Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Biomimetic-inspired synthesis of sporochartines through Diels-Ader reaction between enantiopure (-)-sporothriolide and (+)-trienylfuranol A

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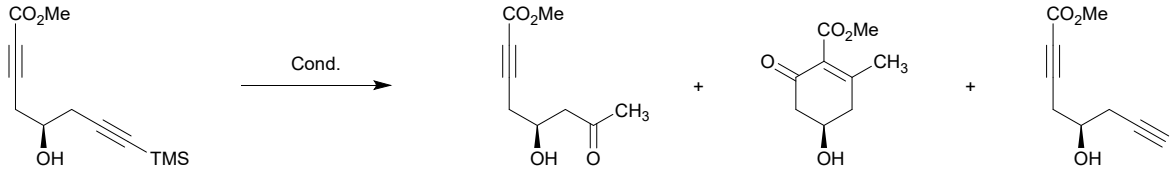
I - General information

All non-aqueous reactions were run under an inert atmosphere (argon), by using standard techniques for manipulating air-sensitive compounds. Anhydrous solvents were obtained by filtration through drying columns (THF, dichloromethane, DMF). All reagent-grade chemicals and other solvents were obtained from commercial suppliers and were used as received. Reactions were monitored by analytical thin-layer chromatography (TLC) on silica gel (60 F_{254}) plates (Merck) and visualized using UV light (254 and 312 nm) and developed by heating the plate after spraying with an aqueous solution of sulfomolybdic acid or $KMnO_4$. Flash column chromatography was conducted on Merck silica gel 60 (40-63 µm) or on Combiflash Companion using Interchim silica columns. Proton magnetic resonance ^1H NMR spectra (500.1 MHz) and carbon magnetic resonance ^{13}C NMR spectra (75.5 and 125.8 MHz) were recorded on Bruker Avance spectrometers. Analyses were acquired in $CDCl_3$ (δ_H 7.26 ppm; δ_C 77.16 ppm) or C_6D_6 (δ_H 7.16 ppm; δ_C 128.06 ppm). The following abbreviations are used for the proton spectra multiplicities: s = singulet, d = doublet, t = triplet, q = quadruplet and m = multiplet. Coupling constants (*J*) are reported in Hertz (Hz). Infrared spectra (IR) were obtained on a Perkin-Elmer Spectrum 100 model instrument and are reported in reciprocal centimeters (cm^{-1}). High-resolution mass spectra (HRMS) were recorded with a Micromass LCT Premier XE instrument (Waters) and were determined by electrospray ionization (ESI) coupled with a time of flight analyser (TOF), while low resolution mass spectrometry (LRMS) on a Waters Acquity QDA detector coupled to a Waters Alliance HPLC system. Optical rotations were measured at 20 °C on an Anton Paar MCP 300 polarimeter and data are reported as follows: optical rotation $[\alpha]_D^{20}$, concentration (*c* in g/100 mL) and solvent.

II - Optimization for selective hydration of bisalkynyl ester 10 and 11

Table S1. Optimization for selective hydration of bisalkynyl ester 10

Table S1. Optimization for selective hydration of bisalkynyl ester **10**.



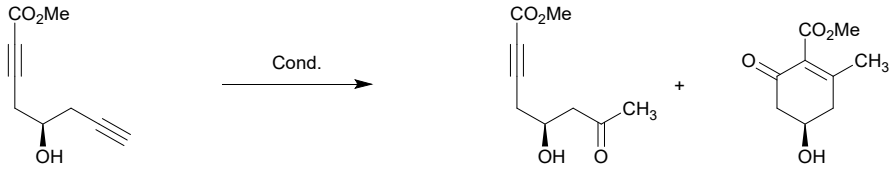
10 **12** **12b** **11**

Entry	catalyst (mol%)	solvent	Temp. (°C)	Time (h)	Conv. (%)	Yield (%) of **12**	Yield (%) of **12b**	Yield (%) of **11**
1[a]	(IPr)AuCl (5) + $AgSbF_6$ (5)	MeOH/H_2O 2:1	20	18	100	decomp.		
2[a]	JohnPhosAu(MeCN)SbF_6 (5)	MeOH/H_2O 2:1	20	18	100	decomp.		
3[a]	(IPr)AuCl (5)	MeOH/H_2O 2:1	20	18	0	starting material		
4[a]	(IPr)AuCl (5)	MeOH/H_2O 2:1	50	72	100	30[b]	30[b]	40[b]
5[a]	(IPr)AuCl (5)	MeOH/H_2O 2:1	110	18	100	-	70[b]	-
6[a]	$AgSbF_6$ (5)	MeOH/H_2O 2:1	80	18	100	decomp.		
7[a]	$HgSO_4$ (3)	THF/H_2O 5:2	0 to 20	24	100	**65%**[c]		

[a] Reactions performed on 0.02 mmol scale. [b] Yield determined by ^1H NMR with trimethoxybenzene as internal standard added at the end of the reaction. [c] Isolated yield. (IPr)AuCl = 1,3-Bis(2,6-diisopropylphenyl-imidazol-2-ylidene)gold(I) chloride.

Table S2. Optimization for selective hydration of bisalkynyl ester 11

Table S2. Optimization for selective hydration of bisalkynyl ester **11**.



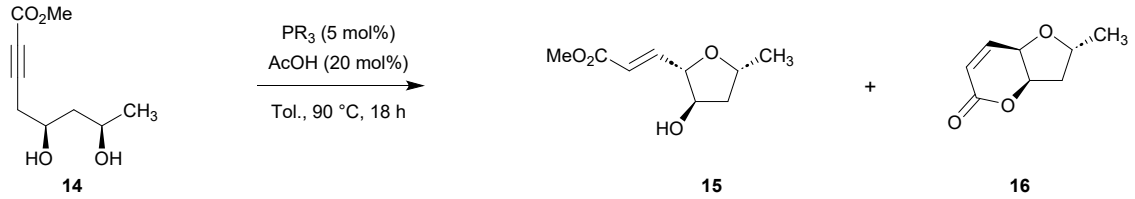
11 **12** **12b**

Entry	catalyst (mol%)	solvent	Temp. (°C)	Time (h)	Conv. (%)	Yield (%) of **12**	Yield(%) of **12b**
1[a]	(IPr)AuCl (5) + $AgSbF_6$ (5)	MeOH/H_2O 2:1	20	18	100	decomp.	
2[a]	JohnPhosAu(MeCN)SbF_6 (5)	MeOH/H_2O 2:1	20	18	100	decomp.	
3[a]	[(IPr)Au(CH_3CN)]BF_4 (5)	MeOH/H_2O 2:1	20	18	100	decomp.	
4[a]	(IPr)AuCl (5)	MeOH/H_2O 2:1	40	140	35	30[b]	5[b]
5[a]	(IPr)AuCl (5)	MeOH/H_2O 2:1	110	18	100	-	100[b]
6[a]	(SIPr)AuCl (5)	MeOH/H_2O 2:1	70	26	80	15[b]	65[b]
7[a]	(AdPr)AuCl (5)	MeOH/H_2O 2:1	70	26	35	20[b]	15[b]
8[a]	$NaAuCl_4.2H_2O$ (5)	MeOH/H_2O 10:1	75	6	10	-	10[b]
9[a]	$PtCl_2$ (5)	DCM+H_2O (few drops)	20	18	0	starting material	
10[a]	$FeCl_3.6H_2O$ (200) + I_2 (200)	CH_3CN	20	6	0	starting material	
11[a]	$HgSO_4$ (3)	THF/H_2O 5:2	0 to 20	21	100	**75%**[c]	

[a] Reactions performed on 0.02 mmol scale. [b] Yield determined by ^1H NMR with trimethoxybenzene as internal standard added at the end of the reaction. [c] Isolated yield. (IPr)AuCl = 1,3-Bis(2,6-diisopropylphenyl-2-imidazolylidene)gold(I) chloride. (SIPr)AuCl = 1,3-Bis(2,6-diisopropylphenyl-2-imidazolidinylidene)gold(I) chloride. (AdPr)AuCl = 1,3-Bis(2,6-adamantyl-2-imidazolylidene)gold(I) chloride.

Table S3. Optimization for the formation of furane derivative 15

Table S3. Optimization of phosphine-catalyzed umpolung γ-hydroalkoxylations of alkynoate derivative **14** for the formation of furane derivative **15**.

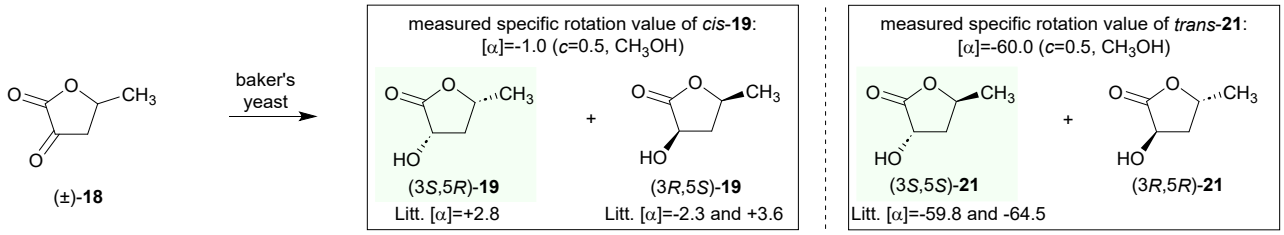


Entry	PR_3	Conv. (%)[c]	Yield (%) of **15**	Yield(%) of **16**
1[a]	PPh_3	70	15[g]	5[g]
2[a]	PPh_2Me	100	40[g]	25[g]
3[a]	$PPhMe_2$	NR	NA	NA
4[a]	dppe[d]	50	20[g]	10[g]
5[a]	dppp[e]	100	40[g]	20[g]
6[a]	dppb[f]	100	40[g]	20[g]
7[b]	dppp[e]	100	**15**[h]	**10**[h]

[a] Reactions performed on 0.1 mmol scale. [b] Reactions performed on 0.5 mmol scale. [c] Based on the consumption of **14** as determined of ^{1}H NMR analysis of the crude mixture. [d] 1,2-Bis(diphenylphosphino)ethane. [e] 1,3-Bis(diphenylphosphino)propane. [f] 1,4-Bis(diphenylphosphino)butane. [g] Yield determined by ^{1}H NMR with dimethylsulfone as internal standard added at the end of the reaction. [h] Isolated yield.

Table S4. Enantioselective reduction of α-oxo-γ-butyrolactone (±)-18 using Baker's yeast

Table S4. Enantioselective reduction of α-oxo-γ-butyrolactone (±)-**18** using Baker's yeast

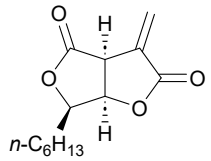


Entry	Time (h)	Conv. (%)	d.r.[c] *cis*-**19**/*trans*-**21**	Yield[d] (%) of *cis*-**19**	Yield[d] (%) of *trans*-**21**
1[a]	15	90	1:1	15	15
2[a]	40	100	1:1	18	16
3[b]	24	100	1:1	20	20

[a] Reactions performed on 0.9 mmol scale in water (250 mL), 30 °C, 150 rpm with 5 g of baker's yeast. [b] Reactions performed on 9 mmol scale in water (1 L), 30 °C, 150 rpm with 20 g of baker's yeast. [c] The diastereoisomeric ratio (d.r.) was determined by ^{1}H NMR on the crude mixture. [d] Isolated yield.

