CHAPTER III

Ultrasound-Accelerated Synthesis of Chiral Allylic Alcohols Promoted by Indium Metal
Introduction:

The chemical synthesis of carbon containing molecules has been a major field of scientific endeavor for over a century. Nevertheless, the subject is still far from fully developed. For example, of the almost infinite number and a variety of organic compounds which are capable of discrete existence, only a minute fraction have actually been prepared and studied. In addition, for the last century there has been a continuing and dramatic growth in the power of science in constructing complex molecules which shows no signs of dwindling. The proven ability of chemists to synthesize compounds which were beyond reach in the past, is exemplified in the literature to a vast extent. Many branches of chemistry like organometallics, bioorganic, photochemical, acoustics have come to the aid of synthetic organic chemist enabling him to achieve an efficient multistep synthesis of complex organic molecules. Larger and larger molecules are now being synthesized using computer aided retrosynthesis and selecting appropriate retrons.1

For a successful synthesis of a considerably large molecule a convergent approach utilizing easily accessible building blocks is considered to be logical. Thus several such building blocks have been previously synthesized and will be synthesized in future. Though early researchers were concentrating on the synthesis of racemic compounds, the demand for chiral synthons has tremendously increased in the last one decade. The change in need of organic chemistry is mostly due to improved understanding of mode of action of drugs and biological system. These chiral synthons generally can be obtained either by asymmetric synthesis, chiron approach or by resolution of racemic compounds. Among the various chiral synthons accessible amicably, chiral allyl alcohols are considered to be
among important class because of their existence in several natural products like pheromones, plant growth regulators, anticancer agents, steroids, terpenoids, sphingolipids, leukotrienes, prostaglandins, fungicides and so on (chart 1). For example, pheromone of comstock melay bug 2 is an acetate of allylic alcohol 2-hydroxy-1-octene (1), isolated from a no. of essential oils has also been shown to be a control factor for growth of pinewood nematodes. Thromaxane\(^3\) (3) a major intermediate in biosynthesis of prostaglandins is an allylic alcohol. The vicinal allylic glycol (4) is the major constituent of Bentozia grandiflora\(^4\).

![Chemical structures](chart)

1. Allylic alcohol 2-hydroxy-1-octene (1)
2. Allylic alcohol 2-hydroxy-1-octene acetate (2)
3. Thromaxane (3)
4. Vicinal allylic glycol (4)
5. Cerabroside (5)
Sphingosines which form a partial structure of cerebrosides\(^4\) (5) contain allyl alcohol functionality. Apart from these, allylic alcohol fragments are found in numerous other natural products. Allylic alcohols are also vital intermediates in the synthesis of prostaglandins, macrolides, vitamins, antibiotics, insecticides, pheromones etc. Both unsaturation and the alcohol functionality in them have been used to carry out several transformations like cyclopropanations, claisen rearrangement, pericyclic reactions.

This little background amply demonstrates that, the allyl alcohol functionality especially in a chiral environment forms not only partial structure of several important natural and uncommon biologically important compounds but also as useful chiral synthons. Accordingly several approaches have been developed for the preparation of this class of compounds which are outlined as follows.

1) Kinetic resolution of racemic allyl alcohols.

2) Enantioselective reduction of vinyl ketones with chiral metal hydrides.
3) Enzymatic approaches

Each of the above methods has been described briefly in the following few pages.

**Kinetic resolution of racemic allylic alcohols**:7

The ready availability of racemic secondary allylic alcohols prompted researchers lead by Prof. Sharpless to discover an unprecedented "kinetic resolution technique" for the preparation of this class of compounds wherein they used the standard asymmetric epoxidation procedure on allylic alcohol and stopped the reaction at 50% conversion to recover the starting chiral allyl alcohol in high ee's (scheme 1).

Though ee's are excellent for the recovered allylic alcohols, the overall efficacy in terms of yields is restricted to only 50%.

![Scheme 1](image)

**Enantioselective reduction of ketones with chiral metal hydrides**:

One of the conventional methods of obtaining optically active alcohols is the asymmetric reduction of prochiral ketones which is generally restricted only to aromatic substrates. Most of the asymmetric reducing agents uniformly provided good ee's during asymmetric reduction of ketones having adjacent aromatic group. However, in the case of simple aliphatic compounds the ee's are awfully poor.
Noyori's method:

Olefonic ketones were readily reduced by the asymmetric reducing agent prepared from Ω-binaphthol and LiAlH₄ to provide 'R' enantiomer, while 'S' enantiomer was obtained from (S)-binaphthol (scheme 2). Though both R1 and R2 in the substrate can be alkyl groups, this methodology has limitations in that simple cyclic enones such as 2-cyclohexenone, 3-methyl-2-cyclohexenone, 2-isopropylidene cyclohexenone etc resisted the BINOL-H reduction.

\[ \text{Scheme 2} \]
Brown's method:

Alkenyl ketones are reduced to the corresponding chiral allyl alcohols with chiral reducing agent, 'Alpine-borane (prepared from 9-BBN an (+) pinene) in moderate enantiomeric purity (scheme 3). As the reduction involves hydride attack, due experimental care is required to avoid 1,4 addition of the hydrogen nucleophile.

\[
\begin{align*}
\text{R}_1 & \quad \text{R}_2 & \quad \text{R}_3 \\
\text{R}_1 & \quad \text{R}_2 & \quad \text{R}_3 \\
\text{OH} & \quad \text{OH}
\end{align*}
\]

Scheme 3

The same research group has developed yet another asymmetric reducing agent starting from carbohydrates namely potassium 1,2 ; 5,6-di-O-isopropylidene D-mannitol

\[
\begin{align*}
\text{R}_1 & \quad \text{R}_2 \\
\text{R}_1 & \quad \text{R}_2 \\
\text{OH} & \quad \text{OH}
\end{align*}
\]

Scheme 4

Thexyl hydridoborate (prepared from thexyl borane, 1,2 ; 5,6-di-O-isopropylidene D-mannitol and potassium hydride). This reagent reduced unsaturated ketones to chiral allyl alcohols (scheme 4). With this reagent optical inductions were low exception being 2-cyclohexen-1-one (71% ee).
Enzymatic approaches:

The microorganisms or enzymes have also been utilized to produce chiral allyl alcohols from prochiral substrates either by reduction or by hydrolysis of corresponding esters. These approaches generally give very pure alcohols (>98% ee), however it has its own limitations in that, reactions have to be run in high dilution and specialized lab reagents are required.

a) Fuganti's method\textsuperscript{11}:

Fuganti et al have reported Baker yeast assisted reduction of alkenyl ketones to obtain chiral allyl alcohols (scheme 5). However this method offers preparation of enantio pure compounds only to a limited scale as high dilutions are required. Chemical yields are also poor in this case (32-40%).

\begin{center}
\begin{tikzpicture}
\node at (0,0) (A) {\textbf{Scheme 5}};
\node at (-2,0) (B) {\text{Baker yeast}};
\node at (-3,0) (C) {R_2};
\node at (-4,0) (D) {R_3};
\node at (-5,0) (E) {R_1};
\node at (0,-0.5) (F) {\text{OH}};
\node at (1.5,0.5) (G) {\rightarrow};
\node at (1.5,-0.5) (H) {\rightarrow};
\node at (3,0) (I) {R_2};
\node at (4,0) (J) {R_3};
\node at (5,0) (K) {R_1};
\end{tikzpicture}
\end{center}

b) Frejd's method\textsuperscript{12}:

Frejd et al, prepared optically active cyclohexenol derivatives from acetates of racemic allyl alcohols by enzymatic ester hydrolysis (scheme 6). Several enzymes viz pig liver esterase, rabbit liver esterase, acetylcholine esterase and aspergillusniger were exposed to this reaction. Pig liver esterase was found to be the best enzyme and gave highest enantiomeric purity (88 - 98% ee).
Though high ee's can be achieved by this method, half of the starting material is wasted and moreover it required longer reaction times (3-4 days).

![Chemical structure from Scheme 6]

**Regio selective Deoxygenation of 2,3-epoxy alcohols**

Recently yet another method for the synthesis of chiral allyl alcohols through Titanocene induced regio selective deoxygenation of 2,3-epoxy alcohols has been reported by our group (scheme 7). Deoxygenation occurred exclusively from the least substituted carbon end to produce terminal alkenic alcohol in high yield (82-91%).

![Chemical structure from Scheme 7]

**Introduction to Indium metal:**

Indium-mediated transformations have attracted great significance because of certain unique properties possessed by indium. Indium metal is quite stable to water or air and does not require any activation or anhydrous reaction conditions. Furthermore, the first ionization potential of indium is much lower than that of zinc or tin, hence it could be a potential reducing agent.
In addition, a variety of iodomethyl-O-isopropylidene acetics underwent smoothly the reductive elimination to afford the corresponding allylic alcohols in high yields. Methanol appears to be the solvent of choice, giving best results. The reaction proceeds smoothly under sonication to give the products in high yields. Owing to vibrational energy of water, the bath temperature reached 60-65 °C under sonication. The reaction rates and yields were dramatically enhanced by ultrasound. The rate enhancement under sonication may be attributed to the cavitation and the activation of the metal surface by sonic waves. In the absence of sonic waves, longer reaction times and high temperature conditions are typical to achieve comparable yields than those that are obtained by ultrasound.

