CHAPTER -II

Enantio- and Diastereocontrolled Total Synthesis of (+)-Boronolide
2.1. INTRODUCTION

Many natural products with different biological activities such as insect growth inhibition, antitumor, antibacterial, antifungal or immunosuppressive properties, possess α,β-unsaturated δ-lactone moiety as an important structural feature. α,β- Unsaturated δ-lactone\(^1\) functionality is presumed to be responsible for biological activities due to its ability to act as a Michael acceptor enabling these molecules to bind to a target enzyme. The pyrone units are widely distributed in all parts of plants (Lamiaceae, Piperaceae, Lauraceae, and Annonaceae families) including leaves, stems, flowers and fruits. α-Pyrone possessing polyhydroxy or polyacetoxy side chains have attracted much attention from synthetic and medicinal chemists due to their broad range of biological activities such as plant-growth inhibition, as well as antifeedant, antifungal, antibacterial, and antitumor properties.\(^2\) Examples of such compounds include (+)-boronolide 1 and its deacetylated 1a and dideacetylated derivative 1b (Fig. 1). Boronolide 1 is an α,β-unsaturated C-12 lactone isolated from the leaves and branches of *Tetradenia fruticosa*\(^3\) and from the leaves of *Tetradenia barberae*,\(^4\) which has been used as a local folk medicine in Madagascar and South Africa.\(^5\) Deacetylated 1a and dideacetylated boronolide 1b have been obtained from *Tetradenia riparia*,\(^6\) a Central African species typically employed by

![Chemical structures](image.png)

**Figure 1.** Structure of (+)-boronolide and its derivatives

---

53
the Zulu as an emetic, which is an infusion of the leaf has also been reported to be effective against malaria. The relative stereochemistry of 1 was determined by X-ray analysis. The R-configuration at the C-6 position was proposed by application of Hudson’s lactone rule to the molecular rotation. Later, the stereochemistry at the C-6 position was confirmed by chemical degradation.

2.2. Review of Literature

The first synthesis of 1 was reported from an acrolein derivative in racemic form. Most of the enantioselective syntheses known for boronolide derive the asymmetry from chiral pool starting materials such as glucose, mannitol, tartaric acid, D-glucono-δ-lactone and L-erythulose etc. However synthetic approaches involving achiral substrate as starting material are rather scarce. A detailed report of these synthesis is described below.

Honda et al. (1996)

Honda and co-workers employed iterative Sharpless asymmetric dihydroxylation (AD) approach for the synthesis of boronolide. As shown in Scheme 1, 1,3-enyne 3, prepared by Pd-catalyzed cross-coupling reaction of (E)-1-iodo-1-hexane with acetylene 2, was subjected to the AD reaction using AD-mix-α to give the diol 4 with 94% ee. To achieve high diastereoselectivity for the second dihydroxylation, they prepared three substrates by protection of diol as acetate and isopropylidene followed by partial hydrogenation to give substrates 6, 7 and 8, which were subjected to second dihydroxylation under the conditions shown in Table 1. Finally, hydrolysis of TBDPS, oxidation, cyclisation, elimination and subsequent acetylation gave boronolide 1 (Scheme 2).
Scheme 1. Reagents and conditions: (a) (E)-1-iodo-1-hexene, (Ph₃P)₂PdCl₂, CuI, Et₂NH, rt (95%); (b) (i) AD-mix-α, CH₃SO₂NH₂, t-BuOH-H₂O, 0 °C (96%, 94% ee); (ii) Ac₂O, Py, rt (99%); (c) (i) Lindlar catalyst, H₂, AcOEt, rt (quant); (ii) K₂CO₃, MeOH, 0 °C to rt (99%); (iii) PPTS, CH₂Cl₂, 2,2-dimethoxypropane, 0 °C to rt (86%); (d) a AD-mix reagent (14 g/mmole of substrate) was used in 50% aqueous t-BuOH (50 mL/mmole of substrate). b OsO₄ (35 mol %), 4-methylmorpholine N-oxide (NMO) (3 mol equiv) in 75% aqueous t-BuOH (30 mL/mmole of substrate). c Yield was that of the corresponding tetraacetate after treatment with acetic anhydride in pyridine.

Table 1. Dihydroxylation of (Z)-olefin.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Oxidant</th>
<th>Product (yield %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7 (R¹ = H)</td>
<td>AD-mix-β</td>
<td>9A (53)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10A (25)</td>
</tr>
<tr>
<td>2</td>
<td>7 (R¹ = H)</td>
<td>AD-mix-α</td>
<td>9A (27)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10A (41)</td>
</tr>
<tr>
<td>3</td>
<td>7 (R¹ = H)</td>
<td>OsO₄-NMO</td>
<td>9A (46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10A (45)</td>
</tr>
<tr>
<td>4</td>
<td>6 (R¹ = Ac)</td>
<td>OsO₄-NMO</td>
<td>9A (46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10A (42)</td>
</tr>
<tr>
<td>5</td>
<td>6 (R¹ = CNMe₂)</td>
<td>OsO₄-NMO</td>
<td>9A (19)</td>
</tr>
</tbody>
</table>

Scheme 2. Reagents and conditions: (e) AcOH-H₂O-THF (3:1:1), rt (97%); (f) PCC, AcONa, rt (76%); (g) NaClO₂, 2-methyl-2-buten, t-BuOH-H₂O, rt (95%); (h) NaOMe, MeOH, rt, then 2N HCl; p-TsOH, benzene-THF, reflux; Ac₂O, Py, rt (79%); (i) [PhSe(O)]₂O, chlorobenzene, reflux (63%).

Ghosh et al. (2000)⁸d

Ghosh and co-workers employed 1-O-benzyl-2,3-O-isopropylidene-D-threitol 16 as the starting material which can be easily prepared from tartaric acid. Isopropylidene derivative 16 was converted into the Weinreb amide 17, which was further treated with butylimagnesium bromide to afford the ketone 18. Reduction of ketone 18 with L-selectride followed by acetyl protection provided the acetate derivative 19. Benzyl deprotection and subsequent oxidation
followed by allylation with diallyl zinc furnished the homoallylic alcohol 21. α,β-Unsaturated-δ-lactone 25 was constructed by RCM of the acrylated derivative of 24, which was subsequently converted into the target molecule 1.

Scheme 3. Reagents and conditions: (a) (i) CrO₃, H₂SO₄, Me₂CO–H₂O, 0°C, 68%; (ii) Me₂CHCH₂OCOC₁, N-methylpiperidine, CH₂Cl₂–THF (10:1); (MeO)NHMe·HCl, N-methylpiperidine, CH₂Cl₂, 83%; (b) CH₃(CH₂)₂MgBr, THF, -20 °C, 96%; (c) (i) L-selectride, THF, -78 °C, 99%; (ii) Ac₂O, Et₃N, DMAP (cat), CH₂Cl₂, 98%; (d) (i) H₂, Pd(OH)₂ (cat), EtOAc–MeOH (4:1), quant.; (ii) DMSO, (COCl)₂, Et₃N, CH₂Cl₂, -78 °C; (e) allylmagnesium bromide, ZnCl₂, THF, -78 °C; (f) CH₂=CHCOCl, Et₃N, 0 °C to 23 °C, CH₂Cl₂, 80%; (g) PhCH=RuCl₂(ChX₃P)₂, (10 mol%), Ti(OiPr)₄ (30 mol%), CH₂Cl₂, 40 °C, (84%); (h) (i) Dowex 50 W-X8 (H⁺), H₂O, 70 °C; (ii) Ac₂O, Et₃N, DMAP (cat), CH₂Cl₂, 0 °C, quant.

Singh et al. (2000)⁸e
Singh and co-workers synthesized (+)-boronolide using D-mannitol 26 as starting material. 1,2,3,4-O-Diisopropylidene-D-mannitol was converted into epoxide 29 with inverted stereochemistry by selective hydroxyl protection followed by mesylation of secondary hydroxyl group of 28 and saponification with K₂CO₃. Ring opening of the epoxide 29 with n-propylmagnesium bromide followed by hydroxyl protection with BnBr provided 30. The other acetonide was converted into epoxide 32 with retention of configuration and opened.
with allyliccuprate followed by hydroboration and oxidation to provide 33, which was lactonized and converted into the target molecule 1 by known methods.\textsuperscript{8a-c}

![Chemical diagram](image)

**Scheme 4. Reagents and conditions:** (a) (i) PhCOCl, Py, DCM, -80 to -20 °C, 4 h (83%); (ii) MeSO\textsubscript{2}Cl\textsubscript{2}, Et\textsubscript{3}N, DCM, -80 to -20 °C, 12 h (95%); (b) K\textsubscript{2}CO\textsubscript{3}, MeOH, rt, 2 h (85%); (c) (i) n-PrLi, CuCN, THF, -80 °C, 12 h (95%); (ii) PhCH\textsubscript{2}Br, NaH, THF, rt, 16 h (90%); (d) (i) CuCl\textsubscript{2}.2H\textsubscript{2}O, MeOH, 0 °C, 40 min (80%); (ii) TsCl, Py, DMAP (cat.), 0 °C, 14 h (65%); (e) K\textsubscript{2}CO\textsubscript{3}, MeOH, 0 °C, 1 h (90%); (f) Allyl magnesium bromide, CuBr.DMS, -80 °C, 8 h (80%); (g) (i) BH\textsubscript{3}.DMS, 0 °C, 12 h, PhH followed by 30% aq. H\textsubscript{2}O\textsubscript{2}, NaOH, EtOH, 0 °C (75%); (ii) AgCO\textsubscript{3} on Celite, PhH, reflux, 12 h (75%); (h) (i) CuCl\textsubscript{2}.2H\textsubscript{2}O, MeCN, rt, 36 h (80%); (ii) H\textsubscript{2}, 10% Pd/C, EtOH, rt, 24 h (95%); (iii) Ac\textsubscript{2}O, Py, rt, (i) Ref. 8a-c

**Carda et al. (2002)\textsuperscript{8f,g}**

Carda and co-workers employed ketone 36, a functionalized d\textsuperscript{3} (homoenolate) synthon as a starting material which can be prepared from L-erythrolulose. Thus, enolization of 36 with ChX\textsubscript{2}BCl/Et\textsubscript{3}N (Chx = cyclohexyl) followed by addition of pentanal generated a boron aldolate intermediate 37, which was reduced in situ with LiBH\textsubscript{4} to give all-syn acetonide 38 as a single stereoisomer. Protection of hydroxyl groups with Ac\textsubscript{2}O followed by oxidative cleavage of acetonide moiety of 40 and allylation of the resulting aldehyde 41 in the presence of indium metal afforded the homoallylic alcohol 42 with 91:9 diastereomeric ratio.
Esterification followed by ring-closing metathesis and deprotection provided the target molecule 1.

Scheme 5. Reagents and conditions: (i) Chx₂BCl, Et₃N, CH₃(CH₂)₃CHO, Et₂O, from -78 to 0 °C, 5 h, then LiBH₄, 2 h (83%); (ii) TBAF, THF, 15 min (96%); (iii) Ac₂O, Et₃N, cat. DMAP, CH₂Cl₂, rt, 12 h (90%); (iv) H₂IO₆, AcOEt, rt, 1 h (85%); (v) allyl bromide, In powder, THF/H₂O (1:1), rt, 18 h; (vi) acryloyl chloride, Et₃N, cat. DMAP, CH₂Cl₂, rt, 12 h (50% overall of two steps); (vii) PhCH=RuCl₂(Chx₃P)₂, Ti(OiPr)₄, CH₂Cl₂, reflux, 24 h (71%).

Trost et al. (2002)⁸th
Trost and co-workers synthesized 46 stereoselectively from hydroxyacetylfluran 44 and valeraldehyde 45 using a novel dizinc aldol catalyst 47. Aldol reaction of 44 and 45 gave the syn-diol 46, which was protected as its corresponding acetonide followed by reduction of ketone under Felkin-Anh control using L-selectride⁹ to furnish the alcohol with excellent diastereoselectivity (98:2).

Scheme 6. Asymmetric Aldol
Protection of secondary alcohol as its TBS ether 48 followed by oxidative cleavage of furan, esterification and reduction furnished the aldehyde 49. Brown's chiral allylboration\(^{10}\) (8:1 dr) of aldehyde followed by esterification, ring-closing metathesis\(^{11}\) and deprotection led to target molecule 1.