III - Experimental Procedures and Characterization Data

III.1 - Sporothriolide production from fermentation culture of *Hypoxylon monticulosum* CLL-205

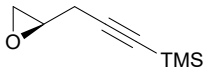


(-)-sporothriolide (**3**)

The crude ethyl acetate extract (3.0 g) from *Hypoxylon monticulosum* culture broth was purified by silica gel column chromatography (eluent: *n*-heptane/EtOAc 1:1). After concentration under reduced pressure, sporothriolide (300 mg, 10%) was obtained as a white powder. The spectra data are consistent to the previous described compound in literature (Leman-Loubière et al., J. Nat. Prod. 2017, 80, 2850-2854).

^{1}H NMR (500.1 MHz, $CDCl_3$) δ 6.47 (d, *J* = 2.0 Hz, 1H), 6.15 (d, *J* = 2.0 Hz, 1H), 5.15 (dd, *J* = 6.8, 4.7 Hz, 1H), 4.68-4.61 (m, 1H), 4.01 (dt, *J* = 6.7, 1.9 Hz, 1H), 1.91-1.82 (m, 2H), 1.55-1.44 (m, 2H), 1.39-1.25 (m, 6H), 0.89 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 172.2 (C), 167.6 (C), 130.0 (C), 127.4 (C), 82.9 (CH), 77.3 (CH), 46.3 (CH), 31.7 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 25.5 (CH_2), 22.6 (CH_2), 14.1 (CH_3). **HRMS (ESI)** *m/z*: calcd. for $C_{13}H_{19}O_4$ $[M+H]^+$ 239.1283, found 239.1282.

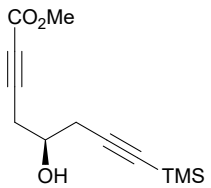
III.2 - Synthetic approach of trienylfuranol by phosphine-organocatalyzed reaction for the formation of furanic moiety



9

(*R*)-2-[3-(Trimethylsilyl)prop-2-yn-1-yl]oxirane (9). Trimethylsilylacetylene (11.2 mL, 81.1 mmol, 1.5 equiv.) was added to anhydrous THF (90 mL) under an argon atmosphere and the solution was cooled to -78 °C. Then, *n*-BuLi 1.6 M (51 mL, 81.1 mmol, 1.5 equiv.) was added dropwise and very carefully to avoid heating the reaction. The mixture was stirred at -78 °C for 10 min, then $BF_3.OEt_2$ (10.0 mL, 81.1 mmol, 1.5 equiv.) was added dropwise and very carefully to avoid heating the reaction and the mixture was stirred for another 10 min. Afterward, a solution of (*R*)-(-)-epichlorohydrin (5.0 g, 54.0 mmol, 1 equiv.) in anhydrous THF (20 mL) under an argon atmosphere at -78 °C was added dropwise along the wall of the flask and very carefully to the reaction mixture. The solution was stirred at -78 °C for 1.5 h and then allowed to warm up to 0 °C. After 1.5 h at 0 °C, the reaction was completed and treated by a saturated aqueous NH_4Cl solution. Then, the organic layer was separated and the aqueous phase was extracted three times by Et_2O. Combined organic layers were washed with brine, dried with $MgSO_4$, filtered and concentrated under *vacuum.* The crude mixture was dissolved in DCM (200 mL) and then NaOH (12.97 g, 324.3 mmol) was added. The mixture was stirred overnight at room temperature. After the reaction was completed, the reaction was treated by a saturated aqueous NH_4Cl solution. Then, the organic layer was separated and the aqueous phase was extracted three times by DCM. Combined organic layers were washed with brine then dried with $MgSO_4$, filtered and concentrated under *vacuum.* The crude product was purified by silica gel flash column chromatography (eluent: Pentane/Et_2O 9:1) to give the alkynylated product **9** as a pale yellow colorless oil (4.7 g, 30.2 mmol, 56 %).

^{1}H NMR (500.1 MHz, $CDCl_3$) δ = 3.11-3.08 (m, 1H), 2.79 (dd, *J* = 5.0, 4.0 Hz, 1H), 2.67 (dd, *J* = 17.4, 4.4 Hz, 1H), 2.66 (dd, *J* = 5.0, 2.6 Hz, 1H), 2.48 (dd, *J* = 17.4, 5.2 Hz, 1H), 0.15 (s, 9H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 100.9 (C_q), 87.4 (C_q), 50.0 (CH), 46.6 (CH_2), 23.7 (CH_2), 0.1 (CH_3). **HRMS (ESI)** *m/z*: calc for $C_{10}H_{18}NOSi$ $[M+ACN+H]^+$ 196.1158, found 196.1149. **IR (neat) ν_{max}** = 3960, 2901, 2180, 1485, 1407, 1250, 1028, 946, 856, 760 cm^{-1}. $[\alpha]_D^{22}$ = - 28.8 (*c* = 1, $CHCl_3$).



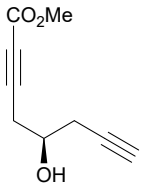
10

Methyl (*S*)-5-hydroxy-8-(trimethylsilyl)octa-2,7-diynoate (10). Methyl propiolate (10.8 mL, 121.9 mmol, 4 equiv.) was added to anhydrous THF (140 mL) under an argon atmosphere and the solution was cooled to -78 °C. Then, *n*-BuLi (76.2 mL, 121.9 mmol, 4 equiv.) was added dropwise along the wall of the flask and very carefully to avoid heating the reaction. The mixture was stirred at -78 °C for 30 min. Afterward, a solution of epoxide **9** (4.70 g, 30.5 mmol, 1 equiv.) in anhydrous THF (30 mL) under an argon atmosphere was added dropwise along the wall of the flask and very carefully to avoid heating the reaction, this was followed by the addition of $BF_3.OEt_2$ (15.0 mL, 121.9 mmol, 4 equiv.) using the same method. Then, the mixture was stirred at -78 °C for 3 h. After the reaction was completed, the reaction was treated by a saturated aqueous NH_4Cl solution. Then, the organic layer was separated and the aqueous phase was extracted three times by Et_2O. Combined organic layers were washed with brine, dried with $MgSO_4$, filtered and concentrated under *vacuum.* The crude product was purified by silica gel flash column chromatography (eluent: Pentane/Et_2O 8:2) to give the alkynylated product **10** as a pale yellow colorless oil (6.48 g, 27.2 mmol, 89 %).

^{1}H NMR (500.1 MHz, $CDCl_3$) δ = 3.99 (quint, *J* = 6.0, 1H), 3.77 (s, 3H), 2.67 (dd, *J* = 17.2, 6.0 Hz, 1H), 2.62 (dd, *J* = 17.2, 6.0 Hz, 1H), 2.58 (dd, *J* = 16.8, 6.0 Hz, 1H), 2.54 (dd, *J* = 16.8, 6.0 Hz, 1H), 0.16 (s, 9H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 153.9 (C_q), 101.5 (C_q), 88.8 (C_q), 85.4 (C_q), 74.9 (C_q), 67.9 (CH), 52.7 (CH_3), 27.9 (CH_2), 26.2 (CH_2), 0.0 (CH_3). **HRMS (ESI)** *m/z*: calc for $C_{12}H_{19}O_3Si$ $[M+H]^+$

239.1103, found 239.1107. **IR (neat) ν_{max}** = 3422, 2958, 2902, 2240, 2177, 1716, 1436, 1356, 1249, 1074, 1028, 858, 753 cm^{-1}. $[\alpha]_D^{20}$ = -3.8 (*c* = 1, $CHCl_3$).

Methyl (*R*)-5-hydroxyocta-2,7-diynoate (11). PTSA monohydrate (13.31 g, 70.0 mmol, 6 equiv.) was added to a solution of diyne **10** (2.78 g, 11.7 mmol, 1 equiv.) in MeOH (20 mL). Then, the mixture was warmed up to 60 °C and the reaction was stirred 65 h at this temperature. The crude was concentrated under *vacuum* and then was dissolved in EtOAc. The reaction was treated by a saturated aqueous Na_2CO_3 solution. Then, the organic layer was separated and the aqueous phase was extracted three times by EtOAc. Combined organic layers were washed with brine, dried with $MgSO_4$, filtered and concentrated under *vacuum.* The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 7:3) to give the deprotected product **11** as a pale yellow colorless oil (1.56 g, 9.4 mmol, 80 %).

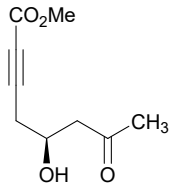


11

^{1}H NMR (500.1 MHz, $CDCl_3$) δ = 4.02 (quint, *J* = 5.8 Hz, 1H), 3.73 (s, 3H), 2.69 (dd, *J* = 17.2, 5.8 Hz, 1H), 2.65 (dd, *J* = 17.2, 5.8 Hz, 1H), 2.55 (ddd, *J* = 16.8, 5.8, 2.6 Hz, 1H), 2.51 (ddd, *J* = 16.8, 5.8, 2.6 Hz, 1H), 2.35 (brs, 1H), 2.10 (t, *J* = 2.6 Hz, 1H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 153.9 (C_q), 85.1 (C_q), 79.4 (C_q), 75.0 (C_q), 71.8 (CH), 67.8 (CH), 52.8 (CH_3), 26.4 (CH_2), 26.2 (CH_2). **HRMS (ESI)** *m/z*: calc for $C_9H_{11}O_3$ $[M+H]^+$ 16.0708, found 167.0701. **IR (neat) ν_{max}** = 3423, 3292, 2956, 2923, 2853, 2239, 1708, 1436, 1252, 1071 cm^{-1}. $[\alpha]_D^{20}$ = - 4.3 (*c* = 1, $CHCl_3$).

Methyl (*S*)-5-hydroxy-7-oxo-oct-2-ynoate (12).

Starting from the protected alkyne 10. A few drops of H_2SO_4 (95 % weight) were added to a solution of $HgSO_4$ (27.7 mg, 0.93 mmol, 3 mol%) in a mixture of THF/H_2O (28 mL, 5:2) at 0 °C. Then, a solution of the diyne **10** (371 mg, 2.20 mmol) in THF (20 mL) was added at the same temperature. The mixture was warmed up to room temperature and stirred for 24 h. The reaction was treated by a saturated aqueous $NaHCO_3$ solution. Then, the organic layer was separated and the aqueous phase was extracted twice by Et_2O. Combined organic layers were washed with brine, dried with $MgSO_4$, filtered and concentrated under *vacuum.* The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 4:6) to give the desired hydration product **12** as a pale yellow colorless oil (267.3 mg, 1.5 mmol, 65 %).

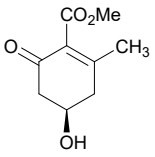


12

Starting from the deprotected alkyne 11. According to the same above procedure and starting from the diyne **11** (703 mg, 4.20 mmol), the desired hydration product **12** was obtained in 75% yield (587.1 mg, 3.2 mmol).

