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Dimethyl Sulphoxide a Useful Reagent for Organic Synthesis

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Abstract

Dimethyl sulphoxide as a reagent brings about N-methylthiomethylation and N,N/-methyl - thiomethylation in substituted barbituric acids. It converts 4-acetoxy coumarins to corresponding ylides and brings about methylene insertion in 1,6-naphtharidenes at reflux temperature.DMSO activated by trifluoro-aceticanhydride brings about formation of mono, bis and tris-sulphonic substituted derivatives when interacted with cyclo pentadiene and trimethylsilyl cyclopentadiene.This reagent converts 3-Nitro-4-hydroxy coumarins to salicylic acid in dichloromethane at low temperature.DMSO-acetic anhydride reagent converts enols to sulphur ylides, introduces methylthiomethyl group into phenols and oxidizes secondary alcohols to corresponding ketones. It brings about oxidative rearrangement in polyporic acid and converts 4-hydroxy coumarins and its 3-substituted derivatives into a wide range of products under different conditions.DMSO-SO3 pyridine complex in presence of triethyl amine oxidizes cis-diols to corresponding quinones.DMSO-activated by N-bromosuccinimide brings about methylation of alcohols and converts diols to their corresponding methylene-acetals.

Keywords: Ylide, Methylthiomethylation, Acetoxy coumarins, Polyporic acid, N-bromosuccinimide DMSO, Acetic anhydride.

Contents

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1. Introduction

In this article I have broadly explained the role of DMSO as reagent either alone or with a number of activators using different substrates and yielding a large number of products under varying conditions Graphics of all the structures have been highlighted in different schemes.

2. Discussion

Dimethyl sulphoxide a viscous hygroscopic liquid, initially used as a dipolar aprotic solvent has found extensive use in synthetic organic chemistry over the years. Kornblum, et al. [1] first used it to bring about oxidation of alcohols and allylic alcohols. Subsequently sulphoxonium ylide was used as a source of methylene in the preparation of oxiranes and cyclopropanes by Corey and coworkers [2].

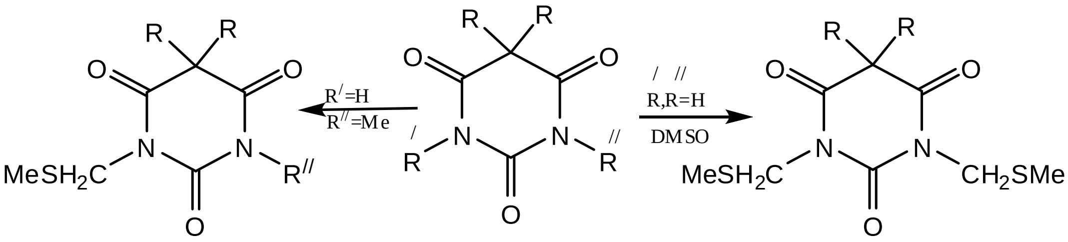
Direct nucleophilic attack on sulphur of DMSO has been found unfavorable in presence of lone pair of electrons on it. Therefore an initial electrophilic attack on oxygen is necessary to facilitate attack by a nucleophile on sulphur to give sulphonium species, formation of which is followed by further reactions. Electrophilic reagents that activate DMSO include trifluoroacetic anhydride [3] acetic anhydride [4] thionyl chloride [5] oxalyl chloride [6] chlorine [7] acetyl chloride [8] SO_3-pyridine [9] polyporic acid [10] Bromine [11] etc.The nucleophiles usually employed are alcohols [12] phenols [13] enols [14] amines [15] oximes [16] alkenes and alkynes [17].

Lately DMSO even in absence of activators has been found as a versatile reagent and can bring about methyl thiomethylation and dimerisation involving methylene insersion in certain substrates.

