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MECHANISTIC DETAILS OF
THE DIMETHYL SULFIDE/N-CHLOROSUCCINIMIDE OXIDATION OF ALCOHOLS

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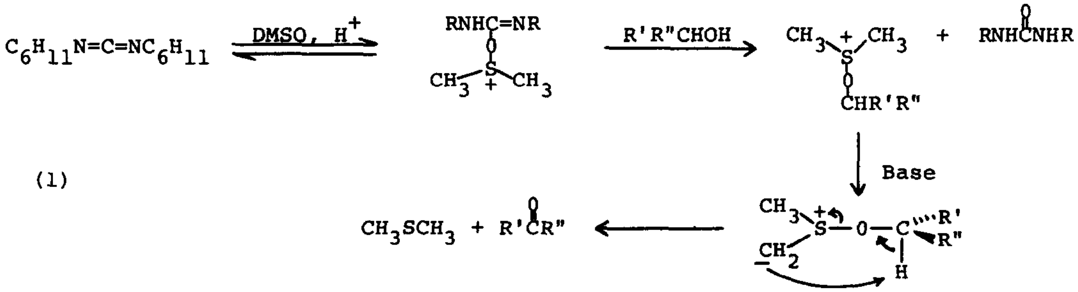
Since the acid-catalyzed DMSO/DCC oxidation of alcohols was uncovered,[1] considerable interest in its application and in development of modifications has ensued.[2] The recent report[3] of the oxidation of alcohols by the dimethyl sulfide/N-chlorosuccinimide (DMS/NCS) complex represents a novel modification which offers practical advantages, to which the rapid application[4] of this and the related DMS/halogen complexes by other groups attests. Full evaluation of its utility to studies in this laboratory and broader interest in the DMS/NCS complex and its chemistry[5] have prompted the mechanistic study of this oxidation reported herein. Two major points are of interest: (1) the nature of the DMS/NCS complex, and (2) the mechanistic pathway of the oxidation. Evidence concerning the former has been published;[5] this report deals with the latter aspect.

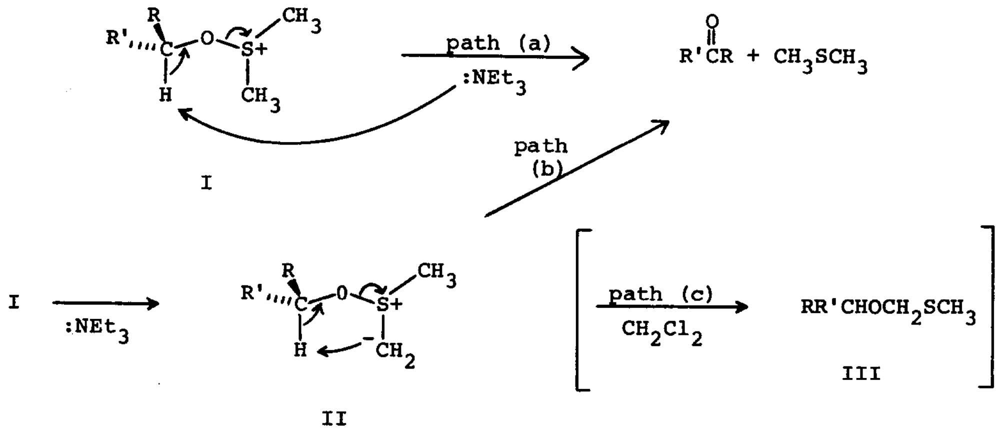
Deuterium and ^{18}O labeling studies[6] have shown the mechanism of the DMSO/DCC oxidation to be that depicted in (1), or a variation[7] of this scheme consistent with the indicated proton and oxygen transfers. No mechanistic



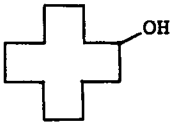
(1)

details of the DMS/NCS oxidation have been reported, but the original studies[3] showed that methylthiomethyl ethers (III) are formed when more polar solvents such as methylene chloride are used, leading the authors to postulate the intermediacy of a sulfur ylid (II) in the generation of this aberrant product (path c). By analogy with the DMSO/DCC oxidation, and in keeping with available evidence concerning the nature of the DMS/NCS complex, it seems reasonable to suggest oxidation of alcohols by the latter reagent involves initial formation of the sulfonium ion I, which, upon the <u>required addition</u> of base, could collapse to products by either path (a) or path (b). The apparent requirement of addition of an external base, in contrast to the DMSO/DCC oxidation, might have been interpreted as evidence for path (a). The labeling studies reported herein demonstrate the abstraction of one proton from the starting DMS and the transfer of the carbinol proton to the regenerated DMS, indicating path (b) obtains, in complete analogy with the DMSO/DCC oxidation.

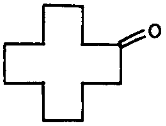
(2)



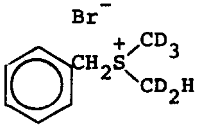
Oxidation of 835 mg. (4.52 m moles) cyclododecanol (IV) was carried out according to the described procedure,[3] using 4.11 m moles DMS-d_6,[8] 4.35 m moles NCS, and 5.78 m moles triethylamine. Before aqueous work-up, the majority of the deuterium-containing DMS was removed by vacuum transfer at -35 to -25°. Work-up provided 790 mg (96% crude yield) of cyclododecanone (V) m.p. 55.5-57.5°. Glc analysis (OV-101) indicated the crude material was a 91:9 mixture of V:IV. This corresponds to oxidation by 4.11 m moles (100%) of DMS/NCS complex. The



IV



V



VI

DMS obtained from the reaction was treated with benzyl bromide in ethanol, affording 207 mg of the sulfonium salt VI [m.p. after recryst. (THF/EtOH), 99.2-99.5° (decomp.), lit.[9] 99-99.5° (unlabeled material)]. NMR analysis of VI indicated a benzyl (5.48 ppm)/methyl (3.32 ppm) proton ratio of 2.0 ± 5%, demonstrating the abstraction of one and only one deuterium atom from the starting DMS-d_6. In corroboration of this result, mass spectral analysis of the DMS obtained in a similar experiment showed the molar amount of DMS-d_5 (m/e 67) which was formed equal to the amount of alcohol oxidized.

Finally, the intramolecular nature of the proton transfer in the ylid II was demonstrated by carrying out the oxidation as described above, using unlabeled DMS and cyclododecanol-1-d.[10] Mass spectral analysis of the DMS produced indicated a large predominance of the monodeuterio species (m/e 63). Owing to the large M-1 peak (rel. abundance 31%), exact determination of the deuterium content was not possible; however, careful examination of the ratios of ions at m/e 63, 62, & 61, and 48 & 47, indicated at least 95% of the DMS contained deuterium.

These results implicate the intermediacy of I (or possibly an equivalent species with tetravalent sulfur)[7] and its collapse to product by path (b). Experiments designed to exploit the intramolecular nature of the proton abstraction to effect regioselective and stereoselective oxidations of alcohols are underway and will be reported later.

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