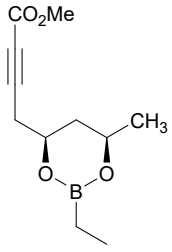
^{1}H NMR (500.1 MHz, $CDCl_3$) δ = 4,27-4.21 (m, 1H), 3.73 (s, 3H), 3.34 (d, *J* = 2.8 Hz, 1H), 2.78 (dd, *J* = 17.8, 3.2 Hz, 1H), 2.67 (dd, *J* = 17.8, 8.6 Hz, 1H), 2.67 (dd, *J* = 17.2, 5.6 Hz, 1H), 2.58 (dd, *J* = 17.2, 7.0 Hz, 1H), 2.18 (s, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 208.7 (C_q), 153.8 (C_q), 85.2 (C_q), 74.9 (C_q), 65.4 (CH), 52.7 (CH_3), 48.5 (CH_2), 30.7 (CH_3), 26.3 (CH). **HRMS (ESI)** *m/z*: calc for $C_9H_{13}O_4$ $[M+H]^+$ 185.0814, found 185.0810. **IR (neat) ν_{max}** = 3423, 2957, 2239, 1720, 1436, 1361, 1258, 1164, 1075, 946, 753 cm^{-1}. $[\alpha]_D^{20}$ = + 35.6 (*c* = 1, $CHCl_3$).

Methyl (*R*)-4-hydroxy-2-methyl-6-oxocyclohex-1-ene-1-carboxylate (12b). ^{1}H NMR (500.1 MHz, $CDCl_3$) δ = 4,27-4.23 (m, 1H), 3.78 (s, 3H), 3.22 (brs, 1H), 2.66 (dd, *J* = 16.0, 4.2 Hz, 1H), 2.65 (dd, *J* = 18.0, 4.4 Hz, 1H), 2.48 (dd, *J* = 16.0, 8.2 Hz, 1H), 2.46 (dd, *J* = 18.0, 6.8 Hz, 1H), 1.98 (s, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 194.0 (C_q), 167.1 (C_q), 157.9 (C_q), 132.7 (C_q), 65.4 (CH), 52.3 (CH_3), 45.7 (CH_2), 40.1 (CH_2), 22.3 (CH_3). **HRMS (ESI)** *m/z*: calc for $C_9H_{13}O_4$ $[M+H]^+$ 185.0814, found 185.0818. **IR (neat) ν_{max}** = 3430, 2955, 2902, 1727, 1666, 1632, 1436, 1381, 1318, 1241, 1185, 1154, 1078, 1019, 933 cm^{-1}.



12b

Methyl 4-((4*S*,6*R*)-2-ethyl-6-methyl-1,3,2-dioxaborinan-4-yl)but-2-ynoate (13). Diethylmethoxy-borane (2.4 mL, 1 *M* in THF, 2.4 mmol, 1.5 equiv.) then MeOH (1.5 mL) were added to a solution of the β-hydroxy-ketone **13** (300 mg, 1.6 mmol, 1 equiv.) in THF (7 mL) under an argon atmosphere and the mixture was stirred for 1 h at room temperature. Afterward, the solution was cooled to -78 °C and $NaBH_4$ (135.6 mg, 3.58 mmol, 2.2 equiv.) was added to the mixture. The solution was stirred for 24 h at -78 °C. Then, a saturated aqueous NH_4Cl solution was added and the solution was allowed to warm up to room temperature. The mixture was extracted three times by AcOEt. Combined organic layers were washed with brine, dried with $MgSO_4$, filtered and concentrated under *vacuum.* The crude mixture was purified by silica gel flash column chromatography

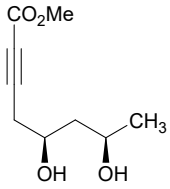


13

(eluent: Petroleum ether/EtOAc 8:2) to give the *cis*-*B*-ethyldioxaborinane **13** as a pale yellow colorless oil (309.7 mg, 1.4 mmol, 85 %).

^{1}H NMR (500.1 MHz, $CDCl_3$) δ = 4.17-4.07 (m, 2H), 3.77 (s, 3H), 2.69 (dd, *J* = 17.2, 5.0 Hz, 1H), 2.50 (dd, *J* = 17.2, 7.6 Hz, 1H), 2.10 (dt, *J* = 13.6, 2.4 Hz, 1H), 1.42 (dt, *J* = 13.6, 11.4 Hz, 1H), 1.26 (d, *J* = 6.4 Hz, 3H), 0.87 (t, *J* = 7.8 Hz, 3H), 0.67 (q, *J* = 7.8 Hz, 2H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 154.0 (C_q), 85.0 (C_q), 74.8 (C_q), 68.9 (CH), 67.4 (CH), 52.7 (CH_3), 39.6 (CH_2), 27.2 (CH_2), 23.1 (CH_3), 7.7 (CH_2), 1.1 (CH_3). **HRMS (ESI)** *m/z*: calc for $C_9H_{15}O_4$ [M-B(Et)+3H]$^+$ 187.0970, found 187.0979. **IR (neat) ν_{max}** = 3377, 2968, 2241, 1713, 1437, 1379, 1263, 1076, 941 cm^{-1}. $[\alpha]_D^{22}$ + 19.1 (*c* = 1, $CHCl_3$).

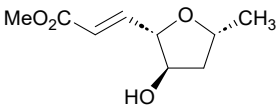
Methyl (5*S*,7*R*)-5,7-dihydroxyoct-2-ynoate (14). A solution of *cis*-*B*-ethyldioxaborinane **13** (309.7 mg, 1.4 mmol) in MeOH (50 mL) was rotary evaporated at 50 °C for 5 times. This gave the crude product as an oil (236.1 mg, 1.3 mmol, 92 %). The crude 1,3-diol **14** was used without further purification.



14

^{1}H NMR (500.1 MHz, $CDCl_3$) δ = 4.11-4.06 (m, 2H), 3.76 (s, 3H), 2.70 (brs, 1H), 2.56 (dd, *J* = 17.2, 6.0 Hz, 1H), 2.50 (dd, *J* = 17.2, 6.2 Hz, 1H), 1.74 (dt, *J* = 14.4, 2.4 Hz, 1H), 1.61 (dt, *J* = 14.4, 10.0 Hz, 1H), 1.24 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 154.1 (C_q), 85.9 (C_q), 74.7 (C_q), 70.3 (CH), 68.8 (CH), 52.7 (CH_3), 43.6 (CH_2), 27.9 (CH_2), 24.1 (CH_3). **HRMS (ESI)** *m/z*: calc for $C_{11}H_{17}NO_4Na$ [M+MeCN+Na]$^+$ 250.1055, found 250.1058. **IR (neat) ν_{max}** = 3385, 2956, 2920, 2853, 2238, 1710, 1436, 1251, 1130, 1073 cm^{-1}. $[\alpha]_D^{20}$ = + 23.5 (*c* = 1, $CHCl_3$).

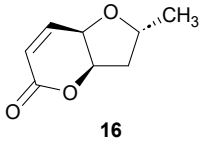
Methyl (*E*)-3-((2*S*,3*R*,5*R*)-3-hydroxy-5-methyltetrahydrofuran-2-yl)acrylate (15). A solution of **14** (54.4 mg, 0.29 mmol) in degassed THF (0.7 mL) was added to a solution of 1,3-bis(diphenylphosphino)propane (6.0 mg, 14.6 µmol, 0.05 eq) in degassed THF (0.7 mL) under argon atmosphere. Then, acetic acid (3.5 mg, 58.4 µmol, 0.2 eq) was added to the solution. The mixture was warm up to 90 °C and allowed to stir during 22 h. The crude mixture was concentrated under *vacuum* and was purified by flash chromatography (eluent: cyclohexane/MTBE 3:7) to give the desired product **15** as an oil (7.8 mg, 41.9 µmol, 14 %) and a mixture of compounds **15** and **16** (6.4 mg).



15

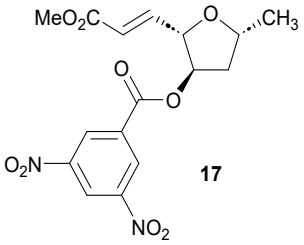
^{1}H NMR (500.1 MHz, $CDCl_3$) δ = 6.97 (dd, *J* = 15.6, 4.8 Hz, 1H), 6.11 (dd, *J* = 15.6, 1.8 Hz, 1H), 4.40-4.33 (m, 2H), 4.24 (m, 1H), 3.74 (s, 3H), 1.97 (ddd, *J* = 13.2, 5.4, 2.0 Hz, 1H), 1.91 (d, *J* = 2.8 Hz, 1H), 1.74 (ddd, *J* = 13.2, 10.0, 6.0 Hz, 1H), 1.32 (d, *J* = 6.0 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 166.9 (C_q), 146.5 (CH), 121.0 (CH), 85.7 (CH), 77.0 (CH), 75.1 (CH), 51.7 (CH_3), 42.1 (CH_2), 20.8 (CH_3). **HRMS (ESI)** *m/z*: calc for $C_9H_{15}O_4$ [M+H]$^+$ 187.0970, found 187.0972. **IR (neat) ν_{max}** = 3434, 2972, 2931, 1724, 1661, 1438, 1383, 1300, 1278, 1195, 1171, 1104, 1042 cm^{-1}. $[\alpha]_D^{20}$ = + 19.4 ° (*c* = 1, $CHCl_3$).

(2*R*,3a*R*,7a*R*)-2-methyl-2,3,3a,7a-tetrahydro-5*H*-furo[3,2-b]pyran-5-one (16). **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ = 6.82 (dd, *J* = 10.0, 5.0 Hz, 1H), 6.11 (d, *J* = 10.2, 1H), 5.12 (td, *J* = 5.0, 1.0 Hz, 1H), 4.48 (t, *J* = 5.0 Hz, 1H), 4.40-4.33 (m, 1H), 2.44 (ddd, *J* = 13.8, 5.4, 1.0 Hz, 1H), 1.90 (ddd, *J* = 13.8, 9.8, 5.4 Hz, 1H), 1.31 (d, *J* = 6.0 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 162.0 (C_q), 141.1 (CH), 122.6 (CH), 81.2 (CH), 74.8 (CH), 68.9 (CH), 42.1 (CH_2), 20.6 (CH_3).