A brief description of DMSO alone and DMSO activated by different electrophiles, as reagents is given below

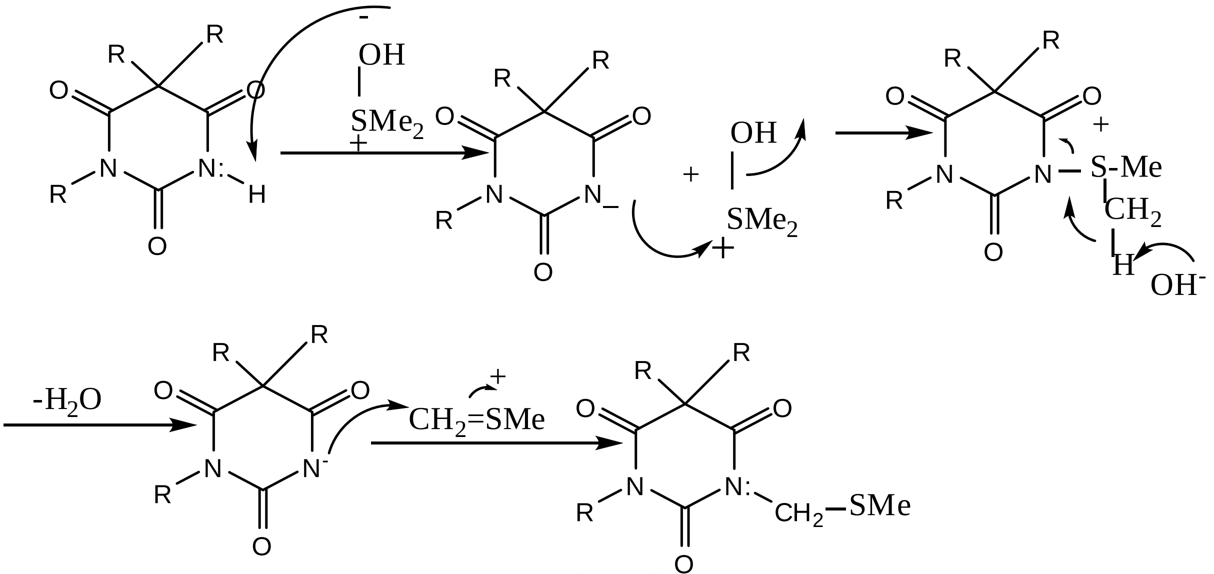
Section A

1. DMSO brings about N-methyl thiomethylation and N,N$^{/}$ -methyl thiomethylation in 5,5-disubstituted barbituric acid (1) which have been prepared by the reaction of corresponding unsubstituted barbiturates with DMSO [18].



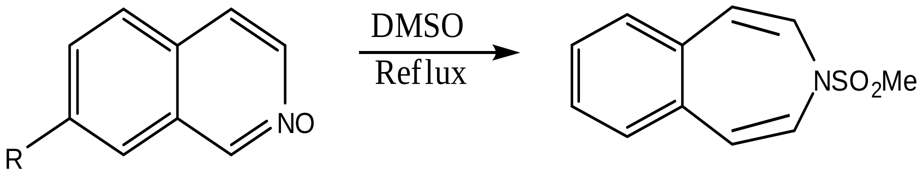
(1)

Formation of N-methyl thiomethylation of (1) can be explained on the basis that oxygen of DMSO gets protonated and forms a sulphur stabilized carbocation which reacts with barbiturate ion and forms the corresponding products.



