CHAPTER IV
SYNTHESIS AND APPLICATIONS OF NOVEL ENANTIOMICALLY PURE 1,2-DIOLS

IV.1 Introduction

Optically active molecules with two chiral centres, especially 1,2-diols and related substrates play significant role as chiral synthons in the synthesis of natural products and biologically active compounds. 1,2-diol ligands have been found to show high enantioselectivity in some asymmetric reactions. The extensive use of this class of compounds is very well established as a large number of 1,2-diol based chiral molecules are even commercially available\textsuperscript{6,101,174} (Fig. IV.1). The usual sources for these chiral molecules are carbohydrates and hydroxy acids.

![Chemical structures](image)

Fig. IV.1
Pharmacological activity of certain naturally occurring chiral molecules is attributed to the presence of vicinal hydroxyl groups. Several examples of natural products bearing distinct 1,2-diol unit are available (Fig. IV.2).

![Chemical structures](image)

**Fig. IV.2**

1,2-diol based chiral synthons are frequently employed in stereoselective syntheses and several instances pertaining to their use in natural product synthesis are available (Scheme IV.1).

![Scheme IV.1](image)
Also a surprisingly large number of naturally occurring compounds with therapeutic activity possess a vicinal amino alcohol unit\(^4\), 1,2-Diols are excellent precursors for vicinal amino alcohols\(^{27,37}\) (Scheme IV.2).

\[\text{Scheme IV.2}\]

1,2-Diol based chiral catalysts and reagents provide high enantioselectivity in epoxidations, preparation of chiral sulphoxides, Diels-Alder reactions, reduction of ketones and many other reactions\(^6\). A few of the catalysts and reagents are depicted in Fig. IV.3

\[\text{Fig. IV.3}\]

Reduction of ketones

\[\text{Hydrogenation of enamides}\]

\[\text{Epoxidation of allylic alcohols}\]

\[\text{Oxidation of sulphides}\]

\[\text{Diels-Alder reactions}\]
Diols are often protected as ketals. Chiral ketals not only offer protection to the hydroxyl groups but are also useful synthetic intermediates\(^\text{101}\). Ketals often act as chiral auxiliary by influencing the face selectivity of a proximal prochiral centre. They also undergo electrophilic or nucleophilic substitution reactions in presence of Lewis acids (Scheme IV.3).

\[
\text{Scheme IV.3}
\]

It is clear from the discussion that chiral 1,2-diols and the corresponding ketals derived from (2S,3S)-Tetrahydro-3-hydroxy-5-oxo-2,3-furandicarboxylic acid (127, Garcinia acid) are yet another set of molecules ideally suited for the aforementioned applications.

**IV.2 Results and Discussion**

**IV.2.i Preparation of Chiral 1,2-Diols and Ketals**

Hitherto unknown triesters of (-)-hydroxycitric acid (142a, 142b and 142c) carry the two chiral centres from 127 and bear a vicinal diol moiety. Hydrolysis of 127 followed by esterification is expected to furnish the triesters (Scheme IV.4).
Esterification in the usual way in presence hydrochloric acid and alcohol was carried out. However, the product was a mixture of diester and triester in almost equal ratio. This could be due to the fact that esterification conditions are favourable for lactonisation as well.

To overcome this difficulty, esterification using alkali salts of carboxylic acids was considered. Accordingly 127 was treated with methyl iodide in presence of a base and an aprotic solvents namely HMPA\textsuperscript{175}, N,N-dimethylacetamide\textsuperscript{176} or DMSO\textsuperscript{177}. However, no appreciable quantity of the product was isolated (Scheme IV.5).

As all these methods failed to furnish the desired triester, an attempt was made to prepare the same by reacting the trisodium salt (143) with thionyl chloride in presence of alcohol. Though trisodium salt of 127 is known, no spectroscopic data is available in the literature. Highly hygroscopic solid 143 was prepared and characterised by \textsuperscript{1}H NMR and \textsuperscript{13}C NMR spectra (Scheme IV.6; Fig. IV.4a,b).
Fig. IV.4a

Fig. IV.4b

Scheme IV.6
The $^{13}$C NMR spectrum of 143 shows appreciable increase in the $\delta$ values of the three carbonyl groups as compared to the free acid.

A suspension of 143 in appropriate alcohol on refluxing with thionyl chloride readily furnished the corresponding triester in high yield and purity (Scheme IV.7). As 143 reacts with thionyl chloride without the generation of HCl, lactonisation leading to the formation of diesters was not observed. This strategy has been generalised by preparing methyl (142a), ethyl (142b), and isopropyl (142c) triesters of 127 and were completely characterised (Fig. IV.5a-d; IV.6a-d; IV.7a-d). Unlike the other triesters, 142c is a solid with a sharp melting point.

\[
\begin{align*}
143 & \xrightarrow{\text{SOCl$_2$ \ ROH}} \\
\text{142a : } R &= \text{CH}_3 \\
\text{142b : } R &= \text{C}_2\text{H}_5 \\
\text{142c : } R &= \text{CH}(\text{CH}_3)_2
\end{align*}
\]

