5.1. Introduction

The complex polycyclic norcembranoid ineleganolide (238) was first isolated from the Taiwanese coral *Sinularia inelegans* in 1999 by the Duh group (Figure 5.1.1). The relative stereochemistry of ineleganolide (238) was unambiguously confirmed by X-ray analysis and spectroscopic method. This complex polycyclic norditerpenoid possesses intriguing architectural features including an ether bridge, which connects two carbocyclic rings and an angular fusion of five-, seven-, and six-membered carbocyclic rings linked with a five-membered lactone ring. Ineleganolide exhibits cytotoxic activity against P-388 murine leukemia cells (ED$_{50}$ = 3.82 µg/mL).  

*Figure 5.1.1. Structure of Ineleganolide (238). (Originally depicted structure shown on the left-hand side; the proposed actual structure from biosynthetic studies shown on the right-hand side.)*
A biosynthetic pathway of ineleganolide was proposed by Pattenden and co-workers (Scheme 5.1.1a). It is hypothesized that ineleganolide (238) is biosynthetically constructed by successive transannular Michael reactions of macrocyclic 5-episinuleptolide (239). An initial intramolecular Michael reaction of 5-episinuleptolide (239) establishes the C4–C13 bond to furnish cyclohexanone 240. Dehydration of 240 at C11 and subsequent bond formation between C7 and C11 by a second Michael reaction affords ineleganolide (238). The Pattenden group proved this biosynthetic route experimentally by a semisynthesis of ineleganolide (238) from 5-episinuleptolide (239), which was isolated from Sinularia scabra species (Scheme 5.1.1b). Acetylation of the hydroxyl group at C11 position of 5-episinuleptolide (239) furnished acetate 242. Ineleganolide (238) was obtained in 26% yield by treatment of acetate 242 with LHMDS.

Scheme 5.1.1. Proposed Biosynthesis of Ineleganolide (238)
Although this intriguing polycyclic norditerpenoid ineleganolide (238) has attracted much attention from the synthetic community over the past decade including extensive efforts from my lab at Caltech, a total synthesis of ineleganolide has not been reported. Herein, we describe new synthetic strategies toward an enantioselective synthesis of ineleganolide (238). We chose to pursue the synthesis of the enantiomer of ineleganolide (238), which was depicted in the original isolation paper.

5.2. Results and Discussion

We envisioned that a total synthesis of ineleganolide (238) could be achieved by successive transannular Michael reactions (Scheme 5.2.1). Disconnections of the C4–C13 and C11–C12 bonds affords domino double-Michael reaction precursor 243. The 1,4-diketone and ester functional groups of macrocycle 243 can be disassembled into α,β-unsaturated ester 244 and bicycle 245.

Scheme 5.2.1. Retrosynthesis of ineleganolide (238)

Our synthesis began with the known acetal 246 to prepare the α,β-unsaturated ester fragment 248 (Scheme 5.2.2). Subjection of acetal 246 to Still-Gennari
olefination conditions\textsuperscript{8,9} afforded the (Z)- and (E)-isomers of enoate 248 in ratios ranging from 10:1 to 2:1, respectively. We were delighted to find that highly (Z)-selective olefination occurred to furnish enoate 248 in 54% yield using conditions developed by the Ando group.\textsuperscript{10}

\textit{Scheme 5.2.2. Synthesis of (Z)-Selective Enoate 248}

Acid-mediated acetal hydrolysis of 248 furnished aldehyde 250 in quantitative yield (Scheme 5.2.3a). Methyl Grignard addition to aldehyde 250 produced diastereomeric mixtures of alcohol 251, which was converted to ketone 252 by Swern oxidation. After extensive experimentation, it was found that employing LiTMP (TMP = 2,2,6,6-tetramethylpiperidine) and TMSCl afforded kinetically favored silyl enol ether 253 selectively.\textsuperscript{11} Silyl enol ether 253 was subsequently transformed to \( \alpha \)-hydroxyketone 254 by Rubottom oxidation.\textsuperscript{12} Surprisingly, tosylation and bromination of \( \alpha \)-hydroxyketone 254 proved to be challenging. However, we were delighted to find that treatment of silyl enol ether 253 with NBS furnished \( \alpha \)-bromoketone 244b (Scheme 5.2.3b).
With $\alpha,\beta$-unsaturated ester fragment 244b in hand, we turned our attention to preparing bicyclic fragment 245. Oxidation of known diol 255 with MnO$_2$ delivered aldehyde 256 (Scheme 5.2.4a). Methyllithium addition to aldehyde 256 provided secondary alcohol 257, which was oxidized with MnO$_2$ to afford ketone 258. Unfortunately, we explored diazo transfer reactions extensively with various diazo sources (e.g., p-ABSA, 4-dodecylbenzenesulfonyl azide) under Danheiser’s conditions, but the desired diazo 259 was not observed. Another strategy was devised to obtain diazo ketone 259 by using Pinnick oxidation of aldehyde 256 to furnish acid 260 (Scheme 5.2.4b). Treatment of acid 260 with ethyl chloroformate or oxalyl chloride generated the corresponding intermediates 261 or 262, respectively. However, attempts to obtain the desired diazo ketone 259 from intermediate 261 or...
with TMS-diazomethane were unsuccessful.\textsuperscript{15,16,17} Alternatively, we envisioned that the diazo functional group could be inserted by addition of ethyl diazoacetate to aldehyde 256 (Scheme 5.2.4c). Deprotonation of ethyl diazoacetate by LDA followed by addition to aldehyde 256 resulted in an alcohol (263) that could be oxidized to diazo compound 264. Disappointingly, intramolecular O–H insertion of the tertiary alcohol to the diazo in 264 was found to be challenging under Lewis acid conditions. Despite screening numerous rhodium catalysts, solvents, and temperature, only undesired lactonization occurred to form 266.\textsuperscript{18}
Having failed to access the bicyclic fragment using diazo strategies, a revised approach was put forward (Scheme 5.2.5). Treatment of methyl ketone 258 with
LiTMP (TMP = 2,2,6,6-tetramethylpiperidine) and TESCl provided silyl ether 267, which was transformed to α-hydroxyketone 268 by Rubottom oxidation. However, the desired bicycle 245 was not observed under various basic conditions (e.g., NaOH, KOtBu, NaH, LHMDS, LDA) from benzoate 269 and mesylate 270, which were prepared from α-hydroxyketone 268.19,20

Scheme 5.2.5. Attempted Williamson Etherifications

The desired bicycle 245 seemed highly angularly strained due to the α,β-unsaturated ketone at the junction of the bicycle. We envisaged that the strain would be reduced by converting the sp²-hybridized carbon to the sp³-hybridized carbon at C6. After considerable experimentation, we found that diastereomeric mixtures of epoxides 271a and 271b could be obtained by a Corey-Chaykovsky reaction (Scheme 5.2.6a).21 Surprisingly, diol 255 was furnished as a major byproduct under these reaction conditions. Treatment of aldehyde 256 with dibromomethane (or chloriodomethane) and n-BuLi also produced diastereomeric mixtures of epoxides 271a and 271b along with diol 255 (Scheme 5.2.6b).22
With epoxide 271 in hand, direct epoxide ring opening reactions were conducted to deliver 272 (Scheme 5.2.7a). Unfortunately, 5-membered ring formation to generate 272 was not observed with various Lewis acids (e.g., CeCl₃, TMSOTf, In(OTf)₃, PPTS) or bases (e.g., KHMDS, NaH). Interestingly, treatment of epoxide 271 with MgI₂ at 40 °C generated iodohydrin 273 along with methyl ketone 258 (Scheme 5.2.7b). Protection of secondary alcohol 273 with TESCl and subsequent intramolecular etherification of iodide 274 with NaH afforded bicyclic 275. Selective removal of TES group in 275 with PPTS furnished mono-silyl ether 276. An attempt to oxidize secondary alcohol 276 to ketone 245 shows promise by TLC analysis but to date we have not successfully isolated and characterized 245.
We next investigated coupling reactions of α-bromoketone 244b and methylketone 258, which could be easily prepared (Scheme 5.2.8a). Despite extensive experimentation, alkylation of methylketone 258 with α-bromoketone 244b failed under basic conditions. Treatment of hydroxyketone 268 with ethyl chloroformate afforded the carbonate intermediate, which was subjected to α-bromoketone 244b to generate 1,4-diketone 279 under basic conditions. However, α-bromoketone 244b appeared to decompose under the basic conditions and only the unreacted cyclopentene fragment was recovered.
Since coupling reactions of α-bromoketone 244b and the cyclopentene fragment by alkylation did not proceed, we next chose to focus on metathesis strategies to combine these two fragments (Scheme 5.2.9). We believed that esterification of acid 280 and secondary alcohol 281 would afford metathesis precursor diene 282. Intramolecular metathesis reaction between the vinyl groups of 282 was expected to produce macrocycle 283. 1,4-Addition of tertiary alcohol to the α,β-unsaturated ketone could deliver 5-membered ether 243, which would proceed domino double-Michael reaction to afford ineleganolide (238).