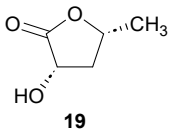
16

(2*S*,3*R*,5*R*)-2-((*E*)-3-Methoxy-3-oxoprop-1-en-1-yl)-5-methyltetrahydrofuran-3-yl 3,5-dinitrobenzoate (17). To a suspension of 3,5-dinitrobenzoic acid (34.2 mg, 0.16 mmol, 1.5 equiv.) in dichloromethane (1 mL) was added DMAP (39.4 mg, 0.32 mmol, 3.0 equiv.) in one portion at 0 °C. The reaction mixture was stirred for five minutes at 0°C then *N*,*N*'-dicyclohexylcarbodiimide (33.2 mg, 0.16 mmol, 1.5 equiv.) was added at 0 °C and the resultant suspension was stirred for 15 min at 0 °C. A solution of the alcohol **15** (20.0 mg, 0.11 mmol) in dichloromethane (1 mL) was added at 0 °C. The cooling bath was removed and the reaction mixture was stirred at room temperature for 40 h. The suspension was filtrated through a pad of Celite® and the filter cake was washed with dichloromethane. The combined organic extracts were dried over $MgSO_4$, concentrated under reduced pressure and purified by silica gel column chromatography (Petroleum ether/EtOAc 4:6) to give benzoate ester **17** (2.7 mg, 7%) as a white solid. **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ = 9.26 (t, *J* = 2.0 Hz, 1H), 9.15 (d, *J* = 2.0 Hz, 2H), 7.10 (dd, *J* = 15.6, 4.4 Hz, 1H), 6.22 (dd, *J* = 15.6, 2.0 Hz, 1H), 5.38 (m, 1H), 4.68 (dt, *J* = 4.4, 2.2 Hz, 1H), 4.46 (m, 1H), 3.78 (s, 3H), 2.28 (ddd, *J* = 14.2, 4.4, 0.6 Hz, 1H), 1.87 (ddd, *J* = 14.2, 10.6, 6.0 Hz, 1H), 1.44 (d, *J* = 6.0 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ = 166.5 (C_q), 166.2 (C_q), 148.8 (C_q), 144.7 (CH), 133.4 (C_q), 129.5 (CH), 122.8 (CH), 122.2 (CH), 83.1 (CH), 81.7 (CH), 75.8 (CH), 51.8 (CH_3), 38.9 (CH_2), 20.3 (CH_3). **HRMS (ESI)** *m/z*: calc for $C_{18}H_{20}N_3O_9$ [M+MeCN+H]$^+$ 422.1200, found 422.1216. **IR (neat) ν_{max}** = 3102, 2975, 2932, 1727, 1630, 1545, 1461, 1437, 1346, 1276, 1167, 1111, 1077 cm^{-1}. $[\alpha]_D^{20}$ = + 12.6° (*c* = 1, $CHCl_3$).



17

III.3 - Enantioselective reduction of α-hydroxy-butenolide (±)-18 using Baker's yeast



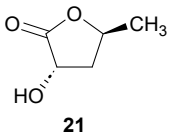
19

(3*S*,5*R*)-3-Hydroxy-5-methyldihydrofuran-2(3*H*)-one (19). To a solution of α-hydroxy-butenolide (±)-**18** (1.0 g, 8.77 mmol) in water (1 L) was added Baker's yeast (*Saccharomyces cerevisiae*, 20 g) and placed on orbital shaker (150 rpm) at 30 °C for 24 h. After this period, the reaction mixture was centrifugated and the supernatant was concentrated to reduce the volume to 200 mL and extracted with ethyl acetate (3x150 mL). The crude mixture was purified by silica gel flash column chromatography (eluent: petroleum ether/EtOAc 1:1) to give the reduced compounds *cis*-**19** as a pale yellow colorless oil (200 mg, 20%) and *trans*-**21** as a pale yellow colorless oil (200 mg, 20%).

The spectra data of **(3*S*,5*R*)-19** are consistent to the previous described compound in Literature.[1]

^{1}H NMR (500.1 MHz, $CDCl_3$) δ 4.56-4.47 (m, 2H), 3.11 (s, 1H), 2.71 (ddd, *J* = 12.8, 8.3, 5.0 Hz, 1H), 1.89-1.83 (m, 1H), 1.46 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$) δ 177.8 (CO), 73.8 (CH), 69.1 (CH), 38.9 (CH_2), 21.0 (CH_3).
$[\alpha]_D^{20}$ = -1.0 (*c* = 0.5, CH_3OH).

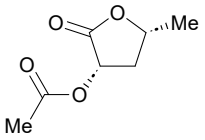
(3*S*,5*S*)-3-Hydroxy-5-methyldihydrofuran-2(3H)-one (21).



21

The spectra data of **(3*S*,5*S*)-21** are consistent to the previous described compound in Literature.[1a,1b]

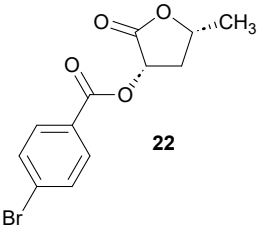
^{1}H NMR (500.1 MHz, $CDCl_3$) δ 4.83-4.77 (m, 1H), 4.55 (t, *J* = 7.8 Hz, 1H), 3.24 (s, 1H), 2.38 (dt, *J* = 13.2, 7.6 Hz, 1H), 2.22 (ddd, *J* = 13.2, 8.1, 4.1 Hz, 1H), 1.40 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 177.6 (CO), 75.2 (CH), 67.7 (CH), 37.2 (CH_2), 21.5 (CH_3).
$[\alpha]_D^{20}$ = -60.0 (*c* = 0.5, CH_3OH).



19b

(3*S*,5*R*)-5-Methyl-2-oxotetrahydrofuran-3-yl acetate (19b). To a solution of DMAP (3.0 mg, 0.03 mmol, 0.2 equiv.) in DCM (2 mL) at 0 °C was added triethylamine (54 µL, 0.39 mmol, 3.0 equiv.), *cis*-**19** compound (15 mg, 0.13 mmol) in DCM (1 mL). Then Ac_2O (19.0 µL, 0.20 mmol, 1.5 equiv.) was added dropwise and the mixture was stirred for 1h at room temperature. Upon completion, solvents were removed under reduced pressure and the crude product was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 7:3) to give the acetate derivative **19b** as a pale yellow colorless oil (16 mg, 80 %).

The spectra data of **(3*S*,5*R*)-19b** are consistent to the previous described compound in Literature.[1c,1d] **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 5.49 (dd, *J* = 10.8, 8.7 Hz, 1H), 4.59-4.52 (m, 1H), 2.81 (ddd, *J* = 13.2, 8.6, 5.4 Hz, 1H), 2.16 (s, 3H), 1.91-1.84 (m, 1H), 1.48 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 172.5 (CO), 169.9 (CO), 73.6 (CH), 69.1 (CH), 36.9 (CH_2), 21.1 (CH_3), 20.7 (CH_3). $[\alpha]_D^{20}$ = + 12.4 (*c* = 1, $CHCl_3$); Literature[1c,1d] $[\alpha]_D^{20}$ = -18.4 (*c* = 0.9, $CHCl_3$) for **(3*R*,5*S*)-19b**.



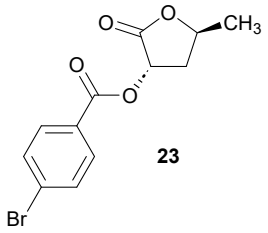
22

(3*S*,5*R*)-5-Methyl-2-oxotetrahydrofuran-3-yl 4-bromobenzoate (22). To a suspension of *p*-bromobenzoic acid (26.0 mg, 0.13 mmol, 1.5 equiv.) in DCM (3 mL) was added DMAP (32.0 mg, 0.26 mmol, 3.0 equiv.) in one portion at 0 °C. The reaction mixture was stirred for five minutes at 0 °C and *N*,*N*'-dicyclohexylcarbodiimide (30.0 mg, 0.14 mmol, 1.5 equiv.) was added at 0 °C and the resultant suspension was stirred for 15 min at 0 °C. Then, a solution of *cis*-**19** (10.0 mg, 0.09 mmol) in DCM (1 mL) was added at 0°C. The cooling bath was removed and the reaction mixture was stirred at room temperature overnight. The suspension was filtrated through a pad of Celite® and the filter cake was washed with DCM. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 7:3) to give the benzoate ester **22** as an off-white solid (9.0 mg, 35%).

The NMR spectra data of **(3*S*,5*R*)-22** are consistent to the racemic sample (±)-**22** (see next page) prepared for the HPLC analysis. **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.95-7.92 (m, 2H), 7.62-7.59 (m, 2H), 5.71 (dd, *J* = 10.8, 8.5 Hz, 1H), 4.67-4.60 (m, 1H), 2.93 (ddd, *J* = 12.7, 8.5, 5.3 Hz, 1H), 2.01 (dt, *J* = 12.7, 10.6 Hz, 1H), 1.53 (d, *J* = 6.2 Hz, 3H). **HRMS (ESI)**: *m/z* calcd. for $C_{12}H_{12}O_4Br$ $[M+H]^+$ 298.9919, found 298.9914.

Enantiomeric excess of compound **22** has been measured to 91% by HPLC analysis (Waters) equipped with a Chiralpak® ID column (5 µm, 10x250 mm) with *n*-heptane/*i*-propanol 85:15 as solvent at a flow rate of 1 mL.min^{-1}, a temperature of 25°C, and a detection at 250 nm. $[\alpha]_D^{20}$ = -27.0 (*c* = 0.1, CH_3OH).

(+)-(3*S*,5*S*)-5-Methyl-2-oxotetrahydrofuran-3-yl 4-bromobenzoate (23). To a suspension of *p*-bromobenzoic acid (26.0 mg, 0.13 mmol, 1.5 equiv.) in DCM (3 mL) was added DMAP (32.0 mg, 0.26 mmol, 3.0 equiv.) in one portion at 0 °C. The reaction mixture was stirred for five minutes at 0 °C then *N*,*N*'-dicyclohexylcarbodiimide (30.0 mg, 0.14 mmol, 1.5 equiv.) was added at 0 °C and the resultant suspension was stirred for 15 min at 0 °C. A solution of *trans*-**21** (10.0 mg, 0.09 mmol) in DCM (1 mL) was added at 0°C. The cooling bath was removed and the reaction mixture was stirred at room temperature overnight. The suspension was filtrated through a pad of Celite® and the filter cake was washed with dichloromethane. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 7:3) to give the benzoate ester **23** as an off-white solid (13.0 mg, 50%).

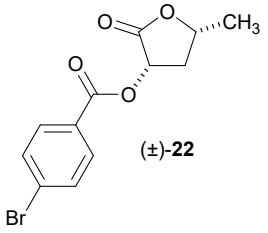


23

The NMR spectra data of **(3*S*,5*S*)-23** are consistent to the racemic sample (±)-**23** (see next page) prepared for the HPLC analysis. **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 7.93-7.90 (m, 2H), 7.61-7.59 (m, 2H), 5.65 (dd, *J* = 8.3, 7.4 Hz, 1H), 4.92-4.86 (m, 1H), 2.54-2.48 (m, 1H), 2.43 (ddd, *J* = 12.9, 8.4, 4.4 Hz, 1H), 1.49 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 172.4 (CO), 164.9 (CO), 132.1 (CH), 132.1 (CH), 131.6 (CH), 131.6 (CH), 129.2 (CH), 127.8 (CH), 75.0 (CH), 69.0 (CH), 35.7 (CH_2), 21.7 (CH_3). **IR (neat) ν_{max}:** 2981, 2932, 1785, 1723, 1589, 1263, 1172, 1103, 1011, 754 cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{12}H_{12}O_4Br$ $[M+H]^+$ 298.9919, found 298.9918.

Enantiomeric excess of compound **23** has been measured to 99% by HPLC analysis (Waters) equipped with a Chiralpak® ID column (5 µm, 10x250 mm) with *n*-heptane/*i*-propanol 85:15 as solvent at a flow rate of 1 mL.min^{-1}, a temperature of 25°C, and a detection at 250 nm. $[\alpha]_D^{20}$ = +14.0 (*c* = 0.1, CH_3OH).

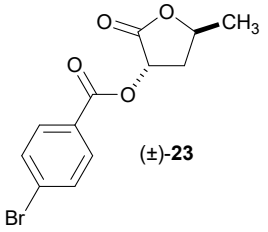
***cis*-5-Methyl-2-oxotetrahydrofuran-3-yl 4-bromobenzoate (±)-22.** To a suspension of *p*-bromobenzoic acid (26.0 mg, 0.13 mmol, 1.5 equiv.) in DCM (3 mL) was added DMAP (32.0 mg, 0.26 mmol, 3.0 equiv.) in one portion at 0 °C. The reaction mixture was stirred for five minutes at 0°C then *N*,*N*'-dicyclohexylcarbodiimide (30.0 mg, 0.14 mmol, 1.5 equiv.) was added at 0 °C and the resultant suspension was stirred for 15 min at 0 °C. A solution of alcohol (±)-**19** (10.0 mg, 0.09 mmol) in DCM (1 mL) was added at 0 °C. The cooling bath was removed and the reaction mixture was stirred at room temperature overnight. The suspension was filtrated through a pad of Celite® and the filter cake was washed with DCM. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 7:3) to give the benzoate ester (±)-**22** as an off-white solid (32 mg, 63%).



(±)-**22**

^{1}H NMR (500.1 MHz, $CDCl_3$) δ 7.95-7.91 (m, 2H), 7.61-7.58 (m, 2H), 5.71 (dd, *J* = 10.8, 8.5 Hz, 1H), 4.67-4.60 (m, 1H), 2.92 (ddd, *J* = 12.8, 8.5, 5.3 Hz, 1H), 2.00 (dt, *J* = 12.6, 10.5 Hz, 1H), 1.52 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 172.2 (CO), 164.9 (CO), 132.1 (CH), 132.1 (CH), 131.6 (CH), 131.6 (CH), 129.2 (CH), 127.8 (CH), 73.7 (CH), 69.8 (CH), 37.0 (CH_2), 21.2 (CH_3). **IR (neat) ν_{max}:** 2979, 2935, 1785, 1727, 1589, 1274, 1200, 1122, 1012, 755 cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{12}H_{12}O_4Br$ $[M+H]^+$ 298.9919, found 298.9919.

***trans*-5-Methyl-2-oxotetrahydrofuran-3-yl 4-bromobenzoate (±)-23.** To a solution of *p*-bromobenzoic acid (45.0 mg, 0.22 mmol, 1.3 equiv.), triphenylphosphine (58.0 mg, 0.22 mmol, 1.3 equiv.) and (±)-**19** (20.0 mg, 0.17 mmol) in THF (5 mL) at 0 °C was slowly added diethyl azodicarboxylate (40% in toluene, 105 µL, 0.22 mmol, 1.3 equiv.). The cooling bath was removed and the reaction mixture was stirred at room temperature overnight. The diethyl ether (20 mL) was added and the mixture was washed with a saturated aqueous $NaHCO_3$ solution (2x10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 7:3) to give the benzoate ester (±)-**23** as an off-white solid (10 mg, 20%).

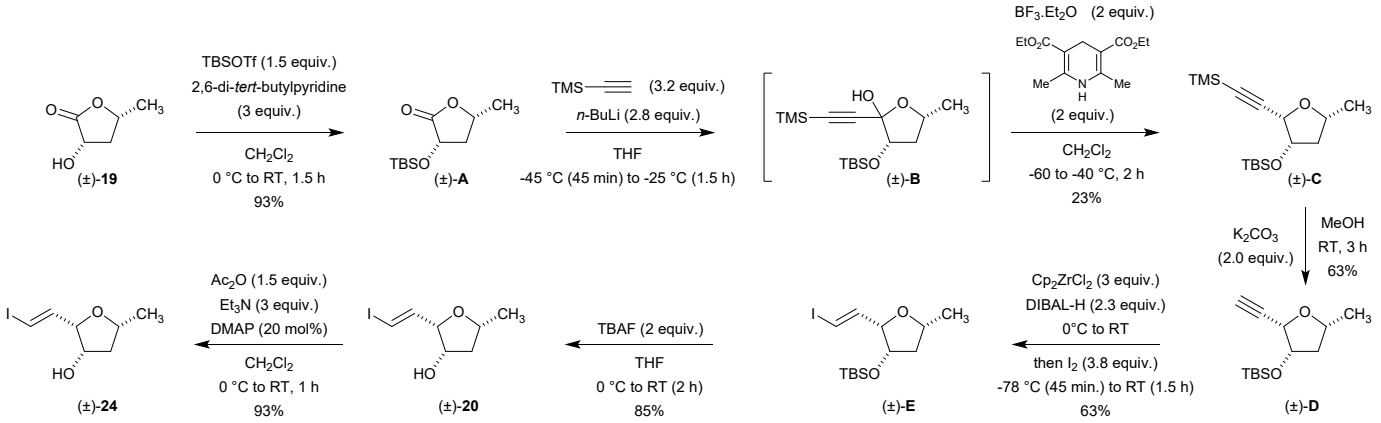


(±)-**23**

^{1}H NMR (500.1 MHz, $CDCl_3$) δ 7.92-7.90 (m, 2H), 7.61-7.59 (m, 2H), 5.66-5.63 (m, 1H), 4.92-4.86 (m, 1H), 2.54-2.48 (m, 1H), 2.43 (ddd, *J* = 12.7, 8.4, 4.3 Hz, 1H), 1.48 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 172.4 (CO), 164.9 (CO), 132.1 (CH), 132.1

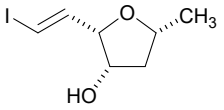
(CH), 131.6 (CH), 131.6 (CH), 129.2 (CH), 127.8 (CH), 75.0 (CH), 69.0 (CH), 35.7 (CH_2), 21.7 (CH_3). **IR (neat) ν_{max}:** 2981, 2932, 1785, 1723, 1589, 1263, 1172, 1103, 1011, 754 cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{12}H_{12}O_4Br$ $[M+H]^+$ 298.9919, found 298.9916.

III.4 - Reaction scheme for synthesis of (±)-20 and (±)-24 from (±)-19



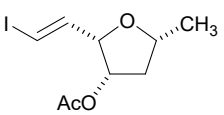
The experimental procedures and characterization of racemic compounds (±)-**A**-**E** are described in our previous synthesis of (±)-trienylfuranol A.[2]

The experimental procedures and characterization of new compounds (±)-**20** and (±)-**24** are given below.


(±)-**20**

(2*S,3*S**,5*R**)-2-((*E*)-2-Iodovinyl)-5-methyltetrahydrofuran-3-ol (±)-20.** To a solution of OTBS-protected of (±)-**20** (250 mg, 0.68 mmol) in THF (12 mL), prepared for the racemic synthesis of trienylfuranol A in our previous study,[2] was added TBAF (1*M* in THF, 1.37 mL, 1.37 mmol, 2.0 equiv.) at 0°C and stirred for 2 h at room temperature. Upon completion, the mixture was quenched with a saturated aqueous NH_4Cl solution (3 mL) and extracted with diethyl ether (3x20 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 6:4) to give the deprotected alcohol (±)-**20** as a pale yellow colorless oil (146 mg, 85%).

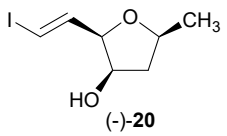
^{1}H NMR (500.1 MHz, $CDCl_3$) δ 6.68 (dd, *J* = 14.6, 6.0 Hz, 1H), 6.53 (dd, *J* = 14.6, 1.1 Hz, 1H), 4.32-4.28 (m, 1H), 4.14-4.11 (m, 1H), 4.02 (qdd, *J* = 6.5, 6.5, 6.5 Hz, 1H), 2.40 (dt, *J* = 13.6, 6.4 Hz, 1H), 1.58-1.55 (m, 1H), 1.34 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 141.5 (CH), 85.0 (CH), 80.3 (CH), 74.1 (CH), 73.8 (CH), 42.7 (CH_2), 22.1 (CH_3). **HRMS (ESI)**: *m/z* calcd. for $C_7H_{12}O_2I$ $[M+H]^+$ 254.9882, found 254.9887. **IR** (**neat**) **ν_{max}:** 3409, 2973, 2928, 1608, 1445, 1387, 1331, 1267, 1179, 1115, 1067, 1027, 947 cm^{-1}.

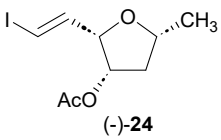

(±)-**24**

(2*S,3*S**,5*R**)-2-((*E*)-2-Iodovinyl)-5-methyltetrahydrofuran-3-yl acetate (±)-24.** To a solution of DMAP (12.0 mg, 0.10 mmol, 0.2 equiv.) in DCM (7 mL) at 0°C was added triethylamine (210 µL, 1.50 mmol, 3.0 equiv.), alcohol (±)-**20** (128 mg, 0.50 mmol) in DCM (3 mL). Then Ac_2O (71.0 µL, 0.75 mmol, 1.5 equiv.) was added dropwise and the mixture was stirred for 1 h at room temperature. Upon completion, solvents were removed under reduced pressure and the crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 8:2) to give the acetylated alcohol (±)-**24** as a pale yellow colorless oil (138 mg, 93%).

^{1}H NMR (500.1 MHz, $CDCl_3$) δ 6.55 (dd, *J* = 14.5, 6.0 Hz, 1H), 6.47 (dd, *J* = 14.5, 0.6 Hz, 1H), 5.31-5.28 (m, 1H), 4.25 (t, *J* = 5.4 Hz, 1H), 4.02 (qdd, *J* = 6.3, 6.3, 6.3 Hz, 1H), 2.46 (dt, *J* = 13.7, 6.8 Hz, 1H), 2.06 (s, 3H), 1.61 (ddd, 13.6, 7.7, 3.9 Hz, 1Hz), 1.33 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 170.5 (CO), 140.8 (CH), 83.1 (CH), 80.1 (CH), 75.3 (CH), 74.0 (CH), 39.9 (CH_2), 21.4 (CH_3), 21.1 (CH_3). **HRMS (ESI)**: *m/z* calcd. for $C_9H_{14}O_3I$ $[M+H]^+$ 296.9988, found 297.0004. **IR** (**neat**) **ν_{max}:** 2976, 2931, 2866, 1737, 1607, 1439, 1374, 1236, 1179, 1104, 1035, 947 cm^{-1}.

III.5 - Enzymatic kinetic resolution of acetate ester (±)-24


(-)-**20**
31% yield, 99% ee

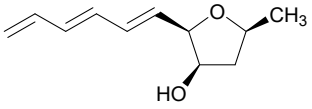

(-)-**24**
35% yield, 99% ee

Enzymatic kinetic resolution of acetate ester (±)-24 for the production of (-)-20 and (-)-24. To a solution of acetate (±)-**24** (130 mg, 0.44 mmol) in 20 mM, pH 7.4 phosphate buffer (130 mL) was added Amano Lipase PS from *Burkholderia Cepacia* (500 mg) and placed on orbital shaker (130 rpm) at 28°C for 6 h. Reaction was monitored by ^{1}H NMR to have 50:50 acetate/alcohol ratio. After this period, the reaction mixture was extracted with ethyl acetate (3x100 mL) and the crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 8:3) to give alcohol (-)-**20** (35 mg, 31%) and acetate (-)-**24** (45 mg, 35%).

Enantiomeric excess of alcohol **20** has been measured to 99% by HPLC analysis (Waters) equipped with a Chiralpak® ID column (5 µm, 10x250 mm) with *n*-heptane/*i*-propanol 80:20 as solvent at a flow rate of 1 mL.min^{-1}, a temperature of 25°C, and a detection at 230 nm. $[\alpha]_D^{20}$ = -19.0 (*c* = 0.1, CH_3OH).