Scheme IV.7

The $^{13}$C NMR spectra of triesters clearly show the presence of three alkoxy groups as expected. However in the case of 142a and 142b, the presence of small quantities of the corresponding diesters are observed which could have formed during storage. 142c was found to be more stable and the $^{13}$C NMR spectrum do not indicate the presence of even traces of its diester. Elemental analysis of 142c also furnished satisfactory results. The mass spectra of the triesters show respective molecular ion peaks.
Fig. IV.7a

Fig. IV.7b

Fig. IV.7c

Fig. IV.7d
These novel triesters are yet another addition to the existing collage of chiral 1,2-diols which are used in asymmetric syntheses. Appropriate modifications of triesters could lead to many novel synthons (Scheme IV.8)

![Scheme IV.8](image)

Concerning the triesters, another important aspect which may receive attention is the pharmacological activity. There exists a controversy whether the acyclic [(-)-hydroxycitric acid] or the cyclic form (Garcinia acid) of 127, is pharmacologically active. It is possible that the chiral 1,2-diol unit present in the molecule is responsible for the pharmacological activity⁴. Usually the formulations involving Garcinia acid are prepared from the crude extract so as to retain the acid in the acyclic form. However, (-)-hydroxycitric acid undergoes lactonisation to give 127 upon isolation.¹⁴⁷,¹⁴⁸ Triester (142b), the first derivative of Garcinia acid produced in the acyclic form, retains the 1,2-diol unit and can be made available with a high degree of chemical and optical purity.

It has been observed that a small amount of diester is formed from the triester, upon storage, through transesterification. This could be avoided by protecting the hydroxyl groups of triesters as ketals. Attempts to prepare ketals of triesters following usual procedures¹⁷⁸, were futile as the molecule underwent lactonisation. This could be due to the fact that conditions for ketal formation are ideally suited for lactonisation also.

The difficulty for the preparation of acetonides was overcome by following a modified known procedure¹⁷⁹. Upon refluxing a solution of the appropriate
triester in acetone in presence of anhydrous copper sulphate and catalytic quantity of concentrated sulphuric acid furnished acetonides 144a, 144b and 144c (Scheme IV.9). These novel chiral ketals were completely characterised by IR, $^1$H NMR, $^{13}$C NMR and mass spectra (Fig. IV.8a-d and IV.9a-d).

IR spectra of the acetonides show the absence of the absorption band corresponding to the lactone carbonyl. $^{13}$C NMR spectra show the expected signal characteristic of the C-2 carbon of the 1,3-dioxolane ring at ~δ 112. 144a and 144b show the corresponding molecular ion peaks in the mass spectra and the fragmentation pattern of the compounds are as expected. However, 144c was found to be quite unstable and decomposes rapidly upon storage and hence mass spectrum of the compound was not recorded.

Protection of hydroxyl groups of the triester is necessary for any further transformation like Grignard reaction, alkylation etc. Ketals are significant even otherwise, as they undergo several useful synthetic transformations (Scheme IV.3)
IV.2.ii Asymmetric Epoxidation Employing Novel 1,2-Diols

To explore the possibility of using triesters of 127 (142a-c) and 128 (145a-c) as chiral ligands, Sharpless epoxidation - a mechanistically intriguing reaction was considered. An examination of the structures of triesters show that the molecular topology matches with 1,2-diol ligands like dialkyltartrates except the fact that one of the C-2 hydrogen is substituted with -CH₂COOR. Hence it is a curiosity to see the effect of replacement of tartrate ester with 142a-c and 145a-c in Sharpless asymmetric epoxidation (Fig IV.10).

![Diagram of (2S,3S)-Tartrate ester](image.png)

**Fig. IV.10**

Prior to the formulation of Sharpless epoxidation, experiments for accomplishing asymmetric epoxidations were run with vanadium catalysts bearing chiral hydroxamic acid as ligands with a maximum e.e. of 80%. With the introduction of diethyl tartrate (DET) by Sharpless et al for the titanium-catalysed epoxidation of allylic alcohols, there was a dramatic increase in the optical purity of the product (up to 95% e.e.). Depending on the nature of the tartrate enantiomer used, this epoxidation system delivers the oxygen from the same enantioface of the olefin regardless of the substitution pattern of the allylic alcohol (Scheme IV.10).
The advantage offered by diols such as tartrate esters, for binding with metal ion of titanium(IV) alkoxides to provide the chiral environment is that they exhibit much higher binding constants over monodentate alcohols. The specific arrangement of ligands about the titanium ion makes it a chiral centre with the absolute configuration being determined by the tartrate ligand. In the transition state proposed by E. J. Corey, there exists hydrogen bonding between the ester carbonyl of the tartrate and the hydrogen of the allylic hydroxyl group\textsuperscript{183}. The chirality about the catalytic titanium and the fixed hydrogen bonding, strongly favour internal epoxidation at only one face of the double bond of the allylic alcohol and thereby explaining the stereochemical preference (Fig. IV.11).