We report herein a novel and highly efficient method for the synthesis of chiral allyl alcohols. The 2-iodomethyl-O-isopropylidene acetics undergo smoothly β-elimination by Indium metal in methanol under sonication to afford the corresponding allyl alcohol. (Scheme 8)

\[ 
\text{Di-O-isopropylidene-D-arabinitol 1 was made according to known procedure}\textsuperscript{17} \text{ by treating commercial}\text{ D-arabinitol with acetone and anhydrous CuSO}_4 \text{ in presence of catalytic H}_2\text{SO}_4.\text{ (Scheme 9) The PMR spectrum of 1 showed two singlets at } \delta 1.36 \text{ and } 1.28 \text{ for two isopropylidene groups. Compound 1 was then treated with 3 eq of TPP, I2} \]
and imidazole to give the corresponding iodo compound 2 in 79% yield. IR spectrum showed the absence of hydroxy absorption. Treatment of iodo compound 2 with two eq of Indium metal in methanol was sonicated for 5.5 h, yielded 92% of allyl alcohol 2a. The PMR spectrum of 2a exhibited resonance's at δ 5.90-5.70 as a ddd having J=17.3 10.2, 6.8 Hz for -CH=CH₂, at δ 5.45 as a dd having J=17.3, 1.9 Hz for -CH=CH₆H₆, at δ 5.25 as a dd having J=10.2, 1.9 Hz for -CH=CH₆H₆ conformed the structure of 2a.

D-Ribose:

Anomeric Wittig esterification was done on the sugar to extend the carbon chain and the C-5 alcohol was converted to iodo compound to facilitated the elimination reaction thereby incorporating three chiral hydroxyl functionalities on adjacent carbons in the resulting alkene polyol.
The mono acetonide of D-ribose 3 was obtained from D-ribose on treatment with acetone, anhydrous CuSO₄ and cat conc, H₂SO₄. This pale yellow viscous liquid was treated with stable ylide carboxethoxy methylene triphenylphosphorane in refluxing CH₃CN for 2h to afford the ester 4 and its α-anomer 5 in 22:1 ratio according to the known procedures. The faster moving kinetic product 4 was isolated from its minor α-analogue 5 on silicagel column chromatography, whose IR spectrum showed absorption's corresponding to the ester carbonyl at 1738 cm⁻¹ and the hydroxyl at 3469 cm⁻¹ and PMR spectrum contained a singlet at δ 3.71 for -O-CH₃ indicated ester group was present, and at δ 2.72-2.52 as a multiplet to the two protons of -CH₂-COOCH₃. The hydroxy ester 4 was then treated with 3 eq of TPP, I₂, imidazole to give the corresponding iodo compound 6 in 92% yield, (Scheme 10) whose IR spectrum showed no hydroxy absorption's in its spectra and in PMR spectrum at δ 3.29 as a doublet for two protons of -CH₂-I having J=5.6 Hz. 6 undergoes smoothly β-elimination by 2 eq of In metal in methanol under sonication to afford the corresponding the allylic alcohol 6a in 86% isolated yield. The PMR spectrum
of 6a showed resonance's at $\delta$ 2.95 as a broad singlet indicated -OH group was present, at $\delta$ 5.25 as a dd having $J=10.2, 2.0$ Hz, at $\delta$ 5.50 as dd, $J=17.3, 2.0$Hz for -CH=CH$_2$, and at $\delta$ 5.90-5.72 as a ddd, $J=17.3, 10.2, 6.8$Hz for -CH=CH$_2$ affirm the structure of 6a.

Table 1

<table>
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<th>Entry</th>
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<th>Product</th>
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<th>Yield (%)</th>
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</table>
D-Ribose:

The mono acetonide of D-ribose 3 was obtained from D-ribose on treatment with acetone, anhydrous CuSO₄ and conc. H₂SO₄, had a boiling of 115°C at 0.05 mm pressure. This on reductive cleavage with LAH in dry THF afforded the triol 7 as a

![Diagram](attachment:diagram.png)

open chain structure, a semi solid, which on its PMR spectrum, showed the absence of anomeric proton in triol thereby confirming the open chain structure. Tosylation²⁰ of triol with 2 eq. of pTsCl in pyridine with catalytic triethyl amine at -15°C gave the tetrahydrofuran derivative 8, as a result of ring closure, whose structure sits on its diagnostic PMR spectrum, at δ 2.50 as a singlet for CH₃-ArH, at δ 4.64 as a doublet with a J=5.4 Hz and at δ 4.81 as a multiplet thereby confirming the CH₂-OTs, at δ 7.39 as a doublet J=8.64 Hz, at δ 7.79 as a doublet J=8.64 Hz for aromatic protons affirms the structures of 8. The OTs compound was then subjected to the NaI in refluxing acetone (75ml) gives iodo derivative 9 yielded in 85 %.(Scheme 11) This iodo compound was confirmed by its PMR spectrum, absence of tosyl group and at δ 3.15-3.05 as a multiplet.
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for CH$_2$I, and in IR spectrum absence of aromatic region at 1620 cm$^{-1}$ indicates the structure of Iodo 9. This title precursor was then subjected to 2 eq. of Indium powder in methanol under sonication yielded allyl alcohol 9a in 89% yield. The structure of 9a confirmed by its PMR spectrum, at $\delta$ 2.05 as a broad singlet indicates the hydroxy groups, at $\delta$ 5.25 as a dd $J$=10.3, 2.0 Hz, at $\delta$ 5.50 as a dd $J$=17.3, 2.0 Hz for terminal olefinic protons, and at $\delta$ 5.72-5.90 as a ddd, $J$= 17.3, 10.3, 6.5 Hz was proving, the olefinic proton. It was further confirmed by its mass spectra having $M^+$ at 158.

Mannose:

The di acetonide of D-mannose 10 was obtained from D-mannose on treatment with anhydrous CuSO$_4$ in dry acetone and catalytic amount of conc. H$_2$SO$_4$. 10 was characterised by PMR spectrum, at $\delta$ 1.45,1.38 as a two singlets each for four methyl groups of acetonide, at $\delta$ 5.34 as a singlet for anomeric proton. This di acetonide gave the diol 11, which was confirmed by absence of the anomeric proton in its PMR spectrum. The diol was then treated with 1eq. of pTsCl, 1eq. of pyridine in dry DCM yielded mono tosyl
derivative of mannose 12, which was used for the next step without purification. 12 was treated with NaI in dry acetone under refluxing conditions to afford lodo derivative of mannose 13,(Scheme 12) which was used for the next step without purification. 13 was subjected to the title reaction with 2 eq. of indium metal in refluxing methanol under sonication to afford 13a in 87% yield. The PMR spectrum of 13a revealed a broad singlet at δ 2.08 for two hydroxy compounds and the presence of three olefinic protons that resonated at δ 5.20, 5.45 as a dd with a J=10.2, 1.9 Hz and 17.3, 1.9 Hz for -CH=CH₂ respectively, at δ 5.80 as a ddd with a J=17.3, 10.2, 6.5 Hz for -CH=CH₂. The compound in its mass spectroscopy (EIMS) showed (M⁺+1) peak at m/z=188.

**L(+) - Diethyl tartate:**

Protection of free hydroxyl groups in diethyl tartrate with 2,2-DMP in dry acetone containing catalytic amount of PTSA furnished 14 in 90% yield. Compound 14 exhibited IR absorption corresponding to ester carbonyl at 1735 cm⁻¹ and absorption due to hydroxyl was absent confirming the complete conversion to 14 which was reduced with LAH in dry THF to afford 15 in 78% yield.

![Scheme 13](image-url)
The diol 15 showed IR absorption between 3300-3540 cm\(^{-1}\) for the free hydroxyl groups. Which was then converted into mono benzyl ether 28 by using NaH and BnBr in dry THF in 90% yield. The PMR spectrum of 16 contained a singlet at \(\delta 4.57\) corresponding to -OCH\(_2\)Ph and a multiplet at \(\delta 7.30\) for aromatic protons, mono benzyl ether 16 was then smoothly converted to the iodide in 85% yield using 1.5 equimolar of each of TPP, iodine and imidazole in a mixture of dry ether and acetonitrile in 3:1 ratio at 0°C. (Scheme 13) The PMR spectrum of 17 showed a doublet at \(\delta 3.1\) for I-CH\(_2\) protons and absence of hydroxyl functional groups in IR spectrum.