Enantiomeric excess of acetate **24** has been measured to 99% by HPLC analysis (Waters) equipped with a Chiralpak® ID column (5 µm, 10x250 mm) with *n*-heptane/*i*-propanol 95:5 as solvent at a flow rate of 1 mL.min^{-1}, a temperature of 25°C, and a detection at 230 nm. $[\alpha]_D^{20}$ = -40.0 (*c* = 0.1, CH_3OH).

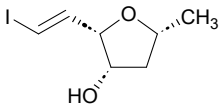
III.6 - Synthesis of both enantiomers of trienylfuranol A (-)-4 and (+)-4.


(-)-**4**

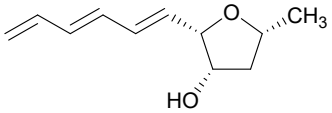
Trienylfuranol A (-)-4 (unnatural enantiomer). To a solution of vinyl iodide (-)-**20** (65 mg, 0.25 mmol) and *(E)*-buta-1,3-dien-1-yltributylstannane (150 mg, 0.44 mmol, 1.8 equiv.) in degassed DMF (8 mL) at room temperature was added $PdCl_2(CH_3CN)_2$ (20.0 mg, 0.08 mmol, 30 mol%) and stirred for 3h. Upon completion, the mixture was quenched with an aqueous KF solution (1*M*, 8 mL). The precipitate was removed by filtration and the mixture was diluted in diethyl ether (50 mL), washed with water (5x3 mL) and the combined organic extracts were concentrated under reduced pressure. The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 5:5) to give the unnatural enantiomer of trienylfuranol A (-)-**4** as a pale yellow colorless oil (26 mg, 56%).

^{1}H NMR (500.1 MHz, C_6D_6) δ 6.46-6.41 (m, 1H), 6.30-6.23 (m, 1H), 6.12-6.09 (m, 2H), 5.72 (dd, J = 15.3, 6.0 Hz, 1H), 5.09 (d, J = 16.7, 1H), 4.98 (d, J = 10.1, 1H), 3.95-3.93 (m, 1H), 3.86-3.83 (m, 1H), 3.80-3.74 (m, 1H), 1.95-1.89 (m, 1H), 1.41 (ddd, J = 13.3, 6.7, 2.7 Hz, 1H), 1.28 (d, J = 6.2 Hz, 3H). **^{13}C NMR** (125.8 MHz, C_6D_6) δ 137.3 (CH), 133.9 (CH), 133.1 (CH), 133.0 (CH), 130.3 (CH), 117.5 (CH), 83.8 (CH), 74.4 (CH), 74.0 (CH), 43.0 (CH_2), 22.3 (CH_3). **HRMS (ESI)**: *m/z* calcd. for $C_{11}H_{17}O_2$ $[M+H]^+$ 181.1229, found 181.1228.

Enantiomeric excess of trienylfuranol A (-)-**4** has been measured to 99% by supercritical fluid chromatography (Thar SFC, Waters) equipped with a Chiralpak® IA column (5 µm, 4.6x250 mm) with 5% *i*-propanol in CO_2 as solvent at a flow rate of 4 mL.min^{-1}, a pressure of 100 bar, and a detection at UV max absorbance. $[\alpha]_D^{20}$ = -8.0 (*c* = 0.1, CH_3CN).


(+)-**20**

(2*S*,3*S*,5*R*)-2-((*E*)-2-iodovinyl)-5-methyltetrahydrofuran-3-ol (+)-20. To a solution of acetate (-)-**24** (78 mg, 0.26 mmol) in anhydrous methanol (3 mL) was added dry K_2CO_3 (110 mg, 0.79 mmol, 3.0 equiv.) and stirred at room temperature for 3h. Upon completion, the mixture was quenched with a saturated aqueous NH_4Cl solution (2 mL), extracted with diethyl ether (3x20 mL) and the combined organic extracts were concentrated under reduced pressure. The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 6:4) to give the deacetylated alcohol (+)-**20** as a pale yellow colorless oil (50 mg, 75%). $[\alpha]_D^{20}$ = +24.0 (*c* = 0.1, CH_3OH).


(+)-**4**

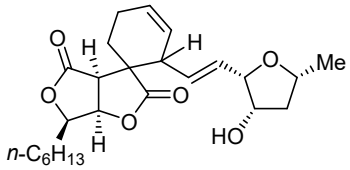
Trienylfuranol A (+)-4 (natural enantiomer). To a solution of vinyl iodide (+)-**20** (50 mg, 0.20 mmol) and *(E)*-buta-1,3-dien-1-yltributylstannane (115 mg, 0.34 mmol, 1.7 equiv.) in degassed DMF (6 mL) at room temperature was added $PdCl_2(CH_3CN)_2$ (15.0 mg, 0.06 mmol, 0.3 equiv.) and stirred for 3h. Upon completion, the mixture was quenched with an aqueous KF solution (1*M*, 5 mL). The precipitate was removed by filtration and the mixture was diluted in diethyl ether (50 mL), washed with water (5x3 mL) and the combined organic extracts were concentrated under reduced

pressure. The crude mixture was purified by silica gel flash column chromatography (eluent: Petroleum ether/EtOAc 5:5) to give the natural enantiomer of trienylfuranol A (+)-**4** as a pale yellow colorless oil (24 mg, 68%).

Enantiomeric excess of trienylfuranol A (+)-**4** has been measured to 99% by supercritical fluid chromatography (Thar SFC, Waters) equipped with a Chiralpak® IA column (5 µm, 4.6x250 mm) with 5% *i*-propanol in CO_2 as solvent at a flow rate of 4 mL.min^{-1}, a pressure of 100 bar, and a detection at UV max absorbance. $[\alpha]_D^{20}$ = +9.0 (*c* = 0.1, CH_3CN).

III.7 - Diels-Alder reaction between (-)-sporothriolide 3 and (+)-trienylfuranol A 4

Sporochartines A-D. Sporothriolide (30 mg, 0.13 mmol) and (+)-trienylfuranol A (26 mg, 0.14 mmol, 1.1 equiv.) were suspended in water/THF 4:1 mixture (3 mL) and warmed at 100 °C, allowing the THF to evaporate then stirred for 3 hours under reflux. After this period, the reaction mixture was concentrated and purified by preparative reversed-phase HPLC (Sunfire C18 5 µm, 10 × 250 mm) eluting with a gradient of 50 to 100% acetonitrile in 40 min at a flow rate of 4 mL.min^{-1} and a detection at 215 nm.



Sporochartine B (11 mg, 21%) was isolated as the major product as a white solid. **Sporochartines A** and **C** (8 mg, 15%) were isolated in 1:1 mixture as a white solid. **Sporochartine D** (1.5 mg, 3%) was isolated as the minor product as a white solid.

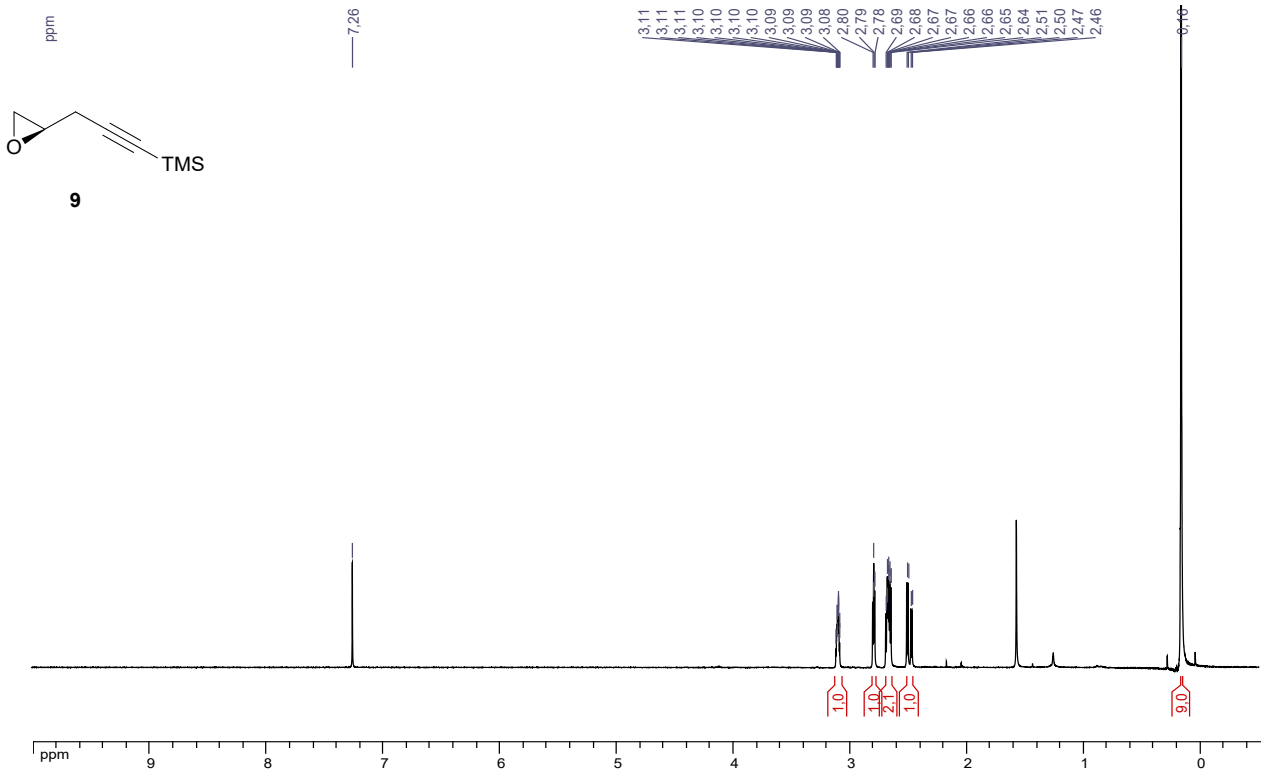
The spectra data of **sporochartines A-D** are consistent to the natural compounds described in Literature: C. Leman-Loubière, G. Le Goff, C. Debitus and J. Ouazzani, Sporochartines A-E, A New Family of Natural Products from the Marine Fungus Hypoxylon monticulosum Isolated from a Sphaerocladina Sponge, *Front. Mar. Sci.*, 2017, **4**, Article 399.[3]

Sporochartine B. ^{1}H NMR (500.1 MHz, $CDCl_3$) δ 5.96-5.92 (m, 1H), 5.83 (dd, J= 15.5, 9.0 Hz, 1H), 5.74 (dd, J= 15.5, 3.9 Hz, 1H), 5.54 (dd, J= 10.0, 1.5 Hz, 1H), 5.14-5.12 (m, 1H), 4.41-4.37 (m, 1H), 4.29-4.26 (m, 1H), 4.20-4.17 (m, 1H), 4.09-4.02 (m, 1H), 3.30 (d, J=5.8 Hz, 1H), 3.25-3.21 (m, 1H), 2.83-2.74 (m, 1H), 2.42-2.36 (m, 1H), 2.29-2.21 (m, 1H), 2.15-2.08 (m, 1H), 2.05-2.00 (m, 1H), 1.88-1.81 (m, 1H), 1.79-1.72 (m, 1H), 1.58 (ddd, J= 13.7, 6.0, 1.5 Hz, 1H), 1.47-1.41 (m, 2H), 1.37-1.31 (m, 2H), 1.32 (d, J=6.1 Hz, 3H), 1.31-1.24 (m, 4H), 0.88 (t, J=6.7 Hz, 3H). **^{13}C NMR** (125.8 MHz, $CDCl_3$) δ 178.7 (CO), 173.0 (CO), 130.9 (CH), 130.1 (CH), 129.9 (CH), 124.7 (CH), 82.8 (CH), 81.1 (CH), 78.7 (CH), 74.1 (CH), 73.8 (CH), 50.8 (C), 47.2 (CH), 46.9 (CH), 42.4 (CH_2), 31.7 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 26.9 (CH_2), 25.2 (CH_2), 22.8 (CH_2), 22.6 (CH_2), 22.4 (CH_3), 14.1 (CH_3). **IR (neat) ν_{max}:** 3471, 2931, 2866, 1771, 1306, 1177, 1070 cm^{-1}. **HRMS (ESI)**: *m/z* calcd. for $C_{24}H_{35}O_6$ $[M+H]^+$ 419.2434, found 419.2421. **[α]** $^{20}_{D}$ + 83° (c=0.6, $CHCl_3$)

Sporochartine D. **^{1}H NMR** (500.1 MHz, $CDCl_3$) δ 5.98-5.94 (m, 1H), 5.64 (dd, J= 15.9, 7.4 Hz, 1H), 5.55 (dd, J= 15.6, 6.0 Hz, 1H), 5.52-5.48 (m, 1H), 5.08-5.06 (m, 1H), 4.45-4.42 (m, 1H), 4.28-4.22 (m, 1H), 4.20-4.17 (m, 1H), 4.07-4.03 (m, 1H), 3.29 (d, J=5.3 Hz, 1H), 2.80-2.78 (m, 1H), 2.62-2.54 (m, 1H), 2.41-2.36 (m, 1H), 2.29-2.20 (m, 1H), 1.96-1.92 (m, 2H), 1.91-1.87 (m, 1H), 1.85-1.77 (m, 1H), 1.61-1.58 (m, 2H), 1.49-1.43 (m, 2H), 1.38-1.33 (m, 2H), 1.32-1.26 (m, 7H), 0.88 (t, J=6.6 Hz, 3H). **HRMS (ESI)**: *m/z* calcd. for $C_{24}H_{35}O_6$ $[M+H]^+$ 419.2434, found 419.2418.

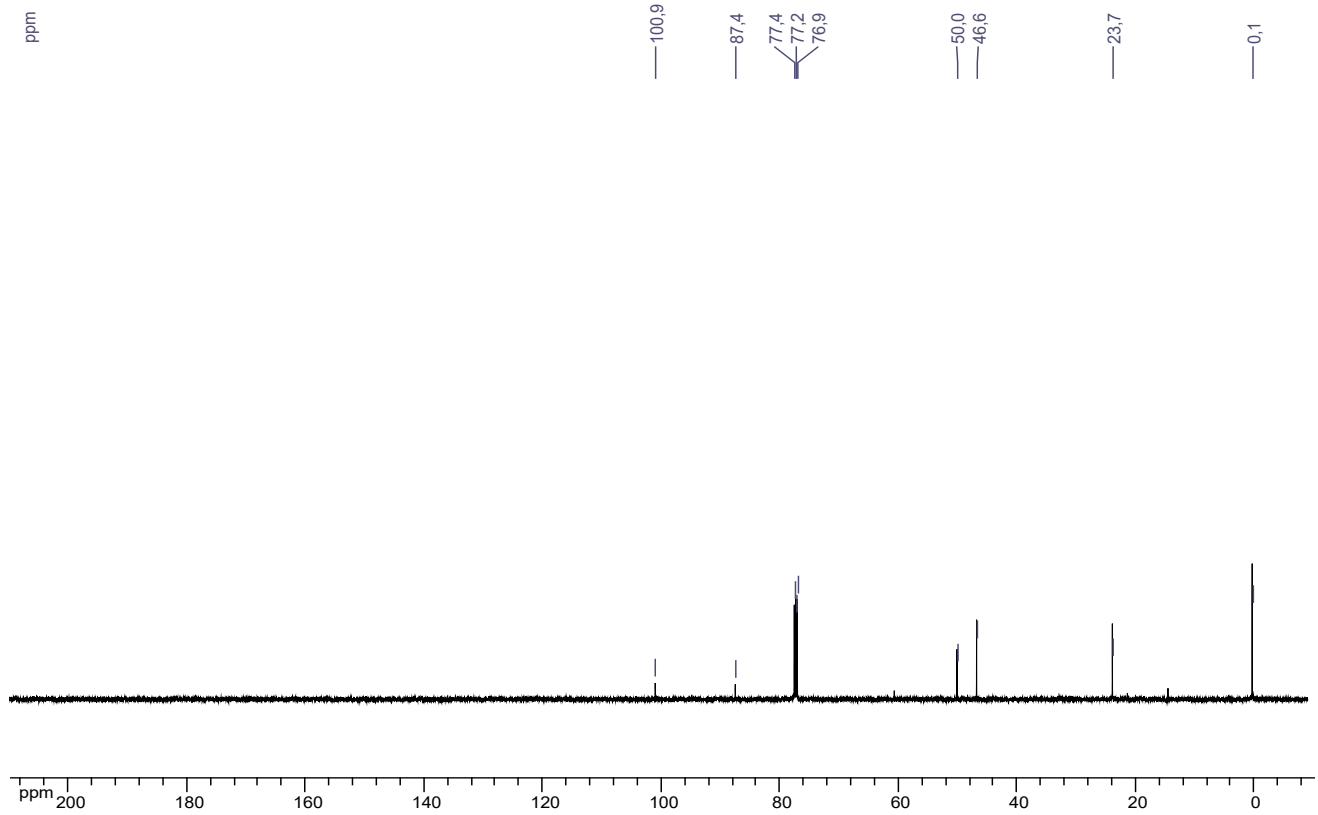
IV - ^{1}H and ^{13}C NMR Spectra

^{1}H NMR ($CDCl_3$, 500.1 MHz) of 9

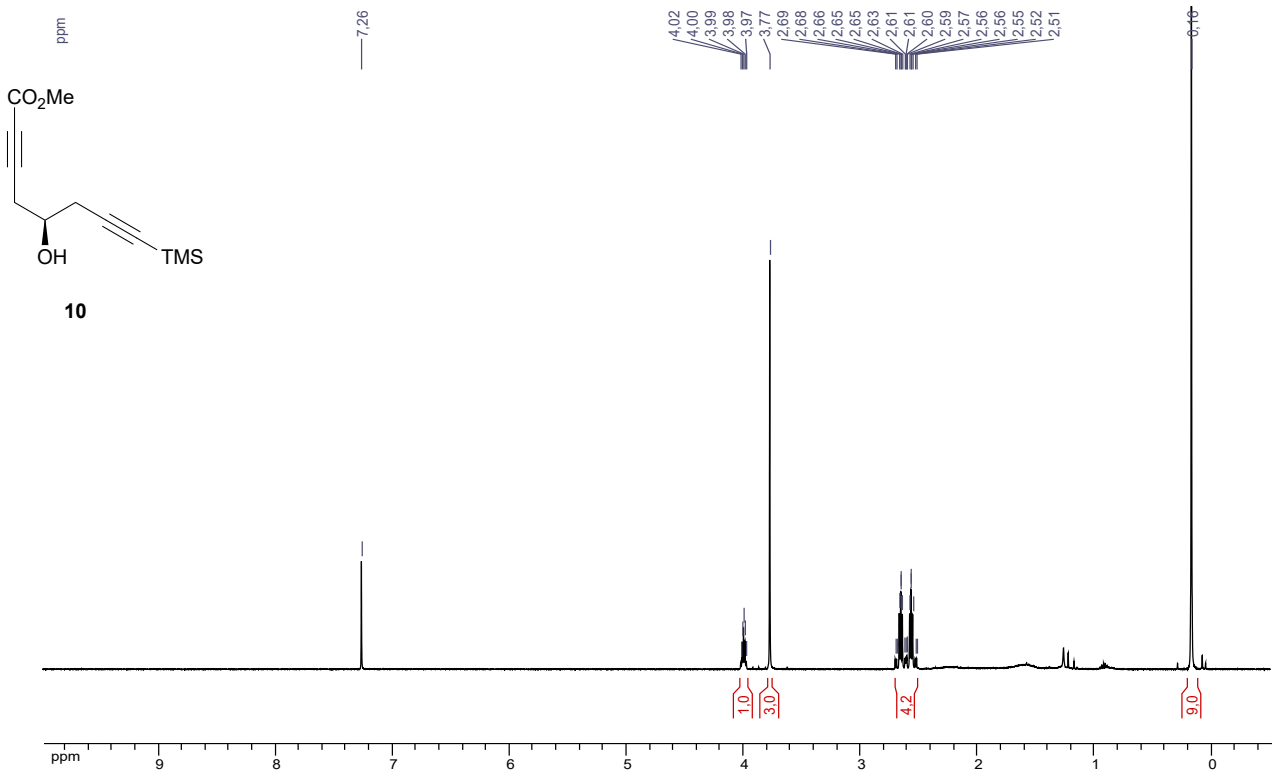


9

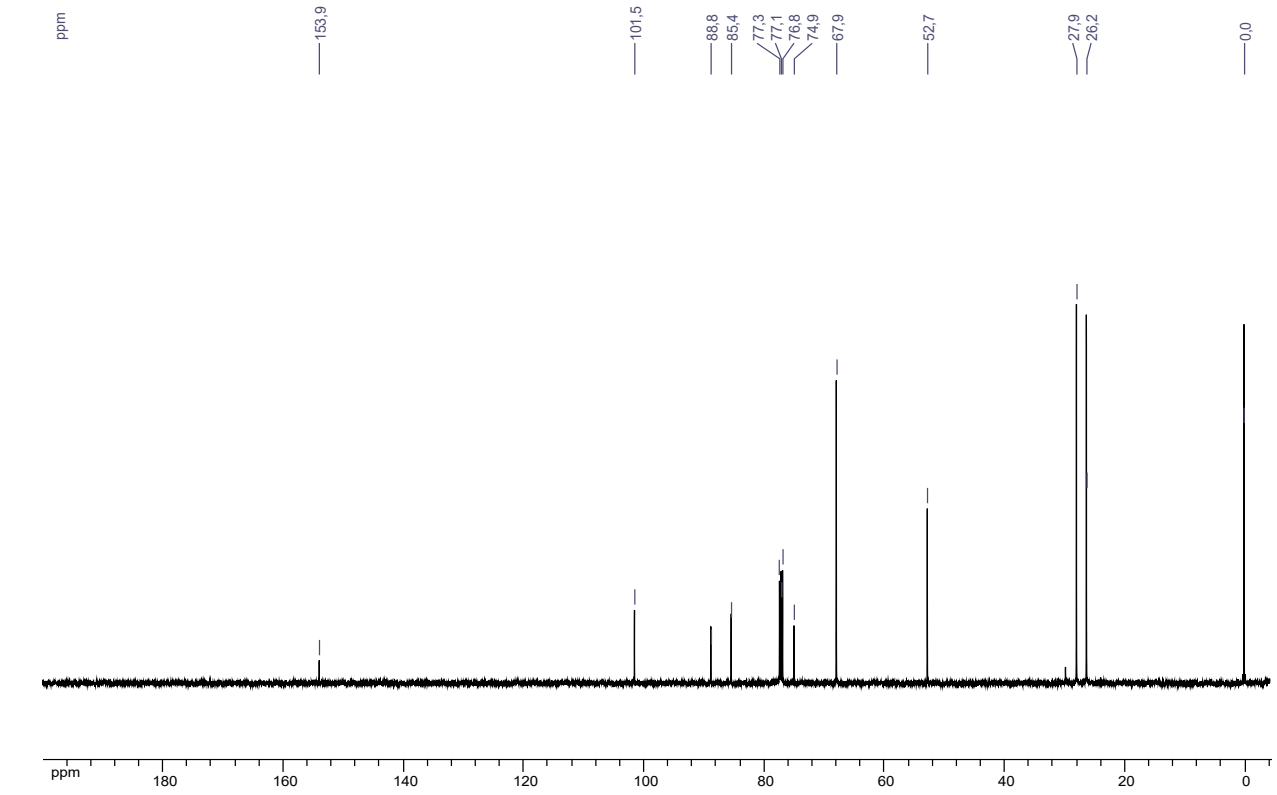
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 9