The formation of hydrogen bond proposed by Corey et al explain the failure of many other chiral 1,2-diols, which do not bear any ester group, to promote enantioselective epoxidation. The catalyst dimer proposed by Sharpless et al allows Ti(IV) centre in the tetraalkoxide to exist in six-coordinate
configuration and suggest co-ordination with oxygen of tartrate ester carbonyl \(^{184}\) (Fig. IV.12).

![Diagram](image)

Fig. IV.12

Hence a study was undertaken to assess the influence of the triesters of 127 and 128, especially the effect of the additional \(-\text{CH}_2\text{COOR}\) group on enantioselectivity in epoxidation. Epoxidation of geraniol was carried out employing 142b as chiral ligand, in place of tartrate ester following the reported procedure.\(^{185}\) The reaction proceeded smoothly and 2,3-epoxygeraniol (146) was isolated by chromatography. The possible transition state involving 142b is shown (Fig. IV.13).

![Diagram](image)

Fig. IV.13

This study has been extended to other triesters of 127 and 128. A standard Sharpless epoxidation reaction using (2R,3R)-DET as chiral ligand was also conducted to compare the results obtained in the epoxidations employing the triesters of 127 and 128 under identical laboratory conditions. The products were identified using IR and \(^1\)H NMR spectra (Fig. IV.14a-d). Initial results are summarised in Table IV.1.
Fig. IV.14a
Ligand used: 142b

Fig. IV.14b
Ligand used: 142c

Fig. IV.14c
Ligand used: 145b

Fig. IV.14d
Ligand used: 145c
Table IV.1

<table>
<thead>
<tr>
<th>Ligand used</th>
<th>$[\alpha]_D$ of 146</th>
</tr>
</thead>
<tbody>
<tr>
<td>142a</td>
<td>-1.73°</td>
</tr>
<tr>
<td>142b</td>
<td>-3.65°</td>
</tr>
<tr>
<td>142c</td>
<td>-2.88°</td>
</tr>
<tr>
<td>145a</td>
<td>-1.0°</td>
</tr>
<tr>
<td>145b</td>
<td>+3.41°</td>
</tr>
<tr>
<td>145c</td>
<td>+1.96°</td>
</tr>
<tr>
<td>(R,R)-DET</td>
<td>-3.80°</td>
</tr>
</tbody>
</table>

Reported$^{185}$ $[\alpha]_D$ for (2S,3S)-Epoxygeraniol with (2R,3R)-DET as ligand = -5.89°

In all the cases the products were found to be optically active. Based on the Specific rotation values, it is observed that esters of 127 yielded products enriched with (2S,3S)-epoxygeraniol and esters of 128 yielded predominantly the opposite enantiomer (Scheme IV.11). It is interesting to note that the enantioselectivity pattern provided by esters of Garcinia acid shows predominant inversion as compared to (2S,3S)-tartrate esters and is in line with the observation made by Sharpless et al regarding structurally modified tartrate ligands$^{186}$. It is also significant that esters of 128 yield (2R,3R)-epoxygeraniol which is usually synthesised employing rather expensive unnatural tartrate esters. However, the extent of e.e need to be confirmed by analysing the products by chromatography using chiral stationary phase.
IV.2.iii Asymmetric Oxidation of Sulphides Employing Novel Diols

Optically pure sulphoxides are often employed as chiral auxiliaries in conjugate addition of organocuprates to enones\textsuperscript{187}. Dienes activated by optically active sulphoxides undergo cycloaddition reactions with high diastereoselectivity. Asymmetric oxidation of sulphides is an important synthetic tool for the preparation of optically active sulphoxides. The usual procedure involves the use of chiral catalysts like Ti(IV)-DET or Ti(IV)-binaphthol etc. with high enantioselectivity.

As an extension to the studies on asymmetric epoxidation employing triesters of 127 and 128, Sharpless type asymmetric oxidation of sulphide to sulphoxide was also carried out following reported procedures\textsuperscript{188,189}. A representative sulphide (Methyl p-tolyl sulphide) was oxidised with cumene hydroperoxide, in presence of Ti(IV)-142b as catalyst (Scheme IV.12).

\[
\text{CH}_3\text{C}_6\text{H}_4\text{S}\text{CH}_3 \xrightarrow{\text{Ti(OiPr)}_4, 142b \text{, 80\% Cumene hydroperoxide} } \text{CH}_3\text{C}_6\text{H}_4\text{SO}\text{CH}_3
\]

Scheme IV.12

The reaction proceeded with the formation of chiral sulphoxide (147) along with certain amount of sulphone. Pure sulphoxide was isolated by chromatography. A tentative structure of the catalyst involving 142b, based on the reported structure of similar catalysts\textsuperscript{189}, is shown in Fig. IV.15.

\[\text{Fig. IV.15}\]
The reaction was repeated using 145b as chiral ligand. To compare the results under identical laboratory conditions a control experiment using (2R,3R)-DET as chiral ligand was also performed. The products isolated by chromatography were identified by $^1$H NMR spectra (Fig. IV.16a-d).

In all the cases the products were found to be optically active, on the basis of specific rotation measurements and the data is summarised in Table IV.2.

<table>
<thead>
<tr>
<th>Ligand used</th>
<th>$[\alpha]_D$ of 147</th>
</tr>
</thead>
<tbody>
<tr>
<td>142b</td>
<td>-11.11°</td>
</tr>
<tr>
<td>145b</td>
<td>+11.21°</td>
</tr>
<tr>
<td>(2R,3R)-DET</td>
<td>+143.95°</td>
</tr>
</tbody>
</table>

Reported$^{188}$ $[\alpha]_D$ for (S)-methyl-p-tolyl sulphoxide with (S,S)-DET as ligand = -142°

It is observed that reaction involving 142b give moderate enantiomeric excess of (S)-methyl-p-tolyl sulphoxide and the enantioselectivity offered is similar to that of expensive (2S,3S)-DET. On the other hand 145b shows selectivity pattern corresponding (2R,3R)-DET and gave the antipode in moderate e.e.

In conclusion, novel diols 142a, 142b and 142c derived from (2S,3S)-Tetrahydro-3-hydroxy-5-oxo-2,3-furandicarboxylic acid (127, Garcinia acid), and 145a, 145b and 145c derived from(2S,3R)-Tetrahydro-3-hydroxy-5-oxo-2,3-furandicarboxylic acid (128, Hibiscus acid) could be used as chiral ligands and they show opposite enantioselectivity pattern in asymmetric epoxidation and oxidation of sulphides. The enantiomeric excess observed is significant as these chiral ligands are devoid of C$_2$-symmetry.
Fig. IV.16a
Ligand used: 142b

Fig. IV.16b
Ligand used: 145b

Fig. IV.16c
Ligand used: (2R,3R)-DET

Methyl-p-tolyl sulphone (formed during reaction)

Fig. IV.16d
IV.3 Experimental

Trisodium (1S,2S)-1,2-dihydroxy-1,2,3-propanetricarboxylate (143):

To an aqueous solution of 127 (2.0 g, 10.5 mmol, in 10 ml water), 2N of sodium hydroxide solution was added at about 80° C, till reaction mixture is alkaline (~ pH = 9.0). The residue obtained after evaporation under reduced pressure, was triturated with dry methanol (5 x 50 ml). The solid obtained was finally dried under vacuum.

Yield : 2.3 g (80 %).

$^1$H NMR (D$_2$O) : $\delta$ 4.08 (s, 1H), 3.36 (s, 1H), 2.82 (d, $J = 15.9$ Hz, 1H), 2.71 (d, $J = 15.9$ Hz, 1H) ppm.

$^{13}$C NMR (D$_2$O) : $\delta$ 181.5, 180.6, 1793, 79.7, 77.9, 44.3 ppm.

Trimethyl (1S,2S)-1,2-dihydroxy-1,2,3-propanetricarboxylate (142a):

To a suspension of 143 (2.0 g, 7.3 mmol) in dry methanol (20 ml), thionyl chloride (3 ml, 40 mmol) was added. After refluxing for two hours, the reaction mixture was cooled and neutralised with saturated aqueous solution of sodium bicarbonate. The residue obtained upon concentration under reduced pressure was extracted with chloroform (3 x 25 ml). The combined extract was dried and concentrated to furnish 142a as yellow oil.

Yield : 0.8 g (44 %).

$[\alpha]_D$ : $+22.14^\circ$ (c 0.52, CHCl$_3$)

IR (film) : 3494, 3009, 2969, 1748, 1452, 1128, 1081, 1013 cm$^{-1}$

$^1$H NMR (CDCl$_3$) : $\delta$ 4.98 (s, 1H), 3.84 (s, 6H), 3.68 (s, 3H), 3.2 (d, $J = 18.0$ Hz, 1H), 2.80 (d, $J = 18.0$ Hz, 1H) ppm.

$^{13}$C NMR (CDCl$_3$) : $\delta$ 172.3, 170.7, 166.9, 77.3, 74.6, 53.07 52.9, 51.7, 39.25 ppm.

Mass spectrum : m/z 251 (M+1) (100), 219 (23), 191 (32), 159 (50), 143 (3), 131 (4.5), 99 (10.5), 90 (15), 59 (6), 43 (15).
Triethyl (1S,2S)-1,2-dihydroxy-1,2,3-propanetricarboxylate (142b):

The procedure adopted for 142a was followed with 143 (2.0 g, 7.3 mmol) in absolute ethanol (20 ml) and thionyl chloride (3 ml, 40 mmol). 142b was isolated as a pale yellow liquid.

**Yield** 1.2 g (85.5%)

[α]_D = +32.2° (c 0.5, CHCl_3)

**IR (film)** 3472, 2970, 1744, 1449, 1372, 1203, 1020 cm⁻¹

**¹H NMR (CDCl₃)** δ 4.87 (s, 1H), 2.19 (q, 4H) 4.03 (q, J = 7.1 Hz, 2H), 3.08 (d, J = 17.6 Hz, 1H), 2.70 (d, J = 17.6 Hz, 1H), 1.18-1.25 (t, 3H), 1.14 (t, J = 7.1 Hz, 3H) ppm.

**¹³C NMR (CDCl₃)** δ 172.7, 170.3, 166.5, 79.0, 74.6, 62.3, 62.1, 60.7, 39.5, 38.5, 1378, 1371 ppm

**Mass spectrum** m/z 292 (M⁺) (100), 276, 147, 246 (53), 218 (47.5), 188 (16.6), 172 (85.8), 157 (14.9), 145 (37.2), 115 (35.8), 99 (47.7), 88 (10.4), 76 (31.3), 43 (50.7)

Triisopropyl (1S,2S)-1,2-dihydroxy-1,2,3-propanetricarboxylate (142c):

The procedure adopted for 142a was followed with 143 (5.0 g, 18.2 mmol) in dry isopropyl alcohol (50 ml) and thionyl chloride (7.5 ml, 50 mmol). The white solid obtained (142c) was recrystallised from hexane.

**Yield** 4.11 g (66.%).

**Melting point** 128° C

**IR (film)** 3500, 3000, 1800, 1740, 1700, 1450, 1380, 1300, 1280, 1200, 1150, 1100, 1050 cm⁻¹

**¹H NMR (CDCl₃)** δ 5.04-5.12 (m, 3H), 4.83 (s, 1H), 3.06 (d, J = 17.5 Hz, 1H), 2.81 (d, J = 17.5 Hz, 1H), 1.62 (s, 6H), 1.26-1.31 (m, 12H) ppm

**¹³C NMR (CDCl₃)** δ 172.7, 169.8, 165.6, 83.9, 78.4, 72.2, 70.6, 39.8, 21.6, 21.5, 21.3 ppm

**Mass spectrum** m/z 334 (M⁺) (31), 238 (7.3), 206 (8.1), 193 (10.5), 170 (16.5), 155 (7.1), 145 (21) 128 (17.9), 115 (20.8), 100 (13.4), 87 (23.8), 69 (13.4), 56 (16.4), 42 (100)
Elemental analysis

Found  
C 52.57, H 6.21

Calculated  
C 53.88, H 7.83

Dimethyl (4S,5S)-2,2-dimethyl-4-(2-oxo-2-methoxyethyl)-1,3-dioxolane-4,5-dicarboxylate (144a):

To a solution of 142a (2.0 g, 8 mmol) in dry acetone (50 ml), anhydrous copper sulphate (10 g) and a few drops of conc. Sulphuric acid were added. After refluxing for four hours, the mixture was filtered, neutralised followed by concentration and extraction with hexane (2 x 25 ml). The combined extract was washed with water, dried and evaporated to yield 144a as a yellow liquid.

Yield  
0.5 g (22 %).

[α]_D  
+29.5° (c 0.95 %, CHCl₃)

IR (film)  
2950, 1740, 1440, 1370, 1200, 1080, 1000 cm⁻¹

¹H NMR (CDCl₃)  
δ 4.93 (s, 1H), 3.86 (s, 3H) 3.81 (s, 3H), 3.68 (s, 3H), 2.98 (d, J = 16.04 Hz, 1H), 2.85 (d, J = 16.04 Hz, 1H), 1.58 (s, 3H), 1.48 (s, 3H) ppm.

¹³C NMR (CDCl₃)  
δ 170.6, 169.3, 167.8, 112.8, 82.5, 78.8, 52.9, 52.3, 51.7, 38.9, 27.4, 25.5 ppm.

Mass spectrum  
m/z 290 (M⁺) (1.0), 274 (19.8), 230 (36.4), 214 (64.4), 198 (19.4), 180 (11.2), 172 (100), 156 (16.4), 144 (29.2), 113 (51.5), 105 (14.2), 73 (41.0), 59 (43.3), 43 (92.5).
Diethyl (4S,5S)-2,2-dimethyl-4-(2-oxo-2-ethoxyethyl)-1,3-dioxolane-4,5-dicarboxylate (144b):

The procedure described for 144a was followed using 142b (1.0 g, 3.4 mmol), dry acetone (25 ml), anhydrous copper sulphate (0.5 g) and conc. Sulphuric acid (one drop). After work-up, 144b was isolated as a pale yellow liquid.

Yield 0.3 g (27 %).

$[\alpha]_D^0 = 36.5^0$ (c 1.1 %, CHCl$_3$)

<table>
<thead>
<tr>
<th>IR (film)</th>
<th>3000, 1740, 1450, 1375, 1200, 1100, 1020 cm$^{-1}$</th>
</tr>
</thead>
</table>

$^1$H NMR (CDCl$_3$) : δ 4.78 (s, 1H), 4.22 (q, $J = 6.5$ Hz, 4H), 4.06 (q, $J = 5.4$ Hz, 2H), 2.90 (d, $J = 15.7$ Hz, 1H), 2.75 (d, $J = 15.7$ Hz, 1H), 1.52 (s, 3H), 1.42 (s, 3H), 1.25 (t, $J = 7.4$ Hz, 6 H), 1.16 (t, $J = 7.4$ Hz, 3H) ppm.

$^{13}$C NMR (CDCl$_3$) : δ 169.4, 168.1, 166.6, 111.9, 81.8, 78.2, 61.3, 61.1, 59.9, 38.3, 26.7, 24.8, 13.1 ppm.

Mass spectrum: m/z 332 ($M^+$) (5), 317 (32), 287 (11), 259 (100), 257 (40), 229 (19), 201 (72), 195 (14), 173, (62), 157 (46), 145 (28), 129 (16), 127 (10), 99 (16), 87 (14), 83 (14), 59 (22), 54 (4).

Diisopropyl (4S,5S)-2,2-dimethyl-4-(2-oxo-2-isopropythyl)-1,3-dioxolane-4,5-dicarboxylate (144c):

The procedure described for 144a was followed with 142c (3.0 g, 9 mmol), dry acetone (75 ml), anhydrous copper sulphate (1.5 g) and concentrated sulphuric acid (a few drops). After work-up, 144c was isolated as a pale yellow liquid.

Yield 1.2 g (32 %).

<table>
<thead>
<tr>
<th>IR (film)</th>
<th>2950, 1740, 1620, 140, 1380, 1220, 1100, 950 cm$^{-1}$</th>
</tr>
</thead>
</table>

$^1$H NMR (CDCl$_3$) : δ 5.06-5.22 (m, 2H), 4.95-5.05 (m, 1H), 4.75 (s, 1H), 2.93 (d, $J = 16.0$ Hz, 1H), 2.77 (d, $J = 16.0$ Hz, 1H), 1.60 (s, 3H), 1.50 (s, 3H), 1.30 (d, $J = 8.0$ Hz, 12 H), 1.22 (d, $J = 8.0$ Hz, 6H) ppm.

$^{13}$C NMR (CDCl$_3$) : δ 171.5, 170.2, 168.6, 112.8, 84.2, 79.3, 70.6, 69.7, 68.5, 39.7, 29.6, 27.6, 22.0 ppm.
2,3-Epoxygeraniol (146) (Employing 142a as chiral ligand):

Powdered, activated molecular sieves (4A, 1.0 g) and dry CH₂Cl₂ (60 ml) was cooled to 0°C. 142a (1.75 g, 7.0 mmol) and Ti(O-i-Pr)₄ (2.0 ml, 7.0 mmol) were added sequentially. After cooling the mixture to -20°C, TBHP (3.3 ml, 14 mmol, 4.0 M in CH₂Cl₂) was added and was stirred for 20 minutes. Geraniol (1.15 ml, 7.0 mmol) was added and the mixture was stirred at -23°C (2.5 h). The reaction was quenched by adding 10% aqueous tartaric acid solution (17 ml) while stirring at -23°C. The organic phase was separated and concentrated. The residue obtained was dissolved in ether (50 ml) and was stirred with 10% NaOH solution in saturated brine (20 ml). The ether phase was separated, washed with brine, dried and concentrated to give clear oil. Purification by chromatography (eluent: CH₂Cl₂) afforded 146.

Yield: 0.5 g (41%).

[α]D: -1.73° (c 0.27, CHCl₃)

IR (film): 3400, 2950, 2900, 1440, 1380, 1250, 1060, 850 cm⁻¹

¹H NMR (CDCl₃): 8 5.32 (t, J = 7.1 Hz, 1H), 3.6-3.9 (m, 2H), 3.12 (dd, J = 6.7 Hz, 1H), 2.25 (q, J = 7.4 Hz, 2H), 1.86 (s, 3H), 1.73 (s, 3H), 1.35-1.71 (m, 2H), 1.31 (s, 3H) ppm.

2,3-Epoxygeraniol (146) (Employing 142b as chiral ligand):

Epoxidation was performed as described in the case of 142a with powdered, activated molecular sieves (1.0 g), dry CH₂Cl₂ (60 ml), 142a (2.0 g, 7.0 mmol), Ti(O-i-Pr)₄ (2.0 ml, 7.0 mmol), TBHP (3.3 ml, 14 mmol, 4.0 M in CH₂Cl₂) and Geraniol (1.15 ml, 7.0 mmol). Work-up followed by chromatography furnished 146.

Yield: 0.6 g (40%)

[α]D: -3.65° (c 0.126, CHCl₃)

IR (film): 3400, 2980, 2900, 2850, 1450, 1360, 1250, 1220, 1200, 1120, 1040, 850 cm⁻¹.
2,3-Epoxygeraniol (146) (Employing 142c as chiral ligand):

Epoxidation was performed as described in the case of 142a with powdered, activated molecular sieves (1.0 g), dry CH₂Cl₂ (60 ml), 142c (2.4 g, 7.0 mmol), Ti(O-i-Pr)₄ (2.0 ml, 7.0 mmol), TBHP (3.3 ml, 14 mmol, 4.0 M in CH₂Cl₂) and Geraniol (1.15 ml, 7.0 mmol). Work-up followed by chromatography furnished 146.