Treatment of iodo compound 17 with two eq of indium metal in methanol was sonicated for 4.5 hrs, yielded 94% of allyl alcohol 29a. The PMR spectrum of 17a exhibited resonance's at \(\delta 5.40\) as a dd for C3-H with \(J = 17.4, 1.7\) Hz and 5.72-5.90 as ddd signal for -CH=CH\(_2\), with \(J = 17.4, 10.3\) and 6.8 Hz and at \(\delta 7.40-7.20\) as a multiplet for aromatic protons and its IR spectrum showed evidence for the hydroxyl group by absorption at 3550,1660 cm\(^{-1}\) corresponding to olefin and hydroxyl group respectively.

Another precursor iodo compound 19 was obtained from diethyl tartrate derived diol 15 in two steps as shown in scheme 13. The diol was converted into monosilyl ether 18 by using imidazole and TBDMSI in DCM in 80% yield. (Scheme 14) The PMR spectrum of 18 contained a singlet at \(\delta 0.0\) for -Si-(CH\(_3\))\(_2\) and at \(\delta 1.10\) corresponding to the t-butyl
group. Mono silyl ether 18 was then converted to the iodo compound in 90% yield, using as mentioned in earlier, which was confirmed by the absence of hydroxyl absorption in IR spectrum. The iodo compound 19 was then subjected to title reaction with two equivalent of indium powder in methanol under sonication to furnish alkenol 19a in 87% yield.

The IR spectrum of 19a exhibited absorption's at 1645, 3445 cm⁻¹ due to olefin and hydroxyl respectively and its PMR spectrum contained singlets at δ 0.00 for Si-(CH₃)₂, at δ 1.10 for t-butyl group, at δ 4.15-4.20 as a multiplet for C2-H, at δ 1.15 as a dd with J=10.3, 1.8 Hz, and at δ 5.40 also a dd for -CH=CH₂ and at δ 5.72- 5.90 as a ddd with J = 17.4, 10.3, 6.9 Hz for (CH=CH₂).

Third example from diethyl tartrate derived diol 15 was obtained in 3 steps as shown in scheme 15. The diol was converted into mono MPM ether 20 by using of NaH, MPMBr in dry THF in 87% yield. The PMR spectrum of 20 contain two doublets at δ 7.25 and 6.88 corresponding to the aromatic protons and at δ 4.56, 3.82 as a singlet corresponding to -OCH₂- and -OCH₃ respectively, 20 was then smoothly converted to the iodide 21 in 90% yield. Which was confirmed by the PMR spectrum, at δ 3.36-3.19 as a multiplet for -CH₂-I.(Scheme 15) The iodide 21 was then subjected to the final reaction with 2 eq of indium metal in MeOH under sonication to furnish the allyl alcohol 21a in 85 % yield. The PMR spectrum of 21a exhibited resonance's at δ 7.20, 6.80 as a doublets for
the aromatic protons, at δ 2.25 as brs for -OH, at δ 3.80 as a singlet for -OCH3 and at δ 4.45 as a singlet for -OCH2- and its IR spectrum, shows evidence for the hydroxyl absorption at 3441 and for alkene at 1612 cm⁻¹.

Sorbitol:

D-Sorbitol was transformed into a tetrahydroxy alkene derivative 30a after simple modifications as shown in the scheme 15 here a six membered 1,3-dioxolane ring opening was administrated in order to get the target poly hydroxy alkene.

D-Sorbitol was converted to 1,3; 5,6-di-O-isopropylidene 2,4-O-methyline-D-sorbitol 29 by the following sequence of reactions in a known route21. D-Sorbitol was first treated with 40% HCHO solution in presence of Conc HCl to provide 22 in 68% yield. Selective cleavage of the bridge methylene occurred when compound 22 was treated with a mixture of acetic acid, Ac₂O and conc H₂SO₄ to give the tetraacetate 23. Which showed an IR absorption at 1720 cm⁻¹. Subsequent Zemplen deacetalization of 23 using cat amount of NaOMe in MeOH afforded the tetrol 24, which was then converted to the isopropylidene derivative on treatment with 2,2-DMP in the presence of cat pTSA. The PMR spectrum of 25 exhibited three sharp singlets between δ 1.38-1.20 corresponding to the isoproylidine methyl groups. The -O- methylene protons of the 1,3-dioxolane ring shown two doublets at δ 5.10 and 4.63, thus confirming the structure of 25. Selective deketalization of the six membered 1,3-O-isopropylidene ring was achieved by using 30% aq AcOH in MeOH to provide the diol 25, whose PMR spectrum was consistent with its structure. IR spectrum of the compound 25 showed a strong absorption at 3150-3560 cm⁻¹ respectively to the hydroxyls. Protection of the C-1 hydroxyl as its TBDMS ether on treatment with
TBDMSCl, imidazole in dry DMF to get 27, followed by the protection of C-3 hydroxyl as its p-methoxybenzyl ether, on treatment with MPM-Br, NaH in dry THF was achieved 28.

Compound 28 contained resonance's at δ 0.10 and 0.90 in the PMR spectrum corresponding to the silyl methyls and tert-butyl's and absorption at 3135-3545 cm⁻¹ in the IR spectrum confirmed the mono protection of 27, whereas compound 28 was confirmed by the absence of IR absorption of hydroxyl and presence of PMR resonance's at δ 7.42, 6.94.
Desilylation of 28 was achieved by using tetra butyl ammonium fluoride solution\textsuperscript{22} in THF to afford the hydroxy precursor 29 as expected in quantitative yields. (Scheme 16) After obtaining satisfactory spectral data, 29 was converted to its iodo derivative as reported earlier on treatment with equimolar ratio of TPP, I\textsubscript{2} and imidazole in 3:1 ether acetonitrile mixture at rt for 1h. Structure of 30 was confirmed by its PMR spectrum resonances at \(\delta\) 3.29-3.04 as a multiplet for \(-\text{CH}_2\text{I}\) and absence of hydroxyl absorption in IR spectrum. The iodo compound 30 was then reacted to the title reaction to furnish allyl alcohol 30a in 91% yield. The structure of the 30a was confirmed by its PMR spectrum, dd at \(\delta\) 5.40, \(J=17.3, 1.9\)Hz, \(\delta\) 5.15 having \(J=10.3, 1.9\)Hz confirmed the terminal olefinic protons having 1,2 and 1,3 shift and at \(\delta\) 5.90 as a ddd having \(J=17.3, 10.3, 6.5\) Hz indicates \(-\text{CH}==\text{CH}_2\) protons. It was further affirmed by IR spectrum, hydroxyl absorption at 3476 and at 1612 cm\(^{-1}\) for olefinic protons was confirmed the structure of 30a.

In conclusion this work describes a novel, convenient and practical method for the synthesis of chiral allyl alcohols from 2-iodomethyl-O-isopropylidene acetals using indium metal in methanol under sonic waves. This method is compatible with acid sensitive 1,2-isopropylidene acetals, silyl ethers, esters and p-methoxybenzyl ethers. In addition to its simplicity and milder reaction conditions, this method provides high selectivity, which makes it a useful and attractive strategy for the synthesis of chiral allyl alcohol.
EXPERIMENTAL SECTION
Experimental Procedures:

General experimental procedure for β elimination of isopropylidene acetals

A mixture of 2-iodomethyl-O-isopropylidene acetals (2 mmol) and Indium powder (4 mmol) in methanol (10mL) was sonicated for an appropriate time (Table 1). The reaction temperature was raised to 60-65°C for 3-5 h. On completion of the reaction, as indicated by TLC, the reaction mixture was filtered and washed with methanol (10mL). The filtrate and washings was concentrated in vacuo and purified by column chromatography on silica gel (ethyl acetate-hexane 1:9) to afford pure allylic alcohol.

5-[2,2-dimethyl-(4R)-1,3-dioxolan-4-yl]-2,2-dimethyl-(4R,5R)-1,3-dioxolan-4-ylmethanol (1):

A mixture of D-arabinitol (12.2g, 80 mmol) anhydrous CuSO₄ (20g), conc. H₂SO₄ (0.7 mL) and dry acetone (250 mL) was stirred at room temperature for 20h and then filtered. The filtrate was neutralized with NaHCO₃. Insoluble material was filtered off, wash it with acetone 2-3 times. The organic solvent was concentrated in vacuo, and chromatographed to afford the oily product 1 (15.05g, 80.73 %)

¹H NMR (200MHz,CDCl₃): δ 4.10-3.55 (m, 5H, 3x-CH-O-, CH₂O), 3.54 (d, 2H, J=3.2 Hz, CH₂OH), 1.58 (brs, -OH), 1.36 and 1.28 (2s, 12H, 4xCH₃)

IR(KBr) : 3546, 2923, 1134cm⁻¹

[α]D₂⁵ -2.3 (c 3.1 CHCl₃):

4-[2,2-dimethyl-(4R)-1,3-dioxolan-4-yl]-5-iodomethyl-2,2-dimethyl-(4R,5S)-1,3-dioxolane (2):
To a stirred solution of 1 (2.50 g, 10.77 mmol) in a mixture of 75 mL dry ether and 25 mL dry acetonitrile was added TPP (4.234 g, 16.16 mmol), imidazole (1.099 g, 16.16 mmol) and iodine (4.105 g, 16.16 mmol) at 0°C. The resulting mixture was stirred at room temperature for 1 hr, solid was filtered and washed with diethyl ether. The filtrate was extracted with ether and washed with 10% aqueous sodium thiosulphate solution, followed by brine and dried over anhydrous Na₂SO₄. Concentration under reduced pressure and purification by silicagel column chromatography afforded 2 (2.911 g, 79%) as a viscous liquid (SiO₂ 15%EtoAc in hexane).

