cases.¹⁰

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10. We are indebted to the National Institutes of Health and the National Science Foundation for financial assistance.