CHAPTER III

Stereoselective Synthesis of C9-C17 Fragment of

(+)-13-Deoxytedanolide
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After preparing the C1-C9 fragment 4 of deoxytanolide (discussed in chapter II) with terminal double bond suitable for cross-metathesis or RCM reaction and carboxylic acid group on the other end to undergo esterification or Yamaguchi macrolactonisation, we started the synthesis of C9-C17 fragment 5. The synthesis of 5 was planned to have terminal double bond to undergo cross-metathesis or RCM reaction with the upper fragment 4 and primary alcohol group on the other end to react with the carboxylic acid group of 4.

Retrosynthetic analysis of C9-C17 fragment 5 (lower fragment):

By retrosynthetic analysis of 5 (Scheme 1) it was envisioned to start the synthesis with 1,5-pentanediol using Evans chiral auxiliaries to fix the stereocenters at C10 and C14. Wittig olefination and Reformatsky reaction are the other key reactions used to accomplish the synthesis of 5.

Stereoselective Synthesis of C9-C17 Fragment of (+)-13-Deoxytanolide:

The chiral auxiliaries 62 and 63 used for chiral methylation and Evans asymmetric aldol reaction, were prepared from D-Valine. D-Valine was reduced to (R)-Valinol using NaBH₄ and I₂ by refluxing in THF. The crude amino alcohol was treated with
diethylcarbonate and K₂CO₃ at 140-145 °C and collection of ethanol formed in the reaction, using Dean-Stark apparatus followed by purification afforded the auxiliary 62 (Scheme 2).

The oxazolidinone auxiliary 62 was treated with propionic anhydride to give propionyl auxiliary 63. The Optical rotation, PMR, ¹³C NMR, IR and Mass spectral data of both the auxiliaries were matched with the reported data.

As per our synthetic plan 1,5-pentane diol was taken as starting material and was first treated with 1 equivalent of benzyl bromide and NaH in dry THF (Scheme 3). The diol was protected on one hydroxyl group leaving the other hydroxyl group free. The alcohol 47 obtained was characterized by ¹H NMR, ¹³C NMR, IR and Mass spectroscopy. ¹H NMR spectrum showed 5 aromatic protons resonated at δ 7.24 ppm, benzylic protons resonated at δ 4.47 ppm and the protons on C1 and C5 resonated as triplets at δ 3.6 ppm and 3.44 ppm respectively. The other 6 protons resonated as a multiplet at δ 1.50 ppm. IR spectrum showed a peak at 3381 cm⁻¹ confirmed the presence of hydroxyl group. Assigned structure 47 was further confirmed by mass spectrum ESI MS m/z 195 [M⁺].
The alcohol 47 was subjected to Swern oxidation to give the aldehyde 47a which was further oxidized to carboxylic acid 48 (Scheme 3) using NaClO\textsubscript{2} and hydrogen peroxide.\textsuperscript{2} \textsuperscript{1}H NMR spectrum showed the carboxylic acid proton resonated at \( \delta \) 8.2 ppm, the two protons on C2 adjacent to carbonyl functional group were resonated as triplet at \( \delta \) 2.36 ppm and the remaining protons resonated at their expected chemical shifts. ESI HRMS \([\text{M+Na}]\) peak at \( m/z \) 231.1005 further confirmed the structure 48.

Mixed anhydride formed by the treatment of carboxylic acid 48 with pivaloyl chloride and triethyl amine in THF. The auxiliary 62 was treated with \( n \)-BuLi in THF at \(-78 \degree C\), and the lithio-oxazolidinone derivative was added to the mixed anhydride at 0 \degree C, (Scheme 4) to afford the imide 49.\textsuperscript{3} The formation of imide 49 was confirmed by the spectral data. ESI HR mass spectrum showed molecular ion peak at \( m/z \) 342.1684 \([\text{M+Na}]\). Strong absorption peaks at 1780, 1701 cm\textsuperscript{-1} in IR spectrum were due to the
presence of two carbonyl groups. In $^1$H NMR spectrum the benzyl protons resonated at $\delta$ 7.30 ppm (5H) and $\delta$ 4.47 ppm (2H). 2' methylene protons resonated at $\delta$ 2.9 ppm as a multiplet, the protons of the isopropyl group resonated at $\delta$ 0.88 ppm (3H, doublet), $\delta$ 0.90 ppm (3H, doublet) and $\delta$ 2.35 ppm (1H, multiplet). $^{13}$C NMR spectrum further confirmed the product 49.

![Scheme 5](image)

The imide 49 was treated with NaHMDS at $-78 \, ^\circ\text{C}$ to generate the carbanion, followed by alkylation with iodomethane at $-78 \, ^\circ\text{C}$ (Scheme 5). In $^1$H NMR spectrum of 50, Protons of the methyl group on C2' resonated at $\delta$ 1.20 ppm as a doublet ($J = 6.79$ Hz) and a multiplet at $\delta$ 2.30 ppm corresponding to C2' proton was seen. The resonance due to other protons confirmed the formation of methylated imide 50. The methylation was further confirmed by ESI HR Mass spectrum $m/z$ 356.1842 [M+Na]; $^{13}$C NMR spectrum and IR spectral data further confirmed the product 50.

![Scheme 6](image)

Conversion of the methylated imide 50 to alcohol 51 was achieved by reduction with NaBH$_4$ in EtOH at $10 \, ^\circ\text{C}$ (Scheme 6). In $^1$H NMR spectrum of 51 benzyl protons
resonated at δ 7.25 ppm (5H) and δ 4.47 ppm (2H) and C2 proton resonated up field at δ 1.50 ppm confirmed the cleavage of the imide and reduction of the carbonyl group. The absence of resonance corresponding to the isopropyl group and C5 protons of the oxazolidinone ring (multiplet at δ ~ 4.10 ppm in imide 49) further confirmed the reductive cleavage of the imide to chiral alcohol 51. A strong and broad peak at 3449 cm⁻¹ confirmed that the product was an alcohol. Molecular ion peak m/z 231.1362 [M+Na] in ESI HR mass spectrum further confirmed the formation of the alcohol 51.

The alcohol 51 was protected as t-butyldiphenylsilyl ether by treating with TBDPSCI and imidazole in DCM at room temperature. t-Butyl protons resonated at δ 1.04 ppm confirmed the formation of TBDPS ether. ESI HRMS m/z 469.2551 [M+Na], IR spectra further confirmed the desired product 52.

