



AN IMPROVED GREEN SYNTHESIS AND APPLICATIONS OF A CHIRON DERIVED FROM 2,3 ISOPROPYLIDENE-D-GLYCERALDEHYDE AND 1,3 PROPANE DITHIOL

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ABSTRACT In the present paper we wish to report the synthesis of a chiron which is produced from the readily available sugar precursor D-Mannitol. The Mannitol was first converted into diisopropylidene derivative and then cleaved oxidatively to yield 2,3-O-isopropylidene-D-Glyceraldehyde. This aldehyde was selectively converted into 1,3 dithiane in quantitative yield employing 1,3 propane dithiol and Montmorillonite (K-10) catalyst. This Chiron can be effectively used for the construction of C-C sigma bond and this methodology can be extensively used for the synthesis of different natural products. This method is eco-friendly and obeys rules of green chemistry principles.

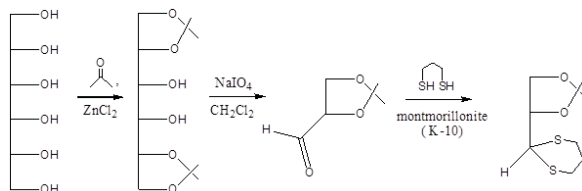
KEYWORDS : 1, 3 dithiane, Montmorillonite, D-Glyceraldehyde, Green chemistry Principles

INTRODUCTION

Synthetic carbohydrate chemistry is one of the fast developing area in synthetic organic chemistry. The potential of sugars as starting points for highly efficient syntheses of non-carbohydrate targets is now well recognised by wider chemical community. Carbohydrates also serve as excellent systems for the study of finer aspects of stereochemical influence and control of chemical transformations, multifunctional and three dimensional matrices. The use of carbohydrates as organic starting materials is due to the fact that they are inexpensive, available in bulk quantities and in enantiomerically pure form. A collection of chemical transformations of sugars into other natural products has been expertly summarised¹.

1,3 Dithianes can easily be prepared from carbonyl compounds with 1,3 propane dithiol in the presence of Bronsted or a Lewis acid catalyst^{2,3}. Removal of dithiane protection group often requires harsh conditions and is usually performed in the late synthetic stage. The normal reactivity of a carbonyl compound is an acceptor reagent and the temporary reversal of the characteristic pattern of reactivity of a functional group is described by the term Umpolung². The 2-lithio 1,3 dithianes derivatives are most successful acyl anion equivalents having stabilisation through sulphur atoms. These anions are easily prepared from the corresponding dithianes and alkyl lithium. The dithio moiety could be hydrolysed after reaction with an electrophile to provide the corresponding ketone.

With this scientific information, we have planned to use this methodology to devise the synthesis of some natural products. 1,3 dithiane of 2,3-O-isopropylidene-D-glyceraldehyde was prepared in few steps from D-Mannitol in excellent yield. Synthesis of The 2,3-isopropylidene-D-Glyceraldehyde was prepared and used for synthesis of some natural products^{4,6}. Since the aldehydic carbonyl group is protected in our compound, we can remove the most acidic hydrogen of the dithiane moiety and can generate a reasonably stable carbanion. This can react with various electrophiles to construct C-C sigma bond and this methodology can be used for the synthesis of numerous organic compounds. The aldehyde functionality can be restored once the desired transformations are accomplished. The protected isopropylidene moiety has two chiral centres which can be incorporated into the target molecule. The 1,3 dithiane 2-carbaldehyde was prepared and its aldol type coupling was reported⁷. A method of dithiane preparation and its reported photolytic degradation has been reported in literature^{8,9}.