**Scheme 5.2.9. Synthetic Plan by Using Metathesis Strategies**
1,2-Addition of vinylmagnesium bromide to aldehyde 256 furnished allyl alcohol 284, which was oxidized by MnO₂ to deliver vinyl ketone 285 (Scheme 5.2.10a). Removal of silyl group on 285 with TBAF afforded diol 281. Vinyl Grignard addition to aldehyde 250 and subsequent oxidation of the resultant alcohol 286 produced ketone 287 (Scheme 5.2.10b). However, an attempted hydrolysis of methyl ester 287 afforded Michael adduct 288 instead of the desired acid 280. Additionally, transesterifications of ester 287 with alcohol 281 were unsuccessful with Otera’s catalyst (Scheme 5.2.10c). Therefore, we decided to explore esterification reactions with silyl ether 289 (Scheme 5.2.10d). Silylation of secondary alcohol 286 with TBSCl and subsequent hydrolysis produced acid intermediate 289. Disappointingly, esterification of acid 289 and alcohol 281 was found to be challenging under several coupling conditions (e.g., EDCI, DCC, BOPCl).
At this stage, we began to investigate intermolecular metathesis between allyl alcohol 286 and vinyl ketone 285 with Grubbs’ catalysts (Scheme 5.2.11a).
However, intermolecular metathesis of 286 and 285 to deliver 291 proved to be difficult. Alternatively, we attempted to connect allyl alcohol 286 and diol 284 via a silyl tether, but the yield was unsatisfactory (Scheme 5.2.11b).

Scheme 5.2.11. Intermolecular Metathesis

Since combining the two fragments appeared to be challenging, we devised a new synthetic strategy that utilized an alkyne functionality (Scheme 5.2.12). Addition of ethynylmagnesium bromide to aldehyde 256 provided intermediate 293, which was oxidized by MnO₂ to generate ynone 294 (Scheme 5.2.12a). Although n-BuLi was subjected to alkyne 294 to form lithium acetylide, which was added to aldehyde 250, little or no conversion was observed (Scheme 5.2.11b). We also attempted the lithium acetylide addition reaction with alcohol 293 or silyl ether 296, but only trace amounts of the respective coupling products 297 or 298 were observed.
5.3. Conclusion

We have described our efforts toward the synthesis of ineleganolide. Highly (Z)-selective olefination at C12–C13 was achieved by a method developed by the Ando group. The C–O bond formation at C5, which proved to be challenging in the other strategy investigated in our group, was accomplished. Although the entire fragmented carbon framework was constructed from this work, unfortunately, coupling of the two fragments was unsuccessful. We will further investigate a total synthesis of ineleganolide using modified strategies.

5.4. Experimental Methods and Analytical Data

5.4.1. Materials and Methods

Unless stated otherwise, reactions were performed at ambient temperature (23 °C) in flame-dried glassware under an argon atmosphere using dry, deoxygenated solvents
(distilled or passed over a column of activated alumina) using a Teflon®-coated magnetic stirring bar. Commercially available reagents were used as received unless otherwise noted. Et₃N was distilled from calcium hydride immediately prior to use. MeOH was distilled from magnesium methoxide immediately prior to use. Reactions requiring external heat were modulated to the specified temperatures using an IKAmag temperature controller. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (250 nm) and visualized by UV fluorescence quenching, potassium permanganate, or p-anisaldehyde staining. Silicycle SiliaFlash P60 Academic Silica gel (particle size 40-63 nm) was used for flash chromatography. ¹H NMR spectra were recorded on a Varian Mercury 300 MHz, a Bruker AV III HD 400 MHz spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe, Varian Inova 500 MHz, and 600 MHz spectrometers and are reported relative to residual CHCl₃ (δ 7.26 ppm), CHDCl₂ (δ 5.32) or C₆D₆ (δ 7.16 ppm). ¹³C NMR spectra are recorded on a Varian Mercury 300 MHz, a Bruker AV III HD 400 MHz spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe, Varian Inova 500 MHz, and 600 MHz spectrometers (75 MHz, 126 MHz, and 151 MHz, respectively) and are reported relative to CHCl₃ (δ 77.16 ppm), CHDCl₂ (δ 53.84) or C₆D₅ (δ 128.06 ppm). Data for ¹H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Infrared (IR) spectra were recorded on a Perkin Elmer Paragon 1000 Spectrometer and are reported in frequency of absorption (cm⁻¹). High resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility using a JEOL JMS-600H High Resolution Mass Spectrometer in fast atom bombardment (FAB+) or electron ionization (EI+) mode or acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in atmospheric pressure
chemical ionization (APCI) or mixed (MultiMode ESI/APCI) ionization mode. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path length cell at 589 nm.

5.4.2. Experimental Procedures

A solution of phosphate 249 (108 mg, 0.322 mmol, 1.20 equiv) in THF (2.68 mL) was treated with NaI (52.0 mg, 0.349 mmol, 1.30 equiv) and DBU (53.0 mg, 0.348 mmol, 1.30 equiv) at 0 °C and stirred for 10 min. After the mixture was cooled to –78 °C, aldehyde 246 was added. The reaction was done in 3 min, and quenched with sat. aq NH₄Cl. The aqueous phase was extracted with EtOAc (3 x 3.00 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford α,β-unsaturated ester 248 (35.5 mg, 54% yield). (The same result was obtained by using 1.05 equiv NaH instead of DBU.)

Rⱽ = 0.62 (1:4 EtOAc:hexanes); ¹H NMR (400 MHz, CDCl₃) δ 6.16 (dt, J = 11.5, 7.2 Hz, 1H), 5.79 (dt, J = 11.5, 1.9 Hz, 1H), 4.79 (ddt, J = 13.6, 2.1, 1.1 Hz, 2H), 4.35 (dd, J = 7.0, 4.7 Hz, 1H), 3.70 (s, 3H), 3.31 (s, 3H), 3.30 (s, 3H), 2.80 – 2.71 (m, 2H), 2.37 (tt, J = 8.5, 6.5 Hz, 1H), 1.76 – 1.64 (m, 2H), 1.65 (dd, J = 1.5, 0.8 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 148.9, 146.3, 120.0, 112.7, 103.0, 53.2, 52.7, 51.2, 43.2, 35.9, 32.6, 18.4; IR (Neat Film NaCl) 2949, 2830, 1723, 1646, 1437, 1408, 1203, 1127, 1053, 892, 819 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C₁₃H₂₁O₄ [M+H]⁺-H₂: 241.1440; found: 241.1431; [α]D²⁵ 3.04° (c 0.30, CHCl₃).
To a solution of acetal 248 (129 mg, 0.494 mmol, 1.00 equiv) in CHCl₃ (2.47 mL) was added 50% aq TFA (1.23 mL) at 0 °C. The reaction mixture was stirred for 3 h at 23 °C before it was quenched by the addition of sat. aq NaHCO₃. The aqueous phase was extracted with CH₂Cl₂ (3 x 4.00 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo to afford aldehyde 250 (95.0 mg, 99% yield), which was used without further purification.

To a solution of aldehyde 250 (95.0 mg, 0.484 mmol, 1.00 equiv) in THF (5.00 mL) was added MeMgBr (3.0 M solution in diethyl ether; 0.21 mL, 0.629 mmol, 1.30 equiv) at −78 °C. The mixture was stirred for 1 h at −78 °C. Then, the solution was quenched by the addition of sat. aq NaHCO₃. The aqueous phase was extracted with EtOAc (3 x 5.00 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford secondary alcohol 251 (65.5 mg, 64% yield).