**1H NMR (200 MHz, CDCl₃):**

δ 4.15-4.08 (m, 1H), 4.05-3.98 (m, 1H), 3.97-3.92 (m, 1H), 3.76-3.70 (m, 1H), 3.60 (t, 1H, J=4.34 Hz), 3.50 (dd, 1H, J =1.3, 6.08 Hz), 3.37-3.28 (m, 1H), 1.44, 1.42, 1.37, 1.30 (4s, 12H, 4xCH₃)

**IR (KBr):** 2920, 1141 cm⁻¹

1-[2,2-dimethyl-(4R)-1,3-dioxolan-4-yl]-(1S)-2-propen-1-ol (2a):

**1H NMR (200 MHz, CDCl₃):**

δ 5.90-5.70 (ddd, 1H, J =17.3 10.2, 6.8, Hz, -CH=CH₂), 5.45 (dd, 1H, J =17.3, 1.9 Hz, -CH=CH₂H₃), 5.25 (dd, 1H, J =10.2, 1.9 Hz, -CH=CH₂H₃), 4.34-4.32 (m, 1H), 4.15-4.10 (m, 1H), 3.90-3.82 (m, 2H), 2.08 (brs, 1H, -OH), 1.45 (s, 3H, -CH₃), 1.35 (s, 3H, -CH₃).

**EIMS: m/z:** 158 [M⁺], 144, 130, 103, 85, 55 and 43

**IR(KBr) ν:** 3475, 2853, 1649, 1451, 1114, 929 and 741 cm⁻¹.

**Anal. Calcd. for C₈H₁₄O₂ (158.19):** C, 60.74; H, 8.92. Found: C, 60.78; H, 8.95.

**[α]D²⁵:** 4.3 (c 1.2, CHCl₃)
To a stirred solution of 1 (2.50 g, 10.77 mmol) in a mixture of 75 mL dry ether and 25 mL dry acetonitrile was added TPP (4.234 g, 16.16 mmol), imidazole (1.099 g, 16.16 mmol) and iodine (4.105 g, 16.16 mmol) at 0°C. The resulting mixture was stirred at room temperature for 1 hr, solid was filtered and washed with diethyl ether. The filtrate was extracted with ether and washed with 10% aqueous sodium thiosulphate solution, followed by brine and dried over anhydrous Na₂SO₄. Concentration under reduced pressure and purification by silicagel column chromatography afforded 2 (2.911 g, 79%) as a viscous liquid (SiO₂ 15%EtoAc in hexane).

¹H NMR (200 MHz, CDCl₃): δ 4.15-4.08 (m, 1H), 4.05-3.98 (m, 1H), 3.97-3.92 (m, 1H), 3.76-3.70 (m, 1H), 3.60 (t, 1H, J=4.34Hz), 3.50 (dd, 1H, J =1.3, 6.08 Hz), 3.37-3.28 (m, 1H), 1.44, 1.42, 1.37, 1.30 (4s, 12H, 4xCH₃)

IR (KBr): 2920, 1141 cm⁻¹

1-[2,2-dimethyl-(4R)-1,3-dioxolan-4-yl]-(1S)-2-propen-1-ol (2a):

¹H NMR (200 MHz, CDCl₃): δ 5.90-5.70 (ddd, 1H, J =17.3 10.2, 6.8, Hz, -CH=CH₂), 5.45 (dd, 1H, J =17.3, 1.9 Hz, -CH=CH₂A), 5.25 (dd, 1H, J =10.2, 1.9 Hz, -CH=CH₂B), 4.34-4.32 (m, 1H), 4.15-4.10 (m, 1H), 3.90-3.82 (m, 2H), 2.08 (brs, 1H, -OH), 1.45 (s, 3H, -CH₃), 1.35 (s, 3H, -CH₃).

EIMS: m/z: 158 [M⁺], 144, 130, 103, 85, 55 and 43

IR(KBr) ν : 3475, 2853, 1649, 1451, 1114, 929 and 741 cm⁻¹.


[α]D²⁵: 4.3 (c 1.2, CHCl₃)
3,4-~quinono~[1,3]diox 6-hydroxy-2,2-dimethyl-(3aS,4S,6aS)-perhydrofuro[3,4-d][1,3]dioxol-4-ylmethyl alcohol (3):

Finely powdered ribose (20 g, 133.33 mmol) was suspended in dry acetone (400 mL) containing 0.2% H₂SO₄. Anhydrous CuSO₄ (40 g) was added and the mixture was shaken at room temperature for 20 h. The CuSO₄ was filtered off, washed thoroughly with small quantities of dry acetone and the filtrate was rendered neutral by shaking with NaHCO₃ for 1 h. Excess NaHCO₃ was removed by filtration and thoroughly washed with small quantities of acetone. The combined filtrate and washings was then evaporated to dryness under reduced pressure. The pale yellow viscous syrup on a silica gel column eluting with n-hexane-ethyl acetate (3:1) to furnish the pure mono acetonide of Ribose 3 (yield, 60%)⁶¹

Methyl,2-[6-hydroxymethyl]-2,2-dimethyl-(3aR,4R,6S,6aS)-perhydrofuro[3,4-d][1,3]dioxol-4-ylacetate (4):

A solution of 2,3-O-isopropylidene-D-ribofuranose 3 (4 g, 21.05 mmol) and carbomethoxy methylene triphenyl phosphorane (5.273 g, 31.57 mmol) in dry acetonitrile (350 mL) was heated under reflux for 4 h. Examination of the reaction mixture by GLC showed the absence of starting material and the formation of two new products in a ratio of 22:1. The solvent was removed in vacuo and the residue was purified by chromatography on silica gel using ethyl acetate-hexane (1:3) as eluent to obtain pure β-substituted compound 4 (2.149 g, 83%), followed by a mixture of 38 and α-substituted compound 5.
\(^1\)H NMR (200 MHz, CDCl\(_3\)) : δ 4.72-4.65 (m, 1H), 4.55-4.25 (m, 1H), 4.23-4.14 (m, 1H), 4.10-4.01 (m, 1H), 3.83-3.75 (m, 1H), 3.71 (s, 3H, -O-CH\(_3\)), 3.68-3.55 (m, 1H), 2.72-2.52 (m, 2H, -CH\(_2\)-COOCH\(_3\)), 1.53, 1.34 (2s, 6H, 2x-CH\(_3\))

IR(KBr): 3469, 2989, 2940, 1738, 1218, 1077, 864, 772 cm\(^{-1}\)

\([\alpha]_D^23\) -5.86 (c 2.0, CHCl\(_3\))

**Methyl2-[6-iodomethyl-2,2-dimethyl-(3aR,4R,6R,6aR)-perhydrofuro[3,4-d][1,3]dioxol-4-yl]acetate (6):**

Iodo compound 6 was obtained from 5 (2.00 g, 8.13 mmol), in 90% yield employing the same procedure described for 2.

\(^1\)H NMR (200 MHz, CDCl\(_3\)) : δ 4.59-4.44 (m, 2H), 4.30 (q, 1H, J=4.4, 11.2 Hz), 3.91 (q, 1H, J=3.2, 8.8 Hz), 3.73 (s, 3H, -O-CH\(_3\)), 3.29 (d, 2H, J=5.6 Hz, -CH\(_2\)-l), 2.70-2.64 (m, 2H, -CH\(_2\)-COOCH\(_3\)), 1.54, 1.34 (2s, 6H, 2x-CH\(_3\))

IR(KBr): 2987, 2936, 1740, 1437, 1378, 1210, 1159, 1075 and 864 cm\(^{-1}\)

\([\alpha]_D^23\) : -9.19 (c -1.9, CHCl\(_3\))

**Methyl3-[2,2-dimethyl-5-vinyl-(4S,5R)-1,3-dioxolan-4-yl]-3-hydroxypropanoate(6a):**

\(^1\)H NMR (200 MHz, CDCl\(_3\)) : δ 5.90-5.72 (ddd, 1H, J=17.3, 10.2, 6.8 Hz, -CH=CH\(_2\)), 5.25 (dd, 1H, J=10.2, 2.0 Hz, -CH=CH\(_2\)H\(_B\)), 4.67-4.63 (m, 1H), 1.38 (s, 3H, -CH\(_3\)), 4.02-3.95 (m, 2H), 3.78 (s, 3H), 2.95 (brs, 1H, -OH), 2.80-2.68 (m, 1H), 2.53-2.38 (m, 1H), 1.43 (s, 3H, -CH\(_3\))

