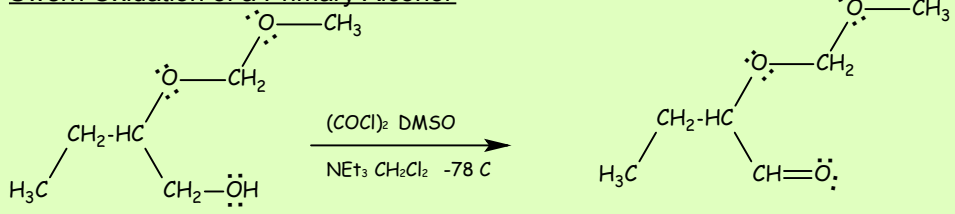
Mechanism & Text By Roderick A Davis, Sr. March 19, 2009

Reference: Organic Chemistry Assignment-Scheme 2, Synthesis of E-Allylic Alcohol, (step 7-rxn (1)) Information from Synthesis of the Piperidine Alkaloid, alpha-Conhydrine. See ACS, "Organic Letters" 2007, Vol.9,No.8, 1609-1611.

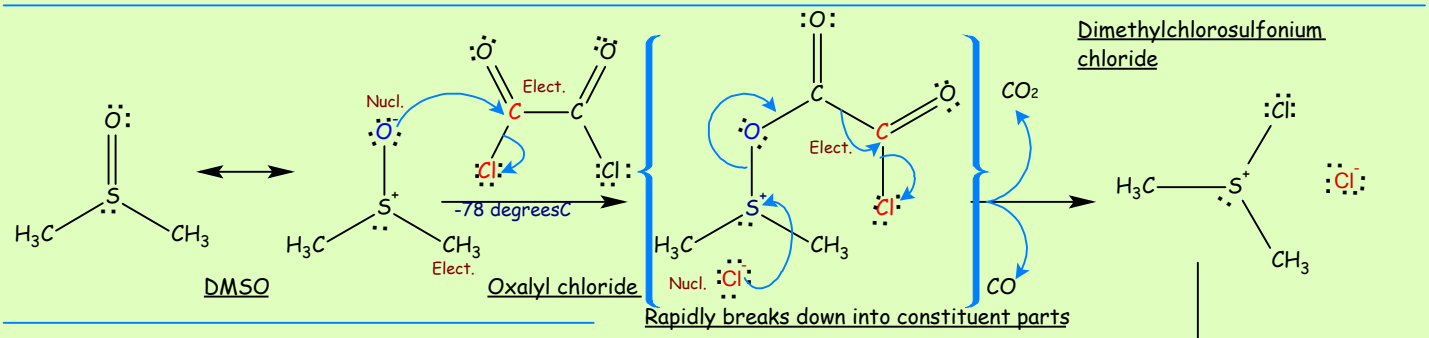
Swern Oxidation of a Primary Alcohol



(2R)-2-(Methoxymethoxy)butan-1-ol **(2R)-2-(Methoxymethoxy)butanal**

Sn2 Reaction:

In this nucleophilic substitution Sn2 reaction, DMSO, which is weakly basic, attacks the electrophilic carbon center of $(COCl)_2$, expelling the chloride ion as the LG-(leaving group), and forming an intermediate in which the two species are linked by a sigma bond. The linked species bond is then quickly broken when the chloride ion attacks the sulfur atom causing a new sigma bond linking DMS with the chloride ion to form Dimethylchlorosulfonium chloride; while giving off CO_2 and CO in the rxn. The oxalyl chloride is the acid electrophile and Dimethyl sulfoxide is the base nucleophile. This follows the order of a Lewis acid/base reaction.