![Scheme 7](image1)

TBDPS ether 52 was debenzylated by catalytic hydrogenolysis with 10% Pd/C to give the alcohol 53 (Scheme 7). The formation of 53 was confirmed by spectral data. In ¹H NMR spectrum the benzyl protons were absent and IR spectrum showed a peak corresponding to the hydroxyl group at 3418 cm⁻¹. In ESI HRMS peak at m/z 379.2077 [M+Na], confirmed the formation of the compound 53.

![Scheme 8](image2)
The alcohol 53 was oxidized under Swern oxidation conditions to give the aldehyde 53a (Scheme 8), and the crude product was used for Evan’s asymmetric aldol reaction\(^4,5\) without purification. Evan’s aldol reaction between chiral auxiliary 63 and aldehyde 53a gave the desired Evan’s \(\text{syn}\) aldol adduct 54 (Scheme 9). By this approach the methyl group at C10 of the deoxytedanolide was successfully fixed with desired stereochemistry.

The structure of aldol adduct was confirmed by \(^1\)H NMR, IR, Mass and \(^{13}\)C NMR spectral data. \(^1\)H NMR spectrum showed the resonance due to isopropyl group of the auxiliary portion at \(\delta\) 0.93 ppm and the newly fixed methyl group as a doublet at \(\delta\) 1.20 ppm (J = 6.98 Hz); t-butyl, aromatic protons of TBDPS group and the remaining protons were found resonated at their expected \(\delta\) values. Mass spectrum (ESI HRMS) showed a peak at \(m/z\) [M+Na] 562.2973; \(^{13}\)C NMR and IR spectra further confirmed the structure of aldol adduct 54.

![Scheme 9](image)

Reduction of the aldol adduct 54 with NaBH\(_4\) in EtOH afforded the diol 55 in excellent yield (Scheme 10). The peaks due to the isopropyl group are absent in \(^1\)HNMR spectrum and the C2 methyl group protons resonated at up field indicating the reduction of the carbonyl group and cleavage of the auxiliary from the adduct 54. In ESI HR mass spectrum molecular ion peak was found at \(m/z\) 437.2505 [M+Na] and IR spectrum showed a strong peak at 3436 cm\(^{-1}\) further confirmed the diol 55.
To protect the secondary alcohol selectively, the diol 55 was first converted into cyclic acetal 56 by treating with p-anisaldehyde dimethyl acetal in DCM (Scheme 10). In $^1$H NMR spectrum of 56 the peaks due to p-methoxybenzyl group were resonated at $\delta$ 3.77 ppm (OCH$_3$, singlet), $\delta$ 5.37 ppm (benzylic proton), $\delta$ 6.80 ppm and $\delta$ 7.62 ppm. The other protons of the acetal resonated at their expected $\delta$ values. In ESI HRMS molecular ion peak was found at $m/z$ 555.2930 [M+Na$^+$] further confirmed the product 56.

![Scheme 10](image)

Regioselective opening from less hindered side of PMB acetal was achieved when 56 was treated with DIBAL-H in DCM at 0 °C. $^1$H NMR spectrum of 57 confirmed the opening of acetal by showing two benzylic protons resonating at $\delta$ 4.43 ppm and rest of the protons resonated at their expected chemical shifts. IR spectrum showed a strong peak at 3446 cm$^{-1}$ due to the hydroxyl group. ESI HRMS showed a peak at $m/z$ 557.8079 [M+Na$^+$] further confirmed the product 57.

Now, the primary alcohol 57 was subjected to Swern oxidation and the aldehyde 57a was treated with non-stabilised ylide Ph$_3$P=CH$_2$ afforded the terminal olefin$^6$ 58 (Scheme 11). The double bond protons of the olefin 58 in $^1$H NMR, resonated at $\delta$ 5.75 ppm (1H) and $\delta$ 5.0 ppm (2H), and the remaining protons resonated at their appropriate chemical
shifts. Mass, $^{13}$C NMR and IR spectra confirmed the formation of the olefin. Base peak in ESI HRMS at $m/z$ 553.3116 [M+Na] gave the molecular weight of the olefin 58. After achieving the terminal double bond which was ready for metathesis reaction, our next attention was to extend the chain on the other side in such a way to have an alcohol group at the end, which could be coupled to the acid group of the upper fragment 4 by Yamaguchi esterification.

![Scheme 11](image)

Desilylation of 58 was achieved using 1M solution of TBAF in THF at room temperature with quantitave yield. The absence of peaks corresponding to the t-butyl and phenyl groups of TBDPS in $^1$H NMR spectrum of 59 confirmed the desilylation. A strong peak at 3439 cm$^{-1}$ in IR spectrum clearly indicated that the product was an alcohol. ESI HR Mass spectrum gave the molecular ion peak at $m/z$ 315.4161 [M+Na] further confirmed the desilylated product 59.
The Swern oxidation of the alcohol 59 readily gave the aldehyde 59a and was used immediately without purification for Reformatsky reaction (Scheme 12) using Zn-Cu couple. The β-hydroxy ester 60 obtained in Reformatsky reaction was a mixture of diastereomers with very close Rf values on TLC. β-Hydroxy group of 60 gave a strong peak at 3451 cm⁻¹ in IR spectrum. α-Methylene protons resonated in ¹H NMR spectrum at δ 2.37 ppm and β-H resonated at δ 3.85 ppm. The ethyl protons resonated at δ 4.15 ppm and δ 0.87 ppm and the rest of the protons were resonated at their expected chemical shifts. Molecular ion peak obtained in ESI HR mass spectrum at m/z 401.2291 [M+Na] further confirmed the product 60.

The β-hydroxy group of 60 was silylated using TESO⁻ and DIPEA in DCM before reducing the ester group to alcohol using DIBAL-H. The six protons (three CH₃) of TES group resonated as a quartet at δ 0.56 ppm (J = 7.9Hz) and the remaining protons resonated at their corresponding δ values confirmed the silylated product 61. IR and mass
profile ESI HRMS at m/z 515.3161 [M+Na] further confirmed the silylation of the β-hydroxy ester.

The compound 61 was treated with DIBAL-H in DCM to give the alcohol 5 the lower fragment (Scheme 12). The disappearance of the ethyl peaks of the ester in $^1$H NMR spectrum of 5 confirmed the reduction, and all the remaining protons were resonated at their respective chemical shifts. IR spectrum showed a peak at 3448 cm$^{-1}$ confirmed the presence of –OH group in 5 and ESI HRMS showed the molecular ion peak at m/z 473.3066 [M+Na] further confirmed the formation of the lower fragment 5.

**Coupling of the fragments 4 with 5:**

To couple the two fragments we tried the cross-metathesis$^8$ reaction using Grubbs' 2$^{nd}$ generation catalyst (10 mol%) by refluxing in DCM. It was noticed that no product was formed even after 4 days (Scheme 13), and the two unchanged substrates 4 and 5 were recovered by silica gel column chromatography.

The reaction was repeated in toluene by stirring the two fragments with Grubbs' 2$^{nd}$ generation catalyst (10 mol%) at 80 °C for 2 days (Scheme 13) but only found the unchanged substrates, and were recovered by silica gel column chromatography.
Chapter III: Present Work (C9-C17 Fragment) Discussion

Scheme 13

Grubbs' 2nd gen. catalyst
reaction 1. DCM, reflux, 4 days
reaction 2. toluene, 80 °C, 2 days
EXPERIMENTAL
To a suspension of NaBH₄ (20.3 g, 534.2 mmol) in THF (250 ml) at room temperature, D-Valine (25 g, 213.6 mmol) was added and cooled to 0 °C, added a solution of iodine (54.25 g, 213.6 mmol) in THF, over a period of 45 min. Stirred the reaction mixture at room temperature for 1 h. After refluxing for 18 h the reaction mixture was cooled to 0 °C and MeOH (100 ml) was added till the reaction mixture become clear. After stirring for 30 min, the solvent was evaporated and dissolved the white precipitate in 20% aqueous KOH (300 ml). The solution was stirred for 4 h and extracted with DCM. The organic layer was dried over Na₂SO₄ and concentrated to get the crude (R)-Valinol.

The crude amino alcohol (R)-Valinol (18.0 g, 174.5 mmol), diethyl carbonate (42.2 ml, 349 mmol) and potassium carbonate (2.45 g, 17.5 mmol) were taken in an RB flask equipped with a Dean-Stark apparatus. The magnetically stirred mixture was heated at 145 °C until 15.7 ml of ethanol was collected. The resultant mixture was cooled to room temperature and diluted with diethylether (200 mL), and the resulting suspension was filtered through a Celite pad to remove the potassium carbonate. The filtered solid was washed with diethyl ether (50 ml). Evaporated the filtrate and purified the residue by column chromatography on silica gel (hexane-ethylacetate, 1:1) afforded the oxazolidinone 62 (14 g, 51%, over 2 steps) as white needles (mp: 70 °C).
1H NMR (300 MHz, CDCl3): δ 7.35 (brs, 1H), 4.44 (m, 1H), 4.10 (m, 1H), 3.61 (m, 1H), 1.76 (m, 1H), 0.94 (d, J = 6.6 Hz, 3H), 0.92 (d, J = 6.7 Hz, 3H).

ESI MS : m/z 130 [M+1].

(4R)-4-Isopropyl-3-propionyl-1,3-oxazolan-2-one (63)

To the solution of oxazolidinone 62 (16.5 g, 127.9 mmol) in THF (80 ml) were added triethylamine (35.6 ml, 255.8 mmol) and LiCl (8.69 g, 204.5 mmol) at room temperature and cooled to -20 °C. Propionic anhydride (2 ml, 155.5 mmol) was added slowly and stirred for 1 hr. The reaction mixture was quenched with saturated aqueous sodium bicarbonate solution and extracted with diethyl ether. The organic layer was washed with brine and dried (Na2SO4), concentrated in vacuo and the residue was purified using silica gel flash chromatography (hexane-ethyl acetate, 8:2) to provide 63 (19.5 g, 83%) as a colorless oil.

1H NMR (300 MHz, CDCl3): δ 4.44 (m, 1H), 4.30 (m, 1H), 4.25 (m, 1H), 2.99 (m, 2H), 2.41 (m, 1H), 1.16 (t, J = 8.3 Hz, 3H), 0.93 (d, J = 7 Hz, 3H), 0.89 (d, J = 7 Hz, 3H).

ESI MS : m/z 208 [M+Na].
5-(Benzzyloxy)-1-pentanol (47)

\[
\text{HOCH}_{2}CH_{2}CH_{2}CH_{2}CH_{2}OH
\]

A solution of 1,5-pentanediol (10 g, 96.15 mmol) in THF (10 ml) was added to a flask containing NaH (50% suspension in mineral oil) (5.5 g, 115.38 mmol) in THF (90 ml) at room temperature. The mixture was stirred at room temperature for 30 min and cooled to 0 °C. Then benzyl bromide (11.5 ml, 96.15 mmol) was added slowly drop-wise and the mixture was stirred for 3 h at room temperature. Water was added slowly to quench the reaction and extracted with ether. The organic layer was dried (Na$_2$SO$_4$) and concentrated in vacuo and the residue was purified using flash chromatography (hexane-ethyl acetate, 6:4) to provide the benzyl ether 47 (14.9 g, 80%) as a colourless oil.

$^1$H NMR (300 MHz, CDCl$_3$) : δ 7.28 (m, 5H), 4.47 (s, 2H), 3.60 (t, $J = 6.5$ Hz, 2H), 3.44 (t, $J = 6.5$ Hz, 2H), 1.79-1.29 (m, 6H).

ESI MS : 195 [M$^+$+1].

IR (neat, cm$^{-1}$) : 3381, 1453, 1096.

5-(Benzzyloxy)pentanoic acid (48)

\[
\text{HOOCCH}_{2}CH_{2}CH_{2}CH_{2}COOH
\]

A solution of dimethyl sulfoxide (DMSO) (11.2 ml, 158.7 mmol) in DCM (30 ml) was added to a stirred solution of (COCl)$_2$ (10 ml, 114.3 mmol) in DCM (30 ml) at -78 °C. After 20 min, a solution of 47 (14 g, 72.16 mmol) in DCM (140 ml) was added at the
same temperature. The mixture was stirred for 20 min at -78 °C and then triethyl amine (50 ml, 360.8 mmol) was added at -78 °C. Removed the dry ice bath and stirring was continued at room temperature for 30 min. Saturated aqueous NH₄Cl (60 ml) was added to quench the reaction, and the mixture was extracted with DCM (2x100 ml). The combined organic layer was washed with brine, dried over Na₂SO₄, concentrated in vacuo and used in the next step without purification.

A solution of NaClO₂ (80% assay) (12.25 g, 108.2 mmol) in water (112 ml) was added to a solution of above aldehyde in acetonitrile (70 ml), NaH₂PO₄·2H₂O (2.25 g, 14.4 mmol) and 35% H₂O₂ (7.7 ml, 79.37 mmol). The reaction mixture was stirred at room temperature for 6 h and Na₂SO₃ was added to quench the unreacted NaClO₂ and H₂O₂ at 0 °C. The reaction mixture was acidified with 10% aqueous HCl and extracted with DCM (2x50 ml). The combined organic layer was dried (Na₂SO₄), concentrated in vacuo and the residue was purified by silica gel flash chromatography (hexane-ethyl acetate, 6:4) to provide the carboxylic acid 48 (7.8 g, 73%) as a colorless viscous oil.

¹H NMR (300 MHz, CDCl₃): δ 8.2 (b, 1H), 7.25 (m, 5H), 4.46 (s, 2H), 3.45 (t, J = 6.0 Hz, 2H), 2.36 (t, J = 6.8 Hz, 2H), 1.78-1.60 (m, 4H).

ESI HRMS: Calculated m/z for C₁₂H₁₆O₃Na [M+Na] 231.0997, Found 231.1005.

IR (neat, cm⁻¹): 3032, 1709, 1452.
A solution of $n$-BuLi in hexane (2.5 M, 23.0 ml, 57.6 mmol) was added dropwise to a stirred solution of 62 (6.2 g, 48 mmol) in anhydrous THF (100 ml) at −78 °C. The mixture was stirred at this temperature for 30 min. To the acid 48 (12 g, 57.69 mmol) and THF (120 ml) taken in a separate flask cooled to 0 °C, triethylamine (11.36 ml, 81.6 mmol) and pivaloyl chloride (7.52 ml, 62.4 mmol) were added. After stirring for 30 min. at 0 °C, the lithio-(4R)-4-isopropyl-2-oxazolidinone was added to the mixed anhydride. The mixture was warmed to room temperature over a period of 2 h. The reaction was quenched with aq. NH$_4$Cl solution and extracted with EtOAc. The organic layer was washed with saturated NaHCO$_3$ solution, saturated NH$_4$Cl solution, and brine. The dried (Na$_2$SO$_4$) organic layer was concentrated in vacuo and the residue was purified using flash chromatography (hexane-ethyl acetate, 8:2) to provide 49 (12.8 g, 70%) as colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$): δ 7.29 (m, 5H), 4.47 (s, 2H), 4.36 (quintet, $J$ = 3.8Hz, 1H), 4.23-4.13 (m, 2H), 3.48 (t, $J$ = 6.0Hz, 2H), 3.03-2.81 (m, 2H), 2.36 (m, 1H), 1.81-1.62 (m, 4H), 0.92 (d, $J$ = 7.2 Hz, 3H), 0.87 (d, $J$ = 6.8 Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$): δ 172.9, 153.9, 138.4, 128.2, 127.4, 127.3, 72.7, 69.8, 63.2, 58.2, 35.0, 28.9, 28.2, 21.0, 17.7, 14.5.
ESI HRMS : Calculated m/z for C_{16}H_{26}NO_4Na [M+Na] 342.1681, Found 342.1684.
IR (neat, cm$^{-1}$) : 1780, 1701, 1456.
Optical rotation [$\alpha$]$^25$ : $-39.0$ (c 0.2, CHCl$_3$).

(4$R$)-3-[(2$S$)-5-(Benzzyloxy)-2-methylpentanoyl]-4-isopropyl-1,3-oxazolan-2-one (50)

The solution of 49 (10.0 g, 31.3 mmol) in THF was cooled to $-78$ °C and 1M solution of NaHMDS (34.5 ml, 34.48 mmol) was added dropwise. The mixture was stirred at $-78$ °C for 1 h then iodomethane (9.75 ml, 156.5 mmol) was added. After stirring for 30 min, the solution was allowed to reach room temperature. The mixture was quenched with aqueous NH$_4$Cl solution and extracted with ether. The organic extract was washed with saturated NH$_4$Cl solution, saturated NaHCO$_3$, and brine and dried over (Na$_2$SO$_4$). The dried organic layer was concentrated in vacuo and the residue was purified by chromatography on silica gel column (hexane-ethyl acetate, 9:1) to give 50 (8.4 g, 81%) as colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.28 (m, 5H), 4.45 (s, 2H), 4.35 (quintet, $J = 3.7$ Hz, 1H), 4.16-4.04 (m, 2H), 3.49-3.39 (m, 2H), 2.34 (m, 1H), 1.80 (m, 1H), 1.67-1.35 (m, 4H), 1.2 (d, $J = 6.8$ Hz, 3H), 0.91 (d, $J = 6.8$ Hz, 3H), 0.87 (d, $J = 6.8$ Hz, 3H).
Chapter III: Experimental

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 176.8, 153.5, 138.5, 129.4, 128.2, 127.4, 127.3, 72.7, 70.1, 63.0, 58.2, 37.4, 29.6, 28.3, 27.2, 17.8, 17.7, 14.5.

ESI HRMS: Calculated m/z for C$_{19}$H$_{21}$NO$_4$Na [M+Na] 356.1837, Found 356.1842.

IR (KBr, cm$^{-1}$): 1778, 1699, 1456.

Optical rotation $[\alpha]_{D}^{25}$: -46.0 (c 0.25, CHCl$_3$).

(2S)-5-(Benzyloxy)-2-methylpentan-1-ol (51)

To a solution of 50 (7.0 g, 21 mmol) in EtOH (70 ml), NaBH$_4$ (1.59 g, 42 mmol) was added at 0 °C and stirred at the same temperature for 15 min. The reaction mixture was quenched with saturated NH$_4$Cl solution, extracted with EtOAc. The organic layer was washed with brine, dried (Na$_2$SO$_4$) and concentrated in vacuo. The residue was purified using chromatography on silica gel column (hexane-ethyl acetate, 7:3) to give 51 (3.7 g, 85 %) as colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.24 (m, 5H), 4.47 (s, 2H), 3.48-3.36 (m, 4H), 1.73-1.42 (m, 5H), 0.91 (d, $J = 6.6$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 138.4, 128.3, 127.6, 72.9, 70.6, 67.9, 35.5, 29.5, 27.0, 16.5.

ESI HRMS: Calculated m/z for C$_{13}$H$_{20}$O$_2$Na [M+Na] 231.1360, Found 231.1362.

IR (neat, cm$^{-1}$): 3449, 1457, 1099.

Optical rotation $[\alpha]_{D}^{28}$: +31.0 (c 0.1, CHCl$_3$).
(2S)-5-(Benzyl oxy)-2-methylpentyl]oxy(tert-butyl)diphenylsilane (52)

The alcohol 51 (3 g, 14.4 mmol) was dissolved in DCM (50 ml), Imidazole (1.95 g ml, 28.8 mmol) and TBDPSCl (4.35 g, 15.84 mmol) were added sequentially at room temperature. After being stirred for 4 h at room temperature the reaction mixture was quenched with saturated aqueous NH₄Cl solution and extracted with DCM. The combined organic layer was dried (Na₂SO₄) and concentrated in vacuo. Purification of the residue by column chromatography on silica gel (hexane-EtOAc, 95:5) gave compound 52 (6.1 g, 95%) as a colorless liquid.

¹H NMR (300 MHz, CDCl₃): δ 7.62 (d, J = 7.5 Hz, 4H), 7.38-7.19 (m, 11H), 4.45 (s, 2H), 3.53-3.36 (m, 4H), 1.71-1.44 (m, 4H), 1.20 (m, 1H), 1.04 (s, 9H), 0.93 (d, J = 6.8 Hz, 3H).

ESI HRMS: Calculated m/z for C₂₉H₃₈O₂NaSi [M+Na] 469.2538, Found 469.2551

IR (neat, cm⁻¹): 1463, 1108

Optical rotation [α]D₂⁵: +22.0 (c 0.17, CHCl₃)

(4S)-5-[1-(tert-Butyl)-1,1-diphenylsilyl]oxy-4-methylpentan-1-ol (53)

To a solution of 52 (5 g, 11.2 mmol) in EtOAc (25 ml), 10% Pd/C (595.8 mg, 0.56 mmol in terms of Pd) was added and the mixture was hydrogenated using a H₂-filled
balloon for 4 h. It was then filtered through Celite bed and the filter cake was washed with EtOAc. The filtrate and washings were combined and concentrated in vacuo. The residue was purified by chromatography on silica gel column (hexane-ethyl acetate, 7:3) to give 53 (3.79 g, 95 %) as colorless oil.

\[ \text{ESI HRMS: Calculated } m/\text{z for C}_{22}\text{H}_{41}\text{O}_6\text{Si} \left[ \text{M+Na} \right] 379.2069, \text{ Found 379.2077.} \]

IR (neat, cm\(^{-1}\))

Optical rotation \( [\alpha]_D^{26} \)

\( +8.1 \) (c 0.5, CHCl\(_3\)).

\( \text{(4S)-3-((2R,3S,6S)-7-[(tert-Butyl)-1,1-diphenylsilyl]oxy-3-hydroxy-2,6-dimethylheptanoyl)-4-isopropyl-1,3-oxazolin-2-one (54)} \)

A solution of dimethyl sulfoxide (DMSO) (1.3 ml, 18.5 mmol) in DCM (15 ml) was added to a stirred solution of (COCl\(_2\)) (1.47 ml, 16.84 mmol) in DCM (15 ml) at -78 °C. After 20 min, a solution of 53 (3 g, 8.42 mmol) in DCM (30 ml) was added at the same temperature. The mixture was stirred for 20 min at -78 °C and then triethylamine (5.86 ml, 42.1 mmol) was added at -78 °C. The reaction was brought to room temperature and
stirring was continued for 30 min at room temperature. Saturated aqueous NH₄Cl (30 ml) was added to quench the reaction, and the mixture was extracted with DCM. The organic extract was washed with brine, dried over Na₂SO₄, concentrated in vacuo proceed to the next step without further purification.

To the auxiliary 63 (1.48 g, 8 mmol) in DCM (15 ml) under nitrogen at 0 °C, added Bu₂BOTf (8.4 ml, 8.42 mmol) followed by DIPEA (1.72 ml, 10.1 mmol). Stirred at 0 °C for 30 min. The reaction mixture was cooled to -78 °C and the solution of aldehyde in DCM (15 ml) was added. The mixture was stirred for 30 min at -78 °C and for 2 h at room temperature. The boron aldolate complex was quenched with pH 7 buffer (15 ml) followed by addition of 30% H₂O₂-MeOH (1:1, 30 ml) at 0 °C and stirred for 1 h. The reaction mixture was extracted with ether (3x20 ml) and the combined organic layer was washed with water, brine dried (Na₂SO₄) and concentrated in vacuo. Purification of the residue by silica gel column chromatography (hexane-EtOAc, 85:15) gave pure Evan's aldol adduct 54 (3.7 g, 82%) as a colorless liquid.

**1H NMR (200 MHz, CDCl₃):** δ 7.67-7.58 (m, 4H), 7.40-7.30 (m, 6H), 4.41 (m, 1H), 4.30-4.14 (m, 2H), 3.83 (brs, 1H), 3.66 (m, 1H), 3.42 (m, 2H), 2.86 (m, 1H), 2.33 (m, 1H), 1.76-1.28 (m, 4H), 1.24 (m, 1H), 1.20 (d, J = 7.0 Hz, 3H), 1.05 (s, 9H), 0.94 (d, J = 6.6 Hz, 3H), 0.93 (d, J = 7.3 Hz, 3H), 0.89 (d, J = 7.3 Hz, 3H).

**13C NMR (50 MHz, CDCl₃):** δ 177.9, 153.4, 135.5, 133.9, 129.4, 127.5, 71.5, 68.6, 63.2, 58.1, 41.8, 35.7, 31.0, 29.4, 28.2, 26.8, 19.2, 17.8, 16.8, 10.5.

**ESI HRMS:** Calculated m/z for C₃₁H₄₃NO₅NaSi [M+Na] 562.2964

Found 562.2973.
(2S,3S,6S)-7-[(1-tert-Butyl)-1,1-diphenylsilyl]oxy-2,6-dimethylheptane-1,3-diol (55)

IR (neat, cm$^{-1}$) : 3447, 1782, 1696, 1109.
Optical rotation $[\alpha]_D^{26}$ : $-15.0$ (c 0.25, CHCl$_3$).

To a solution of 54 (3 g, 5.5 mmol) in EtOH (30 mL), NaBH$_4$ (423 mg, 11.1 mmol) was added at 10 °C and stirred at the same temperature for 15 min. The reaction mixture was quenched with saturated NH$_4$Cl solution, extracted with EtOAc. The organic layer was washed with brine, dried (Na$_2$SO$_4$) and concentrated in vacuo. The residue was purified by column chromatography on silica gel column (hexane-ethyl acetate, 1:1) to give 55 (2.3 g, 85 %) as colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.62 (d, $J$ = 7.5 Hz, 4H), 7.42-7.29 (m, 6H), 3.78-3.59 (m, 3H), 3.54-3.40 (m, 2H), 1.77-1.50 (m, 3H), 1.40 (m, 1H), 1.09 (m, 2H), 1.05 (s, 9H), 0.94 (d, $J$ = 6.8 Hz, 3H), 0.88 (d, $J$ = 6.8 Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 135.6, 133.9, 129.5, 127.5, 75.0, 68.6, 67.3, 38.8, 35.7, 31.4, 29.6, 26.8, 19.2, 16.9, 9.9.

ESI HRMS : Calculated m/z for C$_{25}$H$_{38}$O$_3$NaSi [M+Na] 437.2487 Found 437.2505.

IR (neat, cm$^{-1}$) : 3436, 1464, 1109.
Optical rotation $[\alpha]_D^{26}$ : $+10.0$ (c 0.24, CHCl$_3$).
**Chapter III: Experimental**

*tert*-Butyl((2S)-4-[(4S,5S)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]-2-methylbutyloxy)diphenylsilane (56)

![Structural formula of compound 56](image)

Compound 55 (2.0 g, 4.8 mmol), camphorsulfonic acid (56.0 mg, 0.24 mmol) and p-anisaldehyde dimethylacetal (1.05 ml, 5.76 mmol) in DCM (20 ml) were stirred for 2 h at room temperature. Triethylamine (2.0 ml) was added and the solution was stirred for a further 10 min, the solvent was removed under reduced pressure and the residue was purified by silica gel flash column chromatography (hexane-EtOAc, 95:5) to give 56 (2.2 g, 87%) as a white semi-solid.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.61 (d, $J = 6.0$ Hz, 4H), 7.42-7.28 (m, 8H), 6.8 (d, $J = 9.0$ Hz, 2H), 5.37 (s, 1H), 4.04-3.91 (m, 2H), 3.78 (s, 3H), 3.77 (m, 1H), 3.46 (m, 2H), 1.70-1.31 (m, 6H), 1.13 (d, $J = 6.8$ Hz, 3H), 1.05 (s, 9H), 0.92 (d, $J = 6.0$ Hz, 3H).

ESI HRMS: Calculated m/z for C$_{33}$H$_{44}$O$_4$NaSi [M+Na] 555.2906, Found 555.2930.

IR (neat, cm$^{-1}$): 1462, 1247, 1110, 1035.

Optical rotation $[\alpha]_D^{25}$: +5.0 (c 0.22, CHCl$_3$).

*(2S,3S,6S)-7-[(tert-Butyl)-1,1-diphenylsilyloxy-3-[(4-methoxybenzyl)oxy]-2,6-dimethylheptan-1-ol (57)

![Structural formula of compound 57](image)
A 20% solution of DIBAL-H in toluene (3.25 ml, 3.75 mmol) was added drop wise to a stirred solution of 56 (1.0 g, 1.87 mmol) in DCM (10 ml) at 0 °C, and the mixture was stirred for 1h at 0 °C. The reaction was quenched with saturated aqueous NH₄Cl (5 ml) at 0 °C and saturated aqueous potassium sodium tartrate solution (10 ml). DCM (30 ml) was added, and the mixture was vigorously stirred for 30 min. The organic layer was separated, washed the aqueous layer with DCM and combined organic layer was dried over Na₂SO₄, concentrated in vacuo, and the residue was chromatographed on a silica gel column (hexane-EtOAc, 2 : 1) to give 57 (900 mg, 90%) as a colorless oil.

¹H NMR (200 MHz, CDCl₃): δ 7.67-7.58 (m, 4H), 7.41-7.12 (m, 7H), 6.81 (m, 3H), 4.43 (s, 2H), 3.78 (d, J = 4.4 Hz, 2H), 3.77 (s, 3H), 3.50-3.34 (m, 3H), 1.98 (m, 1H), 1.71-1.38 (m, 3H), 1.37-1.20 (m, 3H), 1.05 (s, 9H), 0.93 (d, J = 6.2 Hz, 3H), 0.83 (d, J = 7.0 Hz, 3H).

ESI HRMS: Calculated m/z for C₃₅H₄₄O₄NaSi [M+Na] 534.8073, Found 557.8079.

IR (neat, cm⁻¹): 3446, 1465, 1247, 1109, 1035.

Optical rotation [α]₂⁵: +19.0 (c 0.25, CHCl₃).

t-Butyl((2S,5S,6S)-5-((4-methoxybenzyl)oxy)-2,6-dimethyl-7-octenyloxy)diphenylsilane (58)
A solution of dimethyl sulfoxide (DMSO) (0.2 ml, 2.88 mmol) in CH$_2$Cl$_2$ (3 ml) was added to a stirred solution of (COCl)$_2$ (0.23 ml, 2.62 mmol) in CH$_2$Cl$_2$ (3 ml) at -78 °C. After 20 min, a solution of 57 (700 g, 1.31 mmol) in CH$_2$Cl$_2$ (5 ml) was added at the same temperature. The mixture was stirred for 20 min at -78 °C and then triethylamine (0.9 ml, 6.55 mmol) was added. The reaction was brought to room temperature and stirring was continued for 30 min at room temperature. Saturated aqueous NH$_4$Cl (30 ml) was added to quench the reaction, and the mixture was extracted with DCM. The combined organic layer was washed with brine, dried over Na$_2$SO$_4$, concentrated in vacuo proceeded to the next step without purification.

Methyltriphenylphosphonium bromide (1.4 g, 3.93 mmol) in THF (20 ml) at 0 °C was treated with sodium bis(trimethylsilyl)amide (2.6 ml, 1 M in THF, 2.62 mmol), and the resulting solution was stirred at 0 °C for 30 min. The aldehyde in THF (5.0 ml) was added, and the mixture was allowed to warm to room temperature and stirred at this temperature for 1 h. The reaction was quenched with saturated aqueous NH$_4$Cl and extracted with Et$_2$O. The combined Et$_2$O fractions were washed with brine and dried over Na$_2$SO$_4$, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (eluting with hexanes-ethyl acetate, 98:2) to afford compound 58 (530 mg, 76%) as a colorless liquid.

$^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 7.62 (d, $J$ = 6.0 Hz, 4H), 7.43-7.29 (m, 6H), 7.18 (d, $J$ = 8.3 Hz, 2H), 6.8 (d, $J$=8.3 Hz, 2H), 5.76 (m, 1H), 4.98 (m, 2H), 4.40 (s, 2H), 3.77 (s, 3H), 3.51-3.36 (m, 2H), 3.16 (m, 1H), 2.42 (m, 1H), 1.59 (m, 2H), 1.46-1.33 (m, 3H), 1.04 (s, 9H), 0.99 (d, $J$ = 6.8 Hz, 3H), 0.91 (d, $J$ = 5.6 Hz, 3H).
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$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 158.9, 140.9, 135.5, 134.0, 129.4, 129.2, 127.5, 114.3, 114.1, 113.6, 82.8, 71.3, 68.7, 55.2, 40.7, 35.8, 29.3, 28.9, 28.3, 27.9, 26.8, 19.3, 16.9, 15.5.

ESI HRMS: Calculated $m/z$ for C$_{16}$H$_{22}$O$_3$Si [M+Na]$^+$ 553.3113, Found 553.3116.

IR (neat, cm$^{-1}$): 1618, 1461, 1247, 1110.

Optical rotation $[\alpha]_D^{28}$: +5.0 (c 0.25, CHCl$_3$).

$(2R,5S,6S)-5$-[(4-Methoxybenzyl)oxy]-2,6-dimethyl-7-octen-1-ol (59)

To a solution of 58 (400 mg, 0.755 mmol) in dry THF (5 ml), TBAF (0.9 ml, 1 M in THF, 0.9 mmol) was added at 0 °C. The reaction mixture was warmed to room temperature and stirred for 4 h. It was quenched with saturated aqueous NH$_4$Cl solution, extracted with EtOAC, washed with brine, dried (Na$_2$SO$_4$) and concentrated in vacuo. The residue was purified by silica gel column chromatography (by eluting with hexane-ethyl acetate, 2:1) to obtained the product 59 (202.5 mg, 92%) as a colorless liquid.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.20(d, $J = 8.4$ Hz, 2H), 6.81 (d, $J = 8.8$ Hz, 2H), 5.78 (m, 1H), 5.05-4.96 (m, 2H), 4.43 (m, 2H), 3.79 (s, 3H), 3.47-3.55 (m, 2H), 3.19 (m, 1H), 2.46 (m, 1H), 1.64-1.22 (m, 5H), 1.02 (dd, $J = 6.8$, 3.6 Hz, 3H), 0.90 (dd, $J = 6.6$, 2.8 Hz, 3H).

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ESI HRMS: Calculated m/z for C_{16}H_{25}O_{3}Na [M+Na] 315.4164, Found 315.4161.

IR (neat, cm⁻¹): 3439, 1615, 1460, 1247, 1037.

Optical rotation [α]_D^{26}: +3.1 (c 0.5, CHCl₃).

Ethyl (4S,7S,8S)-3-hydroxy-7-[(4-methoxybenzyl)oxy]-4,8-dimethyl-9-decanoate (60)

A solution of dimethyl sulfoxide (DMSO) (0.06 ml, 0.9 mmol) in DCM (0.5 ml) was added to a stirred solution of (COCl)₂ (0.07 ml, 0.82 mmol) in DCM (0.5 ml) at -78 °C. After 20 min, a solution of 59 (120 mg, 0.41 mmol) in DCM (2 ml) was added at the same temperature. The mixture was stirred for 20 min at -78 °C and then triethylamine (0.3 ml, 2.15 mmol) was added at -78 °C. The reaction mixture was brought to room temperature and stirring was continued for 30 min. Saturated aqueous NH₄Cl solution was added to quench the reaction, and the mixture was extracted with DCM. The organic layer was washed with brine, dried over Na₂SO₄, concentrated in vacuo, proceeded to next step without purification.

To a warm (60 °C) mixture of acetic acid (2 ml) and cupric acetate dihydrate (8.2 mg, 0.041 mmol) was added zinc dust (157.5 mg, 2.46 mmol) while stirring the reaction mixture vigorously, over a period of 2 min. Instantaneously, a reddish black solid (zinc-copper couple) was formed with an exothermic reaction. The reaction was cooled to room temperature and acetic acid was decanted. The solid was washed with acetic acid.
followed by ether washing (3x3 ml) and the wet Zn-Cu couple used for the reaction immediately.

To the above Zn-Cu couple taken in THF (2 ml), was added the solution of aldehyde 59a and 2-bromoethyl acetate (0.05 ml, 0.45 mmol) in THF (1 ml) under N2 atmosphere at room temperature. The reaction mixture refluxed gently for 1 h, allowed to cool to room temperature. Quenched the reaction mixture with saturated aqueous NH4Cl and the solid was filtered on Celite. The Celite cake was washed with diethyl ether and the filtrate was dried over Na2SO4, and concentrated in rotary evaporator. The residue was purified by flash chromatography on silica gel (eluted with hexane-ethyl acetate, 9:1) to afford the β-hydroxyl ester (diastereomeric mixture) 60 (109.5 mg, 70% after 2 steps) as a colorless oil.

$^1$H NMR (200 MHz, CDCl3): $\delta$ 7.21 (d, $J = 8.4$ Hz, 2H), 6.81 (d, $J = 8.4$ Hz, 2H), 5.79 (m, 1H), 5.0 (m, 2H), 4.43 (s, 2H), 4.15 (q, $J = 7.0$ Hz, 2H), 3.87 (m, 1H), 3.79 (s, 3H), 3.18 (m, 1H), 2.53-2.21 (m, 3H), 1.69-1.34 (m, 5H), 1.28 (t, $J = 7.0$ Hz, 3H), 1.02 (dd, $J = 6.6, 1.8$ Hz, 3H), 0.88 (d, $J = 5.9$ Hz, 3H).

ESI HRMS: Calculated m/z for C22H34O5Na [M+Na] 401.2303, Found 401.2291.

IR (neat, cm$^{-1}$): 3451, 1730, 1613, 1460, 1247.

Ethyl(4S,7S,8S)-7-[(4-methoxybenzyl)oxy]-4,8-dimethyl-3-[1,1,1-triethylallyl]oxy]-9-decanoate (61)
To a solution of 60 (55 mg, 0.14 mmol) in DCM (1 ml) were added DIPEA (0.07 ml, 0.42 mmol.) and the triethyl silyl triflate (0.03 ml, 0.17 mmol) at 0 °C under nitrogen. After 5 min. the cooling bath was removed and the mixture stirred for 1 h at room temperature. Water was added to quench the reaction and separated the layers. The aqueous layer was extracted with DCM and the combined organic layers were dried (Na2SO4), evaporated and purified by chromatography on silical gel column (hexane-ethyl acetate, 95:5) to give the product 61 (66.5 mg, 93%) as a colorless liquid.

1H NMR (300 MHz, CDCl3): δ 7.20 (d, J = 8.3 Hz, 2H), 6.80 (d, J = 8.6 Hz, 2H), 5.78 (m, 1H), 5.0 (m, 2H), 4.41 (s, 2H), 4.09 (m, 3H), 3.79 (s, 3H), 3.17 (m, 1H), 2.52-2.24 (m, 3H), 1.60-1.32 (m, 2H), 1.26 (m, 6H), 1.02 (dd, J = 6.8, 3.8 Hz, 3H), 0.93 (t, J = 7.9 Hz, 9H), 0.89-0.80 (m, 3H), 0.56 (q, J = 7.9Hz, 6H).

ESI HRMS : Calculated m/z for C25H46O5NaSi [M+Na] 515.3168,
Found 515.3161.

IR (neat, cm⁻¹) : 1730, 1613, 1460, 1247, 1108.

(4S,7S,8S)-7-[(4-Methoxybenzyl)oxy]-4,8-dimethyl-3-[(1,1,1-triethylsilyl)oxy]-9-decen-1-ol (S)

Compound 61 (25 mg, 0.05 mmol) in DCM (1 ml), under N2 atmosphere, was cooled to 0 °C, and diisobutylaluminum hydride (20% solution in toluene, 0.17 ml, 0.21 mmol) was slowly added over 10 min. After addition was complete, stirring was continued for 1 h at 0 °C. The reaction mixture was then carefully quenched with
methanol (1 ml). Saturated aqueous solution of potassium sodium tartrate solution (2 ml) and ethyl acetate (2 ml) were added. The mixture was stirred vigorously for 1 h to get the clear separation of organic and aqueous layers. Separated the layers and the aqueous layer was extensively extracted with ethyl acetate. The combined organic layers were dried over (Na₂SO₄), and evaporated to dryness in rotary evaporator to give the alcohol S (21 mg, 92%) as a colorless liquid.

¹H NMR (300 MHz, CDCl₃): δ 7.20 (d, J = 8.3 Hz, 2H), 6.80 (dd, J = 8.6, 2.2 Hz, 2H), 5.79 (m, 1H), 5.0 (m, 2H), 4.51-4.34 (m, 2H), 3.79 (s, 3H), 3.75-3.64 (m, 3H), 3.16 (m, 1H), 2.43 (m, 1H), 1.71-1.44 (m, 3H), 1.34-1.20 (m, 4H), 1.05-0.79 (m, 15H), 0.60 (q, J = 7.9Hz, 6H).

ESI HRMS: Calculated m/z for C₂₆H₄₆O₄NaSi [M+Na] 473.3063, Found 473.3066.

IR (neat, cm⁻¹): 3448, 1613, 1462, 1247, 1109.
Reference:


Conclusion

The work presented in this thesis entitled “Studies Towards the Synthesis of (+)-13-Deoxytedanolide,” the stereoselective synthesis of fragments 4 and 5 was achieved with well planned reactions and protecting groups which can be selectively removed to carry out further reactions, according to our synthetic plan. During this study, the Sharpless asymmetric dihydroxylation has been achieved with excellent regioselectivity, which was an important step of our synthetic plan.

In the present work, the failure in coupling of the two fragments 4 and 5 by cross-metathesis reaction might be due to the presence of the bulky TIPS group in 4 and PMB group in 5 in the close proximity to the double bonds. Hence, our plan was changed so as to remove the bulky protecting groups before subjecting the fragments for cross-metathesis reaction, followed by Yamaguchi macrolactonisation. It was also planned to couple the two fragments by esterification followed by Ring Closing Metathesis and the studies in that direction are under progress.

It was envisioned that after finishing the coupling reactions to give the macrocycle 2, the C2-C3 acetonide can be cleaved and β-hydroxyl group can be methylated after protecting the α-hydroxyl group as silyl ether. Then the TES group can be removed and C15-OH oxidized for coupling with fragment 3 by aldol reaction, followed by the removal of PMB groups and their oxidation to give C5 and C11 carbonyl groups of 1. Finally the substrate controlled epoxidation can be performed to accomplish the total synthesis of (+)-13-deoxytedanolide.
SPECTRA
HOOCC

\[ \text{NMR spectrum of compound 48} \]
$^1$H NMR spectrum of compound 50
$^1$H NMR spectrum of compound S1
'H NMR spectrum of compound 54
'H NMR spectrum of compound 57
$^1$H NMR spectrum of compound 58
$\text{H NMR spectrum of compound 60}$
\text{\textsuperscript{1}H NMR spectrum of compound S}
$^1H$ NMR spectrum of compound 63
$^{13}$C NMR spectrum of compound 54
ESI HRMS of compound 5
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