EIMS: \(m/z\) 230 [M\(^+\)], 215, 127, 98, 69 and 43

IR (KBr) ν : 3465, 2890, 1649, 1465, 1114, 931, 740 cm\(^{-1}\)

1-[5-hydroxymethyl-2,2-dimethyl-(4R,5S)-1,3-dioxolan-4-yl]-(1R)-ethane-1,2-diol (7):

To a stirred suspension of LAH (0.999 g, 26.31 mmol) in dry THF (75 mL), 3 (1.25 g, 13.15 mmol) in dry THF (25 mL) was added dropwise over a period of 30 min at 0°C. The reaction mixture was stirred for 30 min at this temperature and slowly warmed up to room temperature and stirred for another 40 min. Excess LAH was quenched with ethyl acetate (7.5 mL) and water (2.5 mL) by cautious addition, the inorganic solids were removed by filtration and the solid residue was washed with 3x75 mL of ether. The filtrate was washed with water, brine and dried over anhydrous Na2SO4 and evaporated in vacuo. The residual syrup was chromatographed on silica gel column and eluted with 8:2 solution of ethyl acetate and n-hexane respectively, which gave the triol 7 (1.035 g, 82%) as a colorless viscous liquid.

1H NMR (400 MHz, CDCl3): δ 4.34-4.28 (m, 1H, -CH-O), 4.04 (t, 1H, J=6.8Hz, -CH-O), 3.85 (d, 2H, J=9.75Hz, -CH2O), 3.80-3.74 (m, 1H, -CH-O), 3.70-3.62 (m, 2H, -CH2O), 1.70 (brs, -OH), 1.40 (s, 3H, -CH3), 1.35 (s, 3H, -CH3)

IR (KBr): 3240-3540, 3080 and 1610 cm⁻¹.

[α]D²⁵: 8.94 (c 2.5, CHCl₃)

2,2-dimethyl-4-(4-methylphenylsulfonyloxy)methyl)-(3aS,4S,6aS)-perhydrofuro[3,4-d][1,3]dioxole (8):

To a stirred solution of the triol 7 (1.50 g, 7.81 mmol) in dry pyridine (20 mL) was added TsCl (2.978 g, 15.62 mmol) and cat. DMAP at -15°C followed by the addition of few drops of triethyl amine. The reaction mixture was brought to room temperature and stirred
for 3 h and it was diluted to three times of its volume with water, extracted with 100 mL of diethyl ether-petroleum ether (1:1) and the combined organic phase was washed with water, brine, dried over anhydrous Na$_2$SO$_4$ and concentrated under vaccum. The residue was purified on silica gel column eluting with n-hexane-ethyl acetate (5:1) to furnish the tetrahydrofuran tosylate 8 as the product in 87% yield.

$^1$H NMR (400 MHz, CDCl$_3$): δ 7.79 (d, 2H, J=8.64 Hz, Aromatic-H), 7.39 (d, 2H, J=8.64 Hz, Aromatic-H), 4.81 (m, 1H, -CH-O), 4.64 (m, 1H, -CH-O), 4.19-4.09 (m, 2H, -CH$_2$O), 4.03-4.01 (m, 1H, -CH-O), 3.87-3.84 (m, 2H, -CH$_2$O), 2.50 (s, 3H, Ar-CH$_3$), 1.44 (s, 3H, -CH$_3$), 1.36 (s, 3H, -CH$_3$)

2,2-dimethyl-(3aS,4R,6aS)-perhydrofuro[3,4-d][1,3]dioxol-4-ylmethyl iodide (9):

To a solution of 8 (1.25 g, 3.81 mmol) in dry acetone was added NaI (0.714 g, 4.76 mmol) at room temperature, and refluxed for a period of 4h. The resulting mixture was allowed to attain room temperature and concentrated, washed with water followed by brine, compound was extracted into organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated. The resulting yellow color liquid was purified on silicagel column eluting with petroleum ether/ethylacetate (8:1) to afford the iodo compound 9 in 82% yield.

$^1$H NMR (200 MHz, CDCl$_3$): δ 4.82-4.75 (m, 1H, -CH-O), 4.62-4.53 (m, 1H, -CH-O), 4.19-4.09 (m, 1H, -CH-O), 3.98-3.93 (m, 2H, -CH$_2$O), 3.15-3.05 (m, 2H, -CH$_2$I), 1.47 (s, 3H, -CH$_3$), 1.30 (s, 3H,-CH$_3$)

$[\alpha]_D^{25}$: 15.2 (c 1.05, CHCl$_3$)

2,2-dimethyl-5-vinyl-(4S,5R)-1,3-dioxolan-4-ylmethanol (9a):
\[1^H \text{NMR (200 MHz, CDCl}_3): \delta 5.90-5.72 (\text{ddd, 1H, } J=17.3, 10.3, 6.5 \text{ Hz, -CH=CH}_2), 5.50 (\text{dd, 1H, } J=17.3, 2.0 \text{ Hz}, -\text{CH=CH}_2\text{H}_3), 5.25 (\text{dd, 1H, } J=10.3, 2.0 \text{ Hz, -CH=CH}_2\text{H}_3), 4.60 (\text{t, 1H, } J=6.5 \text{ Hz, -CH-O}), 4.20 (\text{q, 1H, } J=6.7 \text{ Hz, -CH-O}, 3.58 (\text{d, 2H, } J=6.7 \text{ Hz, -CH}_2\text{O}), 2.05 (\text{brs, -OH}), 1.37 (s, 3 \text{ H}, -\text{CH}_3), 1.45 (s, 3 \text{ H}, -\text{CH}_3).\]

\[\text{EIMS: } m/z: 158 [M]^+, 144, 130, 102, 85, 55 \text{ and } 43.\]

\[\text{IR (KBr) } \nu: 3450, 2871, 1647, 1459, 1107, 937 \text{ and } 741 \text{ cm}^{-1}.\]

\[\text{Anal. Calcd. for } C_{14}H_{14}O_3 (158.19): \text{C, 60.73; H, 8.91. Found: C, 60.76; H, 8.94.}\]

\[\alpha\text{D}^{25}: +15.1 (c 1.05, CHCl}_3\]

6-[2,2-dimethyl-(4R)-1,3-dioxolan-4-yl]-2,2-dimethyl-(3aS,6S,6aS)-perhydrofuro[3,4-\text{d}][1,3]dioxol-4-ol (10):

Employing the same procedure as mentioned for compound 3, to furnish the pure diacetonide of mannose 10 in 90% yield.

\[1^H \text{NMR (200 MHz, CDCl}_3): \delta 5.34 (s, 1 \text{ H, Anomeric-H}), 4.82-4.74 (m, 1 \text{ H, -CH-O}), 4.58 (d, 1 \text{ H, } J=5.2 \text{ Hz, -CH-O}), 4.41-4.29 (m, 1 \text{ H, -CH-O}), 4.18-4.09 (m, 1 \text{ H, -CH-O}), 4.07-3.95 (m, 2 \text{ H, -CH}_2\text{O}), 2.75 (\text{brs, -OH}), 1.45 (2s, 6 \text{ H, 2xCH}_3), 1.38 (2s, 6 \text{ H, 2xCH}_3)\]

2,2-dimethyl-(4R)-1,3-dioxolan-4-yl-5-hydroxymethyl-2,2-dimethyl-(4S,5R)-1,3-dioxolan-4-yl-R-methanol (11):

Diol 11 was obtained from 10 (2.75 g, 10.82 mmol), in 81% yield employing the same procedure described for 7.

\[1^H \text{NMR (200 MHz, CDCl}_3): \delta 4.44-4.27 (m, 2 \text{ H, 2x-CH-O}), 4.19-3.97 (m, 3 \text{ H, 2x-CH-O, -CH}_2\text{H}_3\text{O}), 3.94-3.75 (m, 2 \text{ H, -CH}_2\text{-O}), 3.63-3.50 (m, 1 \text{ H, -CH}_2\text{H}_3\text{O}), 3.00 (\text{brs, -OH}), 1.52, 1.38 (2s, 12 \text{ H, 4xCH}_3)\]
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Chapter III

[α]D\textsuperscript{25} : -7.62 (c 1.4, CHCl\textsubscript{3})

1-[2,2-dimethyl-(4\textit{R})-1,3-dioxolan-4-yl]-(1\textit{S},2\textit{R})-3-butene-1,2-diol (13a):

\textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{3}):  δ 5.90-5.70 (ddd, 1H, J=17.3, 10.2, 6.5 Hz, -CH=CH\textsubscript{2}), 5.45 (dd, 1H, J=17.3, 1.9 Hz, -CH=CH\textsubscript{A}H\textsubscript{B}), 5.20 (dd, 1H, J=10.2, 1.9 Hz, -CH=CH\textsubscript{A}H\textsubscript{B}), 4.40 (t, 1H, J=6.5 Hz, -CH-O), 4.10 (q, 1H, J=6.5 Hz, -CH-O), 3.82-3.65 (m, 3H, -CH-O, -CH\textsubscript{2}O), 2.08 (brs, -OH), 1.42 (s, 3H, -CH\textsubscript{3}), 1.40 (s, 3H, -CH\textsubscript{3})

EIMS: m/z: 188 [M\textsuperscript{+}], 174, 160, 144, 103, 85 and 55

IR (KBr) ν : 3441, 2861, 1650, 1450, 1100, 925 and 737 cm\textsuperscript{-1}

Anal. Calcd. for C\textsubscript{9}H\textsubscript{16}O\textsubscript{4} (188.22): C, 57.42; H, 8.56. Found: C, 57.45; H, 8.59

[α]D\textsuperscript{25} : 6.1 (c 2.0, CHCl\textsubscript{3})

diethyl 2,2-dimethyl-(4\textit{R},5\textit{R})-1,3-dioxolane-4,5-dicarboxylate (14):

A mixture of L(+) di ethyl tartrate (10g, 48.54 mmol), 2,2 di methoxy propane (11.89 ml, 97.08 mmol), dry acetone (100mL) and cat. PTSA was stirred for 15h at room temperature. Reaction mixture was neutralized with K\textsubscript{2}CO\textsubscript{3} and filtered. The filtrate was concentrated to remove the acetone and unreacted 2,2 di methoxy propane, residue was distilled to afford the 14 (10.269g, 86%).

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}):  δ 4.75 (s, 2H, 2xCH-O), 4.28 (q, 4H, J=10.9Hz, 2xCH\textsubscript{2}-O), 1.52 (s, 6H, 2xCH\textsubscript{3}), 1.35 (t, 6H, 2xCH\textsubscript{2}-CH\textsubscript{3})

5-hydroxymethyl-2,2-dimethyl-(4\textit{S},5\textit{S})-1,3-dioxolan-4-ylmethanol (15):

A solution of 14 (8.50g, 34.55 mmol) in THF (150mL) was added dropwise to a suspension of LAH (2.626g, 69.10 mmol) in dry THF over a period of 2h. After stirring for additional 3h, ethyl acetate (40mL) was carefully added and the reaction mixture was
cooled to 0-5°C. After successive cautious additions of water (2.6mL), 4N NaOH (2.6mL) and water (8mL), the inorganic precipitate formed was removed by filtration and residue was extracted thoroughly with ethyl acetate. The combined extracts were dried and concentrated under reduced pressure. The resulting pale yellow syrup was purified on silica gel column to afford the diol 15 (4.03g, 72%).

\[ {^1}\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 3.95-3.90 \text{ (s, 2H, } 2\times\text{CH-0)}, 3.70 \text{ (s, 4H, } 2\times\text{CH}_2\text{-O)}, 3.35-3.05 \text{ (brs, -OH), 1.40 (s, 6H, } 2\times\text{CH}_3\text{).} \]

5-benzylxoxymethyl-2,2-dimethyl-(4S,5S)-1,3-dioxolan-4-ylmethanol (16):

A suspension of 60% NaH (493 mg, 12.34 mmol), add dry THF (75mL) at 0°C, to the stirred suspension was added dropwise the diol 15 (2.00g, 12.34 mmol) in dry THF (75mL) over 40 min, maintaining the reaction temperature at 0°C, followed by the addition of benzylbromide (1.465mL, 12.34 mmol) over 20 min. The reaction mixture was stirred for 20 min at 0°C and then warmed to room temperature. After 6 h, 15mL water was cautiously added. The aqueous phase was extracted with 3x300 mL ethyl acetate. The combined organic layer was washed with water, brine, dried, concentrated and chromatographed to afford the mono benzyl ether 16 (2.519g, 81%).

\[ {^1}\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 7.36-7.25 \text{ (m, 5H, Ar-H), 4.59 (s, 2H, -O-CH}_2\text{-Ph), 4.30-3.98 \text{ (m, 1H, -CH-O), 3.92-3.88 \text{ (m, 1H, -CH-O), 3.75-3.70 \text{ (m, 1H, -CH}_A\text{H}_B\text{), 3.68-3.62 \text{ (m, 2H, -CH}_2\text{O), 3.543.50 \text{ (m, 1H, -CH}_A\text{H}_B\text{), 2.08 (brs, -OH), 1.40 (s, 6H, 2xCH}_3\text{)}}}}\]

IR(KBr): 3546, 2923, 1601, 1453, 1133 and 684 cm\(^{-1}\)

\[ [\alpha]_D^{25} : 6.62 \text{ (c 2.5, CHCl}_3\text{)} \]

4-benzylxoxymethyl-5-iodomethyl-2,2-dimethyl-(4S,5R)-1,3-dioxolane (17):
Obtained from 16 (1.25g, 4.96 mmol) as in the similar manner described for 2 (1.418g, 85%).

$^1$H NMR (200 MHz, CDCl$_3$): δ 7.27 (m, 5H, Ar-H), 4.54 (s, 2H, -OCH$_2$-Ph), 3.95-3.75 (m, 2H, 2xCH-O), 3.65-3.51 (m, 2H, -CH$_2$O), 3.30-3.19 (m, 2H, -CH$_3$), 1.42, 1.36 (2s, 6H, 2xCH$_3$)

1-benzyloxy-(2R)-3-buten-2-ol (17a):

$^1$H NMR (200 MHz, CDCl$_3$): δ 7.40-7.20 (m, 5H, Ar-H), 5.40 (dd, 1H, $J=17.4, 10.3, 6.8$ Hz, -CH=CH$_2$), 5.10 (dd, 1H, $J=17.4, 1.7$ Hz, -CH=CH$_2$-H$_3$), 5.10 (dd, 1H, $J=10.3, 1.7$ Hz, -CH=CH$_2$-H$_3$), 4.28 (m, 1H, -CH-0), 3.58-3.30 (m, 2H, -CH$_2$O), 2.37 (brs, -OH)

EIMS: m/z: 178 [M$^+$], 91, 87, 77.

IR (KBr): 3440, 2860, 1610, 1529, 1460, 1310, 1255, 1105, 930 and 825 cm$^{-1}$.


$[\alpha]_D^{25}$: 3.8 (c 1.2, CHCl$_3$)

5-(tert-butyldimethylsilyloxy)methyl-2,2-dimethyl-(4S,5S)-1,3-dioxolan-4-ylmethanol (18):

To a mixture of the diol 15 (2.00g, 12.34 mmol) and imidazole (1.678g, 24.68 mmol) in dry DCM (20mL) was added tert-butyldimethylsilyl chloride (1.860g, 12.34 mmol) dropwise. The mixture was then stirred at room temperature overnight, diluted with DCM, washed with brine solution and dried over anhydrous Na$_2$SO$_4$. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel to afford the pure silyl ether 18 (2.964g, 87%) as the product.
1H NMR (300 MHz, CDCl3): \( \delta \) 4.00-3.83 (m, 3H, 2xCH-O, -CH\(_2\)H\(_B\)), 3.75-3.62 (m, 3H, -CH\(_2\)O, -CH\(_A\)H\(_B\)), 2.30 (brs, -OH), 1.40 (s, 6H, 2xCH\(_3\)), 0.91 (s, 9H, -C-(CH\(_3\))\(_3\)), 0.10 (s, 6H, -Si-(CH\(_3\))\(_2\))

IR (KBr): 3445, 3065, 3030, 2869, 1455, 1361, 1104 and 927 cm\(^{-1}\)

\([\alpha]_D^{25}\) : 15.9 (c 1.5, CHCl\(_3\))

**tert-butyl dimethylsilyl** 5-iodomethyl-2,2-dimethyl-(4S,5R)-1,3-dioxolan-4-ylmethyl ether (19):

Obtained from 18 (550 mg, 1.99 mmol) as in the similar manner described for 2 in 82% yield.

1H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 3.85-3.72 (m, 4H, 2xCH-O, -CH\(_2\)O), 3.40-3.20 (m, 2H, -CH\(_2\)-I), 1.39, 1.32 (2s, 6H, 2xCH\(_3\)), 0.83 (s, 9H, -C-(CH\(_3\))\(_3\)), 0.03 (s, 6H, -Si-(CH\(_3\))\(_2\))

\([\alpha]_D^{25}\) : -1.95 (c 1.5, CHCl\(_3\))

1-(*tert*-butyl dimethylsilyloxy)-(2R)-3-buten-2-ol (19a):

1H NMR (200 MHz, CDCl\(_3\)): \( \delta \) 5.90-5.72 (ddd, 1H, J=17.4, 10.3, 6.9 Hz, -CH=CH\(_2\) 5.40 (dd, 1H, J=17.4, 1.8 Hz, -CH=CH\(_A\)H\(_B\)), 5.15 (dd, 1H, J=10.3, 1.8 Hz, -CH=CH\(_A\)H\(_B\)), 4.20-4.15 (m, 1H, -CH-O), 3.65 (dd, 1H, J=12.3, 6.8 Hz, -CH\(_A\)H\(_B\)), 3.40 (dd, 1H, J=12.3, 6.5 Hz, -CH\(_A\)H\(_B\)), 2.37 (brs, 1H, -OH), 0.95 (3s, 9H, -C-(CH\(_3\))\(_3\)), 0.02 (s, 6H, -Si-(CH\(_3\))\(_2\))

EIMS: \( m/z \): 202 [M\(^+\)], 184, 155, 135, 107, 67, 55 and 43.