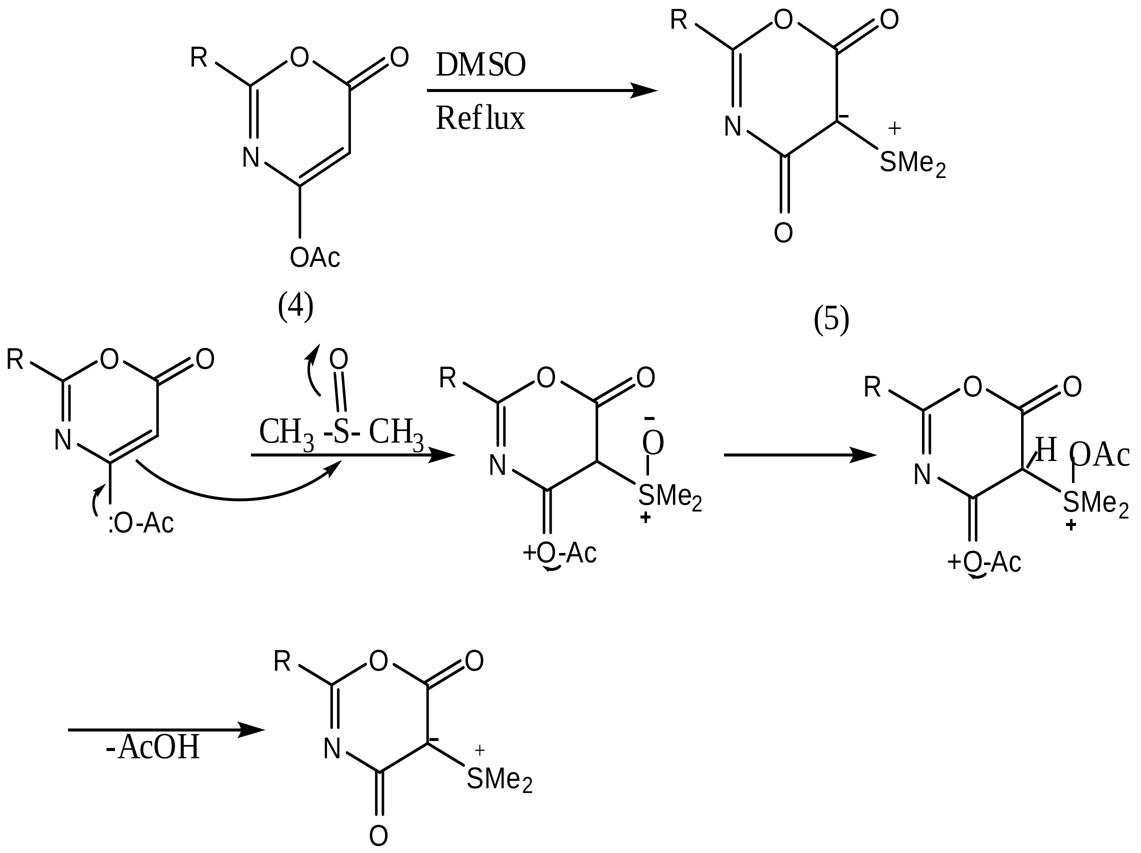
Scheme-1 (**R**$^{/}$=H,**R**$^{//}$=H)

1.1 In a mechanistically interesting reaction ,DMSO converts isoquinoline-2-oxides (2) to Benz(d) azepine (3) in presence of NaOH which generates methyl sulphinyl carbanion ($C^-H_2SOCH_3$) [19].



(2) (3)

1.11 It converts 1,6-naphtharidine an analog of 4-hydroxy coumarin to dinaphtharidinyl methane [20] and also converts oxazinones (4) to the corresponding ylide (5) [21] of mechanistic interest, as in case of 4- acetoxy coumarins [22]. Scheme-2