Rᵣ = 0.22 (1:4 EtOAc:hexanes); (due to the presence of diastereomeric mixtures, the ¹H NMR and ¹³C NMR contained extra peaks. See the attached spectrum) ¹H NMR (400 MHz, CDCl₃) δ 6.18 (ddt, J = 11.5, 9.8, 7.4 Hz, 2H), 5.82 – 5.76 (m, 2H), 4.86 – 4.76 (m, 4H), 3.92 – 3.83 (m, 1H), 3.77 (ddt, J = 9.4, 6.3, 3.1 Hz, 1H), 3.70 (s, 6H), 2.87 (dddd, J = 15.1, 7.3, 5.0, 1.8 Hz, 1H), 2.74 (ddddd, J = 8.3, 7.3, 5.1, 1.8 Hz, 2H), 2.64 – 2.55 (m, 1H), 2.49 (ddddd, J = 10.0, 8.6, 6.5, 4.9 Hz, 1H), 2.37 (ddddd, J = 9.8, 8.1, 6.7, 5.0 Hz, 1H), 1.68 (t, J = 1.2 Hz, 3H), 1.63 (dd, J = 1.5, 0.8 Hz, 3H), 1.55 – 1.42 (m, 4H), 1.19 (s, 3H), 1.17 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 149.2,
To a stirred solution of oxalyl chloride (0.21 mL, 2.40 mmol, 1.50 equiv) in CH₂Cl₂ (8.00 mL) was added DMSO (0.34 mL, 4.79 mmol, 3.00 equiv) dropwise at −78 °C. The reaction mixture was stirred for 15 min, and alcohol 251 (339 mg, 1.60 mmol, 1.00 equiv) in CH₂Cl₂ (1.00 mL) was added dropwise. The solution was stirred for 2 h and 30 min at −78 °C, then Et₃N (1.56 mL, 7.00 equiv) was added. After 90 min at −78 °C, the solution was warmed to 23 °C over 30 min and quenched with H₂O. The aqueous phase was extracted with CH₂Cl₂ (3 x 10.0 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford ketone 252 (295 mg, 88% yield).

Rf = 0.35 (1:4 EtOAc:hexanes); ¹H NMR (400 MHz, CDCl₃) δ 6.19 – 6.10 (m, 1H), 5.81 (dt, J = 11.6, 1.7 Hz, 1H), 4.79 (p, J = 1.5 Hz, 1H), 4.74 (dt, J = 1.7, 0.8 Hz, 1H), 3.70 (s, 3H), 2.84 – 2.73 (m, 3H), 2.61 – 2.46 (m, 2H), 2.12 (d, J = 0.5 Hz, 3H), 1.68 (dd, J = 1.5, 0.8 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 207.8, 166.9, 148.3, 146.2, 120.4, 112.3, 51.3, 47.6, 42.1, 32.4, 30.6, 19.5; IR (Neat Film NaCl) 2951, 1718, 1647, 1437, 1204, 1272, 821 cm⁻¹; HRMS (MM: ESI-APCI+) m/z calc’d for C₁₂H₁₉O₃ [M+H]^+: 211.1329; found: 211.1327; [α]D²⁵ 0 = −9.42° (c 0.15, CHCl₃).
To a solution of 2,2,6,6-tetramethylpiperidine (50 µL, 0.296 mmol, 1.50 equiv) in THF (2.00 mL) was added n-BuLi (2.5 M in hexane; 0.12 mL, 0.296 mmol, 1.50 equiv) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C, and TMSCl (0.13 mL, 0.990 mmol, 5.00 equiv) was added at –78 °C. Then, methyl ketone 252 (42.0 mg, 0.198 mmol, 1.00 equiv) in THF (1.00 mL) was added dropwise at –78 °C. The solution was stirred for 1 h and quenched with Et₃N, followed by sat. aq NaHCO₃. The aqueous phase was extracted with EtOAc (3 x 2.00 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was quickly filtered by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford silyl ether 253, which was used without further purification.

To a solution of m-CPBA (75%; 41.0 mg, 0.178 mmol, 0.90 equiv) in toluene (2.74 mL) was added solid NaHCO₃ (35.0 mg, 0.411 mmol, 2.08 equiv). The heterogeneous mixture was stirred for 15 min at 23 °C, then H₂O (0.40 mL) was added. Silyl ether 253 in toluene (0.50 mL) was added dropwise to the reaction mixture at 0 °C. After the solution was stirred for 30 min at 0 °C, sat. aq NaHCO₃ was added and stirred for 10 min at 0 °C. The aqueous phase was extracted with EtOAc (3 x 3.00 mL). The combined organic phases were washed with NaHCO₃ and brine, dried over MgSO₄ and concentrated in vacuo. To the residue dissolved in THF (0.30 mL) and H₂O (0.17 mL) was added AcOH (0.17 mL). The mixture was stirred for 2 h at 23 °C. Then, the solution was diluted with EtOAc and H₂O, and solid NaHCO₃ was added until the gas evolution ceased. The aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine,
dried over MgSO$_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford α-hydroxyketone 254 (12.0 mg, 56% yield based on recovered starting material, 2 steps).

R$_f$ = 0.35 (1:4 EtOAc:hexanes); $^1$H NMR (400 MHz, CDCl$_3$) δ 6.13 (dt, $J$ = 11.5, 7.1 Hz, 1H), 5.83 (ddd, $J$ = 11.6, 2.0, 1.3 Hz, 1H), 4.82 (p, $J$ = 1.5 Hz, 1H), 4.75 (dt, $J$ = 1.6, 0.8 Hz, 1H), 4.20 (d, $J$ = 3.0 Hz, 2H), 3.71 (s, 3H), 3.05 (s, br, 1H), 2.91 – 2.71 (m, 3H), 2.62 – 2.43 (m, 2H), 1.69 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 208.6, 166.8, 147.6, 145.5, 120.8, 112.8, 68.8, 51.3, 42.3, 42.1, 32.4, 19.5; IR (Neat Film NaCl) 2917, 1716, 1440, 1205, 1172 cm$^{-1}$; HRMS (MM: FAB+) m/z calc’d for C$_{12}$H$_{15}$O$_4$ [M+H]$^+$: 227.1283; found: 227.1288; $[\alpha]_D^{25.0}$ –4.11° (c 0.09, CHCl$_3$).

To a solution of 2,2,6,6-tetramethylpiperidine (0.23 mL, 1.39 mmol, 1.60 equiv) in THF (8.70 mL) was added n-BuLi (1.98 M in hexane; 0.70 mL, 1.39 mmol, 1.60 equiv) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C, and TMSCl (0.55 mL, 4.35 mmol, 5.00 equiv) was added at –78 °C. Then, methyl ketone 252 (183 mg, 0.870 mmol, 1.00 equiv) in THF (1.00 mL) was added dropwise at –78 °C. The solution was stirred for 1 h and quenched with Et$_3$N, followed by sat. aq NaHCO$_3$. The aqueous phase was extracted with EtOAc (3 x 10.0 mL). The combined organic phases were washed with brine, dried over MgSO$_4$ and concentrated *in vacuo*. The residue was quickly filtered by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford silyl ether 253, which was used without further purification.
A solution of silyl ether 253 in THF (8.70 mL) at −78 °C was treated with solid NaHCO$_3$ (132 mg, 1.57 mmol, 1.80 equiv) and stirred for 10 min at −78 °C. NBS (248 mg, 1.39 mmol, 1.60 equiv) was then added portionwise and stirred for 15 min at −78 °C. The solvent was evaporated and the residue was purified by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford α-bromoketone 244b (55.0 mg, 50% yield based on recovered starting material, 2 steps).

R$_f$ = 0.65 (1:4 EtOAc:hexanes); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.14 (dt, $J$ = 11.5, 7.2 Hz, 1H), 5.83 (dt, $J$ = 11.6, 1.6 Hz, 1H), 4.82 (p, $J$ = 1.5 Hz, 1H), 4.77 (dt, $J$ = 1.5, 0.8 Hz, 1H), 3.87 (d, $J$ = 1.0 Hz, 2H), 3.71 (s, 3H), 2.89 – 2.68 (m, 6H), 1.72 – 1.69 (m, 3H), 1.56 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 200.9, 166.9, 147.8, 145.7, 120.7, 112.7, 51.3, 43.7, 42.1, 34.8, 32.2, 19.7; IR (Neat Film NaCl) 2949, 2360, 1716, 1645, 1439, 1203, 1172 cm$^{-1}$; HRMS (MM: FAB) $m/z$ calc’d for C$_{11}$H$_{14}$O$_2$Br [M-OMe]: 257.0177; found: 257.0170; [$\alpha$]$_D^{25.0}$ $-$4.06° ($c$ 0.09, CHCl$_3$).

To a stirred solution of diol 255 (20.0 mg, 0.0774 mmol, 1.00 equiv) in CH$_2$Cl$_2$ (0.80 mL) was added MnO$_2$ (85%; 119 mg, 1.16 mmol, 15.0 equiv). The solution was stirred for 12 h at 23 °C. Solids were removed via a filtration through a celite plug (rinsed with CH$_2$Cl$_2$) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford aldehyde 256 (18.3 mg, 92% yield). All the spectrum data matched with those reported in ref 6a.
To a solution of aldehyde 256 (100 mg, 0.390 mmol, 1.00 equiv) in Et₂O (2.00 mL) was added MeLi (1.6 M in diethyl ether; 1.95 mL, 3.12 mmol, 8.00 equiv) at −10 °C. The solution was stirred for 2 h and quenched with sat. aq NH₄Cl. The solution was poured into H₂O. The aqueous phase was extracted with EtOAc (3 x 3.00 mL), washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:2 EtOAc:hexanes) on silica gel to afford alcohol 257 (93.4 mg, 88% yield).

To a stirred solution of alcohol 257 (162 mg, 0.594 mmol, 1.00 equiv) in CH₂Cl₂ (6.00 mL) was added MnO₂ (85%; 1.20 g, 11.9 mmol, 20.0 equiv). The solution was stirred for 12 h at 23 °C. Solids were removed via a filtration through a celite plug (rinsed with CH₂Cl₂) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford ketone 258 (143 mg, 89% yield). All the spectrum data matched with those reported in ref 6a.

To a stirred solution of aldehyde 256 (18.3 mg, 0.0714 mmol, 1.00 equiv) in MeCN (0.70 mL) were added NaH₂PO₄ (30.0 mg, 0.25 mmol, 3.50 equiv) in H₂O (0.50 mL) and 30% H₂O₂ (10 µL) at 0 °C. Then, a solution of NaClO₂ (23.0 mg, 0.25 mmol, 3.50 equiv) in H₂O (0.70 mL) was added dropwise in 1 h at 0 °C. The reaction
mixture was stirred for 10 min and quenched with sat. aq Na₂SO₃. The aqueous phase was extracted with EtOAc (2.00 mL). The combined aqueous phases were acidified with 2N HCl to make the solution pH 5–6. The aqueous phase was extracted with EtOAc (3 x 4.00 mL) washed with brine, dried over MgSO₄ and concentrated in vacuo to afford acid 260 (17.0 mg, 87% yield).

R₇ = 0.15 (1:1 EtOAc:hexane); ¹H NMR (500 MHz, CDCl₃) δ 6.77 (d, J = 1.8 Hz, 1H), 4.75 (td, J = 6.7, 1.9 Hz, 1H), 2.50 (dd, J = 12.9, 6.9 Hz, 1H), 2.09 – 2.03 (m, 1H), 1.48 (d, J = 0.7 Hz, 3H), 0.90 (s, 9H), 0.10 (d, J = 3.0 Hz, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 168.2, 147.9, 139.6, 79.5, 72.7, 51.3, 27.7, 25.9, 18.2, -4.5, -4.6; IR (Neat Film NaCl) 2929, 2857, 1701, 1362, 1258, 1097, 898, 837, 778 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C₁₂H₁₉O₄ [M+H⁺]-H₂: 271.1366; found: 271.1357; [α]D²⁵ 185.9° (c 0.31, CHCl₃).

To a solution of aldehyde 256 (15.0 mg, 0.0585 mmol, 1.00 equiv) and ethyl diazoacetate (22 µL, 0.205 mmol, 3.50 equiv) in THF (0.60 mL) was added LDA (0.20 M solution in THF; 0.44 mL, 0.088 mmol, 1.50 equiv) at –78 °C. The reaction mixture was stirred for 10 min and quenched with sat. aq NH₄Cl. The aqueous phase was extracted with EtOAc (3 x 1.00 mL) washed with brine, dried over MgSO₄ and concentrated in vacuo to afford alcohol 263, which was used without further purification (13.5 mg, 62% yield).

To a solution of alcohol 263 (13.0 mg, 0.0351 mmol, 1.00 equiv) in CH₂Cl₂ (0.40 mL) was added MnO₂ (85%; 72.0 mg, 0.702 mmol, 20.0 equiv) at 23 °C. The reaction
mixture was stirred overnight. Solids were removed via a filtration through a celite plug (rinsed with CH₂Cl₂) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford diazo 264 (12.0 mg, 93% yield).

Rᶠ = 0.56 (1:2 EtOAc:hexane); ¹H NMR (400 MHz, CDCl₃) δ 6.27 (d, J = 2.0 Hz, 1H), 4.79 (ddd, J = 6.9, 5.6, 2.0 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 2.45 (dd, J = 13.0, 6.9 Hz, 1H), 2.01 (dd, J = 13.0, 5.7 Hz, 1H), 1.39 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 185.4, 161.4, 145.4, 141.0, 82.3, 73.8, 62.0, 51.7, 27.3, 26.0, 25.8, 18.3, 14.4, -4.5, -4.6; IR (Neat Film NaCl) 3499, 2930, 2857, 2141, 1728, 1471, 1370, 1300, 1259, 1094, 906, 837 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C₁₇H₂₉O₅N₂Si [M+H]⁺: 369.1846; found 369.1845; [α]D²⁵ 14.2° (c 0.25, CHCl₃).

To a solution of diazo 264 (12.0 mg, 0.0326 mmol, 1.00 equiv) in toluene (0.30 mL), was added dirhodium tetraacetate (0.70 mg, 0.00163 mmol, 0.05 equiv). The solution was refluxed under argon for 10 min. Solids were removed via a filtration through a celite plug (rinsed with EtOAc) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford lactone 266 (4.0 mg, 36% yield). (Similar result was obtained with benzene solvent at 80 °C.)

Rᶠ = 0.30 (1:2 EtOAc:hexane); ¹H NMR (400 MHz, CDCl₃) δ 6.75 (d, J = 1.6 Hz, 1H), 4.85 (ddd, J = 7.1, 6.4, 1.7 Hz, 1H), 2.72 (dd, J = 12.6, 6.4 Hz, 1H), 2.40 – 2.30
(m, 1H), 1.58 (s, 3H), 0.90 (s, 9H), 0.11 (d, \(J = 4.6\) Hz, 6H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 198.7, 175.1, 142.6, 138.1, 87.6, 73.5, 51.1, 26.9, 25.8, 18.2, 14.3, -4.6, -4.7; IR (Neat Film NaCl) 2953, 2856, 2146, 1713, 1661, 1330, 1302, 1097, 1066, 837 cm\(^{-1}\); HRMS (MM: FAB+) \(m/z\) calc’d for C\(_{15}\)H\(_{23}\)O\(_4\)N\(_2\)Si [M+H]\(^+\): 323.1427; found 323.1417; \([\alpha]_D^{25.0}\) 7.77° (c 0.20, CHCl\(_3\)).

To a solution of 2,2,6,6-tetramethylpiperidine (0.20 mL, 1.19 mmol, 5.00 equiv) in THF (2.40 mL) was added \(n\)-BuLi (1.96 M in hexane; 0.61 mL, 1.19 mmol, 5.00 equiv) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C, and TMSCl (0.20 mL, 1.19 mmol, 5.00 equiv) was added at -78 °C. Methyl ketone 258 (50.0 mg, 0.238 mmol, 1.00 equiv) in THF (0.60 mL) was added dropwise at -78 °C. The solution was stirred for 30 min and quenched with Et\(_3\)N, followed by sat. aq NaHCO\(_3\). The aqueous phase was extracted with EtOAc (3 x 3.50 mL). The combined organic phases were washed with brine, dried over MgSO\(_4\) and concentrated in vacuo. The residue was quickly filtered by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford silyl ether 267, which was used without further purification.

To a solution of \(m\)-CPBA (75%; 50.0 mg, 0.217 mmol, 0.91 equiv) in toluene (3.34 mL) was added NaHCO\(_3\) (55.0 mg, 0.651 mmol, 2.74 equiv). The heterogeneous mixture was stirred for 15 min at 23 °C, then H\(_2\)O (0.56 mL) was added. Silyl ether 267 in toluene (0.50 mL) was added dropwise to the reaction mixture at 0 °C. After the solution was stirred for 45 min at 0 °C, sat. aq NaHCO\(_3\) was added and stirred for 10 min at 0 °C. The aqueous phase was extracted with EtOAc (3 x 3.00 mL).
combined organic phases were washed with NaHCO₃ and brine, dried over MgSO₄ and concentrated in vacuo. To the residue dissolved in THF (0.42 mL) and H₂O (0.21 mL) was added AcOH (0.21 mL). The mixture was stirred for 2 h at 23 °C. After the solution was diluted with EtOAc and H₂O, solid NaHCO₃ was added until the gas evolution ceased. The aqueous phase was extracted with EtOAc (3 x 2.00 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford α-hydroxyketone 268 (12.0 mg, 42% yield based on recovered starting material, 2 steps).

Rᵋ = 0.30 (1:2 EtOAc:hexanes); ¹H NMR (400 MHz, CDCl₃) δ 6.55 (d, J = 1.9 Hz, 1H), 4.79 (td, J = 6.9, 1.9 Hz, 1H), 4.59 (d, J = 18.6 Hz, 1H), 4.51 (d, J = 18.6 Hz, 1H), 3.12 (s, br, 1H), 2.44 (dd, J = 12.8, 7.0 Hz, 1H), 2.05 – 1.99 (m, 1H), 1.47 (s, 3H), 0.90 (s, 9H), 0.10 (d, J = 4.1 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 198.4, 145.8, 143.8, 80.5, 73.4, 65.8, 50.9, 28.0, 25.9, 18.2, -4.5, -4.6; IR (Neat Film NaCl) 3418, 2929, 2857, 1682, 1361, 1259, 1093, 912, 835 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C₁₄H₂₇O₄Si [M+H]⁺:287.1679; found: 287.1677; [α]D₂₅° 78.9° (c 0.10, CHCl₃).

To a solution of α-hydroxyketone 268 (9.80 mg, 0.0342 mmol, 1.00 equiv) in CH₂Cl₂ (0.30 mL) were added DMAP (8.40 mg, 0.0684 mmol, 2.00 equiv) and Et₃N (38 µL, 0.274 mmol, 8.00 equiv). The solution was cooled to 0 °C and benzoic anhydride (15.0 mg, 0.0684 mmol, 2.00 equiv) was added in one portion. After 30 min, the
solution was warmed to 23 °C and stirred for 2 h. After the reaction was done, water was added. The aqueous phase was extracted with CH$_2$Cl$_2$ (3 x 1.00 mL). The combined organic phases were washed with brine, dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford benzoate 269 (11.4 mg, 85% yield).

R$_f$ = 0.75 (1:2 EtOAc:hexanes); $^1$H NMR (400 MHz, CDCl$_3$) δ 8.15 – 8.07 (m, 2H), 7.65 – 7.55 (m, 1H), 7.51 – 7.42 (m, 2H), 6.65 (d, J = 1.9 Hz, 1H), 5.30 (d, J = 16.4 Hz, 1H), 5.18 (d, J = 16.4 Hz, 1H), 4.81 (td, J = 7.1, 1.9 Hz, 1H), 2.44 (dd, J = 12.7, 7.0 Hz, 1H), 2.07 – 1.97 (m, 1H), 1.47 (s, 3H), 0.91 (s, 9H), 0.11 (d, J = 4.4 Hz, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 192.6, 166.0, 145.5, 144.2, 133.6, 130.1, 129.3, 128.7, 80.6, 73.4, 66.3, 50.7, 28.1, 25.9, 18.3, -4.5, -4.6; IR (Neat Film NaCl) 2928, 1728, 1691, 1259, 1098, 836 cm$^{-1}$; HRMS (MM: FAB+) m/z calc’d for C$_{21}$H$_{29}$O$_5$Si [M+H]$^+$-H$_2$: 389.1784; found: 389.1783; [α]$_D^{25.0}$ 40.9° (c 0.16, CHCl$_3$).

To a stirred solution of α-hydroxyketone 268 (49.0 mg, 0.171 mmol, 1.00 equiv) in CH$_2$Cl$_2$ (1.71 mL) were added Et$_3$N (72 µL, 0.513 mmol, 3.00 equiv) and MsCl (20 µL, 0.257 mmol, 1.50 equiv) at 0 °C. The solution was stirred at 0 °C for 2 h and quenched with H$_2$O. The aqueous phase was extracted with CH$_2$Cl$_2$ (3 x 2.00 mL). The combined organic phases were washed with brine, dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford mesylate 270 (44.0 mg, 71% yield).
R<sub>f</sub> = 0.43 (1:4 EtOAc:hexanes); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.58 (d, J = 1.9 Hz, 1H), 5.15 (s, 2H), 4.78 (td, J = 7.0, 1.9 Hz, 1H), 3.23 (s, 3H), 2.44 (dd, J = 12.8, 7.0 Hz, 1H), 2.05 – 1.95 (m, 1H), 1.95 (s, br, 1H), 1.46 (s, 3H), 0.90 (s, 9H), 0.11 (d, J = 4.6 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 191.2, 146.5, 143.8, 80.6, 73.3, 69.8, 50.7, 39.3, 27.9, 25.9, 18.2, -4.5, -4.7; IR (Neat Film NaCl) 2930, 2856, 1693, 1354, 1259, 1173, 1091, 1042, 959, 912, 835, 777 cm<sup>-1</sup>; HRMS (MM: FAB<sup>+</sup>) <sup>m/z</sup> calc’d for C<sub>15</sub>H<sub>27</sub>O<sub>5</sub>SiS [M-OH]<sup>+</sup>: 347.1348; found: 347.1357; [α]<sub>D</sub><sup>25.0</sup> 36.3° (c 0.12, CHCl<sub>3</sub>).

To a solution of trimethylsulfonium iodide (18.0 mg, 0.0877 mmol, 1.50 equiv) in THF (0.60 mL) was added dry KHMDS (17.0 mg, 0.0877 mmol, 1.50 equiv) in portions over 30 min at 0 °C. The mixture was stirred for 1 h. Then, a solution of aldehyde 256 in THF (0.30 mL) was added to a reaction vessel. The solution was stirred for 30 min and quenched with H<sub>2</sub>O. The aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over MgSO<sub>4</sub> and concentrated <i>in vacuo</i>. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford epoxide 271a and 271b (5.50 mg, 35% yield). See below for characterization data.
To a solution of aldehyde 256 (155 mg, 0.604 mmol, 1.00 equiv) and dibromomethane (51.0 µL, 0.725 mmol, 1.20 equiv) in THF (3.02 mL) was added n-BuLi (2.4 M solution in hexane; 0.28 mL, 0.665 mmol, 1.10 equiv) dropwise over 30 min at −78 °C. The reaction mixture was slowly warmed to 23 °C and stirred overnight. Then, the reaction was quenched with sat. aq NH₄Cl. The aqueous phase was extracted with EtOAc (3 x 3.00 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford epoxide 271a and 271b (64.0 mg, 39% yield).

Rₛ = 0.56 (1:2 EtOAc:hexanes); Diastereomer 1: ¹H NMR (400 MHz, CDCl₃) δ 5.72 (dd, J = 2.2, 1.0 Hz, 1H), 4.61 (ddd, J = 6.5, 3.8, 2.3 Hz, 1H), 3.55 (ddt, J = 4.3, 2.7, 0.8 Hz, 1H), 2.97 (dd, J = 6.0, 4.2 Hz, 1H), 2.74 (dd, J = 6.0, 2.7 Hz, 1H), 2.36 (dd, J = 13.5, 6.5 Hz, 1H), 2.06 (dd, J = 15.5 Hz, 1H), 1.89 (dd, J = 13.5, 3.8 Hz, 1H), 1.37 (s, 3H), 0.88 (s, 9H), 0.07 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 148.4, 131.1, 81.3, 73.3, 52.6, 49.7, 48.2, 26.1, 26.0, 18.3, -4.6; IR (Neat Film NaCl) 3408, 2929, 2856, 1361, 1252, 1085, 835 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C₁₄H₂₅O₃Si [M+H]⁺-H₂: 269.1573; found: 269.1568; [α]D²₅ 44.7° (c 0.08, CHCl₃).

Diastereomer 2: ¹H NMR (400 MHz, CDCl₃) δ 5.71 (dd, J = 2.1, 1.0 Hz, 1H), 4.65 (dddd, J = 6.4, 4.4, 2.1, 1.1 Hz, 1H), 3.50 (ddt, J = 3.7, 2.7, 1.0 Hz, 1H), 3.04 (dd, J = 5.7, 4.2 Hz, 1H), 2.88 (dd, J = 5.7, 2.7 Hz, 1H), 2.44 (dd, J = 13.3, 6.5 Hz, 1H), 2.15 (s, 1H), 1.90 (dd, J = 13.3, 4.4 Hz, 1H), 1.44 (s, 3H), 0.90 (s, 9H), 0.09 (d, J = 1.0 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 148.2, 131.1, 81.1, 73.3, 52.6, 49.7, 47.5, 26.1, 26.0, 18.3, -4.6; IR (Neat Film NaCl) 2956, 2929, 2856, 1361, 1252, 1085, 836, 776 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C₁₄H₂₅O₃Si [M+H]⁺-H₂: 269.1573; found: 269.1577; [α]D²₅ 11.5° (c 0.15, CHCl₃).
To a solution of epoxide 271 (64.0 mg, 0.237 mmol, 1.00 equiv) in THF (1.19 mL) was added MgI<sub>2</sub> (69.0 mg, 0.248 mmol, 1.05 equiv). The reaction mixture was stirred overnight at 40 °C and then quenched with H<sub>2</sub>O. The aqueous phase was extracted with EtOAc (3 x 2.00 mL). The combined organic phases were washed with brine, dried over MgSO<sub>4</sub> and concentrated in vacuo. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford iodohydrin 273 (59.0 mg, 63% yield).

To a solution of iodohydrin 273 (13.5 mg, 0.0338 mmol, 1.00 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (0.20 mL) were added imidazole (11.5 mg, 0.169 mmol, 5.00 equiv), DMAP (0.20 mg, 0.0016 mmol, 0.05 equiv), and TESCl (6.20 µL, 0.0371 mmol, 1.10 equiv). The reaction mixture was stirred overnight at 23 °C and then H<sub>2</sub>O was added. The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 0.50 mL). The combined organic phases were washed with brine, dried over MgSO<sub>4</sub> and concentrated in vacuo. The residue was purified by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford silyl ether 274 (11.5 mg, 89% yield).

R<sub>f</sub> = 0.80 (1:4 EtOAc:hexanes); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.89 (ddd, J = 2.1, 1.3, 0.5 Hz, 1H), 4.57 (ddt, J = 5.4, 3.0, 1.4 Hz, 1H), 4.30 (ddt, J = 6.5, 3.9, 1.3 Hz, 1H), 3.59 (dd, J = 10.2, 3.8 Hz, 1H), 3.35 (dd, J = 10.2, 6.4 Hz, 1H), 2.26 – 2.20 (m, 1H), 1.91 – 1.84 (m, 1H), 1.33 (s, 3H), 0.99 – 0.95 (m, 9H), 0.88 (s, 9H), 0.65 – 0.60 (m, 6H), 0.08 (d, J = 0.8 Hz, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 151.8, 132.3, 80.6, 72.8, 69.2, 52.5, 26.0, 25.4, 18.2, 15.4, 7.1, 5.0, -4.4, -4.6; IR (Neat Film NaCl) 2955, 1256,
1088, 836, 740 cm\(^{-1}\); HRMS (MM: FAB+) \(m/z\) calc’d for C\(_{20}\)H\(_{40}\)O\(_3\)Si\(_2\)I [M+H]\(^+\)-H\(_2\): 511.1561; found: 511.1573; \([\alpha]_D^{25.0}\) 4.31° (c 0.20, CHCl\(_3\)).

To a solution of NaH (60%, 1.00 mg, 0.0246 mmol, 1.10 equiv) in THF (1.12 mL) was added silyl ether \(274\) (11.5 mg, 0.0224 mmol, 1.00 equiv) in THF (0.50 mL) at 23 °C. The solution was stirred overnight and then H\(_2\)O was added. The aqueous phase was extracted with EtOAC (3 x 1.00 mL). The combined organic phases were washed with brine, dried over MgSO\(_4\) and concentrated \textit{in vacuo}. The residue was purified by column chromatography (1:8 EtOAc:hexanes) on silica gel to afford ether \(275\) (5.20 mg, 60% yield).

\(R_f = 0.23\) (1:8 EtOAc:hexanes); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.56 (dd, \(J = 2.2, 1.1\) Hz, 1H), 4.99 (dddd, \(J = 7.4, 5.4, 3.2, 1.1\) Hz, 1H), 4.84 (tdd, \(J = 7.5, 3.2, 2.2\) Hz, 1H), 4.16 (t, \(J = 7.9\) Hz, 1H), 3.56 (dd, \(J = 8.2, 7.2\) Hz, 1H), 2.40 (dd, \(J = 11.5, 5.4\) Hz, 1H), 2.00 (ddd, \(J = 11.5, 7.3, 1.0\) Hz, 1H), 1.21 (d, \(J = 0.9\) Hz, 3H), 0.97 (t, \(J = 8.0\) Hz, 9H), 0.90 (s, 9H), 0.68 – 0.52 (m, 6H), 0.10 – 0.06 (m, 9H); \(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 153.1, 126.0, 89.1, 79.3, 73.6, 68.2, 54.4, 26.0, 6.9, 4.8, -4.5; IR (Neat Film NaCl) 2955, 2927, 2875, 2360, 1459, 1256, 1089, 835 cm\(^{-1}\); HRMS (MM: FAB+) \(m/z\) calc’d for C\(_{20}\)H\(_{39}\)O\(_3\)Si\(_2\) [M+H]\(^+\)-H\(_2\): 383.2438; found: 383.2409; \([\alpha]_D^{25.0}\) 12.7° (c 0.15, CHCl\(_3\)).
To a solution of ether 275 (5.10 mg, 0.0132 mmol, 1.00 equiv) in EtOH (0.13 mL) was added PPTS (0.30 mg, 0.00132 mmol, 0.10 equiv) and stirred at 23 °C for 30 min. The reaction was quenched with sat. aq NaHCO₃ and the aqueous phase was extracted with EtOAc (3 x 0.70 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford alcohol 276 (1.61 mg, 45% yield).

Rₛ = 0.23 (1:8 EtOAc:hexanes); ¹H NMR (400 MHz, CDCl₃) δ 5.66 (dd, J = 2.2, 1.2 Hz, 1H), 5.14 – 5.03 (m, 1H), 4.86 (m, br, 1H), 4.35 (dd, J = 9.4, 7.5 Hz, 1H), 3.69 (dd, J = 9.4, 5.5 Hz, 1H), 2.43 (dd, J = 11.7, 5.5 Hz, 1H), 2.02 (ddd, J = 11.7, 7.3, 1.0 Hz, 1H), 1.22 (s, 3H), 0.90 (s, 9H), 0.09 (d, J = 5.8 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 154.7, 126.3, 90.2, 79.9, 75.1, 68.6, 54.0, 26.0, 24.1, -4.5, -4.6; IR (Neat Film NaCl) 2929, 2857, 1361, 1256, 1084, 835, 776 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C₁₄H₂₇O₃Si [M+H]⁺: 271.1730; found: 271.1734; [α]D₂₅ 33.7° (c 0.06, CHCl₃).

A flame-dried flask was charged with aldehyde 256 (399 mg, 1.56 mmol, 1.00 equiv) and THF (7.80 mL). Then, vinylmagnesium bromide (1.0 M solution in THF; 20.5 mL, 20.3 mmol, 13.0 equiv) was added to the solution at −78 °C and stirred for 3 h. The reaction was quenched with sat. aq NH₄Cl and the aqueous phase was extracted with EtOAc (3 x 10.0 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column
chromatography (1:2 EtOAc:hexanes) on silica gel to afford allyl alcohol 284 (371 mg, 84% yield).

To a solution of allyl alcohol 284 (371 mg, 1.30 mmol, 1.00 equiv) in CH₂Cl₂ (13.0 mL) was added MnO₂ (85%; 4.00 g, 39.1 mmol, 30.0 equiv). The mixture was stirred for 12 h. Solids were removed via filtration through a celite plug (rinsed with CH₂Cl₂) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford vinyl ketone 285 (230 mg, 63% yield).

Rₚ = 0.55 (1:2 EtOAc:hexanes); ¹H NMR (400 MHz, CDCl₃) δ 6.88 (dd, J = 17.1, 10.5 Hz, 1H), 6.60 (d, J = 1.9 Hz, 1H), 6.35 (dd, J = 17.1, 1.6 Hz, 1H), 5.80 (dd, J = 10.5, 1.6 Hz, 1H), 4.79 (td, J = 7.1, 1.9 Hz, 1H), 3.67 (s, 1H), 2.44 (dd, J = 12.7, 7.0 Hz, 1H), 2.04 (ddd, J = 12.6, 7.1, 0.9 Hz, 1H), 1.46 (s, 3H), 0.91 (s, 9H), 0.11 (d, J = 4.7 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 189.7, 147.0, 145.9, 132.3, 129.4, 80.4, 73.2, 51.0, 28.2, 25.9, 18.3, -4.4, -4.6; IR (Neat Film NaCl) 2955, 2929, 2856, 1658, 1605, 1361, 1259, 1091, 837, 777 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C₁₅H₂₅O₃Si [M+H]⁺-H₂: 281.1573; found: 281.1569; [α]D²⁵ 33.3° (c 0.06, CHCl₃).

To a solution of ketone 285 (22.1 mg, 0.0782 mmol, 1.00 equiv) in THF (0.80 mL) was added TBAF (1.0 M solution in THF; 0.16 mL, 0.156 mmol, 2.00 equiv) at 23 °C and stirred for 30 min. The reaction was quenched with sat. aq NH₄Cl. The aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was
purified by column chromatography (1:1 EtOAc:hexanes) on silica gel to afford diol 281 (6.00 mg, 46% yield).

\[ R_f = 0.15 \] (1:1 EtOAc:hexanes); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 6.84 (dd, \( J = 17.1, 10.5 \) Hz, 1H), 6.68 (d, \( J = 2.1 \) Hz, 1H), 6.36 (dd, \( J = 17.1, 1.5 \) Hz, 1H), 5.85 (dd, \( J = 10.5, 1.6 \) Hz, 1H), 4.82 (ddd, \( J = 7.4, 5.8, 2.1 \) Hz, 1H), 3.62 (s, br, 1H), 2.51 (dd, \( J = 13.4, 7.1 \) Hz, 1H), 2.01 (dd, \( J = 13.4, 5.7 \) Hz, 1H), 1.48 (s, 3H); \(^13\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 190.3, 148.2, 144.3, 132.6, 130.0, 81.2, 73.5, 50.2, 27.7; IR (Neat Film NaCl) 2922, 1657, 1605, 1407, 1264, 1223, 1148, 1067, 961, 796 cm\(^{-1}\); HRMS (MM: FAB+) \( m/z \) calc’d for C\(_9\)H\(_{13}\)O\(_3\) [M+H]\(^+\): 169.0865; found: 169.0864; \([\alpha]_D^{25.0}\) 25.8° (c 0.10, CHCl\(_3\)).

To a stirred solution of aldehyde 250 (300 mg, 1.53 mmol, 1.00 equiv) in THF (15.3 mL) was added vinylmagnesium bromide (1.0 M solution in THF; 2.29 mmol, 1.50 equiv) at \(-78 \) °C. The reaction was stirred for 1 h at \(-78 \) °C and quenched with sat. aq NH\(_4\)Cl. The aqueous phase was extracted with EtOAc (3 x 6.00 mL). The combined organic phases were washed with brine, dried over MgSO\(_4\) and concentrated \textit{in vacuo}. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford allyl alcohol 286 (227 mg, 66% yield).

\[ R_f = 0.32 \] (1:4 EtOAc:hexanes); (due to the presence of diastereomeric mixtures, the \(^1\)H NMR and \(^13\)C NMR contained extra peaks. See the attached spectrum) \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 6.23 – 6.14 (m, 2H), 5.92 – 5.82 (m, 2H), 5.82 – 5.77 (m, 2H), 5.23 (ddt, \( J = 17.2, 5.0, 1.5 \) Hz, 2H), 5.10 (ddt, \( J = 13.4, 10.4, 1.4 \) Hz, 2H), 4.86 –
Chapter 5 – Synthetic Studies Toward Polycyclic Inelegantolide

4.74 (m, 4H), 4.17 (q, $J = 6.7$ Hz, 1H), 4.13 – 4.07 (m, 1H), 3.71 – 3.68 (m, 6H), 2.91 – 2.81 (m, 1H), 2.76 (dd, $J = 7.3, 6.2, 1.8$ Hz, 2H), 2.69 – 2.62 (m, 1H), 2.54 (dt, $J = 9.8, 7.6, 4.6$ Hz, 2H), 2.37 (dd, $J = 15.1, 9.2, 5.8$ Hz, 1H), 1.65 (dq, $J = 1.5, 0.8$ Hz, 3H), 1.63 – 1.51 (m, 5H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 167.0, 149.1, 149.0, 147.1, 146.5, 141.5, 140.9, 119.9, 115.2, 114.3, 113.2, 112.6, 71.6, 70.9, 51.3, 51.2, 44.2, 40.7, 40.2, 32.9, 32.1, 18.6, 18.2; IR (Neat Film NaCl) 2929, 1722, 1644, 1439, 1202, 1168, 1124, 993 cm$^{-1}$; HRMS (MM: FAB+) $m/z$ calc’d for C$_{13}$H$_{21}$O$_3$ [M+H]$^+$: 225.1491; found: 225.1491.

To a solution of allyl alcohol 286 (10.0 mg, 0.0446 mmol, 1.00 equiv) in CH$_2$Cl$_2$ (0.45 mL) was added MnO$_2$ (85%; 182 mg, 1.78 mmol, 40.0 equiv). The mixture was stirred for 12 h at 23 °C. Solids were removed via a filtration through a celite plug (rinsed with CH$_2$Cl$_2$) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:6 EtOAc:hexanes) on silica gel to afford ketone 287 (8.41 mg, 85% yield). See below for characterization data.

To a stirred solution of oxalyl chloride (29 µL, 0.335 mmol, 1.50 equiv) in CH$_2$Cl$_2$ (1.10 mL) was added DMSO (47 µL, 0.669 mmol, 3.00 equiv) at −78 °C. The
solution was stirred for 15 min, then alcohol 286 (50.0 mg, 0.223 mmol, 1.00 equiv) in CH₂Cl₂ (0.6 mL) was added at −78 °C. The mixture was stirred for 3 h and 30 min at −78 °C, and then Et₃N (0.22 mL, 1.56 mmol, 7.00 equiv) was added. After 90 min at −78 °C, the solution was slowly warmed to 23 °C over 30 min and H₂O was added. The aqueous phase was extracted with CH₂Cl₂ (3 x 2.00 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:6 EtOAc:hexanes) on silica gel to afford ketone 287 (47.9 mg, 97% yield).

R_f = 0.55 (1:4 EtOAc:hexanes); ¹H NMR (400 MHz, CDCl₃) δ 6.34 (dd, J = 17.7, 10.4 Hz, 1H), 6.23 – 6.12 (m, 2H), 5.84 – 5.78 (m, 2H), 4.78 (p, J = 1.5 Hz, 1H), 4.74 (dt, J = 1.7, 0.8 Hz, 1H), 3.70 (s, 3H), 2.88 – 2.77 (m, 3H), 2.73 – 2.61 (m, 2H), 1.69 (dd, J = 1.5, 0.8 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 199.6, 166.9, 148.4, 146.1, 136.8, 128.4, 120.4, 112.3, 51.2, 43.5, 42.2, 32.4, 19.6; IR (Neat Film NaCl) 2950, 1716, 1645, 1439, 1407, 1204, 1173, 992, 895, 818 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C₁₃H₁₉O₃ [M+H]⁺: 223.1334; found: 223.1325; [α]D²⁵ –0.98° (c 0.28, CHCl₃).

![Reaction Scheme](image)

To a solution of ester 287 (10.0 mg, 0.0449 mmol, 1.00 equiv) in THF (0.50 mL) was added a solution of LiOH (2.20 mg, 0.0898 mmol, 2.00 equiv) in H₂O (0.20 mL). After 2 h at 23 °C, the aqueous phase was extracted with EtOAc (3 x 1.00 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:4
EtOAc:hexanes) on silica gel to afford Michael adduct 288 (6.28 mg, 55% yield). See below for characterization data.

To a stirred solution of ester 287 (6.80 mg, 0.00306 mmol, 1.00 equiv) in MeOH (0.10 mL) and H2O (0.10 mL) was added K2CO3 (17.0 mg, 0.122 mmol, 4.00 equiv). After 7 h, the aqueous phase was extracted with EtOAc (3 x 0.50 mL). The combined organic phases were washed with brine, dried over MgSO4 and concentrated in vacuo. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford Michael adduct 288 (4.11 mg, 53% yield).

Rf = 0.25 (1:4 EtOAc:hexanes); 1H NMR (400 MHz, CDCl3) δ 6.14 (dt, J = 11.6, 7.1 Hz, 1H), 5.80 (dt, J = 11.6, 1.7 Hz, 1H), 4.78 (p, J = 1.5 Hz, 1H), 4.77 – 4.70 (m, 1H), 3.70 (s, 3H), 3.61 (t, J = 6.3 Hz, 2H), 3.31 (s, 3H), 2.88 – 2.71 (m, 3H), 2.63 (t, J = 6.3 Hz, 2H), 2.61 – 2.45 (m, 2H), 1.68 (s, 3H); 13C NMR (101 MHz, CDCl3) δ 208.0, 166.9, 148.4, 146.2, 120.3, 112.2, 67.6, 59.0, 51.2, 47.3, 43.3, 41.8, 32.3, 19.6; IR (Neat Film NaCl) 2922, 1719, 1646, 1438, 1203, 1172, 1117, 894, 820 cm⁻¹; HRMS (MM: FAB+) m/z calc’d for C14H23O4 [M+H]+: 255.1596; found: 255.1604; [α]D25.0 – 3.01° (c 0.36, CHCl3).
A flame-dried flask was charged with aldehyde 256 (53.4 mg, 0.208 mmol, 1.00 equiv) and THF (1.04 mL). Then, ethynylmagnesium bromide (0.4M solution in THF; 5.20 mL, 2.08 mmol, 10.0 equiv) was added at –78 °C and stirred for 3 h. The reaction mixture was slowly warmed to 23 °C and stirred for 5 h. The reaction was quenched by adding sat. aq NH₄Cl. The aqueous phase was extracted with EtOAc (3 x 1.50 mL). The combined organic phases were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (1:2 EtOAc:hexanes) on silica gel to afford diol 293 (53.0 mg, 90% yield).

To a solution of diol 293 (11.1 mg, 0.0392 mmol, 1.00 equiv) in CH₂Cl₂ (0.40 mL) was added MnO₂ (85%; 52.0 mg, 0.510 mmol, 13.0 equiv). The mixture was stirred for 12 h. Solids were removed via a filtration through a celite plug (rinsed with CH₂Cl₂) and the resulting solution was concentrated under reduced pressure. The residue was purified by column chromatography (1:4 EtOAc:hexanes) on silica gel to afford ketone 294 (7.50 mg, 68% yield).

Rƒ = 0.56 (1:2 EtOAc:hexanes); ¹H NMR (500 MHz, CDCl₃) δ 6.89 (d, J = 1.9 Hz, 1H), 4.79 (tdd, J = 7.2, 1.9, 0.7 Hz, 1H), 3.29 (s, 1H), 3.09 (s, 1H), 2.47 (dd, J = 12.8, 7.0 Hz, 1H), 2.07 (ddt, J = 12.8, 7.1, 0.8 Hz, 1H), 1.58 (s, br, 1H), 1.46 (s, 3H), 0.91 (s, 9H), 0.11 (d, J = 7.1 Hz, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 176.1, 151.9, 147.9, 79.9, 79.5, 79.3, 72.9, 51.5, 27.8, 25.9, 18.2, -4.6; IR (Neat Film NaCl) 2929, 2955, 2857, 2097, 1638, 1361, 1272, 1259, 1209, 1093, 837, 777 cm⁻¹; HRMS (MM: ESI-APCI+) m/z calc’d for C₁₅H₂₅O₃Si [M+H]⁺: 281.1567; found: 281.1569; [α]D²⁵ 13.3° (c 0.06, CHCl₃).
5.5. References and Notes


(3) The absolute stereochemistry has yet to be confirmed.


(15) Treatment of TMS-diazomethane to acid chloride 262 afforded only methyl ester 299.

(16) Addition of diazomethane to intermediate 261 furnished cyclopropane 300.


(20) Attempted etherifications of α-bromoketone 301, which was prepared from α-hydroxyketone 268, was also unsuccessful.


(25) Only ketone **258** was observed when the reaction was conducted at 80 °C.

(26) Attempts on direct intramolecular etherification of iodohydrin **273** under basic conditions failed to produce **276**. In addition, oxidation of iodohydrin **273** with MnO₂ produced complex mixtures of byproducts.

(27) Because oxidation of secondary alcohol **276** with MnO₂ was conducted on small scale, the amount of the obtained ketone **245** was too little to be characterized by NMR analysis.


(30) An attempt to oxidize secondary alcohol 303, which was prepared by hydrolysis of ester 286 using Swern oxidation conditions, caused lactonization to give 305 instead of the desired 304.


(32) Silyl ether 296 was prepared from diol 293 with TESCl.
APPENDIX 13

Spectra Relevant to Chapter 5:

Synthetic Studies Toward Polycyclic I neleganolide
Figure A13.1. $^1$H NMR (400 MHz, CDCl$_3$) of compound 248.
Figure A13.2. Infrared spectrum (Thin Film, NaCl) of compound 248.

Figure A13.3. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 248.
Figure A13.4. $^1$H NMR (400 MHz, CDCl$_3$) of compound 251.
Appendix 13 – Spectra Relevant to Chapter 5

**Figure A13.5.** Infrared spectrum (Thin Film, NaCl) of compound 251.

**Figure A13.6.** $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 251.
Figure A13.7: $^1$H NMR (400 MHz, CDCl$_3$) of compound 252.
Figure A13.8. Infrared spectrum (Thin Film, NaCl) of compound 252.

Figure A13.9. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 252.
Figure A13.10. $^1$H NMR (400 MHz, CDCl$_3$) of compound 254.
Figure A13.11. Infrared spectrum (Thin Film, NaCl) of compound 254.

Figure A13.12. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 254.
Figure A13.13. $^1$H NMR (400 MHz, CDCl$_3$) of compound 244b.
Appendix 13 – Spectra Relevant to Chapter 5

Figure A13.14. Infrared spectrum (Thin Film, NaCl) of compound 244b.

Figure A13.15. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 244b.
Figure A13.16. $^1$H NMR (400 MHz, CDCl$_3$) of compound 260.
Figure A13.17. Infrared spectrum (Thin Film, NaCl) of compound 260.

Figure A13.18. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 260.
Figure A13.19. $^1$H NMR (400 MHz, CDCl$_3$) of compound 264.
**Figure A13.20.** Infrared spectrum (Thin Film, NaCl) of compound 264.

**Figure A13.21.** $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 264.
Figure A13.22. $^1$H NMR (400 MHz, CDCl$_3$) of compound 266.
Appendix 13 – Spectra Relevant to Chapter 5

*Figure A13.23.* Infrared spectrum (Thin Film, NaCl) of compound 266.

*Figure A13.24.* $^{13}$C NMR (101 MHz, CDCl₃) of compound 266.
Figure A13.25. $^1$H NMR (400 MHz, CDCl$_3$) of compound 268.
Figure A13.26. Infrared spectrum (Thin Film, NaCl) of compound 268.

Figure A13.27. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 268.
Figure A13.28. $^1$H NMR (400 MHz, CDCl$_3$) of compound 269.
Figure A13.29. Infrared spectrum (Thin Film, NaCl) of compound 269.

Figure A13.30. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 269.
Figure A13.31. $^1$H NMR (400 MHz, CDCl$_3$) of compound 270.
Figure A13.32. Infrared spectrum (Thin Film, NaCl) of compound 270.

Figure A13.33. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 270.
Figure A13.34. $^1$H NMR (400 MHz, CDCl$_3$) of compound 271a.
Figure A13.35. Infrared spectrum (Thin Film, NaCl) of compound 271a.

Figure A13.36. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 271a.
Figure A13.37. $^1$H NMR (400 MHz, CDCl$_3$) of compound 271b.
Figure A13.38. Infrared spectrum (Thin Film, NaCl) of compound 271b.

Figure A13.39. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 271b.
Figure A13.40. $^1$H NMR (500 MHz, CDCl$_3$) of compound 274.
Figure A13.41. Infrared spectrum (Thin Film, NaCl) of compound 274.

Figure A13.42. $^{13}$C NMR (126 MHz, CDCl$_3$) of compound 274.
Figure A13.43. $^1$H NMR (400 MHz, CDCl$\textsubscript{3}$) of compound $^{275}$. 

OTBS

TESO

$^{275}$
Figure A13.44. Infrared spectrum (Thin Film, NaCl) of compound 275.

Figure A13.45. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 275.
Figure A13.46. $^1$H NMR (400 MHz, CDCl$_3$) of compound 276.
Figure A13.47. Infrared spectrum (Thin Film, NaCl) of compound 276.

Figure A13.48. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 276.
Figure A13.49. $^1$H NMR (400 MHz, CDCl$_3$) of compound 285.
**Figure A13.50.** Infrared spectrum (Thin Film, NaCl) of compound 285.

**Figure A13.51.** $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 285.
Figure A13.52. $^1$H NMR (400 MHz, CDCl$_3$) of compound 281.
Figure A13.53. Infrared spectrum (Thin Film, NaCl) of compound 281.

Figure A13.54. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 281.
Figure A13.55. $^1$H NMR (500 MHz, CDCl$_3$) of compound 286.
Figure A13.56. Infrared spectrum (Thin Film, NaCl) of compound 286.

Figure A13.57. $^{13}$C NMR (126 MHz, CDCl$_3$) of compound 286.
Figure A13.58. $^1$H NMR (400 MHz, CDCl$_3$) of compound 287.
Figure A13.59. Infrared spectrum (Thin Film, NaCl) of compound 287.

Figure A13.60. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 287.
Figure A13.61. $^1$H NMR (400 MHz, CDCl$_3$) of compound 288.
Figure A13.62. Infrared spectrum (Thin Film, NaCl) of compound 288.

Figure A13.63. $^{13}$C NMR (101 MHz, CDCl$_3$) of compound 288.
Figure A13.64: $^1$H NMR (500 MHz, CDCl$_3$) of compound 294.
Appendix 13 – Spectra Relevant to Chapter 5

Figure A13.65. Infrared spectrum (Thin Film, NaCl) of compound 294.

Figure A13.66. $^{13}$C NMR (126 MHz, CDCl$_3$) of compound 294.