IR (KBr) v: 3445, 2860, 1645, 1455, 1104, 927, 738 and 698 cm\(^{-1}\)


\([\alpha]_D^{25}\) : 4.6 (c 1.0, CHCl\(_3\))
5-(4-methoxybenzylxoxymethyl)-2,2-dimethyl-(4S,5S)-1,3-dioxolan-4-ylmethanol (20):

To a stirred suspension of NaH (986 mg, 24.69 mmol) in dry THF (50mL) under N₂ atmosphere was added 17 (2.00g, 12.34 mmol) in dry THF dropwise at 0°C. After stirring for 30 min at 0°C freshly prepared p-methoxy benzyl bromide (2.486g, 12.34 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 4 hrs, quenched with saturated NH₄Cl solution and extracted with ethyl acetate (2x100mL). The combined organic layers were washed with water, brine and dried over anhydrous Na₂SO₄. Solvent was removed in vacuo and the residue was purified by silicagel column chromatography to afford 20 (2.471g, 71%).

¹HNMR (200 MHz, CDCl₃): δ 7.25 (d, 2H, J=8.0 Hz Ar-H), 6.88 (d, 2H, J=8.0Hz, Ar-H), 4.66 (s, 2H, -CH₂O), 4.03-3.87 (m, 2H, 2xCH-O), 3.82 (s, 3H, -OCH₃), 3.74-3.60 (m, 4H, 2xCH₂O), 2.28 (brs, -OH), 1.40 (s, 6H, 2xCH₃)

IR (KBr): 3450, 2854, 1605, 1529, 1455 and 1315 cm⁻¹

[α]D²⁵ : 9.15 (c 2.0, CHCl₃)

4-iodomethyl-5-(4-methoxybenzylxoxymethyl)-2,2-dimethyl-(4R,5S)-1,3-dioxolane (21):

Obtained from 20 (1.25g, 4.432 mmol), employing the same procedure described for 2 in 77% yield.

¹HNMR(200MHz):δ 7.20 (d, 2H, J=9.3Hz, Ar-H), 6.82 (d, 2H, J=9.3Hz, Ar-H), 4.48 (s, 2H, Ar-CH₂-O), 3.96-3.81 (m, 2H, 2xCH-O), 3.80 (s, 3H, -OCH₃), 3.62-3.51 (m, 2H, -CH₂O), 3.36-3.19 (m, 2H, -CH₂O), 1.41 and 1.38 (2s, 6H, 2xCH₃).

[α]D²⁵ : -9.21 (c 1.5, CHCl₃)
1-(4-methoxybenzyl)oxy)-(2R)-3-buten-2-ol (21a):

$^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 7.20 (d, 2H, $J=8.0$ Hz, Ar-H), 6.80 (d, 2H, $J=8.0$ Hz, Ar-H), 5.72-5.90 (ddd, 1H, $J=17.3$, 10.2, 6.8 Hz, -CH=CH$_2$), 5.40 (dd, 1H, $J=17.3$, 1.7 Hz, -CH=CH$_3$H$_2$), 5.18 (dd, 1H, $J=10.2$, 1.7 Hz, -CH=CH$_3$H$_B$), 4.45 (s, 2H, -O-CH$_2$-Ar), 4.20-4.25 (m, 1H, -CH-O), 3.80 (s, 3H, -OCH$_3$), 3.45 (dd, 1H, $J=12.0$, 6.9 Hz, -CH$_3$H$_B$), 3.25 (dd, 1H, $J=6.7$, 12.0 Hz, -CH$_3$H$_B$), 2.25 (brs, -OH).

$^{13}$C NMR (CDCl$_3$, proton decoupled): $\delta$ 159.0, 136.6, 129.6, 129.1, 115.8, 113.5, 73.5, 72.6, 71.1 and 54.9.

EIMS: m/z: 208 [M$^+$], 167, 137, 121, 109, 95, 83, 69, 57 and 43.

IR (KBr) v: 3441, 2859, 1612, 1514, 1461, 1303, 1251, 1103, 928 and 822 cm$^{-1}$.


$\lbrack\alpha\rbrack_d^{25} : 3.6$ (c 1.5, CHCl$_3$)

4-[(4R)-1,3-dioxolan-4-yl]-(4R,4aR,8aS)-perhydro[1,3]dioxino[5,4-d][1,3]dioxine (22):

A solution of D-Sorbitol (50g) in a mixture of 75mL of 37% aq. formaldehyde and 50mL of conc. HCl was maintained at $5^\circ$C for four days, after cooling the reaction mixture to $5^\circ$C, the trimethylene-D-Sorbitol which had crystallized was separated by filtration. The solid obtained was recrystallized from 50% alcohol to furnish the pure product 22 (40.5g, 68%) m.p: 213$^\circ$C (lit$^{63}$ 212-216$^\circ$C).

$^1$HNMR(400MHz): $\delta$ 5.10 (t, 2H, $J=9.4$Hz, O-CH$_2$-O), 4.94 (s, 1H, O-CH$_3$H$_B$-O), 4.80-4.72 (m, 3H, O-CH$_2$-O, O-CH$_3$H$_B$-O), 4.26-4.04 (m, 2H, 2x-CH-O), 3.94-3.73 (m, 4H, 2x-CH-O, -CH$_2$O), 3.62-3.54 (m, 2H, -CH$_3$O).

$[\alpha]_D^{25} : -31.0^\circ$(c 1.5, CHCl$_3$)
2-methylcarbonyloxymethoxy-2-[5-methylcarbonyloxymethoxy-6-
 methylcarbonyloxymethyl-(4R,5R,6S)-1,3-dioxan-4-yl]ethyl acetate (23):

To a rapidly stirred ice-cooled mixture of acetic anhydride (87.5mL), glacial acetic acid (37.5mL) and conc. H₂SO₄ (1.25mL) was added, dried and powdered trimethylene D-Sorbitol 22 (40gm) and stirring continued for 5 min. The reaction mixture was poured into 1500mL of vigorously stirred ice-water. The acetylolyed product crystallizes after 2 h. The crystalline product was separated by filtration, washed with cold water and air dried. The compound 23 was recrystallized from 12 parts of ethanol as long needles (40g, 52%)
MP: 110°C (lit⁶³.111-112°C)

¹HNMR (400 MHz, CDCl₃) : 5.50 (q, 2H, J=5.2Hz, O-CH₂-O), 5.27-5.06 (m, 3H, -), 4.77-4.62 (m, 2H), 4.20-3.96 (m, 4H, 2xCH₂-O), 3.88-3.60 (m, 3H, 3x-CH-O), 2.09 (2s, 6H, -COCH₃), 2.07 (s, 3H, -COCH₃), 2.05 (s, 3H, -COCH₃)

[α]d²⁵ : 30.2°(c 1.2, CHCl₃)

1-[5-hydroxy-6-hydroxymethyl-(4R,5R,6S)-1,3-dioxan-4-yl]-[1R]-ethane-1,2-diol (24):

A solution of 23 (20g, 47.39 mmol) in chloroform (200mL) was cooled in an ice-bath and 0.2 N Sodium methylate solution (20mL) was added, upon standing at 5°C for 18 h, tetrol 36 (8.734g) was separated from the reaction mixture. The tetrol 24 was recrystallized in ethanol in the form of fine needles.
MP: 163°C
[α]d: -9.9°(c 1.3,H₂O)

8-[2,2-dimethyl-(4R)-1,3-dioxolan-4-yl]-2,2-dimethyl-(4aS,8R,8aR)-perhydro[1,3]dioxino[5,4-d][1,3]dioxine (25)
A Solution of tetrol 24 (7.50g, 38.65 mmol) in dry acetonitrile (50mL) was cooled to 0°C followed by the addition of catalytic amount of PTSA along with 2,2-dimethoxy propane (10.43mL, 85.05 mmol) and the reaction mixture was stirred overnight at room temperature. The reaction was then quenched with solid NaHCO₃ and the solids were filtered off. White crystals of 25 (9.427g, 89%) separated out by the addition of 20 ml of dry petroleum ether.