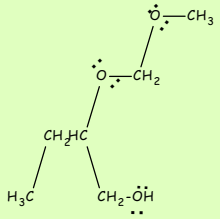


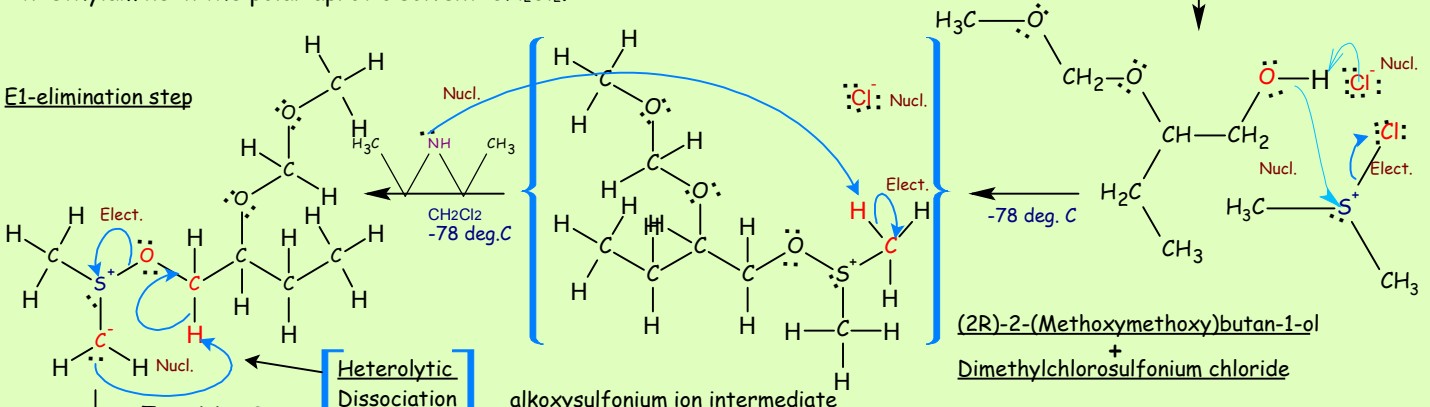
DMSO Oxalyl chloride Rapidly breaks down into constituent parts

Dimethylchlorosulfonium chloride

In this rxn, DMSO is a polar aprotic solvent. The solvent choice for this nucleophilic substitution reaction is polar enough to dissolve the nucleophile-(LG) from the Alkyl halide (oxalyl chloride), which in this case is the chloride ion. This choice of solvent influences the direction of the mechanism to follow an Sn2 rxn. (2R)-2-(Methoxymethoxy)butan-1-ol undergoes oxidation when added to the rxn. The chloride ion dissociates the (H+) atom from the O-H molecule while electrons from oxygen form a new sulfoxide sigma bond causing the other chloride ion to become a nucleophile LG. Hence, the alkoxysulfonium ion intermediate that is formed, undergoes deprotonation upon the addition of triethylamine in the polar aprotic solvent CH_2Cl_2.

-78 degrees C

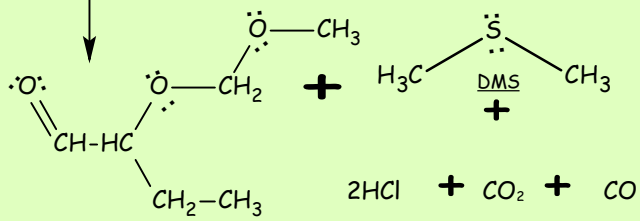




E1-elimination step

Transition State Heterolytic Dissociation alkoxysulfonium ion intermediate

(2R)-2-(Methoxymethoxy)butan-1-ol + Dimethylchlorosulfonium chloride



(2R)-2-(Methoxymethoxy)butanal

E1 Reaction Step:

In the transition state, sulfur ylide undergoes intramolecular deprotonation to yield the dimethyl sulfide and the formation of a pi bond yielding (2R)-2-(Methoxymethoxy)butanal as the product of interest. The rationale behind maintaining such a low temperatures (-78 degrees C) during the rxn, is to prevent the possible formation of mixed thioacetals which are sulfur analogue of acetals .