Experimental**Reaction Scheme****a. Synthesis of 1,2 : 5,6-di-O-isopropylidene-D-mannitol**

A round bottom flask containing zinc chloride (4 gm, 29.3 mmol), was heated in open flame and cooled to room temperature using calcium chloride guard tube. When it cooled to room temperature, anhydrous acetone (40 mL) and D-Mannitol (2.0 gm, 11.1 mmol) was added and the reaction mixture was stirred at room temperature for 5 hours. The reaction mixture was poured to a suspension of 5 gm of potassium carbonate in 50 ml of water. The reaction mixture was filtered and the residue was washed with 5 mL of acetone. The solvent was removed and the solid was dissolved in solvent ether (10 mL). The aqueous layer was extracted with solvent ether. The solvent on evaporation furnished a slurry, which on keeping turned into a white solid when treated with hexane. The overall yield of the diacetone is 2.5 gm, 87%.

M.P. = 119-120 °C

Spectral data

IR (KBr, cm^{-1}): 3403, 3280, 2991, 2984, 1159, 1069, 859, 846¹
 HNMR (δ): 1.36 (s, 6H), 1.42 (s, 6H), 2.66 (d, 2H), 3.74 (dd, J=6, 5.7 Hz), 3.98 (dd, 2H, J=5.4 and 8.4 Hz), 4.09-4.22 (m, 4H)

b. Synthesis of 2,3-O-isopropylidene-D-Glyceraldehyde

In a round bottom flask 1,2:5,6-O-Diisopropylidene-D-Mannitol (2 gm, 7.6 mmol) was placed and 20 mL of methylene chloride was added to it. Sodium periodate (2 gm, 9.3 mmol) was added to the reaction mixture and it was stirred at room temperature for 2 hours. The reaction mixture was filtered to furnish the aldehyde. The yield was 1.0 gm (50%)

Spectral data

IR (cm^{-1}): 2990, 2940, 2890, 2820, 1730, 1375, 1280, 1215, 1150, 1070, 840¹
 HNMR (δ): 9.55 (d, 1H, J=1.8 Hz), 4.25-4.28 (m, 1H), 4.05-3.93 (m, 2H), 1.42 (s, 3H), 1.36 (s, 3H)

c. Synthesis of 1,3 Dithiane Derivative of 2,3-O-Isopropylidene D-Glyceraldehyde

The 2,3-O-isopropylidene-D-Glyceraldehyde (1 gm, 7.6 mmol), 1,3 propane dithiol (1.0 gm, 7.6 mmol) were taken in round bottom flask

and 20 ml of ethyl alcohol was added to it. The montmorillonite (K-10) 0.1 g was introduced and the reaction mixture was refluxed for 1 hr. The reaction mixture was filtered through whatman filter paper and removal of solvent furnished crude product. This product was purified using neutral alumina column and petroleum ether and ethyl acetate as an eluent. The overall yield of the purified product is 1.3 g (80%). This dithiane derivative was characterised by IR and PMR spectroscopy.
M.P. = 130°C

Spectral data

IR (cm⁻¹) : 1679,1530,1420,1276,1050,1010 & 922¹ HMR (δ): 1.38 (s), 3H, 1.46 (s), 3H, 1.58 (t), 2H, 2.05 (m), 1H, 2.90 (m) 1H, 3.78 (m), 1H, 3.93-4.00 (m), 2H, 4.15 (t), 2H, 4.21 (q) 1H

RESULTS AND DISCUSSION

Umpolung of reactivity is very important concept in deciding the polarity at the carbonyl group of aldehydes and ketones. The umpolung of reactivity can be achieved by different means, but dithiane formation remains on the top since it is more useful and selective. The dithiane has less affinity towards lewis acids and bases hence it can sustain those conditions readily as compared to the ketals, acetals tetrahydropyranyl ethers and similar protections. This kind of stability of dithianes make them more versatile and selective for any chemical transformations and removal of dithiane protection can be planned at the end of synthetic sequences. The carbonyl group can be regenerated without affecting the labile functional groups around. In our methodology we have successfully prepared the dithiane derivative of 2,3-O-propylidene-D- Glyceraldehyde in excellent yield and the product is free from any impurities. It is white crystalline solid and is characterised by PMR spectroscopy. Overall this method is very handy and useful for the formation of C-C sigma bond, which is a key step in organic syntheses. The vast utility of this protocol is an advantage to the synthetic organic researchers.

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