STUDY-MATERIAL

M.Sc. IV SEMESTER

PAPER-II C (Organic Synthesis)

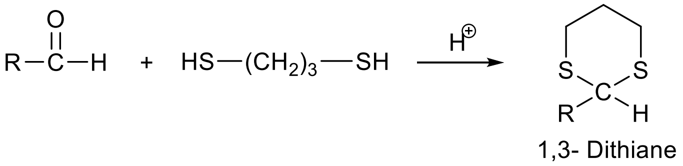
Instructor: Dr. Sachin Kumar Singh

Department of Chemistry, DDU Gorakhpur University

UNIT-4 REAGENTS: 1, 3-DITHIANE (UMPOLUNG)

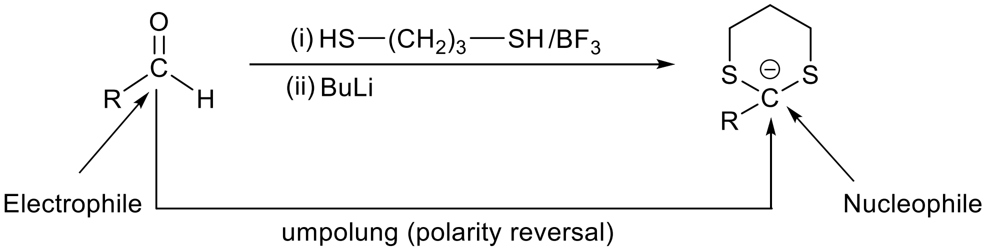
Preparation of 1,3- dithiane:

Carbonyl compounds, aldehydes or ketones reacts 1,3-propanedithiol in the presence of an acid catalyst to form cyclic- thioacetate which is called 1,3- dithiane.

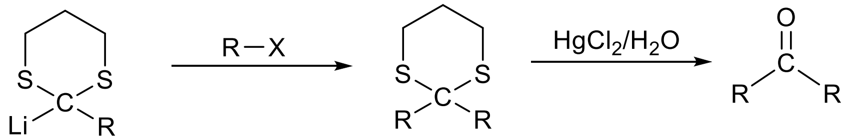


Umpolung (German, Polarity reversal) of 1.3 dithiane:

Normally the carbonyl carbon atom of an aldehyde is partially positive. It is electrohilic and consequently, reacts with nucleophiles, when the aldehyde is converted to 1, 3-dithiane and treated with butyllithium, this same carbon becomes negatively charged and reacts with electrophile. This reversal of polarity of the carbonyl carbon atom is called umpolung (means polarity reversal). Thus the term umpolung refers to the reversal of the normal polarity of a functional group (i.e., electrophilic into nucleophilic and nucleophilic into electrophilic transformation).



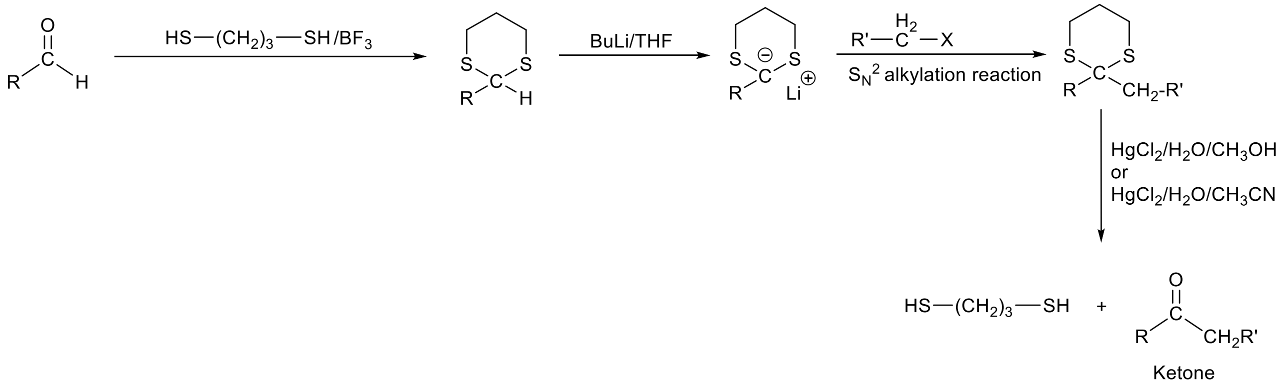
Dithianes are most commonly lithiated (i.e., deprotonated) with butyl lithium in the presence of THF after reaction with the electrophile, removal of the dithiane can be achieved with a variety of reagents including $HgCl_2$ and $CdCO_3$.