1H NMR (400MHz) : δ 5.14 (d, 1H, J=3.2Hz, O-CH₂H₂O), 4.73 (d, 1H, J=3.1Hz, O-CH₂H₂O), 4.30-4.23 (m, 1H, -CH₂O), 4.09-4.03 (m, 1H, -CH₂O), 4.00-3.96 (m, 2H, 2x-CH₂O), 3.88 (t, 2H, J=7.2Hz, -CH₂O), 3.52-3.43 (m, 2H, -CH₂O), 1.48 (2s, 6H, 2xCH₃), 1.39 (s, 3H, -CH₃), 1.34 (s, 3H, -CH₃).

4-[2,2-dimethyl-(4R)-1,3-dioxolan-4-yl]-6-hydroxymethyl-(4R,5R,6S)-1,3-dioxan-5-ol (26)

The di acetonide 25 (7.5g, 27.37 mmol) was treated with 30% solution of acetic acid in methanol (70mL) under vigorous stirring at room temperature for 24h. After completion of the reaction, the mixture was neutralized by PbCO₃ and the insoluble solids were filtered off. The solvents were removed under reduced pressure and the resultant yellow syrup was taken in DCM (20mL) and extracted with water (4x20mL). Combined aqueous layer which contained the diol 38 was concentrated and 10mL of saturated NaCl, was added to it and extracted with dry chloroform (3x30mL) to furnish the pure diol 26 (3.202g, 50%) after evaporation of the solvent.

1H NMR (300MHz, CDCl₃): δ 5.05 (d, 1H, J=5.3Hz, O-CH₂H₂O), 4.74 (d, 1H, J=5.3Hz, O-CH₂H₂O), 4.22-4.15 (m, 1H, -CH₂O), 4.05-3.98 (m, 1H, -CH₂O), 3.90-3.61 (m, 5H, -
Employing the same procedure as mentioned for compound 18 afforded the pure silyl ether 27 (3.479 g, 90%) as the product.

\[
\begin{align*}
\text{HNMR (200 MHz, CDCI\textsubscript{3}): } & \delta 5.06 (d, 1H, J=4.2Hz, -O-CH\textsubscript{2}H\textsubscript{5}-O-), 4.74 (d, 1H, J=4.2Hz, -O-CH\textsubscript{2}H\textsubscript{5}-O-), 4.29-4.20 (m, 1H, -CH-O), 4.11-4.01 (m, 2H, 2x-CH-O), 3.95-3.87 (m, 1H, -CH-O), 3.84-3.68 (m, 4H, 2x-CH\textsubscript{2}-O), 1.40 (s, 3, -CH\textsubscript{3}), 1.36 (s, 3H, -CH\textsubscript{3}), 0.90 (s, 9H, -Si-C(CH\textsubscript{3})\textsubscript{3}), 0.01 (s, 6H, -Si-(CH\textsubscript{3})\textsubscript{2}) \\
\text{IR (KBr): v 3140-3560 cm}\textsuperscript{-1} \\
\text{Mass : m/z 333 (M-15), 233, 117, 75, 43.} \\
\text{[\alpha]D}^{\text{28}} : -3.01^\circ (c 5.4, CHCl\textsubscript{3})
\end{align*}
\]

\text{4-(tert-butyl(dimethyl)silyloxy)methyl)-6-[2,2-dimethyl-(4R)-1,3-dioxolan-4-yl]-5-(4-methoxybenzyl-oxy)-(4S,5R,6R)-1,3-dioxane (28):}

Obtained from 27 (2.40 g, 6.89 mmol) as in the similar manner described for 20 in 85% yield.

\[
\begin{align*}
\text{HNMR (200 MHz, CDCI\textsubscript{3}): } & \delta 7.20 (d, 2H J=7.20Hz, Ar-H), 6.75 (d, 2H, J=7.2Hz, Ar-H), 5.00 (d, 1H, J=5.0Hz, O-CH\textsubscript{2}H\textsubscript{5}O), 4.60 (dd, 2H, J=12.2, 4.2Hz, O-CH\textsubscript{2}H\textsubscript{5}O, -CH\textsubscript{2}H\textsubscript{5}-OAr), 4.26-4.17 (m, 1H, -CH\textsubscript{2}H\textsubscript{5}-OAr), 4.05-3.95 (m, 2H, 2x-CH-O), 3.90-3.82 (m, 2H, 2x-CH-O), 3.74 (s, 3H, -OCH\textsubscript{3}), 3.59-3.50 (m, 3H, -CH\textsubscript{2}O -CH\textsubscript{2}H\textsubscript{5}O), 3.40 (d, 1H,
\end{align*}
\]
To a solution of 28 (3g, 6.40 mmol) in 30 ml of dry THF at 0°C was added a solution of nBu₄NF (1M in THF, 6.4mL, 6.40 mmol) and the reaction mixture was stirred at room temperature for 1 hr. The reaction mixture was diluted with ether (50mL), washed with brine (3x20mL), dried over anhydrous Na₂SO₄, and the solvent was removed under reduced pressure. The resulting liquid was purified in silicagel column by eluting with petroleum ether/ethylacetate(4:1) to afford 29 (2.26, 99.8%).

^1^H NMR (200MHz, CDCl₃): δ 7.30 (d, 2H, J=7.8Hz, Ar-H), 6.85 (d, 2H, J=7.8Hz, Ar-H), 5.09 (d, 1H, J=5.4Hz, O-CH₃H₃B), 4.77-4.68 (m, 2H, O-CH₃H₃B, -CH₃H₃B-OAr), 4.57-4.48 (m, 1H, -CH₃H₃B-OAr), 4.37-4.25 (m, 1H, -CH-O), 4.15-4.03 (m, 1H, -CH-O), 3.96-3.88 (m, 1H, -CH-O), 3.76 (s, 3H, ArOCH₃), 3.72-3.52 (m, 3H, -CH-O, -CH₂O), 3.47-3.33 (m, 2H, -CH₂O), 1.44 (s, 3H, -CH₃), 1.38 (s, 3H, -CH₃).

IR (KBr) : ν 3350-3580cm⁻¹

Mass : m/z 354 (M⁺) 339, (M⁺-15), 233, 121.

[α]D²⁵ : 29.17 (c, 4.3, CHCl₃)
Obtained from 29 (0.5g, 1.412 mmol) as in the similar manner described for 2 in
85% yield.

\([\alpha]_D^{25}\) : 13.28 (c 2.5, CHCl₃)

1-[2,2-dimethyl-(4R)-1,3-dioxolan-4-yl]-2-(4-methoxybenzyloxy)-(1S,2R)-3-buten-1-ol
(30a):

1H NMR (200 MHz, CDCl₃): δ 7.20 (d, 2H, J=8.0 Hz, Ar-H), 6.80 (d, 2H, J=8.0 Hz, Ar-
H), 6.00-5.80 (ddd, 1H, J=17.3, 10.3, 6.5 Hz, -CH=CH₂), 5.40 (dd, 1H, J=17.3, 1.9 Hz, -
CH=CH₃H₃), 5.15 (dd, 1H, J=10.3, 1.9 Hz, -CH=CH₃H₃), 4.50 (d, 1H, J=13.5 Hz, -
CH₃H₂), 4.30 (d, 1H, J=13.5 Hz, -CH₃H₂-O), 4.10-3.90 (m, 4H, 3x-CH-O, -CH₃H₃-
O), 3.80 (s, 3H, -O-CH₃), 3.45-3.38 (m, 1H, -CH₃H₂-O), 2.25 (brs, -OH), 1.30 (s, 3H, -
CH₃), 1.25 (s, 3H, -CH₃)

13C NMR (CDCl₃, decoupled): δ 130.0, 129.4, 118.7, 113.7, 108.9, 79.2, 75.6, 74.6, 70.3,
66.4, 55.2, 26.6 and 25.4.

EI/MS: (m/z): 308 [M⁺], 293, 241, 137, 121, 108, 91 and 77

IR (KBr) v: 3476, 2932, 1612, 1514, 1460, 1376, 1248, 1065, 930, 845 and 770 cm⁻¹


\([\alpha]_D^{25}\) : -24.9 (c 2.0, CHCl₃)
SPECTRA
H NMR SPECTRUM OF COMPOUND 2a
NCMS, IICT, HYDERABAD
06-27-2001

OPEN.LRP  G.PARIMALA RIBOSE/OPEN

Scan 7  RT: 0:31  No.ions= 404  Base: 74.4% F  TIC=366812

EI SPECTRUM OF COMPOUND 6a
$^1$H NMR SPECTRUM OF COMPOUND 9a
$^1$H NMR SPECTRUM OF COMPOUND 17a
1H NMR SPECTRUM OF COMPOUND 19
RSK NPL
CLF-JSY-939-ALKENE
13C IN CDCl3
AV-300, 13/8/02

13C NMR SPECTRUM OF COMPOUND 21a
RSKNFL
CLP-JSY-198-ALKENE
13C IN CDCl3
AV-300, 06/8/02

$^{13}$C NMR SPECTRUM OF COMPOUND 30a
REFERENCES
References


LIST OF PUBLICATIONS:


