CHAPTER 4

Development of an organocatalytic approach to the synthesis of (2R,3S)-hexane-1,2,3,5-tetraol stereoisomers: Application to stereoselective synthesis of Botryolide E, Stagonolide C, 9-epi-Stagonolide C, Decarestrictine O, Ophiocerin A, B and C
4.1 Introduction

Despite extensive research, development of an efficient and simple protocol for the synthesis of complicated organic molecule always throws a challenge to the synthetic organic chemist. Among them, one of the most vital challenge is to construct a pliable and stereodivergent route which leads to various potent compounds from a common starting material. Simple chiral synthons having high functional density and multiple stereogenic centres are common interest in this regard. In continuation of our work on the enantioselective synthesis of hydroxylated pyrans and naturally occurring unsaturated lactones, we have taken up the asymmetric synthesis of some bioactive molecules 1-7 (Figure 1), that contain (2R,3S)-hexane-1,2,3,5-tetraol derivatives 133 (having different stereomers and protecting groups) as the general structural motif. Hence in the present

![Chemical Structures](image)

**Figure 1**: Representative hydroxylated pyrans and unsaturated lactones

work, we have developed a conceptually novel and efficient strategy for the synthesis of the common intermediate 133 employing proline catalyzed intermolecular aldol reaction between acetone and D-(R)-glyceraldehyde acetonide as the key steps. We used all the
stereomers derived from common intermediate 133 for the asymmetric synthesis of following molecules.

(i) **Ophiocerin A, B & C (1,2,3)**, bearing a tetrahydropyran ring with an interesting array of substituents was isolated from freshwater aquatic fungi *Ophioceras venezuelense* and is found in a wide variety of natural products that show broad spectrum biological activity.²

(ii) **Botryolide-E (4)** which was isolated from cultures of the fungicolous *Botryotrichum sp.* (NRRL 38180) and showed promising anti-bacterial activity against *Bacillus subtilis* (MTCC 441), *Staphylococcus aureus* (MTCC 96), *Escherichia coli* (MTCC 443) as well as antifungal activity against *Aspergillus niger* (MTCC 1344) and *Saccharomyces cerevisiae* (MTCC 171).³

(iii) **Decarestrictine O (5)** isolated from various *Penicillium* strains, shows interesting activity against cell line tests with HEP-G2 liver cells as it has inhibitory effect on cholesterol biosynthesis. Due to this property, decarestrictine O has been marked as a new class of cholesterol lowering drugs.⁴

(iv) **Stagonolide C (6)**, a ten membered lactone was isolated from *Cirsium arvense*, have attracted considerable attention due to its potential mycoherbicide nature by causing necrotic leison on leaves.⁵

Due to their wide variety of biological activities and interesting structural features with an array of functionalities, such as stereochemically pure hydroxyl appendage and/or accurately placed olefinic moiety with well defined geometry, the above compounds have attracted attention of synthetic chemists as prominent synthetic targets and therefore a great deal of interest has been devoted for their synthesis.

The synthetic approach described so far for botryolide-E involves either chiral pool approach or asymmetric transformation of chiral propylene oxide or allylation of acetaldehyde. The previous syntheses of ophiocerin A, B and C were reported using chiral pool such as carbohydrate or (R)-(−)-4 penten-2-ol or tartaric acid and asymmetric transformation of chiral epoxide or Sharpless kinetic resolution. Likewise, a few comparatively tedious and lengthy syntheses of decarestrictine O have been reported involving either from chiral building block or asymmetric dihydroxylation. There are some literature reports on synthesis of stagonolide C which employ well established RCM protocol or chiral pool approach or metal-enzyme combined DKR strategies.
4.2 Review of Literature:

Literature precedence of Ophiocerin A, B and C:6,7,8,9,10

The previous syntheses of ophiocerin A, B and C are already discussed in Chapter 2 (Section B, Page 52-57).

Literature precedence of Botryolide E:

There are few synthetic methods described in literature on the synthesis of botryolide E as discussed below.

Venkateswarlu et al. (2011)11

Venkateswarlu et al. reported the first synthesis of botryolide E starting from chiral propylene oxide (Scheme 1). Epoxide opening using THP protected alkyne followed by TBDPS protection provided 8. Later, depyranylnation provided 9 and partial reduction of double bond followed by TBDPS deprotection furnished 10. Selective TBS protection and acetylation (10→11) followed by dihydroxylation and subsequent acetonide protection afforded compound 12. Desilylation of 12 and subsequent oxidation of alcohol followed by Wittig olefination furnished 13. Finally, one-pot acid mediated acetonide deprotection and intramolecular cyclization provided botryolide E.

Scheme 1: Reagents and conditions: (a) THP protected prop-2-yn-1-ol, n-BuLi, BF₃.OEt₂, THF, -78°C, 3h, 75%; (b) TBDPSCI, Imidazole, DMAP, 3h, 93%; (c) PPTS, MeOH, 5h, 85%; (d) Red-Al, THF, 0°C to rt, 12h, 88%; (e) PTSA (cat), MeOH, rt, 6h, 93%; (f) TBSCl, Imidazole, 4h, 92%; (g) Ac₂O, pyr, 0°C to rt, 3h, 93%; (h) AD mix α, MeSO₂NH₂, 1BuOH/water (1:1), 0°C, 24h, 86%; (i) 2,2-DMP, PTSA (cat), DCM, rt, 1h, 88%; (j) (i) IBX,dry DMSO, DCM, 5h, 92%; (ii) Ph₃P=CHCO₂Et, MeOH, 0°C, 24h, 76.1%; (k) 80% aq AcOH, 24h, 0°C to rt, 97%.
Madabhushi et al. (2012)\textsuperscript{12}

Madabhushi et al. described the first chiral pool synthesis of botryolide E in enantiomeric form with 40% overall yield in 12 steps starting from (+)-diethyl-(L)-tartrate using Wacker oxidation, stereoselective keto reduction as well as modified Horner-Wadsworth-Emmons olefination as the key steps. (Scheme 2)

\textit{Scheme 2}: Reagents and conditions: (a) 2,2-DMP, PTSA, dry benzene, 60°C, 8h, 90%; (b) LAH, THF, 70°C, 4h, 95%; (c) BnBr, NaH, THF, rt, 5h, 82%; (d) IBX, dry DMSO, DCM, 5h; (e) PPh\textsubscript{3}+C\textsubscript{2}H\textsubscript{5}I, nBuLi, THF, -78°C, 2h, 90%; (f) PdCl\textsubscript{2}, CuCl, DMF/H\textsubscript{2}O (7:1), O\textsubscript{2}, 60°C, 6h, 91%; (g) (i) K-selectride, THF, -78°C, 2h; (ii) LiEt\textsubscript{3}BH, -78°C, 1h, 90%; (h) Ac\textsubscript{2}O, pyr, 0°C to rt, 5h, 93%; (h) 5% Pd/C, H\textsubscript{2}, 6h, rt, 97%; (i) 2,2-DMP, PTSA (cat), DCM, rt, 1h, 88%; (j) (i) IBX, dry DMSO, DCM, 5h, 92%; (ii) (PhO)\textsubscript{2}P(O)CH\textsubscript{2}CO\textsubscript{2}Et, NaH, THF, -78°C, 3h, 76.1%; (k) 50% aq TFA, 12h, 0°C to rt, 95%.

Das et al. (2012)\textsuperscript{13}

Das et al. reported the asymmetric synthesis of botryolide E starting from acetaldehyde and applying asymmetric allylation, Sharpless asymmetric dihydroxylation, chelation controlled diastereoselective vinylation and ring closing metathesis reaction using Grubbs 1st generation catalyst as the key steps. (Scheme 3)

\textit{Scheme 3}: Reagents and conditions: (a) (i) ref 13 b (ii) Ac\textsubscript{2}O, TEA, 0°C to rt, 54h, 91%; (b) (i) K\textsubscript{3}Fe(CN)\textsubscript{6}, K\textsubscript{2}CO\textsubscript{3}, K\textsubscript{2}OsO\textsubscript{4}.2H\textsubscript{2}O, (DHQD)\textsubscript{2}PHAL, \textsuperscript{1}BuOH/water (1:1), 0°C, 8h,
83%; (ii) TBSCl, imidazole, DMAP, 3h, 81%; (c) (i) TBDPSCI, imidazole, DMAP, 8h, 87%; (ii) PPTS, MeOH, rt, 12h, 79%; (d) (i) PCC, DCM, rt, 5h, 84%; (ii) CH₂=CHMgBr, MgBr₂·OEt₂, DCM, -78°C, 12h, 61%; (e) CH₂=CHCOCl, DIPEA, DCM, 0°C, 5h, 84%; (f) (i) Grubbs I catalyst, DCM, reflux, 6h, 69%; (ii) TBAF, THF, 1h, 64%.

Venkateswarlu et al. (2013)\textsuperscript{14}
After first successful synthesis of botryolide E via HKR, Venkateswarlu et al. also developed a highly concise protecting group free synthesis of botryolide E via Hoveyda-Grubbs cross metathesis, modified Horner-Wadsworth-Emmons olefination and selective asymmetric dihydroxylation. (Scheme 4)

Scheme 4: Reagents and conditions: (a) (i) CH₂=CHMgBr, CuI, THF, -20°C, 12h, 85%; (ii) Ac₂O, TEA, 0°C to rt, 3h, 90%; (c) (i) CH₂=CHCHO, dry DCM, Hoveyda-Grubbs catalyst, 3h, rt, 92% (ii) (CF₃CH₂O)₂P(O)CH₂CO₂Me, NaH, THF, -78°C, 2h, 76%, (e) AD mix α, tBuOH/water (1:1), 0°C, 24h, 86%.

Literature precedence of decarestrictine O:

Krishna et al. (2010)\textsuperscript{15}
Krishna et al. reported the first stereoselective synthesis of decarestrictine O via RCM protocol starting from chiral propylene oxide and 1,3-butane diol. The acid functionalities are derived from Sharpless asymmetric epoxidation followed by allylic alcohol formation and Pinnic oxidation whereas the alcohol fragment was synthesized by the ring opening of propylene oxide using THP protected propargyl alcohol followed by protection-deprotection and LAH reduction.
Synthesis of acid fragment 128 (scheme 5):

Scheme 5: Reagents and conditions: (a) (i) (+) DIPT, Ti(OPr)4, cumenehydroperoxide, DCM, -20°C, 12h, 75%; (b) i) CCl4, PPh3, NaHCO3, reflux, 1h; (ii) Na/ether, 0°C to rt, 3h; (c) PMBBr, NaH, THP, 0°C to rt, 12h, 90%; (d) TBAF, THF, 2h, 91%; (e) (i) (COCl)2, DMSO, NEt3, DCM, 1h; (ii) NaClO2, NaH2PO4, 2H2O, t-BuOH/2-methyl-2-butene, 0°C to rt, 12h.

Synthesis of alcohol fragment (scheme 6):

Scheme 6: Reagents and conditions: (a) ref 15b; (b) BzCl, NEt3, rt; (ii) AD mix β, 75% (iii) 2,2-DMP, PTSA, DCM; (c) K2CO3, MeOH, 2h, 75%; (d) (i) (COCl)2, DMSO, NEt3, DCM; (ii) Ph3P*CH3I, t-BuOK, THF, 0°C, 8h, 78%; (e) DDQ, DCM/H2O (19:1), rt, 1h, 93%.

Completion of synthesis (scheme 7):

Scheme 7: Reagents and condition: (a) (i) 2,4,6-trichlorobenzoylchloride, NEt3, THF, 0°C to rt, 4h, then DMAP, 39, toluene, 0°C to rt, 12h, 88%; (b) TFA, DCM, rt, 1h.
Yadav et al. (2012)\textsuperscript{16}

Yadav et al. described asymmetric total synthesis of decarestrictine O, a polyketide natural product. The total synthesis involves proline catalyzed $\alpha$-aminoxylation, Wittig olefination, HKR and RCM as crucial steps. Improved efficiency was achieved by applying the DIBAL-H mediated reduction of trans-dimethyl L-tartrate acetonide into $\varepsilon$-hydroxy-$\alpha,\beta$-unsaturated ester in a one step.

**Synthesis of alcohol fragment (scheme 8):**
The synthesis of alcohol fragment from dimethyl tartrate is shown in scheme 8.

\begin{align*}
\text{MeOOC} & \quad \text{a} \quad \text{MeOOC} \quad \text{b} \quad \text{c,d} \\
\text{COOMe} & \quad \text{42} \quad \text{OH} \quad \text{COOEt} \\
\text{OH} & \quad \text{e} \quad \text{OH} \quad \text{f} \quad \text{g} \\
\text{COOEt} & \quad \text{44} \quad \text{45} \quad \text{46} \\
\text{O} & \quad \text{h} \quad \text{O} \\
\text{47} & \quad \text{48} \\
\end{align*}

Scheme 8: Reagents and conditions: (a) 2,2-DMP, cat. PTSA, benzene, reflux, 2 h; (b) DIBAL-H, [(EtO)$_2$P(O)CHCO$_2$Et]$^+$ Na$, -78^\circ\text{C}$ to rt; (c) H$_2$, Pd/C, EtOAc, 3 h; (d) (i) IBX, DMSO, DCM, 0$^\circ\text{C}$ to rt, 2 h; (ii) Ph$_3$P$^+$CH$_3$I, $^1$BuOK, THF, -10$^\circ\text{C}$ to rt, 2 h; (e) DIBAL-H, -78$^\circ\text{C}$ to rt, 1 h; (f) (i) IBX, DMSO, DCM, 0$^\circ\text{C}$ to rt, 2 h; (ii) PhNO, D-proline, DMSO, NaBH$_4$, MeOH, CuSO$_4$.5H$_2$O, -20$^\circ\text{C}$ to rt over two steps; (g) TsCl, Et$_3$N, Dibutyl tin oxide (cat), dry DCM, 0$^\circ\text{C}$ to rt, 12 h; (h) LiAlH$_4$, THF, reflux, 3 h.

**Synthesis of acid fragment (scheme 9):**

\begin{align*}
\text{BnO} & \quad \text{a} \quad \text{BnO} \quad \text{b,c} \\
\text{49} & \quad \text{50} \quad \text{51} \quad \text{52} \\
\end{align*}

Scheme 9: Reagents and conditions: (a) Me$_3$S$^+$T, n-BuLi, THF, -20$^\circ\text{C}$, 3 h; (b) TBSCI, imidazole, DMAP, DCM, 0$^\circ\text{C}$ to rt, 2 h, 81%; (c) Li/naphthalene, dry THF, -20$^\circ\text{C}$, 3 h, (d) (i) IBX, DMSO, DCM, 0$^\circ\text{C}$ to rt, 2 h, (ii) NaClO$_2$, NaH$_2$PO$_4$, 2-methyl-2-butene, $^1$BuOH, H$_2$O, 6 h.
Completion of synthesis (scheme 10):

Scheme 10: Reagents and condition: (a) DCC, DMAP, DCM, 0°C to rt; (b) Grubb’s II catalyst, DCM, reflux, 16 h; (c) PTSA, MeOH, 0°C to rt, 2 h.

Srihari et al. (2014)¹⁷

Srihari et al. described a facile chiral pool synthesis of decaerectinie-O using L-(+)-diethyl tartrate as starting material. This conventional and flexible strategy employed Wittig homologation and RCM as key reaction for the synthesis of title molecule.

Synthesis of both acid and alcohol fragment (Scheme 11):

Scheme 11. Reagents and conditions: (a) (i) 2,2-DMP, benzene, cat. pTSA, 80°C, 12 h, 92%, (ii) LiAlH₄, THF, 45°C, 5 h; (b) BnBr, NaH, THF, 0°C to rt, 12 h; (c) (i) (COCl)₂, DMSO, DCM, Et₃N, -78°C, 2.5 h, 85%, (ii) PPh₃CH₂OCH₂Cl, LiHMDS, THF, -10°C to rt, 12 h, (iii) Hg(OAc)₂, THF, then H₂O (1.2 ratio w.r.t THF), NaBH₄, 0°C to rt, 1 h; (d) imidazole, TBDMSCl, DCM, 0°C to rt, 2 h; (e) H₂, Pd/C, THF, rt, 12 h. (f) (i) (COCl)₂,
DMSO, DCM, Et$_3$N, -78°C, 2.5 h, (ii) PPh$_3$CH$_3$I, tBuOK, THF, 0°C to rt, 12 h; (ii) 1.0 M TBAF, THF, 0°C to rt, 2 h; (g) (i) IBX, DCM, DMSO, 0°C to rt, 6 h, (ii) MeMgI, diethylether, -40°C, 5 h; (h) I$_2$, TPP, imidazole, THF, 0°C to rt, 2 h; (i) nBuLi, THF, -78°C, 2 h; (j) MOMCl, DIPEA, DCM, 0°C to rt, 12 h; (k) 1.0 M TBAF, THF, 0°C to rt, 2 h; (l) (i) IBX, DCM, DMSO, 0°C to rt, 6 h, 81%, (ii) 2-methyl-2-butene, NaH$_2$PO$_4$, NaClO$_2$, tBuOH/H$_2$O (1:1), acetone, 0–5°C, 12 h.

**Completion of total synthesis (Scheme 12):**

Both the acid and alcohol fragment were coupled using DCC followed by RCM using Grubbs second generation catalyst to provide compound 159 which, on acidification gave the title compound.

![Scheme 12](image)

**Scheme 12.** Reagents and conditions: (a) DCC, DMAP, DCM, 0°C to rt, 12 h; (b) Grubb’s 2nd generation catalyst, DCM, reflux, 12 h; (c) (i) BF$_3$-$\cdot$OEt$_2$, DMS, 0°C, 20 min, (ii) 1 M HCl, THF, 2 h.

**Literature precedence of stagonolide C:**

*Nanda et al. (2009)*$^{18}$

Nanda described the chemo-enzymatic asymmetric total synthesis of stagonolide C. A metal–enzyme combined DKR strategy was successfully applied to access two advanced intermediates 70 and 78. Coupling of these two intermediates followed by ring-closing metathesis with Grubbs-second generation catalyst afforded the target molecule.
Scheme 13: Reagents and conditions: (a) NaH, TBSCl, 90%; (b) (COCl)$_2$, DMSO, Et$_3$N, -78°C, 88%; (c) Vinylmagnesium bromide, -78°C, 82%; (d) CAL-B, isopropenyl acetate, chlorodicarbonyl(1-(isopropylamino)-2,3,4,5-tetraphenylcyclopentadienyl) ruthenium(II), K$_2$CO$_3$, KO'Bu 90%; (e) K$_2$CO$_3$, MeOH, 94%; (f) PMBO-(C=NH)-CCl$_3$, CSA, 85%; (g) PPTS, MeOH, 88%; (h) PDC, DMF, 72%.

Scheme 14: Reagents and conditions: (a) NaH, PMBBr, TBAI (cat), 80%; (b) CAL-B, isopropenyl acetate, chlorodicarbonyl(isopropylamino)-2,3,4,5-tetraphenylcyclopentadienyl ruthenium (II), K$_2$CO$_3$, KO'Bu, 92%; (c) K$_2$CO$_3$, MeOH, 90%; (d) imidazole, TBDDPSCI, 95%; (e) DDQ, DCM/H$_2$O (19:1), 86%; (f) (COCl)$_2$, DMSO, Et$_3$N, -78°C, 92%; (g) Vinyl MgBr, -78°C, 80%; (h) TPP, DIAD, PhCO$_2$H, NaOH, 90% in two steps; (k) PMBO-(C=NH)-CCl$_3$, CSA, 82%; (l) TBAF, THF, 90%.
Scheme 15: Reagents and conditions: (a) EEDQ, THF, 92%; (b) DDQ, DCM/H2O (19:1), 85%; (c) Grubbs-II, CH2Cl2, 66%.

Nagaiah et al. (2012)\textsuperscript{19}

Nagaiah reported the stereoselective synthesis of stagonolide C. The pivotal functionalities are derived from Barbier allylation, an epoxidation by m-CPBA, a chiral-auxiliary mediated acetate aldol addition, a 1,3-\textit{anti}-reduction, a Sharpless kinetic resolution, a Yamaguchi macro lactonization and ring-closing metathesis.

Scheme 16: Reagents and conditions: (a) Ref. 15; (b) Zn, Allyl bromide, THF, 88%; (c) TBDPSCI, imidazole, DCM, 95%; (d) m-CPBA, DCM, 88%; (e) DIBAL, -78 °C CH2Cl2, 82%; (f) TBAF, THF, 92% (g) TBDPSCI, imidazole, DCM, 92%; (h) PPTS, MeOH, 86%; (i) (i)TPP, I\textsubscript{2}, imidazole, toluene, Reflux, 10%; (ii) Zn, DMF, Reflux, 86% (j) TBAF, THF, 91%; (k) TBDPSCI, imidazole, 90%.

Scheme 17: Reagents and conditions: (a) NaH, BnBr, TBAI (Cat.), 90%; (b) PCC, CH2Cl2, 92%; (c) Vinlymagnesium bromide, THF, -78 °C, 88%; (d) (-)-DET, Ti(O\textsuperscript{Pr})\textsubscript{4}, TBHP, DCM, 4 Å, MS, -20 °C, 6 h, 46%; (e) TBDPSCI, imidazole, DCM, 95%; (f) DDQ, DCM:H2O (9:1), reflux 90%; (g) PCC, NaOAc, DCM, 90%; (h) NaClO\textsubscript{2}, NaH2PO\textsubscript{4}, 2-methyl-2-butene, t-BuOH, H2O, 92%.
Scheme 18: Reagents and conditions: (a) 2,4,6-Trichloro benzoyl chloride, Et$_3$N, THF, DMAP, 0°C rt, 14 h, 86%; (b) HF/pyridine, Pyridine, THF, 0°C to rt, 8 h, 84%; (c) Grubbs-II, DCM, reflux, 24 h, 68%.

Yadav et al. (2012)$^{20}$

Yadav described a flexible, efficient synthesis of stagonolide C, involving Prins cyclization and RCM as the key steps.

Scheme 19: Reagents and conditions: (a) MeCHO, CF$_3$COOH, DCM, then K$_2$CO$_3$, MeOH, r.t, 5 h, 55%; (b) TsCl, Et$_3$N, DCM, 0°C to r.t., 3 h, 90%; (c) MeOCH$_2$Cl, $^i$Pr$_2$EtN, DCM, 0°C to r.t., 6 h, 94%; (d) NaI, acetone, reflux, 24 h, 95%; (e) NaH, DMF, r.t., 6 h; (f) SiO$_2$, 72%; (g) O$_3$, Ph$_3$P, DCM, then Ph$_3$P=CH$_2$, THF, -78 to 0°C, 74%; (h) K$_2$CO$_3$, MeOH, r.t., 2 h, 96%.

Scheme 20: Reagents and conditions: (a) Ref. 17; (b) H$_2$, Pd/C, AcOEt, reflux, 2 h, 90%; (c) I$_2$, Ph$_3$P, imidazole, THF, 0°C to r.t., 4 h, 80%; (d) Zn, EtOH, reflux, 2 h 86%; (e) MeOCH$_2$Cl, $^i$Pr$_2$EtN, DMAP (cat.), DCM, 0°C to r.t., 3 h, 82%; (f) 2N NaOH, MeOH,
r.t., 6 h, 85%; (g) **102**, DCC, DMAP, DCM, 0 °C to r.t., 2 h; 80%; (h) Grubbs II-gen. catalyst, DCM, reflux, 24 h, 60%; (i) Me$_3$SiBr, DCM, -40 °C, 15 min, 76%.

**Qiao et al. (2012)**

This protocol involved the utilization of previously developed chiral epoxide intermediate, Julia–Lythgoe coupling of two fragments and Yamaguchi esterification for intramolecular cyclization to achieve total synthesis of the target compound. This synthesis exemplified the usage of Mulzer epoxide as chiral building block.

**Scheme 21:** Reagents and conditions: (a) NaH, PMBCl, 86%; (b) LiAlH$_4$, 96%; (c) TBSOTf, 2,6-lutidine, DCM, 100%; (d) 50% TFA, DCM, 50%; (e) NaIO$_4$, THF/H$_2$O, quant.

**Scheme 22:** Reagents and conditions: (a) Ref.19; (b) PMBO-(C=NH)-CCl$_3$, PPTS, DCM, 70%; (c) 1-Phenyl-5-mercapto-tetrazole, K$_2$CO$_3$, acetone, 84%; (d) $m$-CPBA, DCM, 82%.

**Scheme 23:** Reagents and conditions: (a) NaHMDS, HMPA, -78 °C, 60%; (b) MeOH, CSA, 90%; (c) LiOH, 98%; (d) 2,4,6-trichlorobenzoyl chloride, Et$_3$N, THF, then DMAP, Benzene, 63%; (e) CAN, MeCN:H$_2$O (10:1), 100%.
Sudalai et al. (2012)\textsuperscript{22}

Sudalai et al. reported the synthesis of stagonolide C from readily available homo allylic alcohol. Proline mediated $\alpha$-aminoxylation and epoxidation of aldehydes are the key steps. The formation of the 10-membered lactone moiety was finally achieved via esterification and RCM reactions.

**Synthesis of alcohol (scheme 24):**

![Scheme 24](image)

**Scheme 24.** Reagents and conditions: (A) TBSCI, imid, DCM, 0–25°C, 6 h; (B) ethyl acrylate, Grubbs-II (10 mol %), DCM, reflux, 12 h; (c) DIBAL-H, toluene, -78°C, 1 h; (d) $\text{H}_2\text{O}_2$, DCM, (10 mol %) (R)-a,a-bis[3,5-bis(trifluoromethyl)phenyl]-2-pyrrolidinemethanol trimethylsilyl ether, 25°C, 4 h then NaBH$_4$, MeOH, 0°C, 1 h; (e) (i) I$_2$, PPh$_3$, imid., Et$_2$O/CH$_3$CN (3:1), 0–25°C, 2 h, (ii) Zn, NaI, MeOH, reflux, 3 h; (f) MOMCl, DIPEA, dry DCM, 16 h; (g) TBAF, THF, 2 h.

**Synthesis of acid fragment (scheme 25):**

![Scheme 25](image)

**Scheme 25.** Reagents and conditions: (a) (i) PhNO (1 equiv), D-proline (20 mol %), CH$_3$CN, -20°C, 24 h then NaBH$_4$, MeOH, 0°C, 1 h, (ii) 10% Pd/C, H$_2$, MeOH, 24 h; (b) (i) TsCl, Et$_3$N, Bu$_2$SnO, DMAP, (ii) K$_2$CO$_3$, MeOH, 30 min; (c) TMSI, NaH, dry THF, 0°C, 2 h; (d) MOMCl, DIPEA, dry DCM, 16 h; (e) TBAF, THF, 2 h; (f) TEMPO, PhI(OAc)$_2$, CH$_3$CN:H$_2$O (4:1), 25°C, 4 h.
Completion of synthesis (Scheme 26):

Scheme 26. Reagents and conditions: (i) EDCI.HCl, Et$_3$N, DMAP, DCM, 0–25°C, 6 h, (ii) Grubbs-II (10 mol %), dry DCM, reflux, 24 h, (iii) Me$_3$SiBr, DCM, -40°C, 6 h.
4.3 Present work

In the present study, we report our successful attempt towards the total synthesis of all these molecule (Fig 1, 1-7) using a common building block derived from very popular environment friendly, non toxic proline catalyzed diastereoselective intermolecular aldol reaction and α-aminoxylation of aldehyde, as the key steps.

4.4 Result and Discussion:

Retrosynthetic analysis of pyrans (1,2,3) and unsaturated lactones (4,5,6,7):

Our retrosynthetic approach for the synthesis of hydroxylated pyrans (1,2,3) and α,β-unsaturated lactone molecules (4,5,6,7) was envisioned via the synthetic route as shown in Scheme 27. From retrosynthetic analysis shown in scheme 27, compound 133 was visualized as a common intermediate for the synthesis of ophiocerin A,B and C.

Preparation of key intermediate (Scheme 28):

To commence the synthesis of key intermediate 133 as shown in scheme 27, the aldol product β-hydroxy ketone 130 was prepared from D-proline catalyzed aldol reaction between acetone and D-(R)-glyceraldehyde acetonide. Protection of alcohol as tert-butyl diphenylsilyl (TBDPS) ether provided compound 131 which, upon subsequent
Scheme 28: Reagents and conditions: (a) 30 mol % D-proline, 5h, rt. 65%; (b) imidazole, TBDPSCl, rt, 8h, 95%; (c) CeCl$_3$·7H$_2$O, NaBH$_4$, MeOH, -78°C, 2h. 80%; (d) (i) PMBCl, NaI, DIPEA, 150°C, 3h (ii) PPTS (catalytic), MeOH, 12h, rt, 90%.

reduction of carbonyl with NaBH$_4$ and CeCl$_3$·7H$_2$O$^{30}$, furnished protected 1,3-diol 132 as a inseparable mixture of diastereomer in a 75:25 ratio. Under weak basic conditions$^{31}$, the free hydroxy group of 132 was protected as PMB ether followed by deprotection of acetonide with PPTS in methanol to furnish 133 as separable diasteromers. Flash column chromatography separation of 133 afforded diastereomer 133a in 75% yield along with the other diastereomer 133b in 25% yield.

Synthesis of ophiocerin A,B and C:
According to retrosynthetic analysis shown in scheme 27, compound 133 was visualized as a commom direct intermediate for the synthesis of ophiocerin A,B and C and all these compounds can be prepared by the fine modulation of both free hydroxy group of 133.

Synthesis of ophiocerin C (1) from intermediate 133a is presented in scheme 29. The diol 133 a was converted to desired syn epoxide 134 in 70% yield via consecutive three steps sequence which involves chemoselective mono benzylation of diol followed by mesylation of secondary alcohol and subsequent in situ internal nucleophilic substitution of secondary mesylate by treatment of base (K$_2$CO$_3$ in MeOH). Desilylation of compound 134 using TBAF in THF at rt furnished 135 in 85% yield. Dimethylsulfonium methylide$^{32}$ (generated from trimethylsulfonium iodide and n-BuLi) mediated ring opening of epoxide 135 followed by protection of diol as acetonide with 2,2-dimethoxypropane in presence of catalytic amount of PPTS in dry DCM afforded 136 in
80% yield. Subsequent removal of the PMB group using DDQ<sup>33</sup> furnished hydroxy alkene 137 in 82% yield. Ozonolysis of 137 followed by reduction with NaBH₄ and

**Scheme 29.** Reagents and conditions: (a) (i) Bu₂SnO, BzCl, NEt₃, DCM (ii) MsCl, NEt₃, DCM (iii) K₂CO₃, MeOH, rt, 1h, 70% (3 steps) (b) TBAF, THF, rt, 2 h, 85% (c) (i)
(CH$_3$)$_3$S$^+$, n-BuLi, THF, -20 °C (ii) 2,2-DMP, PPTS (catalytic), dry DCM, 3 h, 80% (2 steps) (d) DDQ, DCM-H$_2$O (18:1), rt, 1 h, 82% (e) O$_3$, DCM, -78°C, 1 h (ii) NaBH$_4$, MeOH, rt, 0.5 h, (iii) TsCl, NaH, THF, 2 h, 70% (3 steps) ; (f) (i) t-BuO$^+$K$^+$, Et$_2$O, 2 h; (ii) $p$-TSA, MeOH, rt, 2 h, 92%. (g) (i) PPh$_3$, DIAD, PNBA, THF, 0°C to rt, 6 h (ii) K$_2$CO$_3$, MeOH, 79% (2 steps) (h) (i) OsO$_4$, NaIO$_4$, dioxane-H$_2$O (3:1), rt, 1 h, 82% (j) (i) DDQ, DCM-H$_2$O (18:1), rt, 1 h; (2) TsCl, NEt$_3$, DCM, 3 h, 80% (k) (i) Bu$_2$SnO, TsCl, NEt$_3$, DCM (ii) K$_2$CO$_3$, MeOH, (iii) TBAF, THF, rt, 2 h, 82% (after 3 steps). (l) (i) OsO$_4$, NaIO$_4$, dioxane-H$_2$O (18:1), rt, 1 h (ii) (i) t-BuO-K$^+$, Et$_2$O, 2 h; (ii) $p$-TSA, MeOH, rt, 2 h, 82% (after 3 steps).

Selective monotosylation of primary alcohol gave monotosylate 138 in 70% yield, which upon base induced cyclization under known conditions furnished ophiocerin C in 92% yield as a white solid. The physical and spectroscopic data were in full agreement with literature data. [$\alpha$]$_D^{25}$ = + 42.1 (c 0.1, CH$_2$Cl$_2$); lit$^2$ [$\alpha$]$_D^{25}$ = + 45.0 (c 0.1, CH$_2$Cl$_2$)

For the synthesis of ophiocerin A (2), we followed almost the same reaction sequence which we applied for the synthesis of ophiocerin C. So in order to synthesize ophiocerin A, the required anti-epoxy alcohol 139 was achieved in 79% yield via inversion of stereochemistry of the carbon bearing unprotected hydroxy group of syn epoxy alcohol 135 using Mitsonobu reaction$^{34}$ followed by basic hydrolysis (K$_2$CO$_3$ in MeOH). Epoxide 139 was then opened with excess dimethylsulfonium methylide followed by in situ acetonide protection to provide 140 in 80% yield. Oxidative cleavage of olefin 140 using OsO$_4$-NaIO$_4$ followed by NaBH$_4$$^{35}$ reduction gave the corresponding alcohol 141 in good yield. Treatment of 141 with tosyl chloride and the subsequent deprotection of PMB group using DDQ gave tosylate compound 142. Finally, base mediated cyclization with potassium tert-butoxide followed by in situ acetonide deprotection furnished ophiocerin A (2) as a white solid. The spectral data of synthetic compound matched with literature values [$\alpha$]$_D^{25}$ = - 25.2 (c 0.1, CH$_2$Cl$_2$); lit$^2$ [$\alpha$]$_D^{25}$ = - 24.0 (c 0.1, CH$_2$Cl$_2$).

Synthesis of ophiocerin B (3) began with intermediate 133a. In order to get the anti-epoxy alcohol from diol 143 we applied three step sequence: first regioselective primary mono tosylation$^{36,37}$ (using Bu$_2$SnO, tosyl chloride & NEt$_3$) of diol 133a followed by base-induced epoxide formation via intramolecular nucleophilic displacement of tosyl group and then TBAF mediated desilylation of the TBDPS group. Inversion of
stereochemistry of free hydroxy group of 143 using Mitsunobu reaction conditions followed by basic hydrolysis provided the required syn epoxy alcohol 144. Opening of epoxide using excess trimethylsulphonium iodide and n-BuLi produced syn-diol which upon treatment with 2,2-dimethoxy propane and catalytic amount of PPTS provided acetonide compound 145 in good yield. OsO₄-NaIO₄ mediated oxidative cleavage of olefin 146 followed by in situ NaBH₄ reduction gave primary alcohol 147. Esterification of 146 with tosyl chloride afforded the O-tosyl derivative 147. Finally, PMB deprotection using DDQ and base-mediated cyclization followed by acetonide deprotection gave ophiocerin B in 82% yield as pale yellow oil. The correct stereochemistry of three stereogenic centres was confirmed by comparison of its specific rotation value and spectroscopic data with literature data for ophiocerin B. \[ \alpha_D^{25} = -35.2 \text{ (c 1.0, CH}_2\text{Cl}_2) \]; lit\[2\] \[ \alpha_D^{25} = -37.0 \text{ (c 0.1, CH}_2\text{Cl}_2) \].

**Synthesis of Botryolide-E:**

From retrosynthetic analysis shown in scheme 29, we visualized that like ophiocerin A hydroxy olefin 137 is the common intermediate for botryolide-E also and it could be easily accessed from intermediate 133a following the same reaction sequence like ophiocerin A. Towards the synthesis of botrylide E (scheme 30), the hydroxy group of 137 was protected as an acetyl ester using acetic anhydride in pyridine to provide acetylated compound 148.

\[ \text{Scheme 30: Reagents and conditions: (a) Ac}_2\text{O, pyr, rt, 4h, 90\% (b) (i) O}_3, \text{ DMS (ii) (CF}_3\text{CH}_2\text{O})_2\text{P(O)CH}_2\text{CO}_2\text{Et, KHMDS/18 crown 6, -78}^\circ\text{C, 6h, 88\% (c) 1M HCl in THF, 0}^\circ\text{C to rt, 1h, 65\%}. \]

Ozonolysis of olefin followed by modified Horner-Emmons\textsuperscript{38} using electrophilic bis(trifluoroethyl)phosphonoester and KHMDS/18 crown 6 gave the Wittig product 149 in 80% yield with Z:E ratio 95:5. The cis isomer was easily separated by flash column chromatography, which upon treatment with 1M HCl in THF at 0°C for 2 hour provided
botryolide-E (4) in 90% yield. The physical and spectroscopic data of the synthesized compound are in full agreement with the reported data in literature.\textsuperscript{11}

**Synthesis of Decarestrictine O**

Our retrosynthetic analysis of decarestrictine O (as shown in scheme 27) is based on convergent approach. We envisioned that the target molecule could be accessed by the esterification of acid 155 with hydroxy olefin 137 followed by cyclization of diene using Grubbs RCM protocol. The acid fragment 155 could be prepared from sequential \(\alpha\)-aminoxylation of 4-(4-methoxybenzyloxy)butanal 150 whereas the known alcohol fragment 137 which is the common intermediate for both ophiocerin A and botryolide E, could be easily obtained from intermediate 133a via same reaction sequence already applied for synthesis ophiocerin A.

**Synthesis of acid fragment 155:**
The synthesis of acid fragment 155 started from 4-(4-methoxybenzyloxy)butanal 150 as illustrated in scheme 31. Thus \(\alpha\)-aminoxylation of aldehyde 150 using D-proline followed by reduction with NaBH\(_4\) provided unstable anilinoxy compound 151 which was further treated with 30 mole\% CuSO\(_4\).5H\(_2\)O in methanol to cleave O-N bond to afford the diol 152 in 78% yield. Regioselective primary monotosylation of diol 152\textsuperscript{39} and subsequent base treatment furnished epoxide 153\textsuperscript{40} in 80% yield. Opening of epoxide using excess dimethylsulfonium methyldie followed by \textit{in situ} protection of hydroxy group as TBS ether gave olefin 154 in 82% yield. Finally, DDQ mediated deprotection of the PMB group afforded the primary alcohol which upon one-pot oxidation with TEMPO-BAIB provided the required acid 155\textsuperscript{16}.

![Scheme 31: Reagents and conditions:](image)

**Scheme 31:** \textit{Reagents and conditions:} (a) (i) D proline, PhNO, DMSO (ii) NaBH\(_4\), MeOH, rt, 0.5 h ; (b) CuSO\(_4\).5H\(_2\)O, MeOH. 10h, 78 % (3steps) (c) i) Bu\(_2\)SnO, TsCl,
NEt₃, DCM (ii) K₂CO₃, MeOH , 0.5h, rt ,80% (two steps) (d) (i) (CH₃)₃S⁺T, n-BuLi, THF, -20 °C (ii) TBSCl, imidazole, DCM, 82% (two steps) (e) (i) DDQ, DCM-H₂O (18:1), rt,1h (ii) TEMPO (catalytic), BAIB, CH₃CN-H₂O (3:1), rt, 7h. 75% (two steps).

Synthesis of alcohol fragment 137:
The synthesis of alcohol fragment 137 from intermediate 133a is already described in synthesis of ophiocerin A (Scheme 29).

Synthesis of decarestrictine O through RCM (Scheme 32):
With both the cross coupling partners 137 and 155 in hand, the coupling of these two fragments using Shiina's esterification ⁴¹ protocol provided the diene ester 156 in 95% yield. The diene ester was then subjected to ring closing metathesis under high dilution (0.001M in dry DCM) using 10 mole% Grubbs II catalyst to give α,β-unsaturated lactone 157 in 78% yield with exclusively the E-isomer. Compound 157 upon exposure to 1M HCl in THF underwent deprotection of both TBS ether and acetonide to provide decarestrictine O. All the spectroscopic and physical data of synthesized compound were in full agreement with literature data. [α]₂⁵ = - 20.2 (c 0.2,MeOH); lit⁴⁶[α]₂⁵ = - 19.6 (c 0.2, MeOH)

Scheme 32: Reagents and conditions: (a) 2-Methyl-6-nitrobenzoic anhydride, NEt₃, DMAP, DCM, 12h, 95%; (b) Grubbs II catalyst(10 mole%), DCM, reflux, 12h, 75%; (c) 1M HCl in THF, DCM, rt, 1h, 68%.

Synthesis of Stagonolide C and 9-epi-Stagonolide C
Like decarestrictine O, stagonolide C and its 9-epimer could be obtained from coupling of olefinic acid 167 with respective olefinic alcohol (159 and 161) followed by
cyclization of the diene using Grubbs RCM protocol. The acid fragment 167 could be prepared from sequential α-aminoxylation of 5-(4-methoxybenzyloxy)pentanal 162 whereas the olefinic alcohol fragment 159 could be easily obtained from intermediate 133a (scheme 33). Similarly its 9-epimer can be obtained by coupling of alcohol 161 with same olefinic acid 167. Alcohol fragment 161 can also be prepared from other diol isomer 133b via the same sequence of reaction (scheme 34).

Synthesis of alcohol fragment 159:
To synthesize the alcohol fragment, the diol 133a was subjected to direct reductive elimination\textsuperscript{42} with iodine, PPh\textsubscript{3}, imidazole at reflux for 4 h to give olefin 158 in 83% yield. Cleavage of PMB protecting group using DDQ furnished the target alcohol 159 in 80% yield. (scheme 37)

Scheme 33: Reagents and conditions: (a) TPP, I\textsubscript{2}, imidazole, THF, reflux, 4h, 83%; (ii) (b) DDQ, DCM-H\textsubbox{2}O (18:1), rt,1h, 80%.

Synthesis of alcohol fragment 161:
For the synthesis of alcohol fragment 161 for 9-epi-stagonolide C from another diol intermediate 133b, we follow the same reaction sequence as described in earlier scheme 33. (scheme 34)

Scheme 34: Reagents and conditions: (a) TPP, I\textsubscript{2}, imidazole, THF, reflux, 4h, 82%; (ii) (b) DDQ, DCM-H\textsubbox{2}O (18:1), rt,1h, 84%.
Synthesis of common acid fragment 167 for both Stagonolide C and its epimer (scheme 35):
The synthesis of acid fragment commenced from 5-(4-methoxy bezylxylo)pentanal as illustrated in scheme 35. Thus, D-proline catalyzed α-aminoxylation of aldehyde 162 under similar set of reaction conditions as described in scheme 31 (synthesis of acid fragment for decarestrictine O), afforded diol 164 in 77% yield. Selective primary monotosylation of diol and subsequent base treatment gave the epoxide 165 in 81% yield. Dimethylsulfonium methylide mediated epoxide ring opening followed by in situ protection of secondary hydroxy group using TBDPSCI, imidazole afforded TBDPS ether 166 in 78% yield. Later, removal of the PMB group using DDQ furnished primary alcohol which upon one pot oxidation using TEMPO-BAIB gave acid 167 in 75% yield.

Scheme 35: Reagents and conditions: (a) (i) D-proline, PhNO, DMSO (ii) NaBH₄, MeOH, rt, 0.5 h ; (b) CuSO₄,5H₂O, MeOH. 10h, 77 % (3steps); (c) i) Bu₂SnO, TsCl, NEt₃, DCM; (ii) K₂CO₃, MeOH , 0.5h, rt , 81% (two steps); (d) (i) (CH₃)₃S⁺I⁻, n-BuLi, THF, -20°C; (ii) TBDPSCI, imidazole, DCM, 78% (two steps); (e) (i) DDQ, DCM-H₂O (18:1), rt, 1h; (ii) TEMPO (catalytic), BAIB, CH₃CN-H₂O (3:1), rt, 7h, 75%.

Synthesis of Stagonolide C via RCM (scheme 36):
With substantial amount of alcohol 159 and acid 167 in our hand, the platform was set to couple the two fragments for the diene ester formation. To this end, the alcohol 159 was coupled with acid 167 under Shiina protocol to give diene 168 in 93% yield. Deprotection of both TBDPS group with NH₄F in methanol gave the required diol which was immediately subjected for RCM reaction using 10 mole% Grubbs II catalyst to afford the target molecule stagonolide C (6) in 78% yield. The constitution and configuration of the assigned structure were in full agreement with the literature data. 

\[[\alpha]_D^{25} = +45.7 \ (c \ 0.2,\text{CHCl}_3)\]; lit\ [[\alpha]_D^{25} = +48.0 \ (c \ 0.2,\text{CHCl}_3)\].
Scheme 36: Reagents and conditions: (a) 2-Methyl-6-nitrobenzoic anhydride, NEt₃, DMAP, DCM, 6h, 93%; (b) (i)NH₄F, MeOH, 40°C, 24h; (ii) Grubbs II catalyst(10 mole%), DCM, reflux, 48h, 78%.

Completion of the Synthesis of 9-epi-Stagonolide C 7 through RCM (scheme 37):
Towards the synthesis of the 9-epi-isomer, coupling of acid fragment 167 with alcohol 161 was carried out using Shiina's esterification protocol followed by desilylation of both TBDPS group using NH₄F in methanol to give diol 171 in 73% yield. Compound 171 upon treatment with 10 mole% Grubbs II catalyst furnished 9-epi-stagonolide C (7) as the sole product. The geometry of the newly formed double bond was unambiguously determined by the olefinic J trans coupling constant (16.14 Hz between the proton at δ = 5.98 and 5.62 ppm respectively).

Scheme 37: Reagents and conditions: (a) 2-Methyl-6-nitrobenzoic anhydride, NEt₃, DMAP, DCM, 6h, 92%; (b) NH₄F, MeOH, 40°C, 24h, 70%; (C) Grubbs II catalyst(10 mole%), DCM, reflux, 48h, 73%.

4.5 Conclusion
In summary, we have successfully synthesized the key precursors for the synthesis of ophiocerin A, B and C, botryolide E, decaerectistine O, stagonolide C and 9-epi-
stagonolide C by employing proline-catalyzed aldol reaction as the key step. This route exemplifies coupling of two different fragments via esterification and ring closing metathesis sequentially. We believe that this synthetic sequence can be a stepping stone for general synthesis of hydroxylated pyrans and 10-membered unsaturated lactones and other macrolide in particular.
4.6 Experimental

(S)-4-((R)-2,2-Dimethyl-1,3-dioxolan-4-yl)-4-hydroxybutan-2-one (130):

(D)-Proline (46 mg, 0.40 mmol) was added to a solution of aldehyde (260 mg, 2 mmol) in acetone (4 mL) and chloroform (1 mL) and was stirred at RT for 5h. Subsequently, the mixture was diluted with water (5 mL) and diethyl ether (5 mL) and partitioned. The aqueous layer was washed with diethyl ether (5 mL x 3), and the combined organic layers were dried over Na₂SO₄. Evaporation of the solvent and purification by flash column chromatography (100-200 mesh, eluent: 30% EtOAc/pet ether) afforded the desired products 130 as pale yellow liquid.

**Yield:** 244 mg, 65%

**Mol. Formula:** C₉H₁₆O₄

**Mol. Weight:** 188.10

[α]D²⁵: -24.4 (c 4.0, CHCl₃) lit²⁵ [α]D²⁵ = -27.0 (c 1.0, CHCl₃)

**IR (CHCl₃, cm⁻¹)** νmax = 3492, 3018, 2954, 2901, 1720, 1363, 1205, 1069, 859.

**¹H NMR** (500 MHz, CDCl₃): δ = 4.13 - 4.05 (m, 1 H), 4.00 - 3.88 (m, 3 H), 3.21 (br. s., 1 H), 2.89 - 2.80 (dd, J = 1.6, 17.5, 1 H), 2.61 (dd, J = 8.1, 17.9 Hz, 1 H), 2.21 (s, 3 H), 1.40 (s, 3 H), 1.34 (s, 3 H)

**¹³C NMR** (125 MHz, CDCl₃): δ = 209.7, 109.4, 69.0, 66.8, 46.2, 30.8, 26.6, 25.1

(S)-4-((tert-Butyldiphenylsilyloxy)-4-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)butan-2-one (131):

To a stirred solution of compound 130 (0.517 g, 2.75 mmol) in dry DCM and imidazole (0.375 g, 5.5 mmol) at 0°C, TBDPSCI (0.8 mL, 3.3 mmol) was added dropwise and the reaction mixture was stirred for 8h at room temperature. After completion of the reaction,
water was added to quench the reaction mixture and the organic layer was washed with excess water and brine. The organic layer was dried over Na₂SO₄ and concentrated to afford the crude silylated compound, which was purified by silica gel chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to afford 131 (1.11 g, 95%) as a viscous liquid.

Yield: 1.11g, 95%

Mol. Formula: C₂₅H₃₄O₄Si

Mol. Weight : 426.22

[α]D²⁵: - 10.37 (c 3.4, CHCl₃)

IR (CHCl₃, cm⁻¹) νmax = 3392, 3008, 2558, 1732, 1458, 1263, 1099, 759.

¹H NMR (200 MHz, CDCl₃): δ = 7.77 - 7.64 (m, 4 H), 7.47 - 7.34 (m, 6 H), 4.32 - 4.17 (m, 1 H), 4.14 - 4.01 (m, 1 H), 3.92 (dd, J = 6.4, 8.3 Hz, 1 H), 3.64 (dd, J = 6.3, 8.3 Hz, 1 H), 2.60 (dd, J = 3.4, 5.7 Hz, 2 H), 1.91 (s, 3 H), 1.29 (s, 6 H), 1.03 (s, 9 H)

¹³C NMR (50 MHz, CDCl₃): δ = 206.1, 135.92, 135.9, 135.2, 134.8, 133.5, 133.3, 129.9, 129.8, 129.6, 127.7, 127.65, 127.63, 109.3, 78.7, 70.6, 66.9, 48.3, 30.6, 26.9, 26.5, 26.2, 25.1, 19.3

HRMS (ESI) for C₂₅H₃₄O₄SiNa (M + Na)⁺ found 449.2120, calcd 449.2119

(4S)-4-((tert-Butyldiphenylsilyl)oxy)-4-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)butan-2-ol (132):

To a stirred solution of β-hydroxy ketone 131 (0.063 g, 0.147 mmol) in MeOH (1 mL) in a 25 mL flask at −78 °C, CeCl₃·7H₂O (0.057 g, 0.162 mmol) and NaBH₄ (0.006 g, 0.147 mmol) were added to the mixture, and it was allowed to warm to rt. The reaction mixture was stirred for 1 h until analysis of the mixture by TLC (silica gel) indicated completion of reaction. The reaction was diluted with aq NH₄Cl (5 mL) and extracted with DCM (3 × 10 mL), washed with brine, and dried over Na₂SO₄. Removal of the solvent under reduced pressure provided the crude hydroxy compound which was purified by silica gel column chromatography (100-200 mesh, eluent: 20% EtOAc /pet ether ) to afford 132 (0.051 g, 80%) as a pale yellow oil.
Yield: 51 mg, 80%

Mol. Formula: C_{25}H_{36}O_{4}Si

Mol. Weight: 428.24

IR (CHCl_{3}, cm^{-1}) \nu_{\text{max}} = 3382, 3068, 2893, 1632, 1435, 1250, 1136, 889, 743.

^{1}H NMR (500 MHz, CDCl_{3}): \delta = 7.74 - 7.64 (m, 4 H), 7.50 - 7.34 (m, 6 H), 4.17 (qd, J = 6.7, 13.2 Hz, 1 H), 4.05 - 3.96 (m, 1 H), 3.91 - 3.76 (m, 1 H), 3.63 (ddd, J = 7.0, 8.4, 15.7 Hz, 1 H), 2.76 (br. s., 1 H), 1.77 - 1.61 (m, 2 H), 1.34 - 1.18 (m, 5 H), 1.10 - 1.04 (m, 9 H), 1.01 - 0.96 (m, 3 H)

^{13}C NMR (125 MHz, CDCl_{3}): \delta = 135.9(135.94), 135.9(135.91), 135.9(135.85), 135.8, 133.6, 133.3, 133.1, 130.1, 130.0, 129.9, 129.9, 127.9, 127.8, 127.7, 127.7, 127.6, 109.4, 109.3, 78.63, 78.58, 74.3, 73.9, 72.4, 71.9, 67.8, 67.7, 64.8, 64.1, 63.7, 63.4, 43.9, 43.6, 41.3, 30.9, 27.0, 26.99, 26.94, 26.3, 25.31, 25.30, 24.0, 23.7, 23.5, 19.4

HRMS (ESI) for C_{25}H_{36}O_{4}SiNa (M + Na)^{+} found 451.2268, calcd 451.2275

(2R,3S,5R)-3-((tert-Butyldiphenylsilyl)oxy)-5-((4-methoxybenzyl)oxy)hexane-1,2-diol (133a):

Alcohol 132 (0.428 g, 1 mmol), p-methoxybenzyl chloride (0.172 g, 0.15ml, 1.1 mmol) and DIPEA (0.34 ml, 2 mmol) were charged in reaction vessel equipped with magnetic stirring bar under argon atmosphere. The mixture was refluxed in 150°C bath for 3 h. Consumption of the starting material was monitored by TLC. The resulting mixture was diluted with ethyl acetate (5 mL) and 10% aqueous sodium bisulphate (5 mL) and extracted twice with EtOAc (2 \times 10 mL). Combined organic layer was dried over Na_{2}SO_{4} and the solvent evaporated in vacuo. The crude PMB protected product was used for the next step without further purification.

To a stirred solution of crude PMB protected compound (0.45 g, 0.82 mmol) in MeOH (10 mL) was added PPTS (21 mg, 0.082 mmol) and then stirred overnight at room temperature. After completion of the reaction, a saturated aq.NaHCO_{3} solution (10 mL) was added to the reaction mixture and then concentrated under reduced pressure and extracted with DCM (4 \times 15 mL). The combined organic layers were washed with brine...
and dried over Na₂SO₄. Solvent was concentrated under vacuum. The crude residue was purified by column chromatography on silica gel (230-400 mesh. eluent: 45% EtOAc /petether) to give major product 133a (380 mg, 75%) along with minor product 133b (127 mg, 25%) as a colorless liquid.

Data of 133a:
Yield: 0.38 g, 75%
Mol. Formula: C₃₀H₄₀O₅Si
Mol. Weight: 508.26
[α]D²⁵: -12.59 (c 3.3, CHCl₃)
IR (CHCl₃, cm⁻¹) νmax = 3479, 2978, 1554, 1358, 1063, 851, 742.
¹H NMR (400 MHz, CDCl₃): δ = 7.68-7.70 (m, 4 H), 7.48 - 7.33 (m, 6 H), 7.05 (d, J = 8.1 Hz, 2 H), 6.82 (d, J = 8.1 Hz, 2 H), 4.29 (d, J = 10.8 Hz, 1 H), 3.96 (d, J = 4.6 Hz, 1 H), 3.87 (d, J = 11.0 Hz, 1 H), 3.80 (s, 3 H), 3.74 - 3.61 (m, 3 H), 3.11 - 2.97 (m, 1 H), 2.55 (br. s., 2 H), 1.78 (ddd, J = 5.9, 9.5, 15.2 Hz, 1 H), 1.57 (td, J = 3.4, 15.2 Hz, 1 H), 1.07 (s, 9 H), 0.90 (d, J = 6.1 Hz, 3 H)
¹³C NMR (100 MHz, CDCl₃): δ = 159.2, 135.9, 133.8, 133.1, 129.9, 129.9, 129.8, 129.4, 127.8, 127.7, 113.7, 75.0, 73.7, 72.8, 70.0, 63.3, 55.2, 42.2, 27.0, 19.4, 19.3
HRMS (ESI) for C₃₀H₄₀O₅Si Na (M + Na)⁺ found 531.2537, calcd 531.2537

(2R,3S,5S)-3-((tert-Butyldiphenylsilyl)oxy)-5-((4-methoxybenzyl)oxy)hexane-1,2-diol (133b):

Yield: 0.127 g, 25%
Mol. Formula: C₃₀H₄₀O₅Si
Mol. Weight: 508.26
[α]D²⁵: +38.2 (c 2.5, CHCl₃)
IR (CHCl₃, cm⁻¹) νmax = 3379, 2988, 1546, 1308, 1136, 987, 842.
¹H NMR (500 MHz, CDCl₃): δ = 7.68 -7.63 (m, 4 H), 7.49 - 7.36 (m, 6 H), 7.26 - 7.19 (m, J = 8.2 Hz, 2 H), 6.92 - 6.85 (m, J = 8.5 Hz, 2 H), 4.53-4.50 (m, 1 H), 4.35-4.33 (m, 1 H), 3.94 - 3.87 (m, 1 H), 3.84 - 3.80 (m, 4 H), 3.79 - 3.75 (m, 1 H), 3.68 - 3.63 (m, 1 H),
3.45 (dd, J = 7.0, 11.0 Hz, 1 H), 2.66 (br. s., 2 H), 1.82 (ddd, J = 2.3, 8.8, 15.2 Hz, 1 H), 1.53 (dd, J = 4.3, 15.3 Hz, 1 H), 1.07 (s, 9 H), 0.97 (d, J = 6.1 Hz, 3 H)

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 159.4, 135.9, 134.0, 133.2, 129.9, 129.8, 129.7, 129.6, 128.6, 127.7, 127.6, 113.9, 113.7, 73.6, 71.7, 70.5, 70.3, 64.1, 55.2, 39.9, 27.0, 19.4, 19.2

HRMS (ESI) for C$_{30}$H$_{40}$O$_5$Si Na (M + Na)$^+$ found 531.2538, calcd 531.2537

**tert-Butyl((1S,3R)-3-((4-methoxybenzyl)oxy)-1-((S)-oxiran-2-yl)butoxy)diphenylsilane (134)**

![Chemical Structure](image)

To a mixture of diol 133a (0.665 g, 1.31 mmol) in dry CH$_2$Cl$_2$ (2 mL) under argon atmosphere was added Bu$_2$SnO (0.007 g, 0.0262 mmol) followed by addition of benzoyl chloride (0.178 mL, 1.44 mmol), Et$_3$N (0.22 mL, 1.57 mmol). The resulting mixture was stirred at room temperature for 2 h quenched with water and then extracted with CH$_2$Cl$_2$. Removal of volatiles under reduced pressure gave an oily crude monobenzoyl ester. This compound was then dissolved in dry CH$_2$Cl$_2$ (10 mL) under argon and treated with MsCl (0.11 mL, 1.44 mmol), Et$_3$N (0.22 mL, 1.57 mmol), and catalytic amount of DMAP. The reaction mixture was stirred at room temperature for 2 h and then diluted with water. The water layer was extracted with CH$_2$Cl$_2$ (3 x 15 mL) and the combined organic layer was washed with brine, dried (Na$_2$SO$_4$), and concentrated to give a crude product, which was dissolved in MeOH (10 mL) and treated with K$_2$CO$_3$ (0.180 g, 1.31 mmol). This mixture was stirred for 1 h at room temperature and then filtered through celite. Removal of the volatiles under reduced pressure, followed by column chromatography on silica gel (100-200 mesh, eluent: 5% EtOAc/ pet ether) produced the epoxide 134 (0.11 g, overall yield 70%) as a yellow liquid.

**Yield:** 0.675 g, 70%

**Mol. Formula:** C$_{30}$H$_{38}$O$_4$Si

**Mol. Weight:** 490.25

$[\alpha]_D^{25}$: -43.5 (c 1.8, CHCl$_3$)

IR (CHCl$_3$, cm$^{-1}$) $\nu_{\text{max}} =$ 2818, 1632, 1521, 1498, 1332, 1063, 809.
**H NMR** (400 MHz, CDCl$_3$): $\delta = 7.81 - 7.66$ (m, 4 H), 7.43 - 7.30 (m, 6 H), 7.00 (d, $J = 8.8$ Hz, 2 H), 6.80 (d, $J = 8.6$ Hz, 2 H), 4.28-4.25 (m, 1 H), 3.92 (d, $J = 10.8$ Hz, 1 H), 3.80 (s, 3 H), 3.68 - 3.48 (m, 2 H), 3.03 (ddd, $J = 2.7, 4.1, 6.9$ Hz, 1 H), 2.65 (t, $J = 4.5$ Hz, 1 H), 2.43 (dd, $J = 2.7, 4.9$ Hz, 1 H), 1.84 - 1.61 (m, 2 H), 1.10 (s, 9 H), 1.06 (d, $J = 6.1$ Hz, 3 H)

**C NMR** (50 MHz, CDCl$_3$): $\delta = 158.9, 136.1, 136.0, 133.9, 133.8, 130.8, 129.1, 127.5, 127.4, 113.6, 73.1, 71.4, 70.0, 56.0, 55.2, 45.0, 42.6, 27.0, 19.9, 19.5

**HRMS (ESI)** for C$_{30}$H$_{38}$O$_4$Na (M + Na)$^+$ found 513.2435, calcd 513.2432

(1S,3R)-3-((4-Methoxybenzyl)oxy)-1-((S)-oxiran-2-yl)butan-1-ol (135)

To a stirred soln. of epoxide 134 (0.170 g, 0.349 mmol) in dry THF (10 mL) was added 1M TBAF(0.52 mL, 0.52 mmol) in THF at RT and the mixture was stirred for 4 h. The reaction was diluted with satd aq NH$_4$Cl (20 mL), and the mixture was extracted with ethylacetate (2 X 15 mL). The combined organic layers were washed with brine then dried over Na$_2$SO$_4$ and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to give 135 (0.075 g, 85%) as a light yellow oil.

**Yield:** 0.075 g, 85%

**Mol. Formula:** C$_{14}$H$_{20}$O$_4$

**Mol. Weight**: 252.14

$[\alpha]_D^{25}$: -28.75 (c 3.0, CHCl$_3$)

**IR** (CHCl$_3$, cm$^{-1}$) $\nu_{\text{max}}$ = 3410, 3118, 2584, 1638, 1239.

**H NMR** (200 MHz, CDCl$_3$): $\delta = 7.32 - 7.22$ (d, $J = 8.5$ Hz, 2 H), 6.95 - 6.83 (d, $J = 8.5$ Hz, 2 H), 4.57 (d, $J = 11.0$ Hz, 1 H), 4.40 (d, $J = 11.0$ Hz, 1 H), 3.98 - 3.88 (m, 1 H), 3.85 - 3.76 (m, 4 H), 2.99 (dt, $J = 2.9, 4.2$ Hz, 1 H), 2.80 - 2.73 (m, 2 H), 2.72 (d, $J = 5.8$ Hz, 1 H), 1.78 (ddd, $J = 2.4, 4.4, 7.5$ Hz, 2 H), 1.27 (d, $J = 6.1$ Hz, 3 H)

**C NMR** (50 MHz, CDCl$_3$): $\delta = 159.2, 130.5, 129.3, 113.8, 71.9, 70.4, 68.2, 55.3, 55.2, 44.4, 40.8, 19.6

**HRMS (ESI)** for C$_{14}$H$_{20}$O$_4$Na (M + Na)$^+$ found 275.1255, calcd 275.1254

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(4S,5S)-4-((R)-2-((4-Methoxybenzyl)oxy)propyl)-2,2-dimethyl-5-vinyl-1,3-dioxolane (136)

To a stirred solution of dry THF was added trimethylsulfonium iodide (1.23 g, 6.05 mmol) at -20°C followed by n-BuLi (3.8 mL, 1.6 M, 6.05 mmol). The reaction mixture was stirred for 1h after which epoxide 135 (0.3 g, 1.21 mmol) in THF was added dropwise. The reaction mixture was stirred at -20°C for 3 h and completion of the reaction was monitored by TLC. The reaction mixture was diluted with saturated solution of ammonium chloride and extracted with EtOAc (2x50 mL). The combined organic layers were washed with water (2 x 50 mL), brine, dried over Na₂SO₄, and concentrated. The crude diol was used for the next step without further purification.

2,2-DMP (0.25 mL, 2 mmol) and PPTS (23 mg, 0.1 mmol) were added to a solution of crude diol (0.28 g, 1 mmol) in dry DCM (30 mL), and the mixture was stirred for 4 h. The reaction mixture was then quenched with satd aq NaHCO₃ (15 mL). The aqueous layer was extracted with DCM (3x15 mL) and the combined organic layers were dried over Na₂SO₄ and concentrated in vacuo. The crude product was purified by silica gel column chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to give 136 (0.29 g, 80%) as a pale yellow oil.

**Yield:** 0.29 g, 80%

**Mol. Formula:** C₁₈H₂₆O₄

**Mol. Weight:** 306.18

\[ [\alpha]_{D}^{25} \text{ : } -3.7 \text{ (c 3.5, CHCl₃) lit}^{15} [\alpha]_{D}^{25} = - 4.0 \text{ (c 1.0, CHCl₃)} \]

**IR (CHCl₃, cm⁻¹):** ν_max = 3092, 2954, 1658, 1563, 1412, 1099, 829.

**¹H NMR (500 MHz, CDCl₃):** δ = 7.27 (d, J = 8.5 Hz, 2 H), 6.88 (d, J = 8.9 Hz, 2 H), 5.85 - 5.74 (m, 1 H), 5.40 - 5.31 (m, 1 H), 5.29 - 5.15 (m, 1 H), 4.55 (d, J = 11.3 Hz, 1 H), 4.41 (d, J = 11.6 Hz, 1 H), 4.08 - 3.88 (m, 2 H), 3.81 (s, 3 H), 3.78 - 3.70 (m, 1 H), 1.81 - 1.73 (m, 1 H), 1.62 - 1.55 (m, 1 H), 1.42 (s, 3 H), 1.41 (s, 3 H), 1.23 (d, J = 6.4 Hz, 3 H)

**¹³C NMR (125 MHz, CDCl₃):** δ = 159.1, 135.1, 131.0, 129.2, 129.1, 118.8, 113.7, 108.5, 82.9, 77.3, 71.8, 70.4, 55.2, 39.5, 27.4, 27.3, 26.9, 20.3
HRMS (ESI) for C_{18}H_{26}O_{4}Na (M + Na)^+ found 329.1718, calcd 329.1723

(R)-1-((4S,5S)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)propan-2-ol (137)

Compound 136 (0.168 g, 0.55 mmol) was dissolved in 10 mL of DCM/ H_{2}O (18:1). DDQ (0.187 g, 0.82 mmol) was added to it in one portion. The reaction mixture was stirred at room temperature for 1 h. Completion of the reaction was monitored by TLC. The reaction mixture was diluted with 5% NaHCO_{3} solution, water and brine and extracted with DCM (3X20 ml). The organic layer was dried over Na_{2}SO_{4} and concentrated in vacuo. Purification by silica gel chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) afforded the pure compound 137 as light yellow oil.

Yield: 0.083 g, 82%

Mol. Formula: C_{10}H_{18}O_{3}

Mol. Weight: 186.13

[α]_{D}^{25}: -11.91 (c 2.2, CHCl_{3}) lit^{16}[α]_{D}^{25} = - 12.25 (c 0.4, CHCl_{3})

IR (CHCl_{3}, cm^{-1}) \nu_{max} = 3414, 2987, 2918, 1736, 1408.

{^{1}H} NMR (500 MHz, CDCl_{3}): \delta = 5.77 (ddd, J = 7.3, 10.2, 17.2 Hz, 1 H), 5.34 (d, J = 17.1 Hz, 1 H), 5.24 (d, J = 10.4 Hz, 1 H), 4.08 - 3.99 (m, 2 H), 3.90 (dt, J = 3.4, 8.4 Hz, 1 H), 2.71 (br. s., 1 H), 1.70 - 1.67 (m, 1 H), 1.65 - 1.58 (m, 1 H), 1.40 (s, 3 H), 1.39 (s, 3 H), 1.20 (d, J = 6.4 Hz, 3 H)

{^{13}C} NMR (125 MHz, CDCl_{3}): \delta = 134.8, 119.1, 108.8, 82.3, 77.7, 64.9, 39.4, 27.2, 26.8, 23.6

HRMS (ESI) for C_{10}H_{18}O_{3} (M + Na)^+ found 209.1149, calcd 209.1148

((4S,5S)-5-((R)-2-Hydroxypropyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl 4-methylbenzenesulfonate (138)

Olefine 137 (0.084 g, 0.45 mmol) was dissolved in 10 mL of DCM and cooled to -78 °C. Ozone was passed through the solution until a blue tint was observed and 3 mL of
dimethyl sulfide was added to this resulting blue solution. The reaction mixture was allowed to warm to room temperature and stirred for 12h at which point the reaction mixture was concentrated and the crude aldehyde was used for the next step without purification. The residue was redissolved in MeOH(10 mL), and NaBH₄ (45 mg) was added. After 30 min, the mixture was concentrated, and the residue was partitioned between EtOAc(50 mL) and H₂O (20 mL). The organic layer was dried over Na₂SO₄, filtered and concentrated, and the residue was purified by silica gel column chromatography.

To the stirred solution of alcohol in dry THF cooled to 0°C was added NaH (0.010 g, 0.45 mmol) and to this, after 10 minute TsCl (0.086 g, 0.45 mmol) was added and the reaction mixture was stirred at same temperature for another 3 h at which time TLC analysis of the reaction mixture shows consumption of starting material. The reaction mixture was diluted with water and extracted with EtOAc (3 X20 mL). The combined organic layers were washed with water, brine, dried over Na₂SO₄ and concentrated. The residual oil was purified by silica gel column chromatography using 15% EtOAc/ pet ether as eluent to furnish compound 138 as a colourless oil.

**Yield:** 0.108 g, 70%

**Mol. Formula:** C₁₆H₂₄O₆S

**Mol. Weight:** 344.13

[α]²⁵ : +3.2 (c 0.3 , CHCl₃)

**IR (CHCl₃, cm⁻¹)** νₘₐₓ = 3455, 2903, 1445, 1185, 790.

**1H NMR (500 MHz, CDCl₃):** δ 7.79 (d, J = 8.2 Hz , 2H), 7.35 (d, J = 8.2 Hz , 2H), 4.14-4.11 (m, 2H), 4.09- 4.05 (m, 1H), 4.02-3.99 (m, 1H), 3.88-3.85 (m, 1H), 2.47 (s, 3H), 1.71-1.68 (m, 2H), 1.37 (s, 3H),1.31 (s, 3H), 1.21 (d, J = 6.2 Hz, 3H)

**13CNMR (125 MHz, CDCl₃):** δ 145.1, 132.6, 129.9, 127.9, 109.5, 78.0, 75.3, 68.9, 65.0, 41.0, 27.2, 26.6, 23.8, 21.6

**Ophiocerin C (1)**

![Ophiocerin C](image)

To the stirred solution of tosylate 138 in dry Et₂O (3 mL) was added t-BuOK (124 mg, 1.1 mmol) at 0°C, and the mixture was stirred for 1 h at 0°C and monitored by TLC. After
completion of the reaction it was diluted with satd aq NH₄Cl (10 mL), and the mixture was extracted with Et₂O (4x 5 mL). The combined organic layers were washed with H₂O and brine and concentrated in vacuo, then treated with PTSA (3 mg) and MeOH (5 mL) with stirring at RT for another 2 h. The reaction was quenched with satd aq NaHCO₃ solution extracted with DCM (3 X 20 mL) and the combined organic layers were washed with H₂O and brine, then dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to furnish ophiocerin C (3) (0.059 g, overall yield 82%) as a white solid.

Yield: 0.059 g, 82%

Mol. Formula: C₆H₁₂O₃
Mol. Weight: 132.16

[α]D²⁵⁺42.4 (c 1.3, CH₂Cl₂) lit²[α]D²⁵⁺45.0 (c 0.1, CH₂Cl₂)
IR (CHCl₃, cm⁻¹) νmax = 3392, 3018, 2854, 1458, 1263, 1099, 759.

¹H NMR (200 MHz, CDCl₃): δ 3.97 (dd, J = 5.0, 11.3 Hz, 1H), 3.65-3.45 (m, 3H), 3.16 (dd, J = 9.9, 11.0 Hz, 1H), 2.00 (ddd, J = 1.8, 4.3, 12.6 Hz, 1H ), 1.38 (ddd, J = 11.1, 11.1, 12.8 Hz, 1H), 1.22 (d, J = 6.2 Hz, 3H)

¹³CNMR (50 MHz, CDCl₃): δ 73.3, 72.7, 72.2, 69.6, 40.5, 21.2.

(1R,3R)-3-((4-Methoxybenzyl)oxy)-1-((S)-oxiran-2-yl)butan-1-ol (139):

To a precooled (0°C) solution of alcohol 135 (0.116 g, 0.46 mmol), triphenylphosphine (0.366 g, 1.39 mmol) and p-nitrobenzoic acid (0.386 g, 2.32 mmol) in dry THF (2 mL) was added DIAD (0.36 mL, 1.86 mmol). The reaction mixture was stirred at room temperature for 5 h and monitored by TLC. After completion of the reaction, the solvent was concentrated and the crude residue was purified by silica gel column chromatography using petroleum ether/EtOAc (9:1) to give p-nitrobenzoate as a yellow colored oil along with DIAD impurity.

To the solution of p-nitrobenzoate (obtained above) in MeOH (3 mL) was added K₂CO₃ (0.190 g, 1.38 mmol) and the mixture stirred at room temperature for 1 h at which point it was filtered through Celite and washed with ethylacetate (20 mL). The solvent was
concentrated in vacuo and the crude residue was purified by column chromatography using 15% EtOAc/ pet ether as eluent to furnish compound 139 as a colourless oil.

**Yield:** 0.091 g, 79%

**Mol. Formula:** C$_{14}$H$_{20}$O$_{4}$

**Mol. Weight:** 252.14

$[\alpha]_D^{25}$: -53.13 (c 1.8, CHCl$_3$)

**IR** (CHCl$_3$, cm$^{-1}$) $\nu_{max}$ = 3402, 3108, 2564, 1618, 1219.

**$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ = 7.25 (d, $J$ = 8.6 Hz, 2 H), 6.88 (d, $J$ = 8.6 Hz, 2 H), 4.60 (d, $J$ = 11.0 Hz, 1 H), 4.36 (d, $J$ = 11.0 Hz, 1 H), 3.92 - 3.82 (m, 1 H), 3.82 - 3.77 (s, 3 H), 3.70 - 3.64 (m, 1 H), 2.94 - 2.87 (m, 1 H), 2.81 - 2.71 (m, 2 H), 1.84 - 1.76 (m, 2 H), 1.28 (d, $J$ = 5.9 Hz, 3 H)

**$^{13}$C NMR** (100 MHz, CDCl$_3$): $\delta$ = 19.6, 40.6, 45.2, 54.3, 55.2, 70.0, 71.0, 74.9, 113.9, 129.4, 129.9, 159.3

**HRMS (ESI)** for C$_{14}$H$_{20}$O$_{4}$Na (M + Na)$^+$ found 275.1251, calcd 275.1254

(4$R$,5$S$)-4-((R)-2-((4-Methoxybenzyl)oxy)propyl)-2,2-dimethyl-5-vinyl-1,3-dioxolane (140):

![Structure](image)

Compound 140 was synthesized using the same procedure as described for compound 136 in 82% yield.

**Mol. Formula:** C$_{18}$H$_{26}$O$_{4}$

**Mol. Weight:** 306.18

$[\alpha]_D^{25}$: +69.9 (c 1.0, CHCl$_3$)

**IR** (CHCl$_3$, cm$^{-1}$) $\nu_{max}$ = 3102, 2964, 1668, 1573, 1422. 1199, 839.

**$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ = 7.27 (d, $J$ = 8.6 Hz, 2 H), 6.88 (d, $J$ = 8.6 Hz, 2 H), 5.85 - 5.71 (m, 1 H), 5.27 - 5.17 (m, 2 H), 4.52 (d, $J$ = 11.5 Hz, 1 H), 4.42 - 4.35 (m, 2 H), 4.27 (td, $J$ = 5.6, 8.6 Hz, 1 H), 3.81 (s, 3 H), 3.67 - 3.56 (m, 1 H), 1.91 (ddd, $J$ = 6.2, 8.3, 14.1 Hz, 1 H), 1.53 - 1.49 (m, 1 H), 1.48 (s, 3 H), 1.36 (s, 3 H), 1.22 (d, $J$ = 6.1 Hz, 3 H)

**$^{13}$C NMR** (100 MHz, CDCl$_3$): $\delta$ = 159.1, 134.4, 130.9, 129.3, 118.4, 113.8, 108.2, 79.8, 75.0, 71.6, 69.8, 55.3, 37.1, 28.3, 25.7, 19.3
HRMS (ESI) for C_{18}H_{26}O_{4}Na (M + Na)^+ found 329.1721, calcd 329.1723

\((4S,5R)-5-((R)-2-((4\text{-Methoxybenzyl})\text{oxy})\text{propyl})-2,2\text{-dimethyl-1,3-dioxolan-4-yl})\text{methanol (141)}\)

To a stirred solution of compound 140 (0.248 g, 0.812 mmol) in dioxane-water (3:1, 8 mL) were added 2,6-lutidine (0.189 mL, 1.62 mmol) followed by OsO_4 (165 mg, 0.016 mmol) and NaIO_4 (695 mg, 3.25 mmol). The reaction was stirred at room temperature for 12 h. After completion of the reaction (checked by TLC), water (10 mL) was added to it and extracted with DCM (2X20 mL). The combined organic layer was washed with brine and dried over Na_2SO_4. The solvent was concentrated and the crude aldehyde was used for next step immediately. The aldehyde was dissolved in MeOH (10 mL) and NaBH_4 (30 mg) was added. After 30 min the mixture was concentrated and the residue was partitioned between EtOAc (50 mL) and H_2O (20 mL). The organic layer was dried over Na_2SO_4, concentrated and the residue was purified by silica gel column chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to afford the pure compound 141 as a colorless liquid. in 80% yield.

Yield: 0.2 g, 80%

Mol. Formula: C_{17}H_{26}O_{5}

Mol. Weight: 310.18

[α]^D_{25}^{25}: +48.2 (c 1.5, CHCl_3)

IR (CHCl_3, cm^{-1}) ν_{max} = 3392, 3018, 2854, 1458, 1263, 1099, 759.

\(^1H\) NMR (400 MHz, CDCl_3): δ = 7.27 (d, J = 8.3 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 4.53 (d, J = 11.5 Hz, 1 H), 4.39 (d, J = 11.2 Hz, 1 H), 4.36 - 4.26 (m, 1 H), 4.11 - 4.07 (m, 1 H), 3.81 (s, 3 H), 3.73 - 3.64 (m, 1 H), 3.62 - 3.54 (m, 2 H), 1.96 (ddd, J = 5.5, 8.4, 13.8 Hz, 1 H), 1.80 (br. s., 1 H), 1.69 - 1.56 (m, 1 H), 1.46 (s, 3 H), 1.36 (s, 3 H), 1.26 (d, J = 6.1 Hz, 3 H)

\(^13C\) NMR (50 MHz, CDCl_3): δ = 159.2, 130.6, 129.3, 113.8, 108.0, 77.9, 73.6, 71.9, 70.0, 61.7, 55.3, 35.5, 28.2, 25.5, 19.0

HRMS (ESI) for C_{17}H_{26}O_{5}Na (M + Na)^+ found 333.1670, calcd 333.1672

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To the stirred solution of alcohol 141 (1.1 g, 3.6 mmol) in dry DCM, Et3N (1.0 mL, 7.2 mmol) and DMAP (44 mg, 0.4 mmol) were added at RT and the mixture was stirred for 10 minute. TsCl (0.9 g, 4.8 mmol) was added to it and stirring was continued at rt for another 3 h. The reaction was diluted with saturated aq NH4Cl (20 mL) and extracted with DCM (5 x 10 mL). The combined organic layers were washed with H2O and brine, then dried over Na2SO4, and concentrated in vacuo. The crude tosylate product was used in the next step without further purification.

Crude tosylate (1.1 g, 2.37 mmol) was dissolved in 15 mL of DCM/ H2O (18:1). DDQ (0.805 g, 3.55 mmol) was added to it in one portion. The reaction mixture was stirred at room temperature for 1 h. Completion of the reaction was monitored by TLC. The reaction mixture was diluted with 5% NaHCO3 solution, water and brine and extracted with DCM (3X20 ml). The organic layer was dried over Na2SO4 and concentrated in vacuo. Purification by silica gel chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) afforded the pure compound 142.

**Yield:** 0.975 g, 80%

**Mol. Formula:** C16H24O6S

**Mol. Weight:** 344.13

[α]D^25: -6.2 (c 1.0, CHCl3)

IR (CHCl3, cm⁻¹) νmax = 3455, 2903, 1445, 1185, 790.

**1H NMR (200 MHz, CDCl3):** δ 7.80 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.2 Hz, 2H), 4.40–4.22 (m, 2H), 4.05–3.88 (m, 3H), 2.46 (s, 3H), 1.73–1.49 (m, 2H), 1.35 (s, 3H), 1.32 (s, 3H), 1.18 (d, J = 6.2 Hz, 3H)

**13CNMR (50 MHz, CDCl3):** δ 145.0, 132.5, 129.9, 127.9, 109.2, 74.7, 71.8, 68.7, 64.7, 34.0, 29.8, 22.0, 21.6, 19.6;

**Anal. Calcd** for C16H24O6S: C, 55.80; H, 7.02; Found: C, 55.69; H, 6.99.
Ophiocerin A (2):

To the stirred solution of tosylate 142 in dry Et₂O (3 mL) was added t-BuOK (124 mg, 1.1 mmol) at 0°C, and the mixture was stirred for 1 h at 0°C and monitored by TLC. After completion of the reaction it was diluted with satd aq NH₄Cl (10 mL) and the mixture was extracted with Et₂O (4x 5 mL). The combined organic layers were washed with H₂O and brine, concentrated in vacuo and then treated with PTSA (3 mg) and MeOH (5 mL) with stirring at rt for another 2 h. The reaction was quenched with satd aq NaHCO₃ solution extracted with DCM (3 X 20 mL) and the combined organic layers were washed with H₂O and brine, then dried over Na₂SO₄ and concentrated. The residue was purified by silica gel column chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to produce ophiocerin A (3) (0.059 g, overall yield 82%) as a white solid.

Yield: 0.059 g, 92%

Mol. Formula: C₆H₁₂O₃

Mol. Weight : 132.16

M.P = 62–64°C

[α]D²⁵⁻23.4 (c 1.9, CH₂Cl₂); lit²[α]D²⁵ = -24.0 (c 0.1, CH₂Cl₂)

IR (CHCl₃, cm⁻¹): νmax 3401, 2930, 1454, 1389,1185, 1011

¹H NMR (500 MHz, CDCl₃): δ 4.10 (m, 1H), 3.83 (ddq, J = 2.0, 6.4, 11.3 Hz, 1H), 3.71–3.78 (m, 2H), 3.60–3.53 (m, 1H), 1.89 (ddd, J = 2.1, 3.5, 14.3 Hz, 1H), 1.53 (ddd, J = 2.5, 11.0,13.9 Hz, 1H), 1.16 (d, J = 6.3 Hz, 3H)

¹³C NMR (125 MHz, CDCl₃): δ 67.3, 67.1, 67.0, 65.9, 39.0, 20.8

(1S,3R)-3-((4-Methoxybenzyl)oxy)-1-((R)-oxiran-2-yl)butan-1-ol (143)
resulting mixture was stirred at room temperature for 2 h and quenched with water and then extracted with DCM (3x10 mL). The combined organic phase was washed with water, dried (Na₂SO₄) and concentrated to give a crude monotosylate product, which was dissolved in MeOH (10 mL) and treated with K₂CO₃ (0.5 g, 3.61 mmol). This mixture was stirred for 1 h at room temperature and then filtered through celite. Removal of the volatiles under reduced pressure gave crude epoxide.

To a stirred soln. of crude epoxide (0.85 g, 1.73 mmol) in dry THF (10 mL) was added 1M TBAF(2.5 mL, 2.6 mmol) in THF at rt and the mixture was stirred for 4 h. The reaction was diluted with satd aq NH₄Cl (20 mL) and the mixture was extracted with ethylacetate (2 X 15 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated in vacuo. The crude product was purified by silica gel column chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to give 143 (0.365 g, 79%) as a light yellow oil.

**Yield:** 0.365 g, 79%

**Mol. Formula:** C₁₄H₂₀O₄

**Mol. Weight:** 252.14

**[α]D²⁵:** -32.3 (c 0.3, CHCl₃)

**IR (CHCl₃, cm⁻¹) Vₚₚₚₚ = 3420, 3128, 2594, 1648, 1249.**

**¹H NMR** (500 MHz, CDCl₃): δ = 7.27 (d, J = 8.5 Hz, 2 H), 6.89 (d, J = 8.5 Hz, 2 H), 4.59 (d, J = 11.0 Hz, 1 H), 4.39 (d, J = 11.3 Hz, 1 H), 3.99 - 3.86 (m, 2 H), 3.81 (s, 3 H), 3.02 - 2.94 (m, 1 H), 2.80 - 2.68 (m, 2 H), 1.87 - 1.66 (m, 2 H), 1.27 (d, J = 6.1 Hz, 3 H)

**¹³C NMR** (125 MHz, CDCl₃): δ = 159.3, 129.4, 113.9, 71.9, 70.3, 67.1, 55.3, 54.3, 44.4, 39.8, 19.4

**HRMS (ESI)** for C₁₄H₂₀O₄Na (M + Na)⁺ found 275.1248, calcd 275.1254

(1R,3R)-3-((4-Methoxybenzyl)oxy)-1-((R)-oxiran-2-yl)butan-1-ol (144)

![Structure](image)

Compound 144 was synthesized using the same procedure as described for compound 139 in 75% yield.

**Mol. Formula:** C₁₄H₂₀O₄
Mol. Weight: 252.14  
$[\alpha]_{D}^{25}$: -42.4 (c 2.5, CHCl$_3$)  
IR (CHCl$_3$, cm$^{-1}$) $\nu_{\text{max}}$ = 3410, 3118, 2584, 1638, 1239.  

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.25 (d, $J= 8.6$ Hz, 2 H), 6.88 (d, $J= 8.3$ Hz, 2 H), 4.59 (d, $J= 11.0$ Hz, 1 H), 4.36 (d, $J= 11.2$ Hz, 1 H), 3.86 - 3.81 (m, 1 H), 3.80 (s, 3 H), 3.75 - 3.67 (m, 1 H), 3.37 (d, $J= 2.7$ Hz, 1 H), 3.02 - 2.94 (m, 1 H), 2.78 - 2.72 (m, 1 H), 2.70 - 2.60 (m, 1 H), 1.86 (td, $J= 9.2$, 14.4 Hz, 1 H), 1.74 - 1.61 (m, 1 H), 1.26 (d, $J= 6.1$ Hz, 3 H)  

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 159.3, 130.0, 129.4, 113.9, 74.1, 70.7, 69.9, 55.2, 54.9, 44.3, 40.3, 19.6  

HRMS (ESI) for C$_{14}$H$_{20}$O$_{4}$Na (M + Na)$^+$ found 275.1249, calcd 275.1254  

(4R,5S)-4-((R)-2-((4-Methoxybenzyl)oxy)propyl)-2,2-dimethyl-5-vinyl-1,3-dioxolane (145)  

Compound 145 was synthesized using the same procedure as described for compound 136.  

Mol. Formula: C$_{18}$H$_{26}$O$_{4}$  
Mol. Weight: 306.18  
$[\alpha]_{D}^{25}$: -8.47 (c 2.0, CHCl$_3$)  
IR (CHCl$_3$, cm$^{-1}$) $\nu_{\text{max}}$ = 3082, 2964, 1648, 1573, 1402, 1119, 789.  

$^1$H NMR (400MHz, CDCl$_3$): $\delta$ = 7.27 (d, $J= 8.6$ Hz, 2 H), 6.88 (d, $J= 8.6$ Hz, 2 H), 5.79 (ddd, $J= 7.3$, 10.1, 17.3 Hz, 1 H), 5.36 (d, $J= 17.1$ Hz, 1 H), 5.24 (d, $J= 10.3$ Hz, 1 H), 4.50 (d, $J= 11.2$ Hz, 1 H), 4.38 (d, $J= 11.0$ Hz, 1 H), 4.05 (t, $J= 7.8$ Hz, 1 H), 3.81 (s, 3 H), 3.80 - 3.77 (m, 1 H), 3.76 - 3.66 (m, 1 H), 1.96 (td, $J= 7.1$, 14.0 Hz, 1 H), 1.68 (ddd, $J= 4.4$, 6.5, 14.1 Hz, 1 H), 1.43 (s, 3 H), 1.41 (s, 3 H), 1.24 (d, $J= 5.9$ Hz, 3 H)  

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 159.1, 135.2, 130.9, 129.2, 119.0, 113.7, 108.6, 82.8, 77.6, 71.8, 69.9, 55.3, 38.5, 27.3, 26.9, 19.6  

HRMS (ESI) for C$_{18}$H$_{26}$O$_{4}$Na (M + Na)$^+$ found 329.1725, calcd 329.1723
Compound 146 was synthesized using the same procedure as described for compound 141.

**Mol. Formula:** C₁₇H₂₆O₅  
**Mol. Weight:** 310.18  
[α]D²⁵: +0.81 (c 5.8, CHCl₃)  
**IR (CHCl₃, cm⁻¹)** νmax = 3412, 3018, 2854, 1458, 1263, 1099, 759.  
**¹H NMR** (400 MHz, CDCl₃): δ = 7.26 (d, J = 8.3 Hz, 2 H), 6.87 (d, J = 8.3 Hz, 2 H), 4.51 (d, J = 11.2 Hz, 1 H), 4.38 (d, J = 11.0 Hz, 1 H), 4.06 - 3.96 (m, 1 H), 3.80 (s, 3 H), 3.74 (m, 2 H), 3.66 - 3.56 (m, 1 H), 2.09 - 1.92 (m, 2 H), 1.76 - 1.65 (m, 2 H), 1.41 (s, 3 H), 1.39 (s, 3 H), 1.26 (d, J = 6.1 Hz, 3 H)  
**¹³C NMR** (100 MHz, CDCl₃): δ = 159.1, 130.6, 129.3, 129.2, 113.8, 108.5, 81.4, 74.1, 71.8, 69.9, 61.9, 55.3, 39.6, 27.3, 27.0, 19.4  
**HRMS (ESI)** for C₁₇H₂₆O₅Na (M + Na)⁺ found 333.1674, calcd 333.1672

To the stirred solution of alcohol 146 (0.56 g, 1.8 mmol) in dry DCM, Et₃N (0.5 mL, 3.6 mmol) and DMAP (22 mg, 0.2 mmol) were added at rt and the mixture was stirred for 10 minute. TsCl (0.9 g, 4.8 mmol) was added to it and stirring was continued at rt for another 3 h. The reaction was diluted with saturated aq NH₄Cl (20 mL) and extracted with DCM (5 x 10 mL). The combined organic layers were washed with H₂O and brine, dried over Na₂SO₄ and concentrated in vacuo. The crude tosylate product was purified by column chromatography(100-200 mesh, eluent: 5% EtOAc/ pet ether) to give the tosyl ester 147 (0.67g, overall yield 80%) as a yellow liquid.

**Yield:** 0.67 g, 80%
Mol. Formula: C$_{24}$H$_{32}$O$_7$S
Mol. Weight: 464.19
$[\alpha]_D^{25}$: -12.3 (c 0.3, CHCl$_3$)

IR (CHCl$_3$, cm$^{-1}$) $\nu_{\text{max}}$ = 3392, 2754, 1858, 1463, 1009, 959.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta =$ 7.83 - 7.72 (d, $J =$ 8.2 Hz, 2 H), 7.32 (d, $J =$ 8.5 Hz, 2 H), 7.25 (d, $J =$ 8.2 Hz, 2 H), 6.91 - 6.85 (d, $J =$ 8.5 Hz, 2 H), 4.56 - 4.46 (m, 1 H), 4.35 (d, $J =$ 11.3 Hz, 1 H), 4.14 - 4.02 (m, 2 H), 3.96 (dt, $J =$ 4.9, 7.5 Hz, 1 H), 3.91 - 3.85 (m, 1 H), 3.81 (s, 3 H), 3.73 - 3.67 (m, 1 H), 2.44 (s, 3 H), 1.93 (td, $J =$ 6.8, 13.9 Hz, 1 H), 1.74 - 1.62 (m, 1 H), 1.37 (s, 3 H), 1.30 (s, 3 H), 1.23 (d, $J =$ 6.4 Hz, 3 H)

$^{13}$C NMR (50 MHz, CDCl$_3$): $\delta =$ 159.1, 144.9, 132.7, 130.7, 129.8, 129.1, 127.9, 113.7, 109.3, 78.3, 74.6, 71.5, 69.8, 69.0, 55.3, 39.5, 27.3, 26.6, 21.6, 13.4

HRMS (ESI) for C$_{24}$H$_{32}$O$_7$SNa (M + Na)$^+$ found 487.1762, calcd 487.1761

**Ophiocerin B (3)**

![Ophiocerin B](image_url)

The compound 147 (0.255 g, 0.55 mmol) was dissolved in 15 mL of DCM/ H$_2$O (18:1) and DDQ (0.187 g, 0.825 mmol) was added to it in one portion. The reaction mixture was stirred at room temperature for 1 h. Completion of the reaction was monitored by TLC. The reaction mixture was diluted with 5% NaHCO$_3$ solution, water and brine and extracted with DCM (3X20 ml). The organic layer was dried over Na$_2$SO$_4$ and concentrated in vacuo. The crude residue was used for next step without further purification.

To the stirred solution of crude tosylate in dry Et$_2$O (3 mL) was added t-BuOK (124 mg, 1.1 mmol) at 0°C, and the mixture was stirred for 1 h at 0°C and monitored by TLC. After completion of the reaction it was diluted with satd aq NH$_4$Cl (10 mL), and the mixture was extracted with Et$_2$O (4x 5 mL). The combined organic layers were washed with H$_2$O and brine, concentrated in vacuo and then treated with PTSA (3 mg) and MeOH (5 mL) with stirring at rt for another 2 h. The reaction was quenched with satd aq NaHCO$_3$ solution extracted with DCM (3 X 20 mL) and the combined organic layers were washed with H$_2$O and brine, dried over Na$_2$SO$_4$ and concentrated. The residue was purified by
silica gel column chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to produce the ophiocerin B (3) (0.059 g, overall yield 82%) as a yellow oil.

**Yield:** 0.059 g, 82%

**Mol. Formula:** C_6H_{12}O_3

**Mol. Weight:** 132.16

[α]_D^{25}:-35.2 (c 1.3, CH_2Cl_2); lit^[2] [α]_D^{25} = - 37.0 (c 0.1, CH_2Cl_2)

**IR (CHCl_3, cm^-1) ν_{max} = 3398, 1467, 1389, 1287, 1104, 987**

**^1H NMR** (500 MHz, CDCl_3): δ = 4.01 - 3.94 (m, 2 H), 3.91 - 3.81 (m, 1 H), 3.73 (dd, J = 12.5, 1.8 Hz, 1 H), 3.48 (m, 1H), 2.27 (br. s., 2 H), 1.81 (ddd, J = 3.2, 10.9, 14.3 Hz, 1 H), 1.63-1.60 (m, 1 H), 1.19 (d, J = 6.4 Hz, 3 H)

**^13C NMR** (125 MHz, CDCl_3): δ = 68.4, 68.3, 67.4, 67.3, 36.0, 21.2

**HRMS (ESI) for C_6H_{12}O_3Na (M + Na)^+ found 155.0680, calcd 155.0679**

(R)-1-((4S,5S)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)propan-2-yl acetate (148)

To a precooled (0°C) solution of 137 (0.725 g, 3.9 mmol) in dry pyridine (5 mL) was added acetic anhydride (1.0 mL, 7.74 mmol) and DMAP (cat.) and stirred at room temperature for 4 h. After completion of the reaction, the reaction was diluted with 10% aq.CuSO_4·5H_2O solution and extracted with ethyl acetate (3 x 20 mL). The combined organic extract was washed with brine solution, dried over Na_2SO_4 and evaporated under vacuum to furnish the crude residue, which was purified over silica gel column chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to give acetate compound 148 (0.8 g, 90%) as a yellow oil.

**Yield:** 0.800 g, 90%

**Mol. Formula:** C_{12}H_{20}O_4

**Mol. Weight:** 228.16

[α]_D^{25}:-16.48 (c 2.5, CHCl_3)

**IR (CHCl_3, cm^-1) ν_{max} = 3081, 2854, 1685, 1458, 1263, 1009, 917.**

**^1H NMR** (400 MHz, CDCl_3): δ = 5.86 - 5.71 (m, 1 H), 5.38 (d, J = 17.1 Hz, 1 H), 5.27 (d, J = 10.3 Hz, 1 H), 5.14 - 4.97 (m, 1 H), 4.01 - 3.90 (m, 1 H), 3.80 - 3.61 (m, 1 H),
2.03 (s, 3 H), 1.92 - 1.79 (m, 1 H), 1.74 - 1.64 (m, 1 H), 1.40 (s, 3 H), 1.38 (s, 3 H), 1.27 (d, J = 6.4 Hz, 3 H)

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 170.5, 134.9, 119.2, 108.8, 82.7, 77.2, 68.6, 38.2, 27.2, 26.9, 21.3, 20.6

HRMS (ESI) for C$_{12}$H$_{20}$O$_4$Na (M + Na)$^+$ found 251.1254, calcd 251.1254

Ethyl(Z)-3-((4S,5S)-5-((R)-2-Acetoxypropyl)-2,2-dimethyl-1,3-dioxolan-4-yl)acrylate (149)

Olefin 148 (0.205 g, 1.1 mmol) was dissolved in 10 mL of DCM and cooled to -78 °C. Ozone was passed through the solution until a blue tint was observed (ca. 3 min) and 6 mL of dimethyl sulfide was added to this resulting blue solution. The reaction mixture was allowed to warm to room temperature and stirred for 12h at which point the reaction mixture was concentrated and crude aldehyde was used for next step without purification.

Ethyl [bis(2,2,2-trifluoroethoxy)phosphinyl]acetate (320 mg, 1.4 mmol), 18-crown-6 (2.47 g, 9.36 mmol) was taken in dry THF (10 mL) at -78 °C and KHMDS (0.67 g, 2.93 mmol) was added to the reaction mixture and stirred for 1h. Then, the above crude aldehyde (0.179 g, 0.95 mmol) dissolved in THF (5 mL) was added to it and stirred for another 6 h at -78°C, at which time it shows complete consumption of starting material. Then the reaction mixture was quenched with saturated aq NH$_4$Cl and extracted with ethyl acetate (3x20 ml). The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, evaporated in vacuo and the residue was purified over silica gel (100-200 mesh, eluent 10% EtOAc/hexane) to give the product 149 (0.290 g, 88%) as colorless syrup.

Yield: 0.290 g, 88%

Mol. Formula: C$_{15}$H$_{24}$O$_6$

Mol. Weight: 300.16

IR (CHCl$_3$, cm$^{-1}$) $\nu_{max}$ = 2975, 2940, 1732, 1645, 1357, 1263, 1199, 1019.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.11 (dd, $J$ = 8.8, 11.7 Hz, 1 H), 5.95 (d, $J$ = 12.2 Hz, 1 H), 5.28-5.23 (m, 1 H), 5.14 - 4.94 (m, 1 H), 4.18 (q, $J$ = 7.3 Hz, 2 H), 3.84 - 3.66 (m, 1 H), 2.00 (s, 3 H), 1.91 - 1.69 (m, 2 H), 1.42 (s, 3 H), 1.39 (s, 3 H), 1.29 (t, $J$ = 7.1 Hz, 3 H), 1.24 (d, $J$ = 6.4 Hz, 3 H)
\( ^{13}\text{C NMR} \) (100 MHz, CDCl\(_3\)): \( \delta = 170.4, 165.4, 145.2, 123.3, 109.5, 77.9, 76.4, 68.5, 60.5, 38.2, 29.6, 27.3, 26.9, 21.3, 14.1 \)

HRMS (ESI) for C\(_{13}\)H\(_{24}\)O\(_6\)Na (M + Na\(^{+}\)) found 323.1460, calcd 323.1465

**Botryolide -E (4)**

The ester 149 (150 mg, 0.5 mmol) was dissolved in THF and 1M HCl solution (1mL) was added to it and stirred for 2 h at 0\(^{\circ}\)C. After consumption of starting material (monitored by TLC), the reaction was quenched with saturated NaHCO\(_3\) and extracted into EtOAc (3x10 mL). The combined organic layers were washed with brine solution, dried (Na\(_2\)SO\(_4\)) and concentrated under reduced pressure to provide crude lactone, which was purified by column chromatography (silica gel 100-200 mesh, 40% EtOAc/pet ether) to afford pure lactone 4 (100mg, 95%).

**Yield:** 0.100 g, 95%

**Mol. Formula:** C\(_{10}\)H\(_{14}\)O\(_5\)

**Mol. Weight:** 214.16

\([\alpha]_{D}^{25}:-36.1 \; (c \; 2.5, \; \text{CHCl}_3); \; \text{lit}^{11}[\alpha]_{D}^{25} = -38.0 \; (c \; 0.05, \; \text{CHCl}_3)\)

**IR** (CHCl\(_3\), cm\(^{-1}\)) \( \nu_{\text{max}} = 3432, 3008, 2844, 1743, 1720, 1658, 1256. \)

\(^1\text{H NMR} \) (500 MHz, CDCl\(_3\)): \( \delta = 7.50 \) (dd, \( J =1.5,6.1 \) Hz, 1H), 6.19 (dd, \( J = 2.1, 5.8 \) Hz, 1H), 5.18 - 5.08 (m, 1 H), 5.07 - 4.98 (m, 1 H), 3.96 - 3.84 (m, 1 H), 2.04 (s, 3 H), 1.95 - 1.88 (m, 1 H), 1.80 - 1.73 (m, 1 H), 1.31 (d, 3H, \( J = 6.1 \) Hz)

\(^{13}\text{C NMR} \) (50 MHz, CDCl\(_3\)): \( \delta = 172.8, 170.8, 153.7, 122.8, 85.3, 69.0, 68.7, 39.1, 21.3, 20.0 \)

HRMS (ESI) for C\(_{10}\)H\(_{14}\)O\(_5\)Na (M + Na\(^{+}\)) found 237.0733, calcd 237.0733

(S)-4-((4-Methoxybenzyl)oxy)butane-1,2-diol (152):
To a solution of PMB-protected butanal 150 (1.13 g, 5.43 mmol) and nitroso benzene (0.581 g, 5.43 mmol) in anhydrous DMSO (29 mL), D-proline (0.187 g, 1.63 mmol) was added at room temperature turning the solution green. The reaction mixture was vigorously stirred for 1h under argon (the reaction color changed from green to yellow during this time). Then the temperature was lowered to 0 °C followed by addition of methanol and sodium borohydride to the reaction mixture. After completion of the reaction (monitored by TLC), the resulting mixture was diluted with water and extracted with EtOAc (4 x 20 mL) and the combined organic phases were washed with brine, dried over Na₂SO₄ and concentrated to give the crude aminooxy alcohol, which was directly taken for the next step without purification. To a well stirred solution of this aminooxy alcohol in methanol, CuSO₄·5H₂O (1.35 g, 5.43 mmol) was added and stirred for overnight at rt. The reaction mixture was filtered through celite and concentrated in vacuo. The compound was purified by column chromatography (silica gel mesh 100-200, 40% EtOAc/pet ether ) to afford diol 32 in 78% yield.

**Yield:** 0.958 g, 78%

**Mol. Formula:** C₁₂H₁₈O₄

**Mol. Weight:** 226.12

[α]D²⁵: -4.8 (c 1.7, CHCl₃); lit³⁹[α]D²⁵ = - 5.2 (c 2.0, CHCl₃)

**IR (CHCl₃, cm⁻¹)** νmax = 3446, 2980, 2932, 2853, 1623,1533

**¹H NMR** (400 MHz, CDCl₃): δ = 7.24 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 4.44 (s, 2 H), 3.91 - 3.82 (m, 1 H), 3.79 (s, 3 H), 3.68 - 3.54 (m, 3 H), 3.50 - 3.41 (m, 1 H), 3.17 (br. s., 2 H), 1.81 - 1.68 (m, 2 H)

**¹³C NMR** (100 MHz, CDCl₃): δ = 159.2, 129.8, 129.3, 113.8, 72.8, 71.0, 67.6, 66.4, 55.2, 32.7

**HRMS (ESI)** for C₁₂H₁₈O₄Na (M + Na)⁺ found 249.1095, calcd 249.1097

(S)-2-(2-((4-Methoxybenzyl)oxy)ethyl)oxirane (153):

To a mixture of diol 152 (0.4 g, 1.77 mmol) in dry CH₂Cl₂ (20 mL) under argon atmosphere was added dibutyltinoxide (9 mg, 0.0354 mmol) followed by addition of p-toluene sulfonyl chloride (0.337 mg, 1.77 mmol), Et₃N (0.25 mL, 1.77 mmol). The
resulting mixture was stirred at room temperature for 2 h and quenched with water and then extracted with DCM (3x10 mL). The combined organic phase was washed with water, dried (Na$_2$SO$_4$) and concentrated to give a crude monotosylate product, which was dissolved in MeOH (10 mL) and treated with K$_2$CO$_3$ (0.5 g, 3.61 mmol). This mixture was stirred for 1 h at room temperature and then filtered through celite. Removal of the volatiles under reduced pressure gave crude epoxide which was purified by column chromatography (silica gel mesh 100-200, 20% EtOAc/pet ether) to provide compound epoxide 153 in 80% yield.

**Yield:** 0.295 g, 80%

**Mol. Formula:** C$_{12}$H$_{16}$O$_3$

**Mol. Weight:** 208.11

[α]$^D_{25}$-13.5 (c 2.5, CHCl$_3$); lit$^{40}[α]D_{25}$ = -13.1 (c 0.58, CHCl$_3$)

**IR** (CHCl$_3$, cm$^{-1}$) $\nu_{max}$ = 3036, 2987, 2915, 2870, 1643

**$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ = 7.26 (d, $J = 8.5$ Hz, 2 H), 6.90 (d, $J = 8.5$ Hz, 2 H), 4.47 (s, 2 H), 3.81 (s, 3 H), 3.62 - 3.57 (m, 2 H), 3.09 - 3.03 (m, 1 H), 2.78 (t, $J = 4.5$ Hz, 1 H), 2.52 (dd, $J = 2.7$, 4.9 Hz, 1 H), 1.95 - 1.84 (m, 1 H), 1.77 (qd, $J = 6.0$, 14.3 Hz, 1 H)

**$^{13}$C NMR** (50 MHz, CDCl$_3$): $\delta$ = 159.1, 130.3, 129.2, 113.7, 72.7, 66.6, 55.2, 50.0, 47.0, 32.9

**HRMS (ESI)** for C$_{12}$H$_{16}$O$_3$Na (M + Na)$^+$ found 231.0988, calcd 231.0992

(S)-tert-Butyl((5-((4-methoxybenzyl)oxy)pent-1-en-3-yl)oxy)dimethylsilane (154):

![Chemical Structure](attachment:image)

To a stirred solution of dry THF was added trimethylsulfonium iodide (1.23 g, 6.05 mmol) at -20°C followed by n-BuLi (3.8 mL, 1.6 M, 6.05 mmol). The reaction mixture was stirred for 1 h after which epoxide 153 (0.251 g, 1.21 mmol) in THF was added dropwise. The reaction mixture was stirred at -20°C for 3 h and completion of the reaction was monitored by TLC. The reaction mixture was diluted with saturated solution of ammonium chloride and extracted with EtOAc (2x50 mL). The combined organic layers were washed with water (2 x50 mL), brine, dried over Na$_2$SO$_4$ and concentrated. The crude alcohol was used for the next step without further purification.
To a stirred solution of crude alcohol (0.210 g, 0.95 mmol) and imidazole (0.129 g, 1.9 mmol) in dry DCM at 0°C, t-butyldimethylchlorosilane (0.212 g, 1.41 mmol) was added dropwise and the reaction mixture was stirred for 4 h at room temperature. After completion of the reaction, water was added to quench the reaction mixture and the organic layer was washed with excess water and brine. The organic layer was dried over Na₂SO₄ and concentrated to afford the crude silylated compound, which was purified by silica gel chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to afford 154 (0.330 g, 82%) as a viscous liquid.

Yield: 0.330 g, 82%

Mol. Formula: C₁₉H₃₂O₃Si

Mol. Weight: 336.21

[α]D²⁵: +3.5 (c 1.6, CHCl₃)

IR (CHCl₃, cm⁻¹) νmax = 3072, 3028, 2967, 2912, 1709, 1613, 1485, 1203, 1099.

¹H NMR (200 MHz, CDCl₃): δ = 7.27 (d, J = 8.2 Hz, 2 H), 6.89 (d, J = 8.5 Hz, 2 H), 5.81 (ddd, J = 6.1, 10.5, 16.9 Hz, 1 H), 5.16 (d, J = 17.1 Hz, 1 H), 5.02 (d, J = 10.4 Hz, 1 H), 4.48 - 4.36 (m, 2 H), 4.30 (q, J = 6.0 Hz, 1 H), 3.82 (s, 3 H), 3.59 - 3.43 (m, 2 H), 1.78 (q, J = 5.7 Hz, 2 H), 0.90 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 3 H)

¹³C NMR (50 MHz, CDCl₃): δ = 159.1, 141.6, 130.7, 129.3, 113.7, 72.6, 70.8, 66.4, 55.3, 38.1, 25.9, 18.2, -4.4, -4.9

HRMS (ESI) for C₁₉H₃₂O₃Si Na (M + Na)⁺ found 359.2014, calcd 359.2013

(S)-3-(((tert-Butyldimethylsilyl)oxy)pent-4-enoic acid (155):

Olefin 154 (0.250 g, 0.744 mmol) was dissolved in 15 mL of DCM/ H₂O (18:1). DDQ (0.253 g, 1.12 mmol) was added to it in one portion. The reaction mixture was stirred at room temperature for 1 h. Completion of the reaction was monitored by TLC. The reaction mixture was diluted with 5% NaHCO₃ solution, water and brine and extracted with DCM (3X20 ml). The organic layer was dried over Na₂SO₄ and concentrated in vacuo. The crude alcohol was used for next step without further purification.

To a stirred solution of crude primary alcohol (0.194 g, 0.9 mmol) in CH₃CN (3 mL) and H₂O (1 mL) were added TEMPO (29 mg, 0.1 mmol) and BAIB (0.9 g, 2.8 mmol) at 0°C
and monitored by TLC. The reaction mixture was stirred for 7h, until TLC indicated the complete consumption of starting material. The reaction was diluted by the addition of saturated aqueous Na₂SO₃ (20 mL), and the aqueous layer was extracted with EtOAc (3x20 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexane, 25%) to give 155 (0.128 g, 75%) as light yellow oil.

Yield: 0.128 g, 75%

Mol. Formula: C₁₁H₂₂O₃Si

Mol. Weight : 230.13

[α]D²⁵: + 2.8 (c 1.8, CHCl₃); lit⁶[α]D²⁵ = + 2.1 (c 0.4, CHCl₃)

IR (CHCl₃, cm⁻¹) νmax = 2954, 2856, 1741, 1446, 812

¹H NMR (400 MHz, CDCl₃): δ = 5.86 (ddd, J = 6.2, 10.5, 17.0 Hz, 1 H), 5.27 (dd, J = 1.1, 17.2 Hz, 1 H), 5.13 (dd, J = 1.1, 10.4 Hz, 1 H), 4.69 - 4.50 (m, 1 H), 2.56 (dd, J = 2.7, 6.1 Hz, 2 H), 0.90 (s, 9 H), 0.09 (s, 3 H), 0.07 (s, 3 H)

¹³C NMR (100 MHz, CDCl₃): δ = 175.7, 139.4, 115.4, 70.6, 43.0, 25.7, 18.1, -4.4, -5.2

HRMS (ESI) for C₁₁H₂₂O₃Si Na (M + Na)⁺ found 253.1231, calcld 253.1230

(R)-1-((4S,5S)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)propan-2-yl-(S)-3-((tert-butyldimethylsilyl)oxy)pent-4-enoate (156):

To a stirred solution of triethylamine (66.1 mg, 0.653 mmol) in dry DCM (5 mL) was added DMAP (2.5 mg, 0.020 mmol) followed by MNBA (82.9 mg, 0.241 mmol) and acid 155 (0.056 g, 0.242 mmol). The reaction mixture was stirred for another 45 minute, then hydroxy olefin 17 (0.037g, 0.2mmol) in dry DCM was added to it and progress of the reaction was monitored by TLC. Then this reaction mixture was stirred for 12 h and quenched by addition of satd aqueous NH₄Cl solution. The aqueous layer was extracted with DCM (3x20 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using petroleum ether : EtOAc (80:20) as an eluent to afford 156 (0.075 g, 95%) as a colorless liquid.
Yield: 0.075 g, 95%

Mol. Formula: C_{21}H_{38}O_{5}Si

Mol. Weight: 398.11

$[\alpha]_D^{25}$ = -6.92 (c 1.1, CHCl$_3$); lit$^{16}[\alpha]_D^{25}$ = -5.25 (c 0.4, CHCl$_3$)

IR (CHCl$_3$, cm$^{-1}$) $\nu_{\text{max}}$ = 3023, 2909, 2875, 1773, 1664, 1436, 1337, 1252.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 5.90 - 5.71 (m, 2 H), 5.37 (d, $J = 17.1$ Hz, 1 H), 5.29 - 5.17 (m, 2 H), 5.13 - 4.98 (m, 2 H), 4.63 - 4.52 (m, 1 H), 4.02 - 3.90 (m, 1 H), 3.78 - 3.60 (m, 1 H), 2.52 (dd, $J = 7.0$, 15.0 Hz, 1 H), 2.41 (dd, $J = 5.8$, 14.6 Hz, 1 H), 1.95 - 1.79 (m, 1 H), 1.77 - 1.59 (m, 1 H), 1.39 (s, 3 H), 1.38 (s, 3 H), 1.27 (d, $J = 6.1$ Hz, 3 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H)

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 170.3, 140.2, 134.8, 119.3, 114.6, 108.9, 82.8, 77.2, 68.9, 43.8, 38.4, , 27.2, 26.9, 25.8, 20.6, 18.1, -4.4, -4.5

HRMS (ESI) for C$_{21}$H$_{38}$O$_5$Si Na (M + Na)$^+$ found 421.2381, calcd 421.2381

(3S,5R,9S,11S,E)-9-(tert-Butyl dimethyl silyloxy)-2,2,5-trimethyl-4,5,8,9-tetrahydro-3-(1,3)dioxolo(4,5)oxecin-7-one (157):

To the solution of diene 156 (0.125 g, 0.314 mmol) in 250 ml freshly distilled DCM (degassed for 15 minute through bubbling of argon, Grubbs’ II catalyst (0.027 g, 10 mol %) was added to it and then again the solution was degassed for 1 h. The reaction mixture was refluxed at 45°C for 24 h (completion of the reaction was checked by TLC). The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (silica gel, 230-400 mesh, 30% EtOAc/pet ether) to afford compound 157 (0.14 g, 75%) as a colourless oil.

Yield: 0.087 g, 75%

Mol. Formula: C$_{19}$H$_{34}$O$_5$Si

Mol. Weight: 370.15

$[\alpha]_D^{25}$ = -9.81 (c 1.5, CHCl$_3$); lit$^{16}[\alpha]_D^{25}$ = -8.1 (c 0.4, CHCl$_3$)

IR (CHCl$_3$, cm$^{-1}$) $\nu_{\text{max}}$ = 2919, 2837, 1753, 1126, 1087.
**1H NMR** (400 MHz, CDCl$_3$): $\delta = 5.97 - 5.87$ (m, 1 H), 5.70 - 5.58 (m, 1 H), 5.04 - 4.92 (m, 1 H), 4.72 - 4.63 (m, 1 H), 4.10 (t, $J = 8.8$ Hz, 1 H), 3.63 (t, $J = 8.8$ Hz, 1 H), 2.46 (d, $J = 3.4$ Hz, 2 H), 2.06 - 1.85 (m, 2 H), 1.41 (s, 6 H), 1.22 (d, $J = 6.4$ Hz, 3 H), 0.93 (s, 9 H), 0.11 (s, 3 H), 0.07 (s, 3 H)

**13C NMR** (50 MHz, CDCl$_3$): $\delta = 168.4, 138.1, 122.8, 107.9, 84.1, 81.6, 69.0, 67.9, 45.2, 38.5, 27.0, 26.9, 25.7, 21.8, 18.3, -5.0, -5.2

**HRMS (ESI)** for C$_{19}$H$_{34}$O$_5$Si Na (M + Na)$^+$ found 393.2064, calcd 393.2068

**Decarestrictine O (5)**

The protected lactone 157 (0.087 mg, 0.235 mmol) was dissolved in THF and 1M HCl solution (1mL) was added to it and stirred for 2 h at 0°C. After consumption of starting material (monitored by TLC), the reaction was quenched with saturated NaHCO$_3$ and extracted into EtOAc (3x10 mL). The combined organic layers were washed with brine solution, dried (Na$_2$SO$_4$) and concentrated under reduced pressure to provide crude lactone, which was purified by column chromatography (silica gel 100-200 mesh, 40% EtOAc/pet ether) to afford pure lactone 5 (101mg, 68%) as colourless thick liquid.

**Yield:** 0.034 g, 68%

**Mol. Formula:** C$_{10}$H$_{16}$O$_5$

**Mol. Weight:** 216.10

$\left[\alpha\right]_{D}^{25}$: -20.13 (c 0.8, MeOH); lit$^{16}$ $\left[\alpha\right]_{D}^{25}$ = -19.6 (c 0.2, MeOH)

**IR** (CHCl$_3$, cm$^{-1}$) $\nu_{\text{max}}$ = 3412, 2918, 1754, 1485.

**1H NMR** (400 MHz, CD$_3$OD): $\delta = 5.89$ (dd, $J = 3.1$, 15.8 Hz, 1 H), 5.52 (dd, $J = 10.8$, 15.8 Hz, 1 H), 4.80 - 4.69 (m, 1 H), 4.63-4.62 (m, 1 H), 3.75 (t, $J = 9.2$ Hz, 1 H), 3.38 (t, $J = 9.3$ Hz, 1 H), 2.52 (dd, $J = 3.8$, 11.9 Hz, 1 H), 2.43 (dd, $J = 3.5$, 11.9 Hz, 1 H), 1.95 - 1.88 (m, 1 H), 1.75 (d, $J = 15.9$ Hz, 1 H), 1.20 (d, $J = 6.6$ Hz, 3 H)

**13C NMR** (50 MHz, CD$_3$OD): $\delta = 171.9, 137.6, 127.1, 80.0, 77.2, 70.9, 68.1, 44.5, 44.2, 23.4

**HRMS (ESI)** for C$_{10}$H$_{16}$O$_5$Na (M + Na)$^+$ found 239.0889, calcd 239.0890

193
tert-Butyl(((3S,5R)-5-((4-methoxybenzyl)oxy)hex-1-en-3-yl)oxy)diphenylsilane (158)

To a stirred solution of compound 133a (1.93 g, 3.8 mmol) in dry THF (150 ml), triphenylphosphine (3.0 g, 11.4 mmol) and imidazole (1.56 g, 22.9 mmol) was added followed by iodine (2.9 g, 11.4 mmol) at 0°C. Then the reaction mixture was refluxed for 4 h, cooled to room temperature after which it was diluted with saturated aqueous Na$_2$S$_2$O$_3$ (100 ml) and extracted with ethyl acetate (2 x 30 mL). The combined organic phase was washed with brine, dried (Na$_2$SO$_4$) and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (100-200 mesh silica gel, 5%EtOAc/hexane as an eluent) to afford olefin 158 (1.5 g, 83%) as a colorless oil.

Yield: 1.5 g, 83%

Mol. Formula: C$_{30}$H$_{38}$O$_3$Si

Mol. Weight: 474.26

$[\alpha]_D^{25}$: +13.45 (c 5.0, CHCl$_3$)

IR (CHCl$_3$, cm$^{-1}$): $\nu_{\max}$ = 3072, 2932, 2866, 1614, 1459, 1426, 1377, 1260, 1106, 992.

$^{1}$H NMR (500 MHz, CDCl$_3$): $\delta$ = 7.71-7.67 (m, 4H), 7.46 - 7.32 (m, 6 H), 7.14 (d, $J$ = 8.2 Hz, 2 H), 6.85 (d, $J$ = 8.2 Hz, 2 H), 5.85 - 5.75 (m, 1 H), 4.95 - 4.85 (m, 2 H), 4.40 - 4.29 (m, 2 H), 4.15 (d, $J$ = 10.7 Hz, 1 H), 3.81 (s, 3 H), 3.63 - 3.54 (m, 1 H), 1.81 (td, $J$ = 6.5, 13.5 Hz, 1 H), 1.74 - 1.64 (m, 1 H), 1.09 - 1.05 (m, 12 H)

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 158.9, 141.0, 136.0, 135.9, 134.3, 131.1, 129.5, 129.4, 129.1, 129.0, 127.5, 127.3, 114.5, 113.6, 72.5, 71.7, 69.8, 55.3, 45.6, 27.0, 19.9, 19.3

HRMS (ESI) for C$_{30}$H$_{38}$O$_3$SiNa (M + Na)$^+$ found 497.2479, calcld 497.2482

(2$R$,4$S$)-4-((tert-Butyldiphenylsilyl)oxy)hex-5-en-2-ol (159)
Olefin 158 (0.15 g, 0.316 mmol) was dissolved in 15 mL of DCM/ H\textsubscript{2}O (18:1). DDQ (0.108 g, 0.474 mmol) was added to it in one portion. The reaction mixture was stirred at room temperature for 1 h. Completion of the reaction was monitored by TLC. The reaction mixture was diluted with 5% NaHCO\textsubscript{3} solution, water and brine and extracted with DCM (3X20 ml). The organic layer was dried over Na\textsubscript{2}SO\textsubscript{4} and concentrated \textit{in vacuo}. The crude product was purified by column chromatography (100-200 mesh silica gel, 15%EtOAc/hexane as an eluent) to afford olefin 159 (0.093 g, 80\%) as a colorless oil.

\textbf{Yield:} 0.089 g, 80\%

\textbf{Mol. Formula:} C\textsubscript{22}H\textsubscript{30}O\textsubscript{2}Si

\textbf{Mol. Weight :} 354.20

\([\alpha]\textsubscript{D}\textsuperscript{25}:-6.25 (c 1.2, CHCl\textsubscript{3}); \text{lit} \_[\alpha]\textsubscript{D}\textsuperscript{25} = -5.3 (c 1.3, CHCl\textsubscript{3})

\textbf{IR (CHCl\textsubscript{3}, cm\textsuperscript{-1})} \nu_{\text{max}} = 3479, 2924, 2845, 1436, 1471, 1206, 1119, 969, 942, 812, 716.

\textbf{\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}):} \delta = 7.76 - 7.64 (m, 4 H), 7.49 - 7.36 (m, 6 H), 5.86 (ddd, \(J = 5.9, 10.7, 16.9\) Hz, 1 H), 5.12 - 4.99 (m, 2 H), 4.47 (q, \(J = 5.1\) Hz, 1 H), 4.11 - 4.03 (m, 1 H), 1.69 (ddd, \(J = 4.4, 9.8, 14.4\) Hz, 1 H), 1.55 - 1.47 (m, 1 H), 1.10 (s, 12 H)

\textbf{\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}):} \delta= 139.5, 136.0, 135.9, 133.3, 133.2, 129.9, 129.8, 127.7, 127.5, 115.0, 73.8, 64.6, 44.8, 27.0, 23.4, 19.2

\textbf{HRMS (ESI) for C\textsubscript{22}H\textsubscript{30}O\textsubscript{2}SiNa (M + Na)}\textsuperscript{+} found 377.1904, calcd 377.1907

\textit{tert-Butyl((3S,5S)-5-((4-methoxybenzyl)oxy)hex-1-en-3-yl)oxy)diphenylsilane (160)}

\[
\begin{array}{c}
\text{PMBO} \\
\text{OTBDPS}
\end{array}
\]

Compound 160 was synthesized using the same procedure as described for the synthesis of compound 158 in 82\% yield.

\textbf{Mol. Formula:} C\textsubscript{30}H\textsubscript{38}O\textsubscript{3}Si

\textbf{Mol. Weight :} 474.26

\([\alpha]\textsubscript{D}\textsuperscript{25}:+22.58 (c 8.0, CHCl\textsubscript{3})

\textbf{IR (CHCl\textsubscript{3}, cm\textsuperscript{-1})} \nu_{\text{max}} = 3052, 2922, 2836, 1617, 1449, 1416, 1317, 1267, 1162, 1056.

\textbf{\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}):} \delta = 7.72-7.67 (m, 4 H), 7.48 - 7.35 (m, 6 H), 7.13 (d, \(J = 8.2\) Hz, 2 H), 6.83 (d, \(J = 8.2\) Hz, 2 H), 5.86 - 5.75 (m, 1 H), 4.93 (d, \(J = 10.4\) Hz, 1 H),
4.84 (d, J = 17.7 Hz, 1 H), 4.41 - 4.30 (m, 2 H), 4.24 (d, J = 11.3 Hz, 1 H), 3.82 (s, 3 H), 3.58 - 3.48 (m, 1 H), 2.04 - 1.95 (m, 1 H), 1.59 - 1.50 (m, 1 H), 1.08 (s, 12 H)

\(^{13}\text{C} \text{ NMR} \) (125 MHz, CDCl\(_3\)): \(\delta = 158.9, 140.7, 136.0, 135.9, 134.2, 134.1, 131.1, 129.5, 129.4, 129.0, 127.5, 127.3, 114.6, 113.6, 72.6, 71.3, 69.5, 55.2, 45.2, 27.0, 19.8, 19.3\)

\(\text{HRMS (ESI)}\) for C\(_{30}\)H\(_{38}\)O\(_3\)SiNa (M + Na)^+ found 497.2476, calcd 497.2482

(2S,4S)-4-((tert-Butyldiphenylsilyl)oxy)hex-5-en-2-ol (161):

[Chemical structure image]

Compound 161 was synthesized using the same procedure as described for the synthesis of compound 159 in 84% yield.

**Mol. Formula**: C\(_{22}\)H\(_{30}\)O\(_2\)Si

**Mol. Weight**: 354.20

\([\alpha]_D^{25}\) : -2.87 (c 2.5, CHCl\(_3\))

**IR (CHCl\(_3\), cm\(^{-1}\))** \(\nu_{\text{max}} = 3472, 2942, 2855, 1466, 1451, 1216, 1039, 869, 802, 746\).

\(^1\text{H} \text{ NMR} \) (400 MHz, CDCl\(_3\)): \(\delta = 7.79 - 7.61 \) (m, 4 H), 7.48 - 7.33 (m, 6 H), 5.79 (ddd, J = 6.7, 10.4, 17.1 Hz, 1 H), 4.95 - 4.85 (m, 2 H), 4.40 (q, J = 6.3 Hz, 1 H), 4.04 - 3.96 (m, 1 H), 2.13 (br. s., 1 H), 1.71 (ddd, J = 6.7, 9.0, 14.3 Hz, 1 H), 1.53 (ddd, J = 2.9, 5.9, 14.2 Hz, 1 H), 1.11 (d, J = 6.4 Hz, 3 H), 1.08 (s, 9 H)

\(^{13}\text{C} \text{ NMR} \) (100 MHz, CDCl\(_3\)): \(\delta = 140.5, 136.0, 135.9, 133.8, 133.7, 129.8, 129.6, 127.6, 127.4, 114.9, 74.3, 65.8, 46.3, 27.0, 23.7, 19.3\)

**HRMS (ESI)** for C\(_{30}\)H\(_{38}\)O\(_3\)SiNa (M + Na)^+ found 377.1907, calcd 377.1907

(S)-5-((4-Methoxybenzyl)oxy)pentane-1,2-diol (164):

[Chemical structure image]

Compound 164 was synthesized in 83% yield using the same procedure as described for the synthesis of compound 152.

**Mol. Formula**: C\(_{13}\)H\(_{20}\)O\(_4\)
Mol. Weight : 240.14
$[\alpha]_{D}^{25}$: -2.51 (c 4.2, CHCl₃); lit$^{43}[\alpha]_{D}^{25} = -2.0$ (c 1.1, CHCl₃)

IR (CHCl₃, cm⁻¹) $\nu_{\text{max}}$ = 3412, 2924, 2872, 1602, 1522, 1236, 1076, 809

$^{1}H$ NMR (400 MHz, CDCl₃): $\delta = 7.21 - 7.14$ (m, $J = 8.6$ Hz, 2 H), 6.84 - 6.78 (m, $J = 8.6$ Hz, 2 H), 4.37 (s, 2 H), 3.73 (s, 3 H), 3.64 - 3.55 (m, 1 H), 3.51 (dd, $J = 3.1$, 11.1 Hz, 1 H), 3.45 - 3.31 (m, 3 H), 2.90 (br. s., 2 H), 1.74 - 1.59 (m, 2 H), 1.58 - 1.45 (m, 1 H), 1.43 - 1.34 (m, 1 H)

$^{13}C$ NMR (100 MHz, CDCl₃): $\delta = 159.2$, 129.9, 129.4, 113.8, 72.7, 71.9, 70.1, 66.7, 55.2, 30.7, 26.1

HRMS (ESI) for C₁₃H₂₀O₄Na (M + Na)$^+$ found 263.1252, calcd 263.1254

(S)-2-((3-((4-Methoxybenzyl)oxy)propyl)oxirane (165):

Compound 165 was synthesized in 81% yield using the same procedure as described for the synthesis of compound 153.

Mol. Formula: C₁₃H₁₈O₃
Mol. Weight : 222.13

$[\alpha]_{D}^{25}$: - 5.2 (c 3.5, CHCl₃); lit$^{43}[\alpha]_{D}^{25} = -4.5$ (c 0.88, CHCl₃)

IR (CHCl₃, cm⁻¹) $\nu_{\text{max}}$ = 2913, 2836, 1652, 1510, 1266, 1074, 1034, 811

$^{1}H$ NMR (400 MHz, CDCl₃): $\delta = 7.27 - 7.22$ (m, $J = 8.6$ Hz, 2 H), 6.89 - 6.84 (m, $J = 8.6$ Hz, 2 H), 4.42 (s, 2 H), 3.79 (s, 3 H), 3.54 - 3.41 (m, 2 H), 2.96 - 2.87 (m, 1 H), 2.73 (t, $J = 4.5$ Hz, 1 H), 2.45 (dd, $J = 2.8$, 5.0 Hz, 1 H), 1.79 - 1.55 (m, 4 H)

$^{13}C$ NMR (50 MHz, CDCl₃): $d = 159.1$, 130.5, 129.2, 113.7, 72.5, 69.4, 55.2, 52.1, 47.0, 29.3, 26.1

HRMS (ESI) for C₁₃H₁₈O₃Na (M + Na)$^+$ found 245.1145, calcd 245.1148

(S)-tert-Butyl((6-((4-methoxybenzyl)oxy)hex-1-en-3-yl)oxy)diphenylsilane (166):
To a stirred solution of dry THF was added trimethylsulfonium iodide (2.46 g, 12.1 mmol) at -20°C followed by n-BuLi (7.6 mL, 1.6 M, 12.1 mmol). The reaction mixture was stirred for 1h after which epoxide 165 (0.537 g, 2.42 mmol) in THF was added dropwise. The reaction mixture was stirred at -20°C for 3 h and completion of the reaction was monitored by TLC. The reaction mixture was diluted with saturated solution of ammonium chloride and extracted with EtOAc (2x50 mL). The combined organic layers were washed with water (2 x50 mL), brine, dried over Na$_2$SO$_4$ and concentrated. The crude alcohol was used for the next step without further purification. To a stirred solution of alcohol (0.510 g, 2.16 mmol) and imidazole (0.294 g, 4.32 mmol) in dry DCM at 0°C, TBDPSCI (0.6 ml, 2.6 mmol) was added dropwise and the reaction mixture was stirred for 4 h at room temperature. After completion of the reaction, water was added to quench the reaction mixture and the organic layer was washed with excess water and brine. The organic layer was dried over Na$_2$SO$_4$ and concentrated to afford the crude silylated compound, which was purified by silica gel chromatography (100-200 mesh, eluent: 5% EtOAc/ pet ether) to afford 166 (0.895 g, 78%) as a viscous liquid.

**Yield:** 0.895 g, 78%

**Mol. Formula:** C$_{30}$H$_{38}$O$_3$Si

**Mol. Weight:** 474.26

[α]$_D^{25}$: +16.9 (c 3.0, CHCl$_3$)

**IR** (CHCl$_3$, cm$^{-1}$) $\nu_{\text{max}}$: 3408, 3049, 2912, 2867, 1632, 1445, 1406,1372, 1351, 1109, 1031, 963, 851, 717, 652.

**$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ = 7.74-7.70 (m, 4 H), 7.48 - 7.37 (m, 6 H), 7.25 (s, 2 H), 6.91 (d, $J$ = 8.5 Hz, 2 H), 5.83 (ddd, $J$ = 6.3, 10.5, 17.1 Hz, 1 H), 5.07 - 4.97 (m, 2 H), 4.41 (s, 2 H), 4.28 - 4.20 (m, 1 H), 3.84 (s, 3 H), 3.40 - 3.31 (m, 2 H), 1.68 - 1.55 (m, 4 H), 1.12 (s, 9 H)

**$^{13}$C NMR** (100 MHz, CDCl$_3$): $\delta$ = 159.0, 140.5, 135.9, 135.8, 134.4, 134.2, 129.5, 129.4, 129.1, 127.4, 127.3, 114.5, 113.7, 74.3, 72.3, 70.0, 55.2, 34.0, 27.0, 24.6, 19.3

**HRMS (ESI)** for C$_{30}$H$_{38}$O$_3$SiNa (M + Na)$^+$ found 497.2482, calcd 497.2482
(S)-4-((tert-Butyldiphenylsilyl)oxy)hex-5-enoic acid (167):

![Structure of compound 167]

Compound 167 was synthesized in 75% yield using the same procedure as described for the synthesis of compound 155.