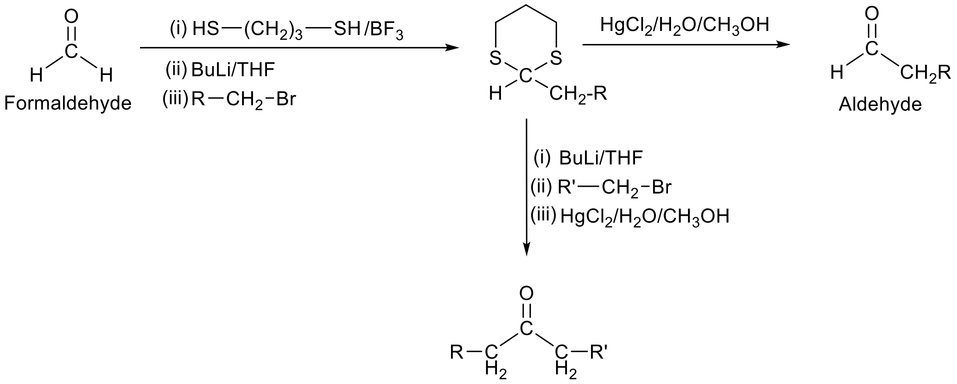


Synthetic Applications:

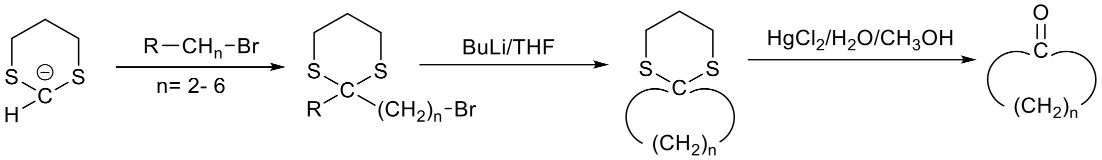
(I) Reaction with Halides and Sulphonates:

1, 3-dithiane anion (*i.e.*, 2-lithio-1, 3-dithiane) is an excellent nucleophile and reacts by S_N2 pathway with primary, secondary alkyl halides, allylic halides or primary sulphonates to give a disubstituted dithiane. Hydrolysis of this product in the presence of $HgCl_2$, either in methanol or in aqueous acetonitrile gives a ketone. Thus formaldehyde can be converted into other aldehydes and ketones whereas aldehydes are converted into ketones by 1, 3-dithiane.



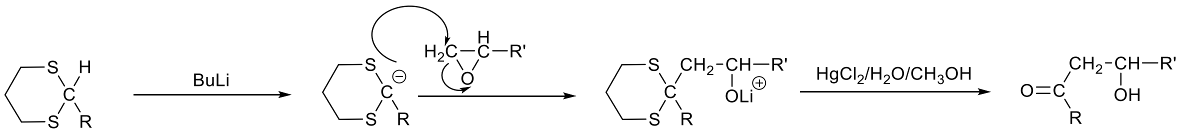


Macro cyclic products are obtained with bifunctional electrophile.



(II) Reaction with epoxides:

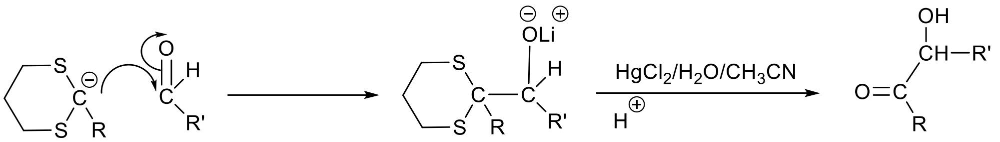
Anion of 1, 3-dithiane gives nucleophilic substitution reaction with epoxide to from β-hydroxy aldehydes and ketones. Ring opening with anion of 1, 3-dithaiane proceeds in general with good regio- and stereochernical control, following the rules of $S_N{}^2$ processes in basic medium and affording the β-hydroxy carbonyl compounds.



β–hydroxy carbonyl compound

(III) Reaction with carbonyl compounds:

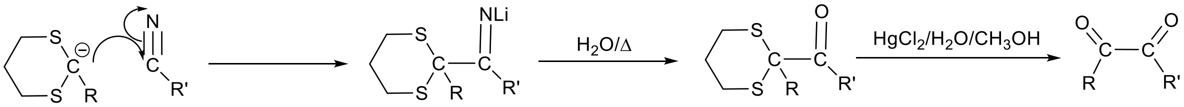
Anions of 1, 3-dithiane add to the carbonyl group of aldehydes and ketones to form tetrahedral carbonyl addition compounds which, on hydrolysis, give α-hydroxy carbonyl compounds.



α–hydroxy carbonyl compound

(IV) Reaction with Nitrites:

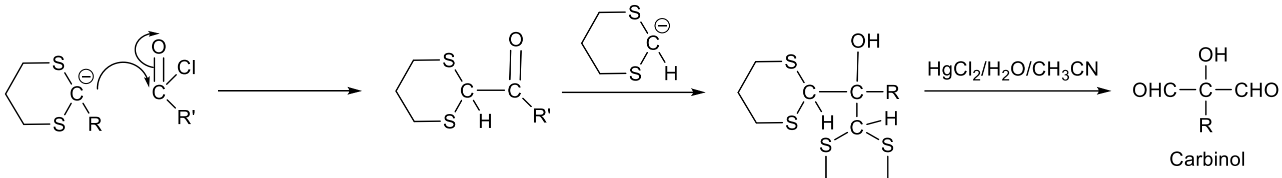
Anion of 1, 3-dithiane gives nucleophilic addition with nitriles. The adduct on hydrolysis gives vie dicarbonyl compounds.



vic dicarbonyl compound

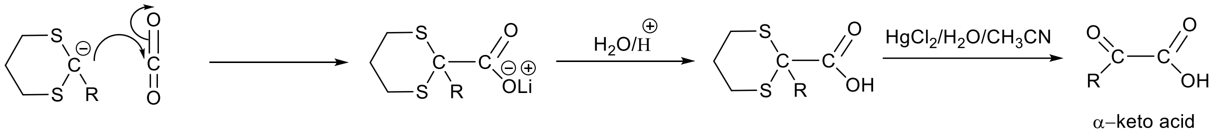
(V) Reaction with Acid chlorides:

Acid chlorides give the double addition carbinol product.

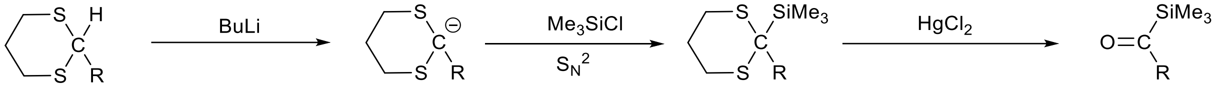


(VI) Reaction with CO_2 :

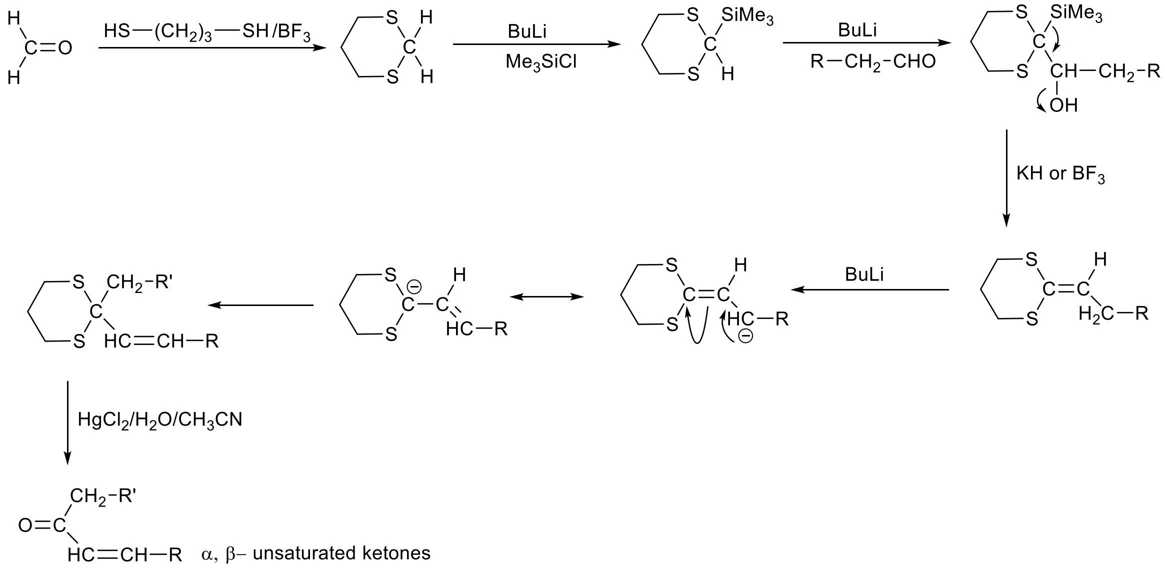
Anion of 1, 3-dithiane reacts with solid carbon dioxide to give addition product which on hydrolysis gives α-keto acid.



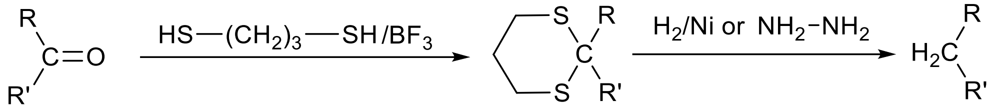
Apart from carbon electrophiles other electrophiles such as silicon electrophile also react with the anion of 1, 3-dithiane. Trimethylsilyl chloride reacts wtih anion of 1, 3-dithiane to give 2-trimethylsily1-1, 3-dithiane.



2-trimethylsily1-1, 3-dithiane of formaldehyde is very useful compound for the preparation of α, β-unsaturated carbonyl compounds.



A dithiane may also be converted into —CH_2— group by reaction with Raney Nickel. This reduction method of carbonyl compound into the corresponding hydrocarbon is known as Mozingo method.



Reference Books:

1. Organic Synthesis By Michael B Smith , Mc-Graw Hill, 2010
2. Organic Synthesis By J. Singh and LDS Yadav, Pragati Prakashan, 2010
3. Advanced Organic Chemistry Part. A & B By F. A. Carey and R. J. Sundberg, Plenum Publisher , New York, 2002
4. Advanced Organic Chemistry By J. March, 2007