Yield : 0.6 g (49%).

\[ \alpha \]D : -2.88° (c 0.22, CHCl₃)

IR (film) : 3400, 2980, 2900, 1450, 1380, 1250, 1220, 1190, 1100, 1040, 840 cm⁻¹

\[ \delta \]H NMR (CDCl₃) : δ 5.1 (t, \( J = 7.1 \) Hz, 1H), 3.6-3.8 (m, 2H), 2.05 (q, \( J = 7.2 \) Hz, 2H), 1.6 (s, 3H), 1.5 (s, 3H), 1.3-1.7 (m, 2H), 1.2 (s, 3H) ppm.

\[ \delta \]C NMR (CDCl₃) : δ 132.1, 123.4, 63.1, 61.4, 61.2, 38.5, 25.6, 23.7, 17.6, 16.7 ppm.

2,3-Epoxygeraniol (146) (Employing 145a as chiral ligand):

Epoxidation was performed as described in the case of 142a with powdered, activated molecular sieves (1.0 g), dry CH₂Cl₂ (60 ml), 145a (1.75 g, 7.0 mmol), Ti(O-i-Pr)₄ (2.0 ml, 7.0 mmol), TBHP (3.3 ml, 14 mmol, 4.0 M in CH₂Cl₂) and Geraniol (1.15 ml, 7.0 mmol). Work-up followed by chromatography furnished 146.

Yield : 0.5 g (41%).

\[ \alpha \]D : -1.0° (c 1.1, CHCl₃)

IR (film) : 3400, 2980, 2900, 2850, 1440, 1380, 1250, 1220, 1100, 1030, 870 cm⁻¹

\[ \delta \]H NMR (CDCl₃) : δ 5.3 (t, \( J = 7.2 \) Hz, 1H), 3.6-3.8 (m, 2H), 3.05 (dd, 1H), 2.25 (q, \( J = 6.3 \) Hz, 2H), 1.9 (s, 3H), 1.7 (s, 3H), 1.3-1.7 (m, 2H), 1.25 (s, 3H) ppm.
2,3-Epoxygeraniol (146) (Employing 145b as chiral ligand):

Epoxidation was performed as described in the case of 142a with powdered, activated molecular sieves (1.0 g), dry CH₂Cl₂ (60 ml), 145b (2.0 g, 7.0 mmol), Ti(O-i-Pr)₄ (2.0 ml, 7.0 mmol), TBHP (3.3 ml, 14 mmol, 4.0 M in CH₂Cl₂) and Geraniol (1.15 ml, 7.0 mmol). Work-up followed by chromatography furnished 146.

Yield : 0.7 g (57%).

[α]₀ᵈ : +3.41° (c 0.53, CHCl₃)

IR (film) : 3400, 2980, 2900, 2850, 1450, 1380, 1250, 1220, 1100, 1050, 870 cm⁻¹

¹H NMR (CDCl₃) : δ 5.05 (t, J = 7.05 Hz, 1H), 3.6-3.8 (m, 2H), 2.94 (dd, J = 4.08, 6.83 Hz, 1H), 2.1 (q, J = 7.3 Hz, 2H), 1.7 (s, 3H), 1.6 (s, 3H), 1.3-1.7 (m, 2H), 1.2 (s, 3H) ppm.

2,3-Epoxygeraniol (146) (Employing 145c as chiral ligand):

Epoxidation was performed as described in the case of 142a with powdered, activated molecular sieves (0.5 g), dry CH₂Cl₂ (30 ml), 145c (1.2 g, 3.5 mmol), Ti(O-i-Pr)₄ (1.0 ml, 3.5 mmol), TBHP (1.65 ml, 7 mmol, 4.0 M in CH₂Cl₂) and Geraniol (0.6 ml, 3.5 mmol). Work-up followed by chromatography furnished 146.

Yield : 0.4 g (67%).

[α]₀ᵈ : +1.96° (c 0.17, CHCl₃)

IR (film) : 3400, 2900, 2850, 1450, 1360, 1250, 1220, 1100, 1050, 870 cm⁻¹

¹H NMR (CDCl₃) : δ 5.1 (t, J = 7.1 Hz, 1H), 3.6-3.8 (m, 2H), 3.1 (dd, J = 4.5, 6.3 Hz, 1H), 2.1 (q, J = 7.3 Hz, 2H), 1.7 (s, 3H), 1.6 (s, 3H), 1.3-1.7 (m, 2H), 1.2 (s, 3H) ppm.
2,3-Epoxygeraniol (146) (Employing (2R,3R)-DET as chiral ligand):

Epoxidation was performed as described in the case of 142a with powdered, activated molecular sieves (0.5 g), dry CH₂Cl₂(30 ml), (2R,3R)-DET (1.15 ml, 7.0 mmol), Ti(O-i-Pr)₄ (2.0 ml, 7.0 mmol), TBHP (3.3 ml, 14 mmol, 4.0 M in CH₂Cl₂) and Geraniol (1.15 ml, 7.0 mmol). Work-up followed by chromatography furnished 146.

Yield : 0.8 g (67 %).

[α]D : -3.80° (c 0.612, CHCl₃)

IR (film) : 3400, 2980, 2920, 2850, 1440, 1380, 1250, 1230, 1200, 1120, 1060, 860 cm⁻¹

¹H NMR (CDCl₃) : δ 5.05 (t, J = 7.05 Hz 1H), 3.6-3.8 (m, 2H), 3.1 (dd, J = 4.1, 6.8 Hz 1H), 2.1 (q, J = 7.0 Hz, 2H), 1.7 (s, 3H), 1.6 (s, 3H), 1.3-1.7 (m, 2H), 1.2 (s, 3H) ppm.

Methyl p-tolyl sulphoxide (147) (Employing 142b as chiral ligand):

To a flask containing dry CH₂Cl₂ (32 ml), 142b (2.2 g, 7.5 mmol), Ti(O-i-Pr)₄ (1.12 ml, 3.75 mmol) were added under stirring at room temperature. After a few minutes, distilled water (.068 ml, 3.75 mmol) was added. Vigorous stirring was maintained till a homogeneous solution is obtained. After adding methyl p-tolyl sulphide (1.02 ml, 7.5 mmol in 1.25 ml CH₂Cl₂), the reaction mixture was cooled to -30° C and stirred for 40 minutes. 80% cumene hydroperoxide (1.4 ml, 7.5 mmol) was added and stirring was continued for 8 hours at -25-20°C. Hydrolysis was then effected by adding 1 ml of water and stirring was continued for further 90 minutes. After filtration (over celite), 2N aqueous sodium hydroxide solution (20 ml) and saturated brine (10 ml) were added and stirring was continued for 1 hour. Separation and concentration of organic phase gave the crude product. Pure sulphoxide was isolated by chromatography using Hexane-Ethyl acetate(9:1).
Yield: 0.5 g (43%).

\([\alpha]_D^\circ = -11.11^\circ \) (c 0.7, Acetone)

\(\text{IR} \) (film): 3010, 2900, 2850, 1700, 1480, 1400, 1300, 1150, 1080, 810 cm\(^{-1}\)

\(^1\text{H NMR} \) (CDCl\(_3\)): \(\delta 2.4\) (s, 3H), 2.7 (s, 3H), 7.2-7.6 (m, 4H) ppm.

\(^1\text{C NMR} \) (CDCl\(_3\)): \(\delta 142.5, 141.6, 130.1, 123.6, 44.0, 21.4\) ppm.

**Methyl p-tolyl sulfoxide (147) (Employing 145b as chiral ligand):**

The oxidation was carried out as described in the case of 142b with dry CH\(_2\)Cl\(_2\) (32 ml), 145b (2.2 g, 7.5 mmol), Ti(O-i-Pr)\(_4\) (1.12 ml, 3.75 mmol), distilled water (0.68 ml, 3.75 mmol), methyl p-tolyl sulphide (1.02 ml, 7.5 mmol in 1.25 ml CH\(_2\)Cl\(_2\)), 80% cumene hydroperoxide (1.4 ml, 7.5 mmol). Pure sulfoxide was isolated by chromatography using Hexane-Ethyl acetate (9:1).

Yield: 0.5 g (43%).

\([\alpha]_D^\circ = +11.21^\circ \) (c 0.42, Acetone)

\(\text{IR} \) (film): 3010, 2900, 2850, 1700, 1480, 1400, 1300, 1150, 1080, 810 cm\(^{-1}\)

\(^1\text{H NMR} \) (CDCl\(_3\)): \(\delta 2.4\) (s, 3H), 2.7 (s, 3H), 7.2-7.6 (m, 4H) ppm.

**Methyl p-tolyl sulfoxide (147) (Employing (2R,3R)-DET as chiral ligand):**

The oxidation was carried out as described in the case of 142b with dry CH\(_2\)Cl\(_2\) (32 ml), (2R,3R)-DET (1.34 ml, 7.5 mmol), Ti(O-i-Pr)\(_4\) (1.12 ml, 3.75 mmol), distilled water (0.68 ml, 3.75 mmol), methyl p-tolyl sulphide (1.02 ml, 7.5 mmol in 1.25 ml CH\(_2\)Cl\(_2\)), 80% cumene hydroperoxide (1.4 ml, 7.5 mmol). Pure sulfoxide was isolated by chromatography using Hexane-Ethyl acetate (9:1).

Yield: 0.6 g (52%).

\([\alpha]_D^\circ = +143.9^\circ \) (c 0.42, Acetone)

\(\text{IR} \) (film): 3010, 2900, 2850, 1700, 1490, 1400, 1300, 1150, 1080, 810 cm\(^{-1}\)

\(^1\text{H NMR} \) (CDCl\(_3\)): \(\delta 2.4\) (s, 3H), 2.7 (s, 3H), 7.2-7.6 (m, 4H) ppm.