**Mol. Formula:** C_{22}H_{28}O_{3}Si

**Mol. Weight:** 368.18

\[ [\alpha]_D^{25} = +15.2 \ (c \ 2.5, \ CHCl_3); \text{lit}^{19} [\alpha]_D^{25} = +14.5 \ (c \ 0.6, \ CHCl_3) \]

**IR** (CHCl\_3, cm\-1) \( \nu_{\text{max}} = 3460, 3051, 2941, 2869, 1721, 1637, 1453, 1412, 1215, 1119, 947. \)

**\(^1\)H NMR** (500 MHz, CDCl\_3): \( \delta = 7.70-7.66 \) (m, 4 H), 7.47 - 7.30 (m, 6 H), 5.76 (ddd, \( J = 5.8, 10.6, 16.9 \) Hz, 1 H), 5.12 - 4.95 (m, 2 H), 4.28 (d, \( J = 4.9 \) Hz, 1 H), 2.46 - 2.26 (m, 2 H), 1.86 - 1.72 (m, 2 H), 1.09 (s, 9 H)

**\(^{13}\)C NMR** (125 MHz, CDCl\_3): 179.7, 139.6, 135.9, 135.8, 133.9, 133.8, 129.7, 129.5, 127.5, 127.4, 115.4, 73.2, 31.8, 28.8, 27.0, 19.3

**HRMS (ESI)** for C\_22H\_28O\_3SiNa (M + Na)\(^+\) found 391.1696, calcd 391.1700

(2R,4S)-4-((tert-Butyldiphenylsilyl)oxy)hex-5-en-2-yl((tert-butyldiphenylsilyl)oxy)hex-5-enoate (168)

![Structure of compound 168]

Compound 168 was synthesized in 93% yield using the same procedure as described for the synthesis of compound 156.

**Mol. Formula:** C\_44H\_56O\_4Si\_2

**Mol. Weight:** 704.37

\[ [\alpha]_D^{25} = -44.26 \ (c \ 3.0, \ CHCl_3); \text{lit}^{19} [\alpha]_D^{25} = -48.3 \ (c \ 0.33, \ CHCl_3) \]

**IR** (CHCl\_3, cm\-1) \( \nu_{\text{max}} = 3079, 2942, 2891, 2837, 1744, 1617, 1417, 1334, 1265, 1027, 957, 830, 682 \)
**Stagonolide C (6)**

A solution of 168 (0.138 g, 0.196 mmol) and NH₄F (0.110 g, 2.94 mmol) in MeOH (5 mL) was stirred at 40°C for 24 h and monitored by TLC. After completion of the reaction, the reaction mixture was concentrated and immediately filtered through small pad of silica gel (60-120 mesh, eluent: 50 % EtOAc/ pet ether) to give RCM precursor diol which was for the next RCM reaction.

To the solution of diene (0.04 g, 0.175 mmol) in 150ml freshly distilled DCM (was degassed for 15 minute through bubbling of argon), Grubbs’ II catalyst (0.015g, 10 mol %) was added to it and then again the solution was degassed for 1h. The reaction mixture was refluxed at 45°C for 24 h (completion of the reaction was checked by TLC). The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (Silica gel, 230-400 mesh, 50% EtOAc/pet ether) to afford compound 6 (0.03g, 78%) as a colourless oil.

**Yield:** 0.03 g, 78%

**Mol. Formula:** C₁₀H₁₆O₄

**Mol. Weight:** 200.10

[α]D²⁵: +45.92 (c 0.08, MeOH); lit¹⁹[α]D²⁵ = +43.9 (c 1.0, MeOH)

**IR (CHCl₃, cm⁻¹) νmax =** 3389, 2918, 2854, 1725, 1453, 1367, 1213, 1023.

**¹H NMR (500 MHz, CDCl₃):** δ = 5.60 (dd, J = 9.3, 15.4 Hz, 1 H), 5.44 (dd, J = 9.2, 15.3 Hz, 1 H), 5.21 - 5.10 (m, 1 H), 4.18 - 4.02 (m, 2 H), 2.32 - 2.28 (m, 1 H), 2.24 - 2.14 (m,
2 H), 2.09-2.01 (m, 3 H), 1.90 (dd, J = 2.6, 13.9 Hz, 1 H), 1.78 (td, J = 11.1, 13.7 Hz, 1 H), 1.23 (d, J = 6.4 Hz, 3 H)

$^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ = 174.4, 135.8, 133.0, 74.4, 72.1, 67.7, 43.3, 34.4, 31.5, 21.3

(2S,4S)-4-((tert-Butyldiphenylsilyl)oxy)hex-5-en-2-yl(S)-4-((tert-butyldiphenylsilyl)oxy)hex-5-enoate (170)

Compound 170 was synthesized using the same procedure as described for the synthesis of compound 168.

**Mol. Formula:** C$_{44}$H$_{56}$O$_4$Si$_2$

**Mol. Weight:** 704.37

$[\alpha]_D^{25}$: +18.48 (c 2.3, CHCl$_3$)

**IR** (CHCl$_3$, cm$^{-1}$) $\nu$$_{\text{max}}$ = 3077, 2937, 2899, 1749, 1626, 1423, 1343, 1255, 1020, 977, 840.

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = $^1$H NMR (500MHz ,CHLOROFORM-d) $\delta$ = 7.72 - 7.60 (m, 8 H), 7.44 - 7.31 (m, 12 H), 5.81 - 5.65 (m, 2 H), 5.03 - 4.83 (m, 5 H), 4.20 (q, $J$ = 5.8 Hz, 1 H), 4.17 - 4.10 (m, 1 H), 2.24 - 2.05 (m, 2 H), 1.85 (ddd, $J$ = 4.6, 8.9, 13.7 Hz, 1 H), 1.74 - 1.63 (m, 2 H), 1.56 - 1.53 (m, 1 H), 1.07 (s, 18 H), 1.05 (d, $J$ = 6.4 Hz, 3 H)

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 172.8, 139.8, 139.7, 135.94, 135.92, 135.89, 135.8, 134.1, 134.06, 134.0, 133.9, 129.7, 129.6, 129.5, 127.6, 127.5, 127.4, 127.3, 115.1, 115.0, 73.5, 72.0, 67.6, 43.8, 32.1, 29.4, 27.1, 27.0, 20.5, 19.4, 19.3

**HRMS (ESI)** for C$_{44}$H$_{56}$O$_4$Si$_2$Na (M + Na)$^+$ found 727.3610, calcd 727.3609
(2S,4S)-4-Hydroxyhex-5-en-2-yl (S)-4-hydroxyhex-5-enoate (171):

A solution of 170 (0.069 g, 0.098 mmol) and NH₄F (0.055 g, 1.47 mmol) in MeOH (5 mL) was stirred at 40°C for 24 h and monitored by TLC. After completion of the reaction, the reaction mixture was concentrated. The crude diol was purified by silica gel column chromatography (60-120 mesh, 40% EtOAc/pet ether) to afford compound 171 (0.016 g, 70%) as a colourless oil.

Yield: 0.016 g, 70%

Mol. Formula: C₁₀H₁₆O₄

Mol. Weight : 228.14

[α]D²⁵: +12.4 (c 1.5, CHCl₃)

IR (CHCl₃, cm⁻¹) νmax = 3411, 3071, 2837, 1779, 1403, 1313, 1020, 907, 841.

¹H NMR (200 MHz, CDCl₃): δ = 5.93 - 5.76 (m, 2 H), 5.31 - 5.06 (m, 5 H), 4.18 (qd, J = 6.1, 12.1 Hz, 2 H), 2.45 - 2.37 (m, 2 H), 2.30 (br. s., 2 H), 1.93 - 1.80 (m, 3 H), 1.70 - 1.62 (m, 1 H), 1.26 (d, J = 6.4 Hz, 3 H)

¹³C NMR (50 MHz, CDCl₃): δ = 173.6, 140.3, 136.2, 115.1, 115.0, 72.2, 70.6, 69.0, 43.0, 31.6, 30.6, 20.3

HRMS (ESI) for C₁₂H₂₀O₄Na (M + Na)⁺ found 251.1253, calcd 251.1254

9-epi-Stagonolide C (7)

To the solution of diene 171 (0.016 g, 0.07 mmol) in 100 ml freshly distilled DCM (was degassed for 15 minute through bubbling of argon), Grubbs’ II catalyst (0.006 g, 10 mol %) was added to it and then again the solution was degassed for 1h. The reaction mixture was refluxed at 45°C for 24 h (completion of the reaction was checked by TLC). The solvent was removed in vacuo and the crude product was purified by silica gel column
chromatography (Silica gel, 230-400 mesh, 30% EtOAc/pet ether) to afford compound 7 (0.01g, 73%) as a colourless oil.

Yield: 0.010 g, 73%

Mol. Formula: C_{10}H_{16}O_{4}

Mol. Weight: 200.10

[α]_{D}^{25} : +164.28 (c 0.5, CHCl_{3})

IR (CHCl_{3}, cm^{-1}) \nu_{\text{max}} = 3402, 2981, 2864, 1735, 1413, 1347, 1231, 1033.

^{1}H NMR (400 MHz, CDCl_{3}): \delta = 5.98 (d, J = 16.1 Hz, 1 H), 5.62 (d, J = 16.1 Hz, 1 H), 5.46 - 5.29 (m, 1 H), 4.61 - 4.53 (m, 2 H), 2.54 - 2.40 (m, 1 H), 2.22 (t, J = 13.7 Hz, 1 H), 2.06 (ddd, J = 2.4, 5.4, 14.1 Hz, 1 H), 1.98 - 1.85 (m, 3 H), 1.68 (br. s., 2 H), 1.23 (d, J = 6.6 Hz, 3 H)

^{13}C NMR (100 MHz, CDCl_{3}): \delta = 176.6, 130.6, 127.4, 69.0, 68.2, 64.5, 42.0, 32.9, 28.0, 21.1

HRMS (ESI) for C_{10}H_{16}O_{4}Na (M + Na)^{+} found 223.0940, calcd 223.0941
4.7 Spectra

1. $^1$H and $^{13}$C NMR spectra of 130
2. $^1$H and $^{13}$C NMR spectra of 131
3. $^1$H and $^{13}$C NMR spectra of 132
4. $^1$H and $^{13}$C NMR spectra of 133a
5. $^1$H and $^{13}$C NMR spectra of 133b
6. $^1$H and $^{13}$C NMR spectra of 134
7. $^1$H and $^{13}$C NMR spectra of 135
8. $^1$H and $^{13}$C NMR spectra of 136
9. $^1$H and $^{13}$C NMR spectra of 137
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11. $^1$H and $^{13}$C NMR spectra of ophiocerin C
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18. $^1$H and $^{13}$C NMR spectra of 144
19. $^1$H and $^{13}$C NMR spectra of 145
20. $^1$H and $^{13}$C NMR spectra of 146
21. $^1$H and $^{13}$C NMR spectra of 147
22. $^1$H and $^{13}$C NMR spectra of ophiocerin B
23. $^1$H and $^{13}$C NMR spectra of 148
24. $^1$H and $^{13}$C NMR spectra of 149
25. $^1$H and $^{13}$C NMR spectra of botryolide E
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27. $^1$H and $^{13}$C NMR spectra of 153
28. $^1$H and $^{13}$C NMR spectra of 154
29. $^1$H and $^{13}$C NMR spectra of 155
30. $^1$H and $^{13}$C NMR spectra of 156
31. $^1$H and $^{13}$C NMR spectra of 157
32. $^1$H and $^{13}$C NMR spectra of **decarestrictine O**
33. $^1$H and $^{13}$C NMR spectra of 158
34. $^1$H and $^{13}$C NMR spectra of 159
35. $^1$H and $^{13}$C NMR spectra of 160
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37. $^1$H and $^{13}$C NMR spectra of 164
38. $^1$H and $^{13}$C NMR spectra of 165
39. $^1$H and $^{13}$C NMR spectra of 166
40. $^1$H and $^{13}$C NMR spectra of 167
41. $^1$H and $^{13}$C NMR spectra of 168
42. $^1$H and $^{13}$C NMR spectra of **stagonolide C**
43. $^1$H and $^{13}$C NMR spectra of 170
44. $^1$H and $^{13}$C NMR spectra of 171
45. $^1$H and $^{13}$C NMR spectra of **9-epi-stagonolide C**
$^{1}H$ NMR spectrum of Compound 130 in CDCl$_3$

$^{13}C$ NMR spectrum of Compound 130 in CDCl$_3$
\textbf{\textsuperscript{1}H NMR spectrum of Compound 131 in CDCl\textsubscript{3}}

\textbf{\textsuperscript{13}C NMR spectrum of Compound 131 in CDCl\textsubscript{3}}
$^1$H NMR spectrum of Compound 132 in CDCl$_3$

$^{13}$C NMR spectrum of Compound 132 in CDCl$_3$
$^1$H NMR spectrum of Compound 133a in CDCl$_3$

$^{13}$C NMR spectrum of Compound 133a in CDCl$_3$
$^1$H NMR spectrum of Compound 133b in CDCl$_3$

$^{13}$C NMR spectrum of Compound 133b in CDCl$_3$
$^1$H NMR spectrum of compound 134 in CDCl$_3$

$^{13}$C NMR spectrum of compound 134 in CDCl$_3$
**$^1$H NMR spectrum of compound 135 in CDCl$_3$**

![NMR spectrum of compound 135 in CDCl$_3$](image)

**$^{13}$C NMR spectrum of compound 135 in CDCl$_3$**

![C NMR spectrum of compound 135 in CDCl$_3$](image)
$^1$H NMR spectrum of compound 136 in CDCl$_3$

$^{13}$C NMR spectrum of compound 136 in CDCl$_3$
$^1$H NMR spectrum of compound 137 in CDCl$_3$

$^{13}$C NMR spectrum of compound 137 in CDCl$_3$
$^1$H NMR spectrum of compound 138 in CDCl$_3$

$^{13}$C NMR spectrum of compound 138 in CDCl$_3$
\(^1\)H NMR spectrum of Ophiocerin C in CDCl\(_3\)

\[^{13}\text{C} \text{NMR spectrum of Ophiocerin C in CDCl}_3\]
\textbf{\textsuperscript{1}H NMR spectrum of compound 139 in CDCl\textsubscript{3}}

\begin{center}
\includegraphics[width=\textwidth]{hnmr.png}
\end{center}

\textbf{\textsuperscript{13}C NMR spectrum of compound 139 in CDCl\textsubscript{3}}

\begin{center}
\includegraphics[width=\textwidth]{cnmr.png}
\end{center}
$^1$H NMR spectrum of compound 140 in CDCl$_3$

$^{13}$C NMR spectrum of compound 140 in CDCl$_3$
\textbf{\textsuperscript{1}H NMR spectrum of compound 141 in CDCl$_3$}

\textbf{\textsuperscript{13}C NMR spectrum of compound 141 in CDCl$_3$}
$^1$H NMR spectrum of ophiocerin A in CDCl$_3$

$^{13}$C NMR spectrum of ophiocerin A in CDCl$_3$
$^1$H NMR spectrum of compound 143 in CDCl$_3$

$^{13}$C NMR spectrum of 143 in CDCl$_3$
$^1$H NMR spectrum of compound 144 in CDCl$_3$

$^{13}$C NMR spectrum of compound 144 in CDCl$_3$
\(^1\)H NMR spectrum of 145 in CDCl\(_3\)

\(^{13}\)C NMR spectrum of 145 in CDCl\(_3\)
\[^1\text{H NMR spectrum of 146 in CDCl}_3\]

\[^{13}\text{C NMR spectrum of 146 in CDCl}_3\]

\begin{center}
\includegraphics[width=\textwidth]{hnmr.png}
\end{center}

\begin{center}
\includegraphics[width=\textwidth]{cnmr.png}
\end{center}
$^1$H NMR spectrum of 147 in CDCl$_3$

$^{13}$C NMR spectrum of 147 in CDCl$_3$
\textsuperscript{1}H NMR spectrum of Ophiocerin B in CDCl$_3$

\textsuperscript{13}C NMR spectrum of Ophiocerin B in CDCl$_3$
Chapter 4

$^1$H NMR spectrum of 148 in CHCl$_3$

$^{13}$C NMR spectrum of 148 in CHCl$_3$
$^1$H NMR spectrum of 149 in CDCl$_3$

$^{13}$C NMR spectrum of 149 in CDCl$_3$
\(^1\)H NMR spectrum of botryolide E in CDCl\(_3\)

\(^1\)C NMR spectrum of botryolide E in CDCl\(_3\)
Chapter 4

$^1$H NMR spectrum of 152 in CDCl$_3$

$^{13}$C NMR spectrum of 152 in CDCl$_3$
\(^1\)H NMR spectrum of 153 in CDCl\(_3\)

\(^{13}\)C NMR spectrum of 153 in CDCl\(_3\)
\(^1\)H NMR spectrum of 154 in CDCl\(_3\)

\(^{13}\)C NMR spectrum of 154 in CDCl\(_3\)
$^{1}H$ NMR spectrum of 155 in CDCl$_3$

$^{13}C$ NMR spectrum of 155 in CDCl$_3$
$^1$H NMR spectrum of 156 in CDCl$_3$

$^{13}$C NMR spectrum of 156 in CDCl$_3$
\(^1\)HNMR spectrum of 157 in CDCl\(_3\)

\(^{13}\)CNMR spectrum of 157 in CDCl\(_3\)
\(^1\)H NMR spectrum of Decarestrictine O in MeOD\(_4\)

\(^{13}\)C NMR spectrum of Decarestrictine O in MeOD\(_4\)
$^1$HNMR spectrum of 158 in CDCl$_3$

$^{13}$CNMR spectrum of 158 in CDCl$_3$
1\textsuperscript{HNMR} spectrum of 159 in CDCl\textsubscript{3}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{hnmr_spectrum.png}
\caption{1\textsuperscript{HNMR} spectrum of 159 in CDCl\textsubscript{3}}
\end{figure}

1\textsuperscript{3}CNMR spectrum of 159 in CDCl\textsubscript{3}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{cnmr_spectrum.png}
\caption{1\textsuperscript{3}CNMR spectrum of 159 in CDCl\textsubscript{3}}
\end{figure}
**Chapter 4**

$^1$HNMR spectrum of 160 in CDCl$_3$ 

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$^1$C NMR spectrum of 160 in CDCl$_3$
**Chapter 4**

**$^1$HNMR spectrum of 161 in CDCl$_3$**

![HNMR spectrum](image)

**$^{13}$CNMR spectrum of 161 in CDCl$_3$**

![CNMR spectrum](image)
**Chapter 4**

\(^{1}\text{H}NMR\) spectrum of 164 in CDCl\(_3\)

\[^{13}\text{C}NMR\) spectrum of 164 in CDCl\(_3\)

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\[ ^1\text{HNMR spectrum of 165 in CDCl}_3 \]

\[ ^{13}\text{C NMR spectrum of 165 in CDCl}_3 \]
$^{1}$HNMR spectrum of 166 in CDCl$_3$

$^{13}$CNMR spectrum of 166 in CDCl$_3$
\( ^1 \text{HNMR spectrum of 167 in CDCl}_3 \)

\( ^{13} \text{C NMR spectrum of 167 in CDCl}_3 \)
$^1$H NMR spectrum of 168 in CDCl$_3$  

13C NMR spectrum of 168 in CDCl$_3$
\(^1\text{H} \) NMR spectrum of stagonolide C in CDCl\(_3\)

\(^{13}\text{C} \) NMR spectrum of stagonolide C in CDCl\(_3\)
**Chapter 4**

\[^1H\text{NMR spectrum of 170 in CDCl}_3\]

![HNMR spectrum of 170 in CDCl₃](image)

\[^{13}C\text{ NMR spectrum of 170 in CDCl}_3\]

![C NMR spectrum of 170 in CDCl₃](image)
$^1$HNMR spectrum of 171 in CDCl$_3$

$^{13}$C NMR spectrum of 171 in CDCl$_3$
\(^1\)HNMR spectrum of 9-epi-stagonolide C in CDCl\(_3\)

\(13^C\) NMR spectrum of 9-epi-stagonolide C in CDCl\(_3\)
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