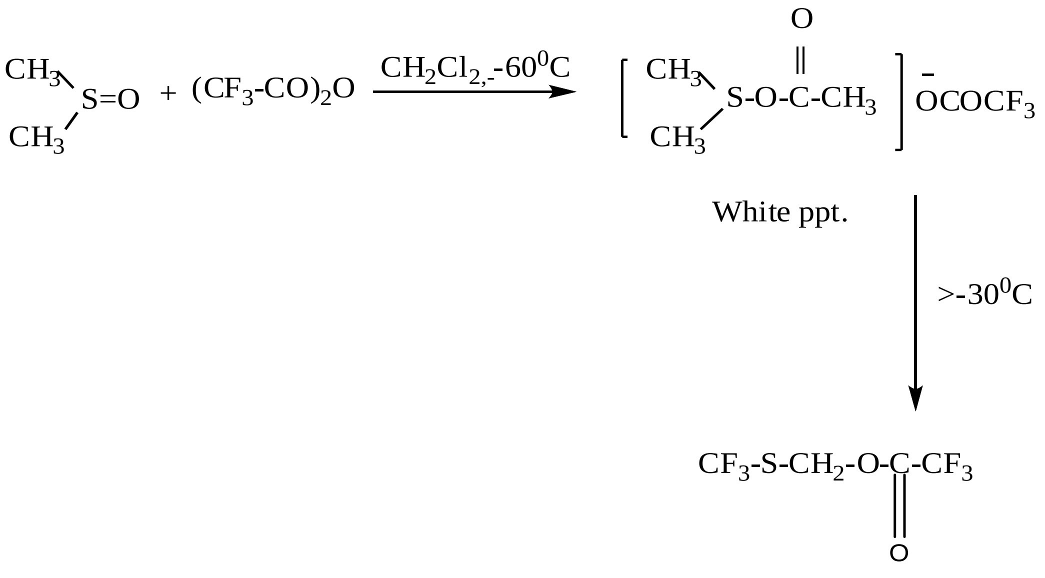


Scheme-2

Section B. DMSO with activators:

2. DMSO/ trifluoro acetic anhydride

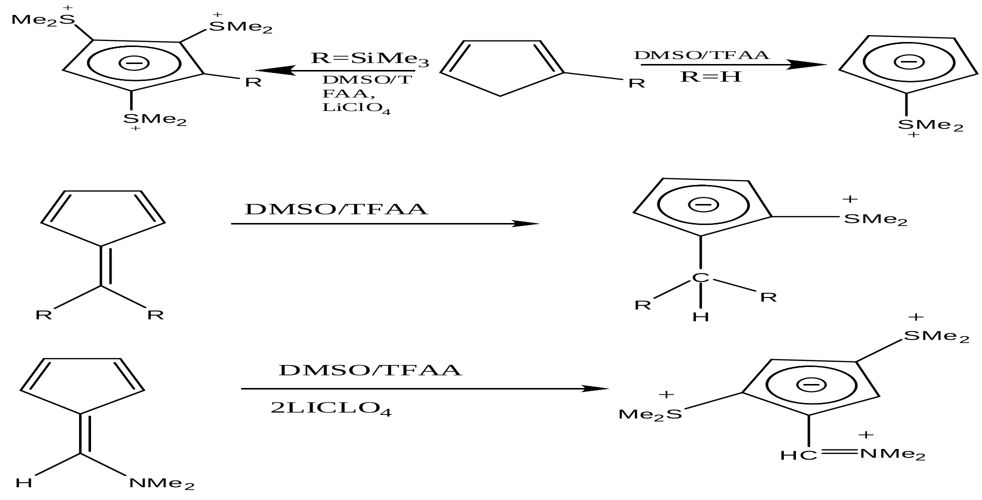
DMSO-trifluoro acetic anhydride reaction, which is violent can be moderated by working at low temperature (< -30^0C) in an unreactive solvent (dichloromethane). The reaction proceeds instantly and exothermically at -60^0C in dichloro methane and produces a white precipitate but upon warming above -30^0C, the system becomes homogeneous and the Pummerer rearrangement product (6) is formed [23].Scheme-3



(6)

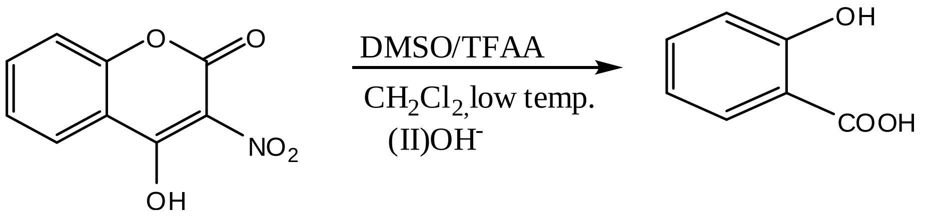
Scheme-3

Formation of mono , bis and tris sulphonic substituted derivatives takes place when TFAA activated DMSO react with cyclo pentadiene and trimethyl silyl cyclo pentadiene and fulvenes [24]. Scheme-4



Scheme-4

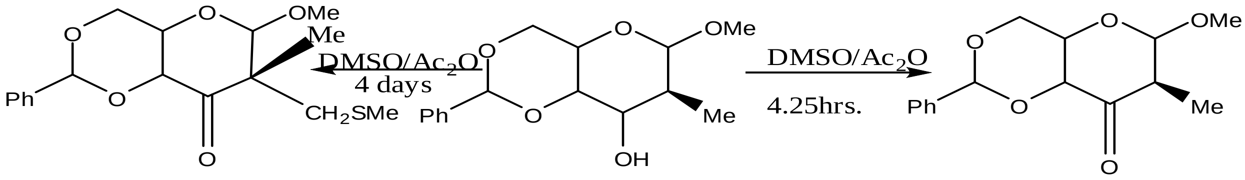
DMSO/ TFAA reagent has been found to afford salicylic acid as a major product along with other minor products, when interacted with 3-nitro-4-hydroxy-coumarin in dichloromethane at low temperature.



2.1 DMSO/acetic anhydride

Dimethyl sulphoxide activated by acetic anhydride has been used to convert enols into sulphur ylide, introduces methyl-thiomethyl group into phenols and oxidizes secondary alcohols to corresponding carbonyl compounds.

DMSO/Ac_2O reagent methyl thiomethylates –OH group in sugar units [25] and reacts with certain medicinally useful secondary alcohols to yield the corresponding ketones and its 2-methyl thiomethyl derivative on prolonged exposure [26]. Scheme-5.



Scheme-5

In an interesting reaction this reagent induces oxidative rearrangement in polyporic acid (7) to pulvinic acid dilactone (8) with excellent yield of the product (95%) [27].

(7)

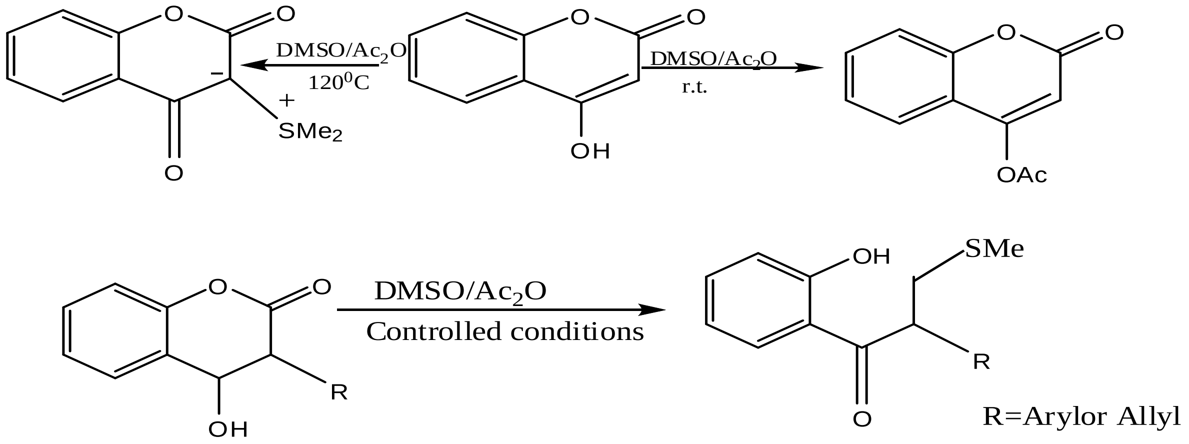
(8)

Oxidation of yohimbine to yohimbinone

Yohimbine was oxidized to yohimbinone in 80-85% yield by DMSO/Ac_2O reagent.

A mixture of yohimbine (886g),DMSO(7.5 l) and acetic anhydride(5.05 l) was stirred at room temperature for 18 h.The mixture was diluted with ethanol(16.8 l) ,stirred for 1 h and diluted with water(4.2 l).Concentrated ammonium hydroxide(11 l) is added while maintaining the temperature at 15-30^0C by cooling and the mixture is diluted with water(16.8).Filtration gives a solid which is washed with water and dried to give a tan colored solid. This is slurried twice with ethanol and filtered. Yield(84%),m.p.253-254^0C [28].

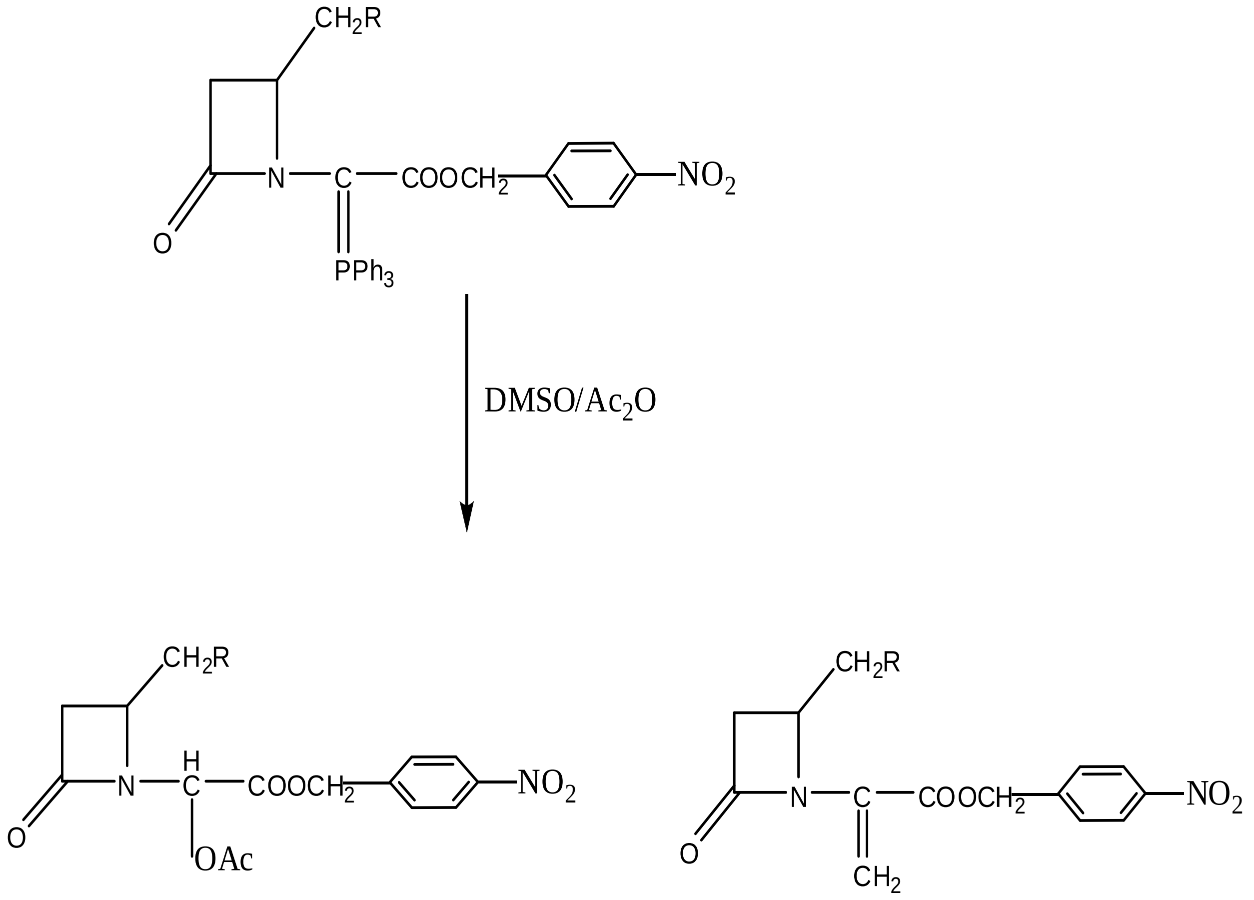
DMSO/Ac_2O reagent has been found to yield a wide range of products with 4-hydroxy coumarins and its 3-substituted derivatives both of pharmacological and chemical importance under different conditions [29]. Scheme-6



Scheme-6

This reagent brings about N-methyl thiomethylation and N-hydroxy methylation in phthalimide.

DMSO/Ac_2O reagent also brings about Wittig type methylene insersion accompanied by acetate formation in certain triphenylphosphine compounds depending upon the temperature. Fetter, et al. [30] scheme-7.

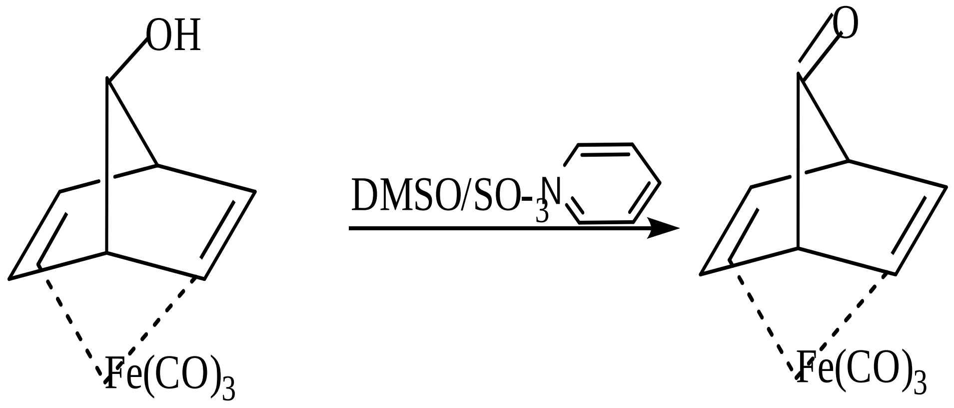


Scheme-7

2.2 DMSO/SO_3/pyridine

DMSO and SO_3-pyridine complex yields a reagent in presence of triethyl amine that rapidly oxidizes primary and secondary alcohols to corresponding aldehydes and ketones respectively in good yields. This reagent also oxidizes allylic alcohols to the corresponding α, β- unsaturated carbonyl compounds.

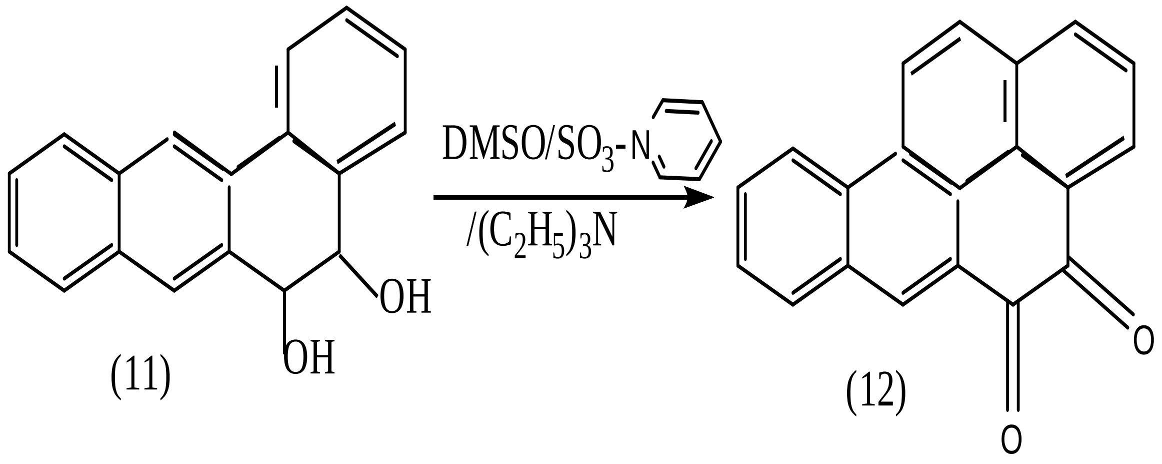
The combination of DMSO with SO_3 / pyridine complex oxidizes tricarbonyl (7-norbornadienol) iron (9) to tricarbonyl (7-norbornadienone) iron (10) [31].



(9)

(10)

The SO_3/pyridine complex in DMSO/ triethylamine has been used to oxidize cis-diols (11) to its corresponding quinone (12) in good yields.

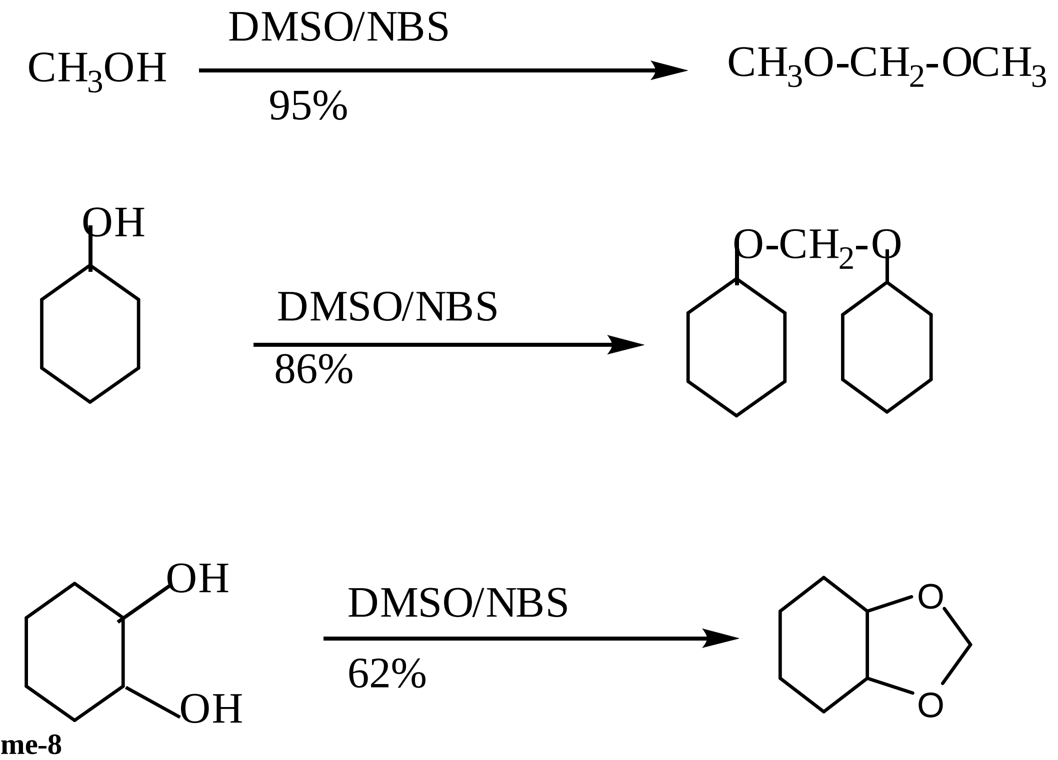


(11)

(12)

2.3 DMSO/N-Bromosuccinimide

DMSO/NBS has also been used as a versatile reagent. Methylation of alcohols and diols to their corresponding methylene acetals in high yield has been observed with this reagent. Scheme-8.-



Scheme-8

2.4 DMSO-KOH reagent

DMSO/KOH reagent has also found wide applications in synthetic organic chemistry. It brings about dimerisation of acetylenes [32] Aldolcondensation of acetophenone,condensation of acetophenone with methylsulphinylmethyl carbanion [33] and converts pyrrole to 1and 2-pyrrole dithiocarboxylic acids in the presence of carbondisulphide [34]. N-vinylation of pyrroles have been achieved in excellent yields through interaction of acetylene and pyrrole in KOH/DMSO [35].

3. Conclusion

This article has focused on the role of DMSO and activated DMSO as reagents in the synthesis of a wide range of products using different substrates.Ylides,dimers,oxidative-cyclization products, certain polymer units have been synthesized by using DMSO and activated Dimethyl sulphoxide as reagents with substrates like 4-hydroxy-coumarins,1,3-indandione ,Phthalimide etc.

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