Table 1. Optimization of the Aldol Reaction\(^{a}\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>ligand</th>
<th>isolated yields</th>
<th>ee</th>
<th>syn/anti</th>
<th>dr(^{b})</th>
<th>syn/anti(^{c})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^{d})</td>
<td>47a</td>
<td>56/14</td>
<td>4.3:1</td>
<td>97/84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>47a</td>
<td>78/16</td>
<td>4.6:1</td>
<td>97/84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>47a(^{e})</td>
<td>58/13</td>
<td>3.5:1</td>
<td>95/81</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>47b</td>
<td>77/15</td>
<td>4:1</td>
<td>93/83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>47c</td>
<td>78/12</td>
<td>6:1</td>
<td>97/86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6(^{f})</td>
<td>47a</td>
<td>76/17</td>
<td>4.2:1</td>
<td>96/83</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{a}\)All reactions were carried out on 2 mmol scale using 5 mol % catalyst, 1.1 equiv of ketone and 100 mg of 4 Å molecular sieves in 0.33 M of THF solution at -35 \(^{\circ}\)C for 12 h unless noted otherwise. \(^{b}\)Determined by NMR of the crude reaction isolate. \(^{c}\)Determined by chiral HPLC using Chirapak AD column; \(^{d}\)This reaction was run for 4 h. \(^{e}\)2.5 mol % catalyst was used. \(^{f}\)This reaction was done on a 16 mmol scale of valeraldehyde 45.

Scheme 7. Reagents and conditions: (b) (i) DMP, Amberlyst 15, CH\(_{2}\)Cl\(_{2}\), rt, 98%; (ii) L-selectride, THF, -100 \(^{\circ}\)C; H\(_{2}\)O, NaOH, 89%, dr 98:2; (iii) TBSOTf, 2,6-lutidine, CH\(_{2}\)Cl\(_{2}\), 0 \(^{\circ}\)C, 98%; (c) (i) RuCl\(_{3}\) (cat.), NaI\(_{2}\), CCl\(_{4}\), CH\(_{3}\)CN, H\(_{2}\)O, CH\(_{2}\)N\(_{2}\), Et\(_{2}\)O, 70%; (ii) LiBH\(_{4}\),
Chapter II: Enantio- and Diastereoccontrolled Total Synthesis of (+)-Boronolide

Et₂O, MeOH, 0 °C, 98%; (iii) Dess-Martin periodinane, CH₂Cl₂, rt, 100%; (d) (+)-(Ipc)₂B-allyl, Et₂O, 100 °C; H₂O₂, NaOH, 85%, dr 8:1; (e) acryloyl chloride, i-Pr₂NET, CH₂Cl₂, 0 °C, 89%; (f) 2 mol % Grubbs’ cat., CH₂Cl₂, 40 °C, 92%; (g) aq HF, CH₃CN, 65%; (h) Ac₂O, DMAP, i-Pr₂NET, CH₂Cl₂, 0 °C, 86%.

Wu et al. (2004)³

Wu and co-workers synthesized 8-epi-(+)-boronolide 1c and (+)-boronolide 1, starting from readily available carbohydrates such as D-tartaric acid 55 and D-glucano-8-lactone derivative 67 respectively.

Scheme 8. Reagents and conditions: (a) (i) Propargyl bromide, Zn powder, DMF–Et₂O. (ii) TBSCl, DMF, imidazole. DMAP, rt, 44% for three steps. (iii) BuLi (1.15 eq, 1.6 M in hexane), CH₃I, THF, −78 °C to rt, 83%. (c) n-BuLi (1.5 eq, 1.6 M in hexane), ClCO₂Me, THF, −78 °C to rt, 81.3%. (d) H₂, Lindlar’s cat., quinoline, ethyl acetate, 50–60 °C, 91%. (e)
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boronolide

TBAF, THF, 72%, (f) HF (40%)–acetonitrile (16 : 1), 62: 21%, 63: 37%, 64: 32%. (g) NH₄F, MeOH, 60 °C, 2 days, 62: 70%; 63: 24%, (h) PPTS (cat.) or p-TSOH (cat.), toluene, 50–60 °C, 88%, (i) H₂, (Ph₃P)RhCl, benzene–EtOH (6 : 1), rt, 86%, (j) CuCl₂·2H₂O, MeCN–MeOH (6 : 1), rt to 50 °C. (ii) Ac₂O, Py, DMAP, CH₂Cl₂, 77% for two steps.

Dialdehyde 56 prepared from diethyl (2S,3S)-2,3-O-isopropylidenetartrate¹³ was subjected to two-directional propargylation¹² with propargylzinc bromide followed by TBS protection to give 57, which was desymmetrised by selective methylation followed by methoxycarbonylation to furnish the intermediate 59. Partial hydrogenation of 59 with Lindlar catalyst afforded cis,cis-diene 60. TBS deprotection-ring closing with NH₄F followed by regioselective hydrogenation with Wilkinson’s catalyst and global deprotection furnished 8-epi-(+)-boronolide 1c (Scheme 8). (+)-boronolide was synthesized from D-glucano-δ-lactone derivative 67 as described in Scheme 9.

Scheme 9. Reagents and conditions: (a) TBSCI, Im, DMAP(cat.), CH₂Cl₂, 94%. (b) (i) DIBAL-H (1 M solution in toluene), toluene, −78 °C. (ii) Ph₃PC₃H₂Br, n-BuLi (1.6 M solution in hexanes), −40 to 0 °C; (iii) Pd/C, H₂, 35 atm, EtOAc–CH₃OH (5 : 1), 58% for three steps; (c) H₃IO₆, ether, rt. (d) (i) Propargyl bromide, DMF–Et₂O, Zn powder, total yield 59% for two steps. (ii) TBSCI, DMF, Im., DMAP, rt, 92%; (e) n-BuLi (1.2 eq, 1.6 M in hexanes), ClCO₂Me, THF, −78 °C to rt, 87%; (f) Lindlar cat., quinoline, ethyl acetate, 91.2%; (i) 6 M HCl–THF (1 : 2), rt; (j) Ac₂O, Py, DMAP, CH₂Cl₂, 73% for two steps.
Barua et al. (2006)\textsuperscript{81}

Barua and co-workers synthesized (+)-boronolide starting from (E)-\(\alpha,\beta\)-unsaturated ester 73 employing Sharpless asymmetric dihydroxylation, Shibasaki’s asymmetric Henry reaction,\textsuperscript{14} asymmetric allylation and ring-closing metathesis as key steps. Thus, AD reaction of 73 and subsequent isopropylidene protection followed by reduction and nitro aldol reaction under the influence of La-(S)-BINOL catalyst gave the nitro alcohol 78 with 13:1 (syn:anti) diastereomeric ratio. The oxime 79 derived from nitro alcohol 78 by Nef reaction\textsuperscript{15} was converted into aldehyde, which was then subjected to asymmetric allylation and ring-closing metathesis to give the target molecule 1.

Scheme 10. Reagents and conditions: (a) (DHQ)\textsubscript{2}PHAL, OsO\textsubscript{4}, K\textsubscript{2}[Fe(CN)]\textsubscript{6}, K\textsubscript{2}CO\textsubscript{3}, \(t\)-BuOH–H\textsubscript{2}O (1/1), 0 °C, 18 h; (b) acetic anhydride, iodine, rt, 10 min; (iii) DIBAL, toluene, -78 to 0 °C; (c) LiBH\textsubscript{4}, ether, 0 °C to rt; (d) 2,2-DMP, Amberlyst 15, CH\textsubscript{2}Cl\textsubscript{2}, rt, 30 min; (e) (i) DIBAL, toluene, -78 °C, 2 h; (ii) nitromethane, La(S)-BINOL, THF, -50 °C, 60 h; (iii) TBSCI, imidazole, DMF, rt, 16 h; (f) anhydride SnCl\textsubscript{2}, Et\textsubscript{3}N, PhSH, MeCN, rt, 30 min; (g) (i) PCC, 30% H\textsubscript{2}O\textsubscript{2}, acetone, rt, 30 min; (ii) (S)-BINOL, Ti(O-iPr)\textsubscript{4}, allyltributyltin, CH\textsubscript{2}Cl\textsubscript{2}, -78 to -20
$^0\text{C}, 36 \text{ h}; (h) \text{ acryloyl chloride, Et}_3\text{N, DMAP, CH}_2\text{Cl}_2, 0 ^\circ\text{C to rt}; (i) \text{ Grubb's catalyst, CH}_2\text{Cl}_2, 40 ^\circ\text{C, 14 h}; (j) (i) \text{ aq HF, CH}_3\text{CN, rt, 12 h}; (ii) \text{ acetic anhydride, pyridine, DMAP, rt, 3 h.}$

**Prasad et al. (2006)**

Prasad and co-workers employed bis-Weinreb amide 83 as starting material for the synthesis of (+)-boronolide 1 and (-)-5-epi-boronolide 1d. As depicted in Scheme 11, mono substitution of bis-Weinreb amide 83\textsuperscript{16} with butylmagnesium bromide followed by reduction with L-selectride.

![Scheme 11](image)

**Scheme 11. Reagents and conditions:** (i) $^\text{tBuMgBr}, \text{THF, -15 \, ^\circ\text{C, 92\%; (ii) (a) L-Selectride, \, THF, -78 \, ^\circ\text{C, 83\%; (b) pentenylmagnesium bromide, THF, 0 \, ^\circ\text{C, 2 h, 94\%; (c) (i) TBSCI, DMF, Im, DMAP, 80 \, ^\circ\text{C, 4 h, 93\%, (ii) DIBAL-H, toluene, -50 \, ^\circ\text{C, 1.5 h, 82\%; (d) O}_3/O_2, Me}_2\text{S, NaHCO}_3, DCM:MeOH, -78 \, ^\circ\text{C to rt, 5 h, (ii) PCC, NaOAc, celite, DCM, rt, 2 h, 89\% for 2 steps; (e) (i) FeCl}_3, 6\text{H}_2\text{O, DCM, rt, 4 h, 75\%, (ii) Ac}_2\text{O, Et}_3\text{N, DMAP, DCM, rt, 8 h, 90\%.}$

![Scheme 11](image)
Scheme 12. Reagents and conditions: (a) (i) pentenylmagnesium bromide, THF, 0 °C, 0.5 h, (ii) n-BuLi, THF, 0 °C, 1 h, 83%; (b) L-selectride, THF, -78 °C, 2.5 h, 89%; (c) (i) O₃/O₂, Me₂S, NaHCO₃, DCM:MeOH, -78 °C to 0 °C, 5.5 h, 87%, (ii) Ag₂CO₃ on celite, toluene, 1.5 h, 98%; (d) LDA/PhSeBr, THF, -78 °C to -30 °C, 4 h, (ii) H₂O₂, DCM, rt, 1 h, 34%; (e) (i) FeCl₃·6H₂O, DCM, 0.5 h, rt, (ii) Ac₂O, Py/DMAP, rt, 10 h, 76% for two steps.

The other amide was substituted with 4-pentenylmagnesium bromide followed by stereoselective reduction with DIBAL-H to afford the required alcohol 86. Ozonolysis of 86, followed by PCC oxidation of resultant lactol afforded the lactone 87. Global deprotection followed acetylation and elimination afforded the target molecule 1. Reaction of bis-Weinreb amide 83 successively with 4-pentenylmagnesium bromide and n-butyllithium in one-pot afforded the diketone 89, which was reduced stereoselectively by L-selectride to furnish the diol 90 as a single diastereomer. Ozonolysis of 90, followed by PCC oxidation of resultant lactol afforded the lactone 91, which was converted into 5-epi-boronolide 1d (Scheme 12).
2.3. PRESENT WORK

2.3.1. Objective

Our synthetic strategy for the synthesis of boronolide 1 is outlined in Scheme 13. We envisioned that the lactone ring could be constructed by the ring closing metathesis of an acrylate ester, which in turn would be obtained from an epoxide. The enantio pure epoxide could be prepared either by the Sharpless asymmetric epoxidation of an allylic alcohol or by hydrolytic kinetic resolution of a racemic epoxide. The chelation-controlled vinylation of an aldehyde would install the third stereogenic centre, while the initial two stereo centers could easily be established by the Sharpless asymmetric dihydroxylation of an olefin.

Scheme 13. Retrosynthetic analysis for (+)-boronolide

2.3.2. Results and Discussion:

The synthesis of boronolide started from commercially available valeraldehyde 93 as illustrated in Scheme 14. Thus, valeraldehyde 93 was subjected to Horner-Emmons olefination with triethyl phosphonoacetate to furnish the (E)-α,β-unsaturated ester 73 in 89% yield. The IR spectrum of 73 showed the ester carbonyl absorption at 1724 cm\(^{-1}\) and olefin C=C stretching at 1655 cm\(^{-1}\). The \(^1\)H NMR spectrum gave olefin protons at δ 5.76 (doublet of doublet) and 6.95 (doublet of triplet) with the coupling constant \(J = 15.76\) Hz indicating...
trans-olefin. The ester 73 was treated with osmium tetroxide and potassium ferricyanide as co-oxidant in the presence of (DHQ)$_2$PHAL ligand under AD conditions$^{17}$ to give the diol (2R, 3S)-74 in 96% yield having $[\alpha]_D^{25} -8.8$ (c 0.9, CHCl$_3$) with 97% ee.$^{18, 8k1}$ The IR spectrum gave hydroxyl absorption at 3400-3300 cm$^{-1}$ and ester carbonyl at 1732 cm$^{-1}$. The $^1$H NMR indicated absence of olefin protons. The chiral protons appeared at δ 3.85 (doublet of triplet) and 4.06 (doublet) in proton NMR spectrum. The chiral carbons appeared at δ 72.4 and 73.2 in the $^{13}$C NMR spectrum. Treatment of diol 74 with 2,2-dimethoxypropane in the presence of p-TSA gave the acetonide ester (2R, 3S)-77 in 95% yield. The IR spectrum of 77 indicated absence of hydroxyl groups. The acetonide methyl protons appeared at δ 1.42 (singlet) and 1.44 (singlet) in the $^1$H NMR spectrum and typical quaternary carbon of acetonide appeared at 110.5 in the $^{13}$C NMR spectrum. The reduction with DIBAL-H furnished the alcohol (2S, 3S)-97 in 91% yield. The IR spectrum of 97 gave hydroxyl absorption at 3440 cm$^{-1}$ and the ester carbonyl group was found to be absent. The resulting alcohol 97 was subjected to oxidation under Swern conditions$^{19}$ to give the aldehyde 98 in excellent yield.

Scheme 14. Reagents and conditions. (a) (EtO)$_2$P(O)(O)CH$_2$CO$_2$Et, LiBr, Et$_3$N, THF, rt, overnight, 89%; (b) (DHQ)$_2$PHAL, K$_2$CO$_3$, K$_3$Fe(CN)$_6$, MeSO$_2$NH$_2$, t-BuOH/H$_2$O 1:1, 0 °C, 24 h, 96%; (c) p-TSA, 2,2-DMP, CH$_2$Cl$_2$, 95%; (d) DIBAL-H, CH$_2$Cl$_2$, 0 °C to rt, 2 h, 91%;
(e) (COCl)₂, DMSO, Et₃N, CH₂Cl₂, -78 °C to -60 °C, 95%. (f) CH₂=CHMgBr, MgBr₂·Et₂O, THF or CH₂Cl₂, -78 °C, 6 h, 92%.

To establish the third stereogenic centre with the required stereochemistry, it was thought worthwhile to examine stereoselective vinylation. Thus, treatment of aldehyde 98 with vinylmagnesium bromide in THF in the presence of MgBr₂·Et₂O at -78 °C furnished the allylic alcohol 99 in 92% yield with moderate diastereomeric selectivity (dr = 3:1; syn:anti) as an inseparable mixture of diastereomers. The IR spectrum of 99 gave broad hydroxyl absorption at 3358-3250 cm⁻¹. The ¹H NMR spectrum of 99 gave olefin peaks at δ 5.81-5.91 (multiplet, one proton) and 5.26-5.34 (multiplet, two protons). The hydroxyl proton appeared at δ 2.42 (broad singlet) and the diastereomeric protons at δ 3.61 (doublet of doublet, minor diastereomer) and δ 3.69 (doublet of doublet, major diastereomer) with coupling constants J = 7.5, 4.5 and 7.9, 3.9 Hz respectively in ¹H NMR spectrum.

![Chemical Structures](image)

**Scheme 15.** Reagents and conditions. (a) MOM chloride, DIPEA, CH₂Cl₂, 0 °C to rt, overnight, 91%; (b) (i) DIBAL-H, CH₂Cl₂, 0 °C to rt, 2 h, 89%, (ii) (COCl)₂, DMSO, Et₃N, CH₂Cl₂, -78 °C to -60 °C, 95%; (c) CH₂=CHMgBr, MgBr₂·Et₂O, THF or CH₂Cl₂, -78 °C, 6 h, 90%.

Even after protection of the hydroxy group of 99 with different protecting groups such as TBS, MOM, Ac, PMB, we were unable to separate the diastereomers by flash chromatography. In order to determine the stereochemistry of newly generated third stereocentre, compound 99 was subjected to acid treatment followed by 1,3-dihydroxy protection as the benzylidene derivative. The required major isomer 104 could easily be separated by silica gel column chromatography. The newly generated stereocentre in 99 was
assigned syn configuration which was based on the NOE studies as strong NOE correlations were observed between the 1,3-diaxial protons of the cyclic derivative 104 (Scheme 16).

Scheme 16. Reagents and conditions. (a) (i) HCl, MeOH, rt, 12 h; (ii) PhCH(O Me)₂, p-TSA, CH₂Cl₂, rt, overnight.

Subsequently several attempts were made to achieve better selectivity with the use of additives such as ZnCl₂ or TiCl₄ and employing addition of vinyl lithium as alkylating reagent with different solvent systems (CH₂Cl₂ or diethyl ether). However, the required syn-selectivity could not be improved. In order to explore the possibility of achieving a better syn-selectivity in vinylation reaction, it was thought worthwhile to change the protecting group. We assumed that the chelation between MOM and aldehyde would be more effective as compared to other protecting groups. Thus the diol 74 was treated with MOMCl in the presence of diisopropylethylamine to afford compound (2R, 3S)-100 in excellent yield (Scheme 15). The IR spectrum of 100 indicated absence of hydroxyl groups. The methylene and methyl protons of MOM group appeared at δ 4.70, 4.62 and 3.37, 3.31 respectively in ¹H NMR spectrum. Subsequent reduction of ester 100 with DIBAL-H followed by Swern oxidation gave the aldehyde 102, which was used immediately in the next reaction without any further purification.

Figure 2. Chelation controlled transition models
Thus when 102 was subjected to chelation controlled vinylation in CH₂Cl₂ at -78 °C with MgBr₂·Et₂O,²⁰ it furnished the allylic alcohol 103 in 90% yield with an excellent diastereoselectivity (dr = 19:1; syn:anti) as determined by \(^1\)H and \(^{13}\)C NMR spectral analysis. The formation of major syn-diastereomer can be explained by the chelated five membered transition state as depicted in Fig. 2.

![Diagram](image)

**Figure 3:** (A) Partial \(^1\)H NMR and \(^{13}\)C NMR spectra of diastereomeric mixture (3:1) 99. (B) Partial \(^1\)H NMR and \(^{13}\)C NMR spectra of diastereomeric mixture (19:1) 103. (C) Partial \(^1\)H NMR and \(^{13}\)C NMR spectra of pure diastereomer 106.

69
The improvement in the syn-selectivity in case of 103 (19:1) as compared to 99 (3:1) could probably be attributed to the extra chelation by MOM protecting group with magnesium as illustrated in Fig.2. After protection of hydroxyl group in compound 103 with TBSCI, the required syn-diastereomer (3R, 4R, 5S)-106 could easily be separated by flash chromatography.

In order to generate the final stereogenic centre with an appropriate functionality, a Sharpless asymmetric epoxidation was employed in the next step (Scheme 17). Thus, treatment of allylic alcohol 103 with titanium tetra-isopropoxide and t-butyl hydroperoxide in the presence of (+)-DIPT for 4 days under Sharpless asymmetric epoxidation conditions\(^{21}\) provided the epoxide 105 albeit in low yield and poor diastereoselectivity. The extra chelation of titanium-tetra isopropoxide with MOM might be possible reason for retarding the rate of epoxidation reaction. As a next alternative, it was thought worthwhile to prepare first the diol 107 by the Sharpless asymmetric dihydroxylation of olefin 106, which could further be converted easily into the required epoxide 108\(^{a}\) by standard transformations. Accordingly, the olefin 106 was treated with osmium tetroxide and potassium ferricyanide as co-oxidant in the presence of (DHQ)\(_2\)AQN ligand under AD conditions\(^{10}\) to give the diol 107 in 91% yield with moderate diastereomeric selectivity \((dr = 5:1; \text{anti}:\text{syn})\) as an inseparable mixture of diastereomers. The IR spectrum of 107 gave broad hydroxyl absorption at 3400 cm\(^{-1}\). The hydroxyl protons appeared at \(\delta\) 1.73 and 1.59 as two broad singlets. In another attempt, to improve the selectivity and to examine the stereochemical outcome of the epoxidation reaction, we carried out epoxidation of olefin 106 using \(m\)-CPBA in various solvent systems in the presence of Na\(_2\)HPO\(_4\). Addition of phosphate could be effective in avoiding the unfavorable acid catalyzed ring opening of epoxide once formed.\(^{22}\) Thus compound 106 was treated with \(m\)-CPBA/Na\(_2\)HPO\(_4\) in CH\(_2\)Cl\(_2\) to afford the epoxide 108 in 92% yield \((dr = 4:1; \text{anti}:\text{syn})\) as a non separable mixture of diastereomers. Even with the use of different solvent systems, we could not improve the selectivity. The \(^1\)H NMR spectrum of 108 showed absence of olefin protons and epoxide protons appeared at \(\delta\) 2.67-2.76 (multiplet, two protons) and 3.27 (multiplet, one proton). The \(^{13}\)C NMR spectrum of 108 showed upfield carbons of epoxide at \(\delta\) 44.5, 43.5 and 52.3, 51.8 as a diastereomeric mixture.
Scheme 17. Reagents and conditions. (a) Ti(OPr-i)₄, (+)-DIPT, t-BuOOH, dry CH₂Cl₂, -20 °C, 4 days, 15%; (b) TBSTf, 2,6-lutidine, CH₂Cl₂, 0 °C, 30 min, 98%; (c) (DHQ)₂AQN (1 mol%), 0.1M OsO₄ (0.4 mol%), K₂CO₃, K₃Fe(CN)₆, t-BuOH/H₂O 1:1, 0 °C, 24 h, 91%; (d) m-CPBA, Na₂HPO₄, CH₂Cl₂, over night, 91%; (e) (R,R)-salen-Co-(OAc) (0.5 mol %), dist H₂O, 42 h, (94% for 108a, 90% for 108b according to the ratio of the starting material).

In order to get the diastereomically pure epoxide, we next attempted at the hydrolytic kinetic resolution method (HKR) developed by Jacobsen. The HKR method uses readily accessible cobalt-based chiral salen complexes as catalyst and water as the only reagent to afford the chiral epoxide and diol of high enantiomeric excess in excellent yields. These advantages have made it a very attractive asymmetric synthetic tool. While the HKR was successfully employed for the resolution of simple epoxides of small molecular weight, mono functional unbranched alkyl substituted epoxides and bis-epoxides, its application to the multifunctional epoxides has not been fully explored. Therefore, we decided to use this method for the resolution of epoxide 108, which would further extend the scope of this protocol for the multifunctionalized large molecules having olefin with pre-existing adjacent chiral centre. Thus epoxide 108 was resolved with R,R-salen-Co(OAc) complex (0.5 mol%) and water (0.4 eq) to yield the epoxide (2R, 3R, 3R, 5S)-108a in 94% yield (as calculated from
80% epoxide) and diol (2S, 3R, 3R, 5S)-108b in 90% yield (as calculated from 20% other epoxide). The diol 108b can be converted into the required epoxide by conventional method. It is interesting to note that while asymmetric epoxidation of 103 gave rather low yield of the product, the treatment of allylic alcohol 99 with titanium tetra-isopropoxide and t-butyl hydroperoxide in the presence of (+)-DIPT under the Sharpless asymmetric epoxidation conditions furnished the desired epoxide (2R, 3R, 3R, 5S)-109 in good yield and high diastereomeric excess (de = 95%) as judged by 1H and 13C NMR spectral analysis (Scheme 18). The 1H NMR spectrum of 109 showed absence of olefinic protons and epoxide protons appeared at δ 2.77-2.89 (multiplet, two protons) and 3.28 (multiplet, one proton). The 13C NMR spectrum of 109 showed upfield carbons of epoxide at δ 44.57 and 52.33. As expected the Sharpless kinetic resolution in the epoxidation reaction has pronounced effect in enhancing the diastereomeric purity of the desired product. The free secondary hydroxyl group was protected with TBSCI in the presence of imidazole and catalytic amount of DMAP to furnish compound 110 in excellent yield. The ring opening of the epoxide 110 with vinylmagnesium bromide in the presence of catalytic amount of CuI in THF at -20 °C furnished the homoallylic alcohol 50 in excellent yield having [α]D25 = -10.1 (c 0.64, CHCl3). The IR spectrum of 50 gave broad hydroxyl absorption at 3475 cm⁻¹. The 1H NMR spectrum of 50 gave olefin peaks at δ 5.91 (multiplet, one proton) and 5.10-5.20 (multiplet, two protons). Treatment of 50 with acryloyl chloride and Et3N in the presence of a catalytic amount of DMAP in CH2Cl2 provided the acrylate 51 in 88% yield having [α]D25 = -2.86 (c 0.64, CH2Cl2). The IR spectrum of 51 indicated absence of hydroxyl group, acryloyl carbonyl appeared at 1726 cm⁻¹. The carbonyl carbon appeared at δ 165.7 in the 13C NMR spectrum. Olefin metathesis of 51 with commercially available Grubbs' 1st generation catalyst26 (2 mol %) in the presence of Ti(OPr-i)4 (0.3 eq) in refluxing CH2Cl2 afforded the α,β-unsaturated δ-lactone 52 in 90% yield having [α]D25 = +71.6 (c 0.44, CH2Cl2). The IR spectrum of 52 showed characteristic carbonyl group absorption of α,β-unsaturated δ-lactone at 1644 cm⁻¹. The olefin protons appeared at δ 5.99 (doublet of doublet of doublet) with J = 8.2, 6.3, 2.0 Hz and 5.92 (doublet of doublet) with J = 9.7, 2.3 Hz in the 1H NMR spectrum. The olefinic carbons appeared at δ 146.84 and 120.67 in 13C NMR spectrum.

72
Global deprotection\textsuperscript{8h} of 52 using aqueous HF in CH\textsubscript{3}CN occurred slowly. Deacetylboronolide 1a was recovered in 65% after stirring 5 days at room temperature. Silyl ether was also recovered in 30% yield and could be recycled under the same deprotection conditions to give 1a and the resulting triol was acetylated with acetic anhydride to give (+)-boronolide 1.

In the same manner, the ring opening of epoxide 108a was carried out with vinylmagnesium bromide in the presence of catalytic amount of CuI in THF at −20 °C to furnish the homoallylic alcohol 111 in excellent yield (Scheme 19). Reaction of 111 with acryloyl chloride and Et\textsubscript{3}N in the presence of catalytic amount of DMAP in CH\textsubscript{2}Cl\textsubscript{2} provided the acrylate ester 112 in 91% yield.

\textbf{Scheme 18. Reagents and conditions.} (a) Ti(OPr-i)\textsubscript{4}, (+)DIPT, t-BuOOH, dry CH\textsubscript{2}Cl\textsubscript{2}, -20 °C, 48 h, 78% (yield based on 75% of syn compound); b) TBSCl, imidazole, cat. DMAP, CH\textsubscript{2}Cl\textsubscript{2}, 0 °C to rt, 98%; (c) CH\textsubscript{2}=CHMgBr, CuI, THF, -30 °C, 90%; d) Acryloyl chloride, Et\textsubscript{3}N, cat. DMAP, CH\textsubscript{2}Cl\textsubscript{2}, 0 °C to rt, 88%; e) 2 mol% (PCy\textsubscript{3})\textsubscript{2} Ru(Cl)\textsubscript{2}=CH-Ph, CH\textsubscript{2}Cl\textsubscript{2}, reflux, 16 h, 90%.

Olefin metathesis of 112 with commercially available Grubbs' 1\textsuperscript{st} generation catalyst\textsuperscript{26} (2 mol%) in the presence of Ti(i-PrO)\textsubscript{4} (0.3 eq) in refluxing CH\textsubscript{2}Cl\textsubscript{2} afforded the \(\alpha,\beta\)-unsaturated lactone 113 in 89% yield having [\(\alpha\)]\textsubscript{D}\textsuperscript{25} +51.4 (c 1.18, CHCl\textsubscript{3}). All protecting groups such as MOM and TBS were deprotected in the presence of BF\textsubscript{3}.SMe\textsubscript{2} and aq. HF to afford triol 1a, which was acetylated with acetic anhydride in the presence of Et\textsubscript{3}N and catalytic amount of DMAP to give (+)-boronolide 1 in 50% overall yield having m.p 101 °C, [lit.\textsuperscript{8h} mp 99-100 °C and [\(\alpha\)]\textsubscript{D}\textsuperscript{25} +57.4 (c 0.71, EtOH); lit.\textsuperscript{8h} [\(\alpha\)]\textsubscript{D}\textsuperscript{25} +56 (c 0.07, EtOH). The IR spectrum of 1
showed presence of acetyl carbonyls at 1744 cm\(^{-1}\). The \(^1\)H NMR spectrum of 1 gave acetyl methyl protons at \(\delta\) 2.11 (singlet, one methyl), 2.05 (singlet, one methyl), 2.03 (singlet, one methyl), the chiral protons at \(\delta\) 5.33-5.38 (multiplet, two protons), 5.01 (quartet with \(J = 6.01\) Hz, one proton), 4.55 (doublet of triplet with \(J = 12.1, 4.5\) Hz, one proton). The \(^{13}\)C NMR spectrum gave chiral carbons at \(\delta\) 75.1, 71.6, 70.6 and 70.5 and four carbonyl carbons at \(\delta\) 170.5, 169.8, 169.5 and 162.5. The physical and spectroscopic data were identical with those reported.\(^{8}\)

![Scheme 19. Reagents and conditions.](image)

**Scheme 19.** *Reagents and conditions.* (a) \(\text{CH}_2\text{CHMgBr, CuI, THF, -30 }^\circ\text{C, 86%},\) (b) Acryloyl chloride, \(\text{Et}_3\text{N, cat. DMAP, CH}_2\text{Cl}_2, 0 \text{ }^\circ\text{C to rt, 91%},\) (c) 2 mol\% (PCy\(_3\))\(_2\) Ru(Cl)\(_2\)=CH-Ph, \(\text{CH}_2\text{Cl}_2, \text{reflux, 8 h, 89%},\) (d) \(\text{BF}_3\text{SMe}_2, -30 \text{ }^\circ\text{C, then aq HF, CH}_3\text{CN, rt, then }\text{Ac}_2\text{O, Et}_3\text{N, cat DMAP, CH}_2\text{Cl}_2, \text{rt, (50% overall).}\)

2.3.3. Conclusion

In conclusion, a practical and stereoselective total synthesis of (+)-boronolide 1 has been achieved in 13 steps from commercially available valeraldehyde 93 in an overall yield of 18% using the Sharpless asymmetric dihydroxylation, chelation controlled addition of vinyl Grignard, epoxidation, Jacobson’s hydrolytic kinetic resolution and ring closing metathesis as the key steps. The HKR on the multifunctional terminal olefin having chiral centers was successfully utilized for the synthesis of boronolide. We believe our new approach is thus the most efficient route to (+)-boronolide reported so far and would permit maximum variability in product structure with regard to stereochemical diversity which is particularly important for making various synthetic analogues required for screening of biological activity.
2.4.1. Experimental Section

Hept-2-enoic acid ethyl ester (73).

To a nitrogen flushed solution of LiBr (35.29 g, 406.40 mmol) in dry THF (150 mL) was added \((\text{EtO})_2\text{P(O)COOEt}\) (21.87 g, 97.53 mmol) dropwise at room temperature for 15 min and followed by addition of \(\text{Et}_3\text{N}\) (22.65 mL, 162.56 mmol). The stirring was continued for another 15 min. To this was added the solution of aldehyde 93 (7 g, 81.28 mmol) in dry THF (20 mL). A white precipitate was formed several minutes after the addition of aldehyde. The reaction was stirred vigorously at room temperature until the full consumption of the aldehyde was observed (TLC). The precipitate was removed by passing the reaction mixture through a pad of silica gel in sintered glass funnel. The pad was washed with 400 mL of hexane/EtOAc 6:1. Concentration gave a colorless oil. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (19:1) as eluent gave compound 73\(^{81}\) as a colorless oil.

**Yield:** 11.30 g (89%).

**Mol. Formula:** \(\text{C}_9\text{H}_{16}\text{O}_2\)

**IR (neat, cm\(^{-1}\)):** \(\nu_{\text{max}}\) 2924, 2856, 1724, 1655, 1466, 1366, 1310, 1178, 1128, 1045, 980, 721.

**\(^1\text{H NMR (200 MHz, CDCl}_3\):** \(\delta \) 6.95 (dt, \(J = 15.7, 7.1\) Hz, 1H), 5.76 (dt, \(J = 15.7, 1.3\) Hz, 1H), 4.18 (q, \(J = 7.1\) Hz, 2H), 2.17 (q, \(J = 8\) Hz, 2H), 1.37-1.40 (m, 4H), 1.27 (t, \(J = 7.6\) Hz, 3H), 0.91 (t, \(J = 7.1\) Hz, 3H).

**\(^{13}\text{C NMR (50 MHz, CDCl}_3\):** \(\delta \) 165.9, 148.5, 132.0, 59.4, 31.4, 21.7, 13.7.

**Analysis:** Calcd.: C, 69.19; H, 10.32%; Found: C, 69.34; H, 10.12%.

(2\(R\), 3\(S\))-2,3-Dihydroxyheptanoic acid ethyl ester (74):

To a mixture of \(\text{K}_2\text{Fe(CN)}_6\) (18.98 g, 57.67 mmol), \(\text{K}_2\text{CO}_3\) (7.96 g, 57.69 mmol) and (DHQ)_2PHAL (149 mg, 1 mol%), in \(\text{t-BuOH-H}_2\text{O}\) (1:1, 75 mL) cooled at 0 °C was added \(\text{OsO}_4\) (0.769 mL, 0.1 M sol in toluene, 0.4 mol%) followed by methane sulfonamide (1.826 g, 19.23 mmol). After stirring for 5 min at 0 °C, the olefin 73 (3 g, 19.23 mmol) was added in

75
one portion. The reaction mixture was stirred at 0 °C for 24 h and then quenched with solid sodium sulfite (25 g). The stirring was continued for 45 min and the solution was extracted with EtOAc (3 × 50 mL). The combined organic phases were washed (10% KOH, then brine), dried (Na₂SO₄) and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (3:2) as eluent gave diol 74 as a colorless syrupy liquid.

Yield: 3.51 g (96%).

Mol. Formula: C₉H₁₈O₄

[α]D²⁴ⁿ : −8.8 (c 0.9, CHCl₃).

IR (neat, cm⁻¹): νmax 3400, 3133, 3018, 2926, 2854, 1732, 1460, 1401, 1215, 760, 667.

¹H NMR (200 MHz, CDCl₃): δ 0.88 (t, J = 7.3 Hz, 3H), 1.24-1.37 (m, 6H), 1.59 (t, J = 13.6 Hz, 3H), 3.20 (brs, 2H), 3.85 (dt, J = 6.8, 2.4 Hz, 1H), 4.06 (d, J = 2.4 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H).

¹³C NMR (50 MHz, CDCl₃): δ 13.7, 13.81, 22.3, 27.6, 32.9, 61.5, 72.4, 73.2, 173.5.

Analysis: Calcd.: C, 56.82; H, 9.54%; Found: C, 56.95; H, 9.33%.

(2R, 3S)-5-Butyl-2,2-dimethyl-[1,3]dioxolane-4-carboxylic acid ethyl ester (77):

To a solution of the diol 74 (2.45 g, 12.90 mmol), p-TSA (100 mg) in CH₂Cl₂ (75 mL) was added 2,2-dimethoxypropane (2.02 g, 19.35 mmol) and mixture stirred overnight. Solid NaHCO₃ (1 g) was added and stirred for 30 min. The reaction was filtered through a pad of neutral alumina and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (9:1) gave 77 as a colorless liquid.

Yield: 2.52 g (95%).

Mol. Formula: C₁₂H₂₂O₄

[α]D²⁴ⁿ : −13.2 (c 3.22, CHCl₃);

IR (neat, cm⁻¹): νmax 3400, 3133, 3018, 2926, 2854, 1732, 1460, 1401, 1215, 760, 667.

¹H NMR (200 MHz, CDCl₃): δ 4.20 (q, J = 8.0 Hz, 2H), 4.09 (m, 2H), 1.62 (t, J = 8.2 Hz, 3H), 1.44 (s, 3H), 1.42 (s, 3H), 1.27-1.35 (m, 6H), 0.89 (t, J = 7.0 Hz, 3H).

¹³C NMR (50 MHz, CDCl₃): δ 170.7, 110.5, 79.1, 60.9, 33.0, 27.0, 25.5, 22.3, 13.9, 13.6.

Analysis: Calcd.: C, 62.58; H, 9.63%; Found: C, 62.72; H, 9.48%.
(2R, 3S)-2,3-Bis-methoxymethoxyheptanoic acid ethyl ester (100).

To a solution of the diol 74 (2.10 g, 11.04 mmol) and diisopropylethyl amine (4.99 g, 38.64 mmol) in dry CH₂Cl₂ (50 mL) was added MOMCl (2.13 g, 26.49 mmol), under argon over 5 min at 0 °C and mixture allowed to warm to room temperature overnight. After cooling to 0 °C, the reaction mixture was quenched with water and extracted with CH₂Cl₂ (3 x 50 ml). The combined organic extracts were washed with water (3 x 50 mL), brine, dried (Na₂SO₄), and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (8:2) gave 100 as a colorless liquid.

Yield: 2.80 g (91%).

Mol. Formula: C₁₃H₂₆O₆

[α]₀²⁰ : +59.2 (c 2.21, CHCl₃).

IR (CHCl₃, cm⁻¹): νmax 3016, 2955, 2824, 2402, 1726, 1466, 1382, 1215, 1102, 1036.

¹H NMR (200 MHz, CDCl₃): δ 4.70 (s, 2H), 4.62 (s, 2H), 4.19 (m, 3H), 3.91 (m, 1H), 3.37 (s, 3H), 3.31 (s, 3H), 1.64 (t, J = 8.2 Hz, 3H), 1.22-1.30 (m, 6H), 0.88 (t, J = 7.1 Hz, 3H).

¹³C NMR (50 MHz, CDCl₃): δ 13.6, 13.8, 22.3, 27.2, 30.2, 55.4, 55.8, 60.5, 76.9, 77.3, 78.1, 96.3, 170.4.

Analysis: Calcd for.: C, 56.10; H, 9.42%; Found: C, 56.44; H, 9.12%.

2,3-Dibenzoylheptanoic acid ethyl ester (74a).

To a solution of the diol 74 (101 mg, 0.53 mmol) and dry pyridine (5 mL) was added benzoyl chloride (184 mg, 1.31 mmol) at 0 °C and mixture stirred over night at room temperature. The reaction mixture was quenched with 6N HCl (10 mL) and aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with water, saturated aqueous NaHCO₃, brine, dried (Na₂SO₄), and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (9.5:0.5) gave 74a as a colorless liquid.
Yield: 190 mg (90%).

Mol. Formula: C_{23}H_{26}O_{6}

\[ \alpha^0_{D} : 67.7 \text{ (c 1.03, CHCl}_3) \].

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 8.15 (dd, \( J = 12.4, 8.1 \text{ Hz, } 4\text{H} \)), 7.38-7.63 (m, 6H), 5.51 (d, \( J = 4.5 \text{ Hz, } 1\text{H} \)), 5.25 (m, 1H), 4.20 (q, \( J = 8.0 \text{ Hz, } 2\text{H} \)), 1.86-1.90 (m, 2H), 1.52 (m, 4H), 1.15 (t, \( J = 12.0 \text{ Hz, } 3\text{H} \)), 0.89 (t, \( J = 6.7 \text{ Hz, } 3\text{H} \)).

\(^{13}\)C NMR (50 MHz, CDCl\(_3\)): \( \delta \) 167.3, 165.7, 133.4, 133.0, 129.8, 129.6, 129.1, 128.4, 128.3, 73.1, 72.7, 61.6, 30.2, 27.2, 22.2, 13.9, 13.7.

Analysis: Calcd.: C, 69.33; H, 6.58%; Found: C, 69.01, H, 6.84%.

\((2S, 3S)-(5\text{-Butyl}-2,2\text{-dimethyl}[1,3]\text{-dioxolan-4-yl})\text{-methanol (97).}\)

To a solution of 77 (2.40 g, 10.42 mmol) in dry CH\(_2\)Cl\(_2\) (80 mL) at 0 °C was added drop wise DIBAL-H (25.8 mL, 25.8 mmol, 1M in toluene) through a syringe. The reaction mixture was allowed to warm to room temperature over 2 h, then re-cooled to 0 °C and treated with saturated sodium/potassium tartrate. The solid material was filtered through a pad of celite and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (7:3) as eluent gave 97 as a colorless oil.

Yield: 1.79 g (91%).

Mol. Formula: C\(_{10}\)H\(_{20}\)O\(_3\)

\[ \alpha^0_{D} : -21.5 \text{ (c 1.08, CHCl}_3) \].

IR (neat, cm\(^{-1}\)): \( \nu_{\text{max}} \) 3440, 2926, 1460, 1361, 1216, 764, 667.

\(^1\)H NMR (200 MHz, CDCl\(_3\)): \( \delta \) 3.75 (m, 2H), 3.58 (dd, \( J = 11.3, 3.9 \text{ Hz, } 2\text{H} \)), 2.17 (s, 1H), 1.44-1.62 (m, 2H), 1.42 (s, 3H), 1.41 (s, 3H), 1.37-1.42 (m, 4H), 0.91 (t, \( J = 6.7 \text{ Hz, } 3\text{H} \)).

\(^{13}\)C NMR (50 MHz, CDCl\(_3\)): \( \delta \) 13.7, 22.5, 26.8, 27.1, 27.9, 32.6, 62.0, 77.00, 81.6, 108.3.

Analysis: Calcd.: C, 63.80; H, 10.71%; Found: C, 64.09; H, 10.58%.

78
2,3-Bis-methoxymethoxyheptan-1-ol (101).

Compound 101 was prepared following the procedure as described for compound 97 as colorless oil.

Yield: 89%.

Mol. Formula: C₁₁H₂₄O₅

[α]D<sup>20</sup>: +7.69 (c 1.04, CHCl₃).

IR (CHCl₃, cm⁻¹): ν<sub>max</sub> 3453, 30.17, 2956, 2826, 2401, 1467, 1381, 1216, 1150, 1035, 918, 756.

¹H NMR (200 MHz, CDCl₃): 4.73 (d, J = 8.0 Hz, 2H), 4.66 (d, J = 6.1 Hz, 2H), 3.60-3.70 (m, 4H), 3.41 (s, 3H), 3.39 (s, 3H), 2.80 (s, 1H), 1.30-1.61 (m, 6H), 0.89 (t, J = 7.0 Hz, 3H).

¹³C NMR (50 MHz, CDCl₃): δ 13.9, 22.6, 27.8, 29.9, 55.6, 55.8, 62.3, 78.2, 81.9, 96.7, 97.5.

Analysis: Caled.: C, 55.91%; H, 10.24%; Found: C, 55.69%; H, 10.56%.

1-(5-Butyl-2,2-dimethyl-[1,3]-dioxolan-4-yl)-prop-2-en-1-ol (99).

To a solution of oxalyl chloride (1.405 g, 9.666 mL, 11.074 mmol) in dry CH₂Cl₂ (100 mL) at -78 °C was added dropwise dry DMSO (1.730 g, 1.57 mL, 22.15 mmol) in CH₂Cl₂ (20 mL). After 30 min, alcohol 97 (1.39 g, 7.382 mmol) in CH₂Cl₂ (20 mL) was added over 10 min giving a copious white precipitate. After stirring for 1 h at -78 °C the reaction mixture was brought to -60 °C and Et₃N (2.988 g, 2.169 mL, 29.53 mmol) was added slowly and stirred for 30 min allowing the reaction mixture to warm to room temperature. The reaction mixture was poured into water (150 mL) and the organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (2 x 50 mL) and combined organic layers were washed with water (3 x 50 mL), brine (50 mL), dried (Na₂SO₄) and passed through short pad of silica gel. The filtrate
was concentrated to give the aldehyde 98 (1.31 g) as pale yellow oil, which was used as such for the next step without purification.

The crude aldehyde 98 dissolved in CH₂Cl₂ under argon was added via cannula to a stirred suspension of MgBr₂·Et₂O in a 250 mL round bottom flask at 0 °C. After stirring for 10 min, the flask was cooled to -78 °C and treated with vinylmagnesium bromide (14.94 mL, 14.94 mmol) (purchased from Aldrich as 1.0 M solution in THF); the solvent was removed in vacuo and diluted with CH₂Cl₂ three times) over 30 min and allowed to warm to 0 °C. The reaction mixture was diluted with saturated NH₄Cl and extracted with CH₂Cl₂ (3 x 50 mL). Combined organic layer was washed with brine, dried (Na₂SO₄), and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (9:1) as eluent gave the allylic alcohol 99 as an inseparable mixture of diastereomers (syn:anti = 3:1) as a pale yellowish oil.

Yield: 1.39 g (92%).

Mol. Formula: C₁₂H₂₂O₃

IR (neat, cm⁻¹): ν max 3358-3250, 2924, 2855, 1466, 1372, 1220, 761, 669.

¹H NMR (200 MHz, CDCl₃): δ 5.81-5.91 (m, 1H), 5.34-5.39 (m, 1H), 5.26 (m, 1H), 4.28 - 4.30 (m, 1H), 3.91-3.96 (m, 1H), 3.69 (dd, J = 7.9, 3.9 Hz, 1H), 3.61 (dd, J = 7.5, 4.5 Hz, 1H, minor diastereomer), 1.49-1.60 (m, 3H), 1.39 (s, 6H), 1.31-1.36 (m, 3H), 0.89 (t, J = 7.1 Hz, 3H).

¹³C NMR (50 MHz, CDCl₃): δ 137.1, 136.3, 116.7, 116.3, 108.6, 108.3, 83.51, 83.0, 77.37, 77.2, 72.7, 72.2, 33.7, 33.0, 28.0, 27.3, 26.9, 22.5, 13.7 (mixture of diastereomers).

Analysis: Calcd.: C, 67.26; H, 10.35%, Found: C, 67.51; H, 10.11%.

4,5-Bis-methoxymethoxynon-1-en-3-ol (103).

Compound 103 was prepared following the procedure as described for compound 99 as an inseparable mixture of diastereomers (syn:anti = 19:1) as a pale yellowish oil. Yield: 90%.

Mol. Formula: C₁₃H₂₆O₅

[α]D²⁰ : +26.43 (c 0.8, CHCl₃).

80
Chapter II: Enantio- and Diastereoccontrolled Total Synthesis of (+)-Borolide

$^1$H NMR (200 MHz, CDCl$_3$): δ 5.87-6.04 (m, 1H), 5.36 (td, $J = 23.8$, 17.2 Hz, 2H), 4.79 (d, $J = 6.7$ Hz, 1H), 4.70 (d, $J = 6.7$ Hz, 1H), 4.68 (s, 2H), 4.32 (tt, $J = 5.5$, 1.6 Hz, 1H), 3.64-3.73 (m, 1H), 3.44 (s, 3H), 3.39 (s, 3H), 2.97 (br s, 1H), 1.58-1.68 (m, 2H), 1.26-1.35 (m, 4H), 0.88 (t, $J = 7$ Hz, 3H).

$^{13}$C NMR (50 MHz, CDCl$_3$): δ 13.8, 22.6, 27.3, 27.7, 30.1, 30.4, 55.7, 56.0, 71.6, 71.9, 78.1, 78.3, 83.0, 83.2, 96.6, 96.9, 97.9, 98.3, 115.9, 116.5, 137.3, 137.7.


[1-(1,2-Bis-methoxymethoxy-hexyl)-allyloxy]-tert-butyl-dimethyl-silane (106).

![Chemical Structure](image)

To a stirred solution of allylic alcohol 103 (1.20 g, 4.57 mmol) in CH$_2$Cl$_2$ (50 mL) and 2,6-lutidine (2.94 g, 3.175 mL, 27.44 mmol) was added TBSTf (1.33 g, 5.031 mmol) at 0 °C and mixture was stirred at the same temperature for 30 min. The reaction mixture was quenched with water and extracted with CH$_2$Cl$_2$ (3 x 30 mL). The combined organic layers were washed with brine, dried (Na$_2$SO$_4$), and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (3:1) as eluent gave compound 106 as a colorless oil.

Yield: 1.69 g (98%).

Mol. Formula: C$_{19}$H$_{40}$O$_5$Si

[$\alpha$]$^D$$_{CHCl_3}$: +31.90 (c 0.9, CHCl$_3$).

$^1$H NMR (200 MHz, CDCl$_3$): δ 5.88-6.04 (m, 1H), 5.16 (dd, $J = 27.3$, 17.8 Hz, 2H), 4.91 (d, $J = 7.04$ Hz, 1H), 4.71 (d, $J = 7.04$ Hz, 2H), 4.63 (s, 2H), 4.37 (t, $J = 6.7$ Hz, 1H), 3.56-3.64 (m, 1H), 3.40 (s, 3H), 3.38 (s, 3H), 1.51-1.74 (m, 2H), 1.26-1.33 (m, 4H), 0.89 (s, 12H), 0.06 (s, 3H), 0.03 (s, 3H).

$^{13}$C NMR (50 MHz, CDCl$_3$): δ 138.1, 115.4, 98.3, 96.9, 81.7, 77.6, 74.1, 55.8, 55.7, 30.9, 27.5, 25.7, 22.7, 17.9, 13.9, -4.8, -4.9.

Analysis: Calcd.: C, 60.60; H, 10.71; Found: C, 60.89, H, 10.42%. 

81
2,3-Bis-methoxymethoxy-1-oxiranyl-heptan-1-ol (105).

\[
\text{OMOMOH} \\
\text{OMOM} \\
\text{105}
\]

To a solution of titanium (IV) isopropoxide (475 mg, 1.67 mmol) (-)-diisopropyl-D-tartrate (0.46 g, 1.97 mmol) in CH\(_2\)Cl\(_2\) (20 mL) at -20 °C was added the olefin 103 (399 mg, 1.52 mmol) in CH\(_2\)Cl\(_2\) (4 mL) followed by tert-butyl hydroperoxide (273 mg, 3.03 mmol). The reaction mixture was stirred for 4 days at -20 °C and then diluted with ether and saturated sodium sulphate. The mixture was stirred vigorously for 2 h at room temperature and filtered. The filtrate was concentrated and residue was chromatographed over silica gel to give epoxide 105 (63 mg, 15%) as a colorless oil.

3-(tert-Butyl-dimethylsilanyloxy)-4,5-bis-methoxymethoxynonane-1,2-diol (107).

\[
\text{OMOMOTBS} \\
\text{OMOMOH} \\
\text{107}
\]

To a mixture of K\(_3\)Fe(CN)\(_6\) (915 mg, 2.78 mmol), K\(_2\)CO\(_3\) (384 mg, 2.78 mmol) and (DHQ)\(_2\)AQN (7.8 mg, 1 mol %), in t-BuOH-H\(_2\)O (1:1, 5 mL) cooled at 0 °C was added OsO\(_4\) (0.79 mL, 0.1 M soln in toluene, 0.4 mol %). After stirring for 5 min at 0 °C, the olefin 106 (346 mg, 0.92 mmol) was added in one portion. The reaction mixture was stirred at 0 °C for 24 h and then quenched with solid sodium sulfite (2 g). The stirring was continued for 45 min and the solution was extracted with EtOAc (3 x 50 mL). The combined organic phases were washed (10% KOH, then brine), dried (Na\(_2\)SO\(_4\)) and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (3:2) as eluent gave diol 107 (347mg, 91%) as an inseparable mixture of diastereomers (5:1) in form of a colorless syrupy liquid.

(2,3-Bis-methoxymethoxy-1-oxiranyloxy)-tert-butyldimethylsilane (108).
To a stirred solution of olefin 106 (0.940 g, 2.49 mmol) and Na$_2$HPO$_4$ (709 mg, 4.99 mmol) in THF (30 mL) was added m-CPBA (1.72 g, 4.99 mmol) at 0 °C. The mixture was stirred for 1 h and then overnight at room temperature. The solution was treated with saturated aqueous NaHCO$_3$ and Na$_2$S$_2$O$_3$ and extracted with CH$_2$Cl$_2$. The organic layer was washed with brine, dried (Na$_2$SO$_4$), and concentrated. Silica gel column chromatography using pet ether/EtOAc (9:1) as eluent gave the epoxide 108 (0.89 g, 91%) as an inseparable mixture of diastereomers (anti:syn = 4:1) as a colorless syrupy liquid.

Hydrolytic kinetic resolution of epoxide 108.

A solution of epoxide 108 (0.574 g, 1.46 mmol) and (R,R)-salen-Co(III)-OAc (4 mg, 0.007 mmol) in THF (10 μL) was stirred at 0 °C for 5 min, and then distilled water (10 μL, 0.584 mmol) was added. After stirring for 42 h, it was concentrated and purified by silica gel column chromatography using pet ether/EtOAc (8:2) to afford 108a as a colorless syrupy liquid as a single diastereomer. (Determined by $^1$H NMR and $^{13}$C NMR analysis). Continued chromatography with pet ether/EtOAc (3:2) provided the diol 108b as a brown color liquid as a single diastereomer.

Data of compound 108a.

Yield: 431 mg (94%).

Mol. Formula: C$_{19}$H$_{40}$O$_6$Si

[α]$_D^2$: -7.1 (c 1.28, CHCl$_3$).

IR (neat, cm$^{-1}$): $\nu_{\text{max}}$ 2954, 2932, 2893, 2859, 1471, 1376, 1361, 1252, 1215, 1102, 1042, 919, 839, 776, 759.

$^1$H NMR (200 MHz, CDCl$_3$): $\nu$ 4.80 (d, $J = 6.1$ Hz, 1H), 4.74 (d, $J = 6.3$ Hz, 2H), 4.65 (d, $J = 6.5$ Hz, 1H), 3.81 (m, 1H), 3.62 (dd, $J = 6.2$, 4.0 Hz, 1H), 3.57 (m, 1H), 3.39 (s, 3H), 3.37 (s, 3H), 3.27 (m, 1H), 2.67-2.76 (m, 2H), 1.61-1.66 (m, 2H), 1.25-1.36 (m, 4H), 0.91 (s, 12 H), 0.08 (s, 3H), 0.06 (s, 3H).

$^{13}$C NMR (50 MHz, CDCl$_3$): $\nu$ 96.6, 96.3, 83.3, 79.9, 55.6, 55.2, 52.9, 44.2, 28.5, 25.7, 22.9, 17.9, 13.9, -4.86, -5.33.
Data of compound 108b.

Yield: 103 mg (90%).

Mol. Formula: C₁₀H₁₄O₇Si

\[ \alpha \] : +19.6 (c 1.03, CHCl₃).

IR (neat, cm⁻¹): \( \nu \)max 3400, 2933, 2862, 1473, 1367, 1214, 1179, 1027, 929, 874, 638, 758.

^1H NMR (200 MHz, CDCl₃): \( \delta \) 4.79 (d, \( J = 6.6 \) Hz, 1H), 4.74 (d, \( J = 6.3 \) Hz, 1H), 4.71 (d, \( J = 6.4 \) Hz, 2H), 3.91 (m, 2H), 3.86 (m, 2H), 3.63 (m, 2H), 3.44 (s, 3H), 3.42 (s, 3H), 1.73 (br s, 1H), 1.59 (br s, 1H), 1.26-1.39 (m, 6H), 0.91 (t, \( J = 7.1 \) Hz, 3H), 0.89 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H).

^13C NMR (50 MHz, CDCl₃): \( \delta \) 97.8, 96.7, 80.5, 77.0, 72.6, 70.6, 63.3, 56.1, 55.8, 30.8, 27.6, 25.7, 22.6, 22.5, 17.8, 13.8, -4.3, -5.0.

Analysis: Calcd.: C, 55.58; H, 10.31%; Found: C, 55.69; H, 10.12%.

(5-Butyl-2,2-dimethyl-[1,3]-dioxolan-4-yl)-oxiranylmethanol (109).

To a solution of titanium (IV)isopropoxide (729 mg, 2.56 mmol), (-)-diisopropyl-D-tartrate (710 mg, 3.03 mmol) in CH₂Cl₂ (20 mL) at -20 °C was added olefin 99 (500 mg, 2.33 mmol) in CH₂Cl₂ (4 mL) followed by tert-butyl hydroperoxide (420 mg, 0.52 mL, 4.66 mmol). After 48 h at -20 °C, the reaction mixture was diluted with ether and saturated sodium sulphate. The mixture was stirred vigorously for 2 h at room temperature and filtered. The filtrate was concentrated and residue was chromatographed over silica gel to give epoxide 109 as a colorless oil.

Yield: 314 mg (78%); yield based on 75% of syn compound.

Mol. Formula: C₁₂H₂₂O₄

\[ \alpha \] : -3.7 (c 0.9, CHCl₃).

IR (neat, cm⁻¹): \( \nu \)max 3453, 2956, 2931, 2893, 2859, 1379, 1254, 1192.
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boronolide

\( ^1H \text{NMR} \) (200 MHz, CDCl\(_3\)): \( \delta \) 4.02-4.09 (m, 1H), 3.83-3.90 (m, 1H), 3.68 (t, \( J = 7.13 \text{ Hz}, 1H \)), 3.22-3.28 (m, 1H), 2.77-2.89 (m, 2H), 2.09 (s, 1H), 1.46-1.66 (m, 3H), 1.42 (s, 3H), 1.39 (s, 3H), 1.26-1.36 (m, 3H), 0.91 (t, \( J = 7.1 \text{ Hz}, 3H \)).

\( ^13C \text{NMR} \) (50 MHz, CDCl\(_3\)): \( \delta \) 108.9, 81.3, 79.5, 71.5, 52.3, 44.6, 33.8, 28.2, 27.4, 27.0, 22.7, 13.9.

**Analysis:** Calculated: C, 62.58%; H, 9.63%; Found: C, 62.78; H, 9.41%.

tert-Butyl-[(5-butyl-2,2-dimethyl-[1,3]-dioxolan-4-yl)-oxiranylmethoxy]dimethyl-silane (110).

![Chemical Structure](image)

To a stirred solution of epoxy alcohol 109 (0.40 g, 1.737 mmol) and imidazole (260 mg, 3.82 mmol) in CH\(_2\)Cl\(_2\) (50 mL) was added TBSCl (0.392 g, 2.61 mmol) at 0°C and the reaction mixture was stirred at the same temperature for 30 min. The reaction mixture was quenched with water and extracted with CH\(_2\)Cl\(_2\) (3 x 30 mL). The combined organic layers were washed with brine, dried (Na\(_2\)SO\(_4\)), and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (9:1) as eluent gave compound 110 as a colorless oil.

**Yield:** 586 mg (98%).

**Mol. Formula:** C\(_{18}\)H\(_{36}\)O\(_4\)Si

\([\alpha]_D^21: -18.1 \text{ (c} 0.8, \text{ CHCl}_3\)."

\( ^1H \text{NMR} \) (200 MHz, CDCl\(_3\)): \( \delta \) 3.91-4.12 (m, 2H), 3.68 (t, \( J = 7.2 \text{ Hz}, 1H \)), 3.24 (m, 1H), 2.72-2.88 (m, 2H), 1.48-1.66 (m, 2H), 1.43 (s, 3H), 1.39 (s, 3H), 1.24-1.37 (m, 4H), 0.91 (s, 12H), 0.08 (s, 3H), 0.06 (s, 3H).

\( ^13C \text{NMR} \) (50 MHz, CDCl\(_3\)): \( \delta \) 108.7, 81.4, 78.9, 72.3, 53.4, 43.9, 33.7, 28.3, 27.4, 27.0, 24.5, 22.8, 16.2, 13.86, -4.8, -4.9.

**Analysis:** Calculated: C, 62.74%; H, 10.53%; Found: C, 62.46; H, 10.87%.

85
1-(5-Butyl-2,2-dimethyl-[1,3]dioxolan-4-yl)-1-(tert-butyldimethylsilyloxy)-pent-4-en-2-ol (50).

A round bottom flask was charged with copper(I)iodide (0.011 g, 0.06 mmol), gently heated under vacuum and slowly cooled with a flow of argon. After the addition of THF (20 mL), this suspension was cooled to –20 °C, stirred and vinylmagnesium bromide (1.22 mL, 1.21 mmol, 1M in THF) was added to it. A solution of epoxide 110 (0.21 g, 0.609 mmol) in THF (5 mL) was added to the above reagent and the mixture was stirred at –20 °C for 1 h. After consumption of starting material, the reaction mixture was quenched with a saturated aqueous solution of NH₄Cl. The water layer was extracted with EtOAc (3 x 50 mL). The combined organic layer was washed with brine, dried (Na₂SO₄), and concentrated. Purification of crude product by silica gel column chromatography using pet ether/EtOAc (8:2) as eluent afforded 50 as a colorless liquid.

Yield: 204 mg (90%).

**Mol. Formula**: C₂₀H₄₀O₄Si

\[ \alpha_{D}^{20} = -10.1 \ (c \ 0.64, \ CHCl₃), \ \text{lit.}^{[3]} -9.10 \ (c \ 0.17, \ CH₂Cl₂). \]

**IR** (neat, cm⁻¹): \( \nu_{\text{max}} \) 3475, 2858, 1608.

**¹H NMR** (200 MHz, CDCl₃): \( \delta \) 5.91 (m, 1H), 5.10-5.20 (m, 2H), 4.07 (m, 1H), 3.75-3.86 (m, 2H), 3.69 (dd, \( J = 4.6, 2.8 \) Hz, 1H), 1.44-1.56 (m, 4H), 1.43 (s, 3H), 1.42 (s, 3H), 1.32-1.41 (m, 2H), 0.95 (s, 9H), 0.92 (t, \( J = 7.2 \) Hz, 3H), 0.12 (s, 3H), 0.11 (3H).

**¹³C NMR** (50 MHz, CDCl₃): \( \delta \) 134.0, 117.2, 108.5, 81, 32, 73.4, 71.9, 38.5, 32.8, 28.3, 27.3, 26.8, 25.9, 22.8, 18.2, 13.9, -4.4, -4.5.

**Analysis: Calcd.**: C, 64.47; H, 10.82; **Found**: C, 64.62; H, 10.71%.
Acrylic acid 1-[(5-buty1-2,2-dimethyl-[1,3]dioxolan-4-yl)-(tert-butyldimethylsilyloxy)-methyl]-but-3-enyl ester (51).

Acryloyl chloride (0.034 g, 0.376 mmol) was added drop wise under argon to a solution of 50 (140 mg, 0.376 mmol) and triethylamine (0.152 g, 1.50 mmol) in dry CH₂Cl₂ (10 mL) at 0 °C. The mixture was stirred overnight at room temperature. The resulting mixture was filtered through a pad of celite and poured into water and organic layer was separated. The aqueous layer was extracted with CH₂Cl₂ (3 x 30 mL) and combined organic layer was washed with brine, dried (Na₂SO₄), and concentrated. Purification of crude product by silica gel column chromatography using pet ether/EtOAc (19:1) as eluent afforded 51 as a yellowish syrupy liquid.

Yield: 173 mg (88%).

Mol. Formula: C₂₃H₄₂O₅Si

[α]D²⁰: -2.86 (c 0.64, CH₂Cl₂); lit.¹ [α]D²⁰: -2.46 (c 0.65, CH₂Cl₂).

IR (neat, cm⁻¹): νₘₐₓ 3029, 2956, 2931, 2859, 1644, 1464, 1255, 1102, 1036, 918, 873, 837, 776.

¹H NMR (200 MHz, CDCl₃): δ 5.83-6.04 (m, 1H), 5.07-5.17 (m, 2H), 4.78 (d, J = 6.7 Hz, 1H), 4.73 (t, J = 1.96 Hz, 3H), 3.60-3.88 (m, 1H), 3.75 (t, J = 3.52 Hz, 1H), 3.61-3.68 (m, 1H), 3.43 (s, 3H), 3.41 (s, 3H), 1.55-1.76 (m, 2H), 1.21-1.36 (m, 6H), 1.21 (s, 12H), 0.12 (s, 3H), 0.10 (s, 3H).

¹³C NMR (50 MHz, CDCl₃): δ 116.2, 99.1, 96.4, 85.8, 79.3, 73.6, 70.1, 55.7, 37.2, 29.4, 28.6, 25.8, 22.7, 18.0, 14.1, -4.4, -4.9.

Analysis: Calcd.: C, 64.75; H, 9.92%; Found: 64.94%; H, 9.72%.
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boropinolide

6-[(5-Butyl-2,2-dimethyl-[1,3]dioxolan-4-yl)-(tert-butyldimethylsilanyloxy)-methyl]-5,6-dihydropyran-2-one (52).

Grubb's catalyst (5 mg, 0.0056 mmol) dissolved in CH$_2$Cl$_2$ (10 mL) was added drop wise to a refluxing solution of acrylate 51 (120 mg, 0.281 mmol), Ti(i-PrO)$_4$ (24 mg, 0.08 mmol) in dry CH$_2$Cl$_2$ (60 mL). Refluxing was continued for 16 h by which time all the starting material was consumed. The solvent was removed under reduced pressure and the crude product was purified by silica gel column chromatography using pet ether/EtOAc (9:1) as eluent to afford 52 as a yellowish syrupy liquid.

Yield: 91 mg (90%).

Mol. Formula: C$_{21}$H$_{38}$O$_3$Si

[α]$_D^2$: +71.6 (c 0.44, CH$_2$Cl$_2$); lit.$^{[3]}$ +69.2 (c 0.30, CH$_2$Cl$_2$).

$^1$H NMR (500 MHz, CDCl$_3$): δ 0.13 (s, 3 H), 0.14 (s, 3 H), 0.91 (t, J = 7.3 Hz, 3 H), 0.92 (s, 9 H), 1.30-1.41 (m, 3 H), 1.38 (s, 6 H), 1.46-1.56 (m, 3 H), 2.56 (ddd, J = 19.3, 5.4, 4.0 Hz, 1 H), 2.75 (ddd, J = 18.8, 12.6, 2.7 Hz, 1 H), 3.61 (dd, J = 8.1, 2.4 Hz, 1 H), 3.96-4.04 (m, 2 H), 4.54 (dd, J = 12.6, 4.0, 2.0 Hz, 1 H), 5.99 (dd, J = 9.8, 3.1 Hz, 1 H), 6.95 (ddd, J = 8.7, 6.3, 2.1 Hz, 1 H).

$^{13}$C NMR (50 MHz, CDCl$_3$): δ 45.3, -4.5, -3.4, 14.2, 18.7, 23.0, 24.5, 26.3, 27.1, 27.8, 28.6, 33.0, 72.2, 76.8, 81.2, 82.4, 108.9, 120.6, 146.8, 164.1.

Analysis: Calcd.: C, 63.28; H, 9.61%; Found: C, 63.44; H, 9.81%.
The spectroscopic data (IR, $^1$H NMR, & $^{13}$C NMR) were in accord with those described.$^{8h}$

5-(tert-Butyldimethylsilanyloxy)-6,7-bis-methoxymethoxy-undec-1-en-4-ol (111).

Compound 111 was prepared following the procedure as described for compound 50 as a colorless liquid.
Yield: 86%.

Mol. Formula: $C_{21}H_{44}O_6Si$

$[\alpha]_D^{25} = +26.3$ (c 0.9, CHCl$_3$).

IR (neat, cm$^{-1}$): $\nu_{max}$ 3029, 2956, 2931, 2859, 1644, 1464, 1255, 1102, 1036, 918, 873, 837, 776.

$^1H$ NMR (200 MHz, CDCl$_3$): $\delta$ 5.83-6.04 (m, 1H), 5.07-5.17 (m, 2H), 4.78 (d, $J = 6.7$ Hz, 1H), 4.73 (t, $J = 1.96$ Hz, 3H), 3.80-3.88 (m, 2H), 3.75 (t, $J = 3.52$ Hz, 1H), 3.64-3.68 (m, 1H), 3.43 (s, 3H), 3.41 (s, 3H), 2.17-2.25 (m, 2H), 1.60-1.72 (m, 2H), 1.21-1.36 (m, 4H), 0.89 (s, 12H), 0.12 (s, 3H), 0.10 (s, 3H).

$^{13}C$ NMR (50 MHz, CDCl$_3$): $\delta$ 136.2, 116.2, 99.1, 96.4, 85.8, 79.3, 73.6, 70.1, 55.7, 37.2, 29.6, 28.6, 25.7, 22.7, 18.0, 13.9, -4.8, -4.9.

Analysis: Caled.: C, 59.96; H, 10.54; Found: C, 60.11; H, 10.61.

Acrylic acid 1-[1-(tert-butyldimethylsilanyloxy)-2,3-bis-methoxymethoxy-heptyl]-but-3-enyl ester (112).

![Chemical Structure](image)

Compound 112 was prepared following the procedure as described for compound 51 as a yellowish syrupy liquid.

Yield: 91%.

Mol. Formula: $C_{24}H_{46}O_7Si$

$[\alpha]_D^{25} = -42.14$ (c 0.84, CHCl$_3$).

IR (neat, cm$^{-1}$): $\nu_{max}$ 2931, 2858, 1726, 1638, 1254, 1256, 1192.

$^1H$ NMR (200 MHz, CDCl$_3$): $\delta$ 6.45 (ddd, $J = 17.2$, 1.6 Hz, 1H), 6.09 (dd, $J = 17.2$, 4.3 Hz, 1H), 5.83 (dd, $J = 10.2$, 1.5 Hz, 1H), 5.75 (dd, $J = 11.7$, 1.6 Hz, 1H), 5.18 (m, 1H), 5.01 (m, 1H), 4.67 (m, 2H), 4.54 (m, 2H), 3.64-3.66 (m, 1H), 3.92 (dt, $J = 8.2$, 1.6 Hz, 1H), 3.37-3.42 (m, 2H), 3.33 (s, 3H), 3.30 (s, 3H), 2.24-2.48 (m, 2H), 1.27-1.34 (m, 6H), 0.81 (s, 12 H), -0.04 (s, 3H), -0.05 (s, 3H).
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boronolide

\[ ^{13}C \text{ NMR} \] (50 MHz, CDCl\(_3\)): \( \delta \) 165.7, 134.6, 131.7, 128.2, 117.1, 98.8, 96.9, 80.8, 79.4, 75.82, 74.4, 74.0, 56.1, 56.0, 32.8, 29.6, 29.4, 28.5, 22.7, 18.2, 14.1, -4.1, -4.7.

Analysis: Calcd.: C, 60.72; H, 9.77%; Found: C, 61.09; H, 9.62%.

6-[1-(tert-Butyldimethylsilyloxy)-2,3-bis-methoxymethoxyheptyl]-5,6-dihydropyran-2-one (113).

![Chemical Structure of 113](image)

Compound 113 was prepared following the procedure as described for compound 52 as a colorless syrupy liquid.

Yield: 89%.

Mol. Formula: C\(_{22}\)H\(_{42}\)O\(_7\)Si

\[ [\alpha]_D^{n} = +51.4 \ (c \ 1.18, \ CHCl_3) \].

IR (neat, cm\(^{-1}\)): \( \nu_{\max} \) 2954, 2934, 2856, 1712, 1469, 1386, 1252, 1149, 1123, 1102, 1018, 923, 838, 779.

\[ ^1H \text{ NMR} \] (200 MHz, CDCl\(_3\)): \( \delta \) 5.92 (ddd, \( J = 8.2, 6.3, 2.0 \) Hz, 1H), 5.99 (dd, \( J = 9.7, 2.3 \) Hz, 1H), 4.58-4.82 (m, 4H), 4.21 (dd, \( J = 8.2, 1.7 \) Hz, 1H), 3.62-3.70 (m, 1H), 3.46-3.49 (m, 2H), 3.39 (s, 6H), 2.77 (m, 1H), 2.17 (ddd, \( J = 19.9, 5.9, 3.9 \) Hz, 1H), 1.31-1.42 (m, 6H), 0.88 (s, 12H), 0.16 (s, 3H), 0.11 (s, 3H).

\[ ^{13}C \text{ NMR} \] (50 MHz, CDCl\(_3\)): \( \delta \) 164.0, 145.6, 120.7, 98.9, 96.4, 79.2, 78.28, 78.21, 73.8, 56.1, 55.9, 29.6, 28.3, 25.9, 22.9, 22.7, 18.2, 14.0, -4.2, -4.3.

Analysis: Calcd.: C, 59.16; H, 9.48%; Found: C, 59.45; H, 9.34%.

Deacetylated boronolide (1a).

![Chemical Structure of 1a](image)

Lactone 113 (182 mg, 0.41 mmol) was dissolved in dimethyl sulfide (3 mL) and cooled to -10 \(^\circ\)C. Then, BF\(_3\).Et\(_2\)O (1.02 mL, 8.15 mmol) was added to the solution, which was stirred at the
room temperature for 30 min. The reaction mixture was quenched with water and extracted with CH₂Cl₂. The combined organic layer was washed with brine, dried (Na₂SO₄), and concentrated to give an oily material which was dissolved in MeCN (5 mL) and treated with 45% aq HF (172 mg, 0.15 mL, 4.1 mmol) at room temperature. After stirring at room temperature for over night, the reaction mixture was quenched with NaHCO₃ (1 g) and the aqueous layer was extracted with CH₂Cl₂ and organic layer was washed with brine, dried (Na₂SO₄), and concentrated. Silica gel column chromatography of the crude product using EtOAc as eluent gave deacetylated boronolide 1a as a white solid.

**Yield:** 106 mg (86%).

**Mol. Formula:** C₁₂H₂₀O₅

**m.p.:** 101 °C, [lit.⁷h m.p 99-100 °C].

[α]D²⁺ : +57.4 (c 0.71, EtOH); lit.⁷h [α]D²⁺ +56 (c 0.07, EtOH).

**¹H NMR** (200 MHz, CDCl₃): δ 6.95 (ddd, J = 9.6, 6.1 Hz, 1H), 6.02 (dd, J = 10.1, 2.6 Hz, 1H), 4.52 (ddd, J = 11.5, 7.3, 4.1 Hz, 1H), 3.85 (d, J = 7.1 Hz, 1H), 3.64 (br s, 2H), 3.01 (br s, 3H), 2.64 (ddd, J = 18.7, 5.2, 4.2 Hz, 1H), 2.51 (ddd, J = 18.8, 11.5, 2.5 Hz, 1H), 1.46-1.66 (m, 2H), 1.26-1.34 (m, 4H), 0.89 (t, J = 7.1 Hz, 3H).

**¹³C NMR** (50 MHz, CDCl₃): δ 163.9, 145.9, 120.9, 77.1, 76.7, 74.3, 70.1, 33.4, 27.7, 25.8, 22.6, 14.0.

**boronolide (1).**

Acetic anhydride (0.18 mL, 1.96 mmol) was added drop wise to a stirred and cooled (0 °C) solution of 1a (48 mg, 0.196 mmol), i-Pr₂EtN (0.5 mL, 2.94 mmol), DMAP (catalytic amount) in CH₂Cl₂ (5 mL). The resulting mixture was allowed to stir for 6 h at room temperature. The resulting mixture was diluted with Et₂O (40 mL). The organic phase was washed with saturated NH₄Cl, water, brine, dried (Na₂SO₄), and concentrated. Silica gel column chromatography of the crude product using petroleum ether/EtOAc (7:3) as eluent gave compound 1 as a clear oil which solidified on standing.
Yield: 62 mg (85%).

Mol. Formula: C_{18}H_{26}O_{8}

m.p: 88-90 °C [lit.\textsuperscript{7} mp 90 °C].

[\alpha]_{D}^{25}: +26.4 (c 0.7, EtOH); lit.\textsuperscript{7b} [\alpha]_{D}^{25} +25 (c 0.2, EtOH).

\textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{3}): \delta 6.89 (ddd, J = 9.7, 6.2, 2.7 Hz, 1H), 6.01 (dd, J = 9.8, 2.4 Hz, 1H), 5.33-5.38 (m, 2H), 5.01 (q, J = 6.1 Hz, 1H), 4.55 (dt, J = 12.1, 4.5 Hz, 1H), 2.51 (dddd, J = 18.1, 11.8, 2.6, 2.5 Hz, 1H), 2.31 (m, 1H), 2.11 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.54 (m, 2H), 1.17-1.30 (m, 4H), 0.89 (t, J = 6.7 Hz, 3H).

\textsuperscript{13}C NMR (50 MHz, CDCl\textsubscript{3}): \delta 170.5, 169.8, 169.5, 162.5, 144.0, 121.2, 75.1, 71.6, 70.6, 70.5, 30.1, 27.1, 25.2, 22.3, 21.1, 20.6, 13.8.
2.4.2. Spectra

1] \(^1\)H NMR Spectrum of 73
2] \(^{13}\)C NMR Spectrum of 73
3] \(^1\)H NMR Spectrum of 74
4] \(^{13}\)C NMR Spectrum of 74
5] \(^{13}\)C NMR Spectrum of 77
6] \(^1\)H NMR Spectrum of 100
7] \(^{13}\)C NMR Spectrum of 100
8] \(^1\)H NMR Spectrum of 74a
9] \(^{13}\)C NMR Spectrum of 74a
10] HPLC of 74a
11] \(^1\)H NMR Spectrum of 97
12] \(^{13}\)C NMR Spectrum of 97
13] \(^1\)H NMR Spectrum of 101
14] \(^{13}\)C NMR Spectrum of 101
15] \(^1\)H NMR Spectrum of 99
16] \(^{13}\)C NMR Spectrum of 99
17] NOSEY of 104
18] \(^1\)H NMR Spectrum of 103
19] \(^{13}\)C NMR Spectrum of 103
20] \(^1\)H NMR Spectrum of 106
21] \(^{13}\)C NMR Spectrum of 106
22] \(^1\)H NMR Spectrum of 108a
23] \(^{13}\)C NMR Spectrum of 108a
24] \(^1\)H NMR Spectrum of 108b
25] \(^{13}\)C NMR Spectrum of 108b
26] \(^1\)H NMR Spectrum of 109
27] \(^{13}\)C NMR Spectrum of 109
28] \(^1\)H NMR Spectrum of 52
29] \(^{13}\)C NMR Spectrum of 52
30] \(^1\)H NMR Spectrum of 111
31] \(^{13}\)C NMR Spectrum of 111
32] \(^1\)H NMR Spectrum of 112
33] \(^{13}\)C NMR Spectrum of 112
34] \(^1\)H NMR Spectrum of 113
35] \(^{13}\)C NMR Spectrum of 113
36] \(^1\)H NMR Spectrum of 1a
37] \(^{13}\)C NMR Spectrum of 1a
38] \(^1\)H NMR Spectrum of 1
39] \(^{13}\)C NMR Spectrum of 1

93
Chapter II: Enantio- and Diastereocntrolled Total Synthesis of (+)-Boronolide

\[ \text{\textsuperscript{1}H NMR Spectrum of 73} \]

\[ \text{\textsuperscript{13}C NMR Spectrum of 73} \]
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (−)-Boronolide

\[ \text{HO} \quad \text{CO} \quad \text{OEt} \]

74

$^1H$ NMR Spectrum of 74

\[ \text{HO} \quad \text{CO} \quad \text{OEt} \]

74

$^{13}C$ NMR Spectrum of 74

94
\[ 13^C \text{ NMR Spectrum of 77} \]
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boronolide

1H NMR Spectrum of 100

13C NMR Spectrum of 100
Chapter II: Enantio- and Diastereoccontrolled Total Synthesis of (+)-Boronolide

$^1$H NMR Spectrum of 74a

$^{13}$C NMR Spectrum of 74a
**Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boronolide**

![Chemical Structure of 74a](image)

**Result Table - Calculation Method Uncal**

<table>
<thead>
<tr>
<th>Peak No.</th>
<th>Retention Time (min)</th>
<th>Area (c.u.)</th>
<th>Height (mV)</th>
<th>WID (min)</th>
<th>Area (%)</th>
<th>Height (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21.17</td>
<td>170.3245</td>
<td>0.574</td>
<td>0.613</td>
<td>1.135</td>
<td>2.995</td>
</tr>
<tr>
<td>2</td>
<td>23.593</td>
<td>13351.8468</td>
<td>280.708</td>
<td>0.780</td>
<td>99.875</td>
<td>97.901</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>13521.1733</td>
<td>256.083</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HPLC of 74a**

98
Chapter II: Enantio- and Diastereocntrolled Total Synthesis of (+)-Boronolide

$^1$H NMR Spectrum of 97

$^{13}$C NMR Spectrum of 97
Chapter II: Enantio- and Diastereocntrolled Total Synthesis of (+)-Boronolide

\[ \text{\textsuperscript{1}H NMR Spectrum of 101} \]

\[ \text{\textsuperscript{13}C NMR Spectrum of 101} \]

100
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boronolide

NOESY

NOE SY of 104
Chapter II. Enantio- and Diastereoccontrolled Total Synthesis of (+)-Boronolide

$^1$H NMR Spectrum of 103

$^{13}$C NMR Spectrum of 103
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boranolide

$^1$H NMR Spectrum of 106

$^{13}$C NMR Spectrum of 106
Chapter II: Enantio- and Diastereoccontrolled Total Synthesis of (+)-Boronolide

$^{1}H$ NMR Spectrum of 108a

$^{13}C$ NMR Spectrum of 108a
Chapter II: Enantio- and Diastereoccontrolled Total Synthesis of (+)-Boranolide

\[ \text{OMOM OTBS} \]
\[ \text{OMOM OH} \]
\[ 108b \]

$^1$H NMR Spectrum of 108b

\[ \text{OMOM OTBS} \]
\[ \text{OMOM OH} \]
\[ 108b \]

$^{13}$C NMR Spectrum of 108b
Chapter II: Enantio- and Diastereocntrolled Total Synthesis of (+)-Boronolide

\[ \text{Spectrum of } 52 \]

\[ ^1H \text{ NMR Spectrum of } 52 \]

\[ \text{Spectrum of } 52 \]

\[ ^{13}C \text{ NMR Spectrum of } 52 \]
Chapter II: Enantio- and Diastereoccontrolled Total Synthesis of (+)-Boronolide

$^1$H NMR Spectrum of 112

$^{13}$C NMR Spectrum of 112
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boronolide

\(^1\)H NMR Spectrum of 113

\(^{13}\)C NMR Spectrum of 113
Chapter II: Enantio- and Diastereocontrolled Total Synthesis of (+)-Boronolide

$^1$H NMR Spectrum of 1a

$^{13}$C NMR Spectrum of 1a
Chapter II: Enantio- and Diastereoccontrolled Total Synthesis of (+)-Boronolide

\[ \text{H NMR Spectrum of 1} \]

\[ \text{\textsuperscript{13}C NMR Spectrum of 1} \]
2.5. REFERENCES


18. For the measurement of enantiomeric excess, the diol 4a was converted into its dibenzoate 4d. The enantiomeric purity of the dibenzoate 4d was estimated to be >96% by chiral HPLC analysis (Chiral Cel OD, petroleum ether- iPrOH (98:2) 1 mL/min, 240 mm.