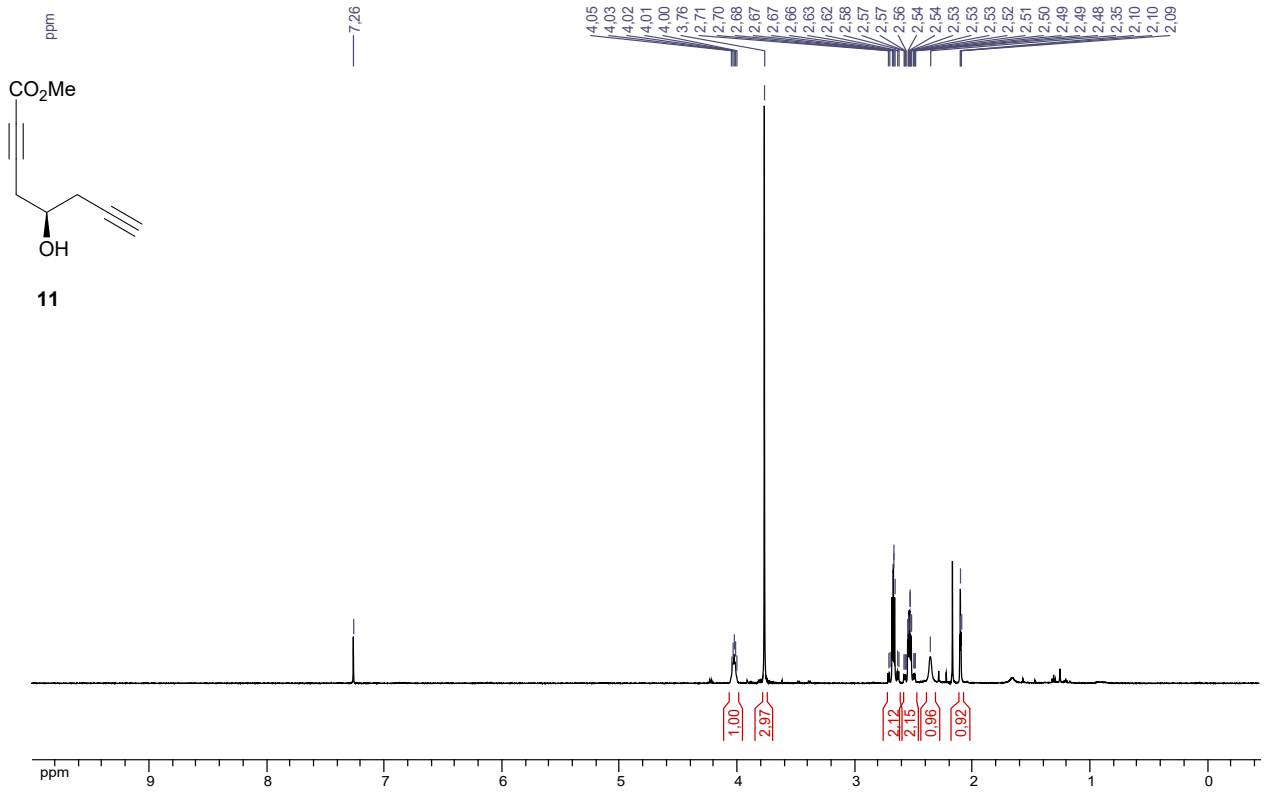
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 10



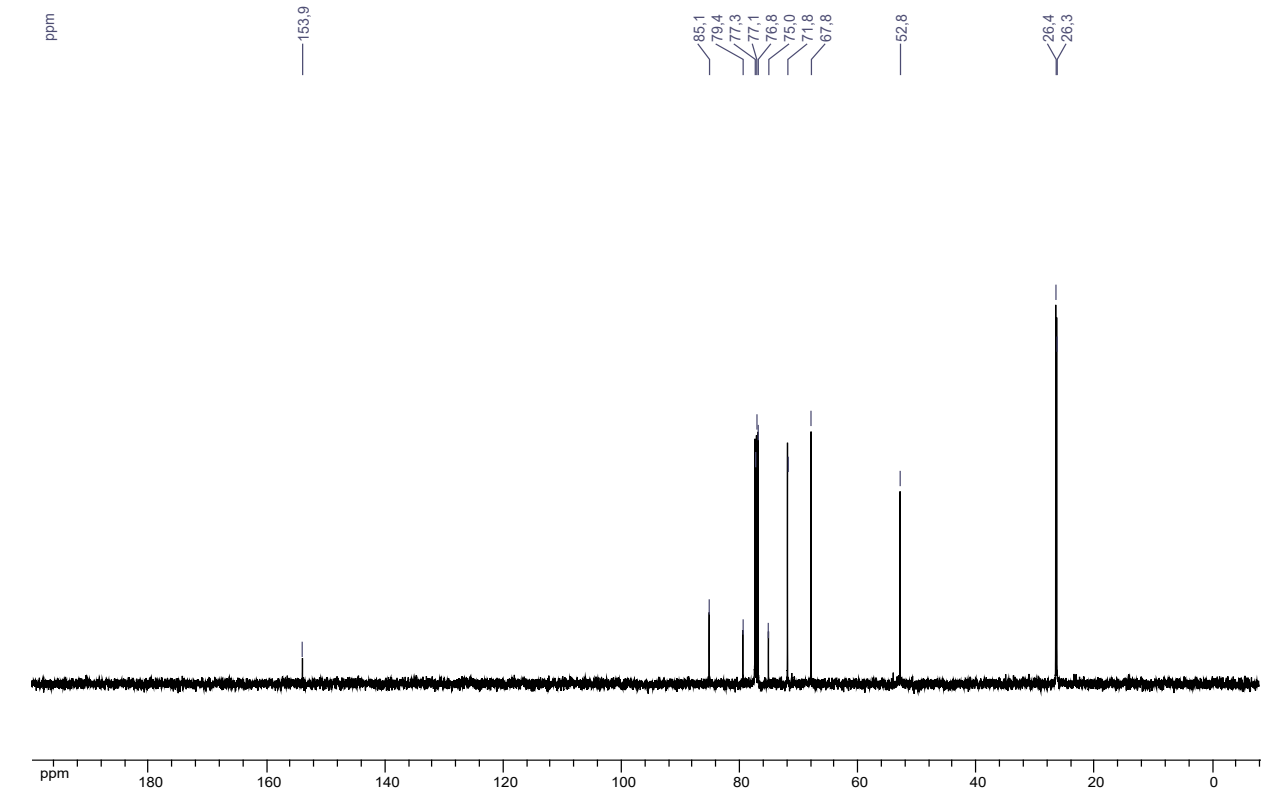
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 10



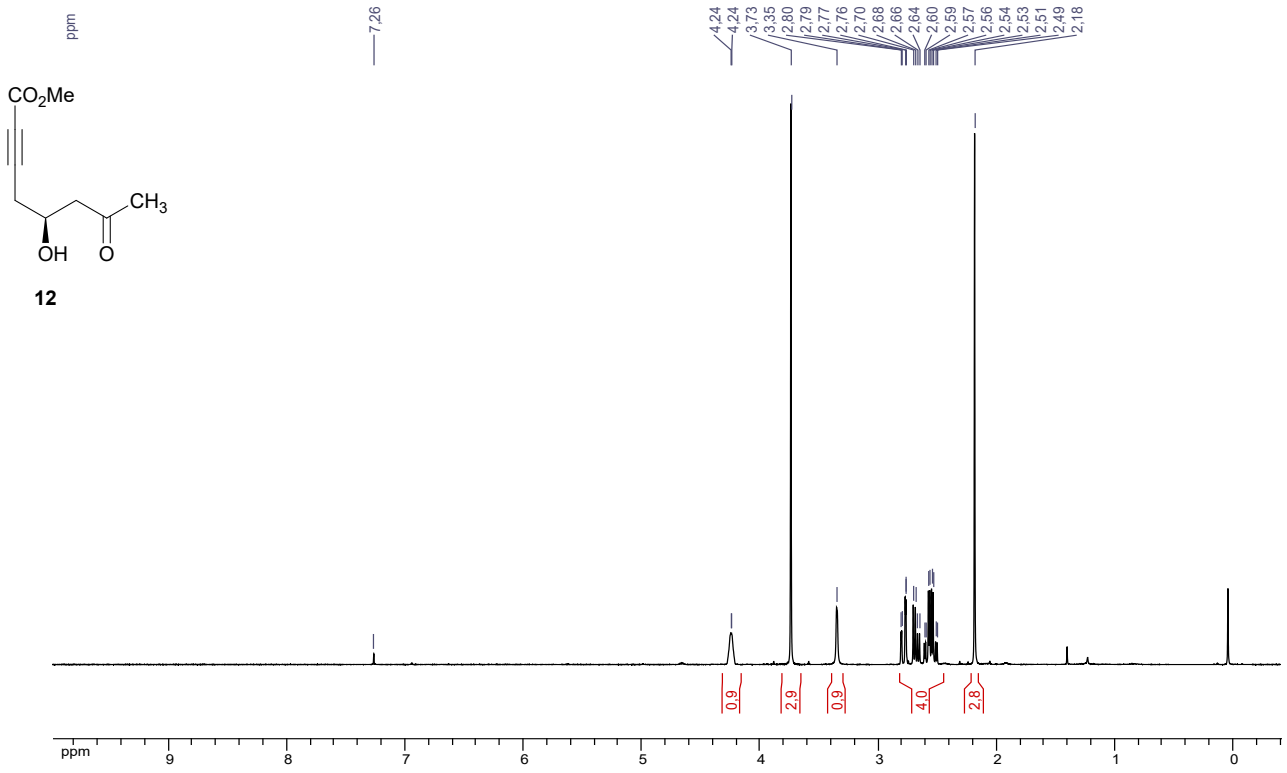
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 11



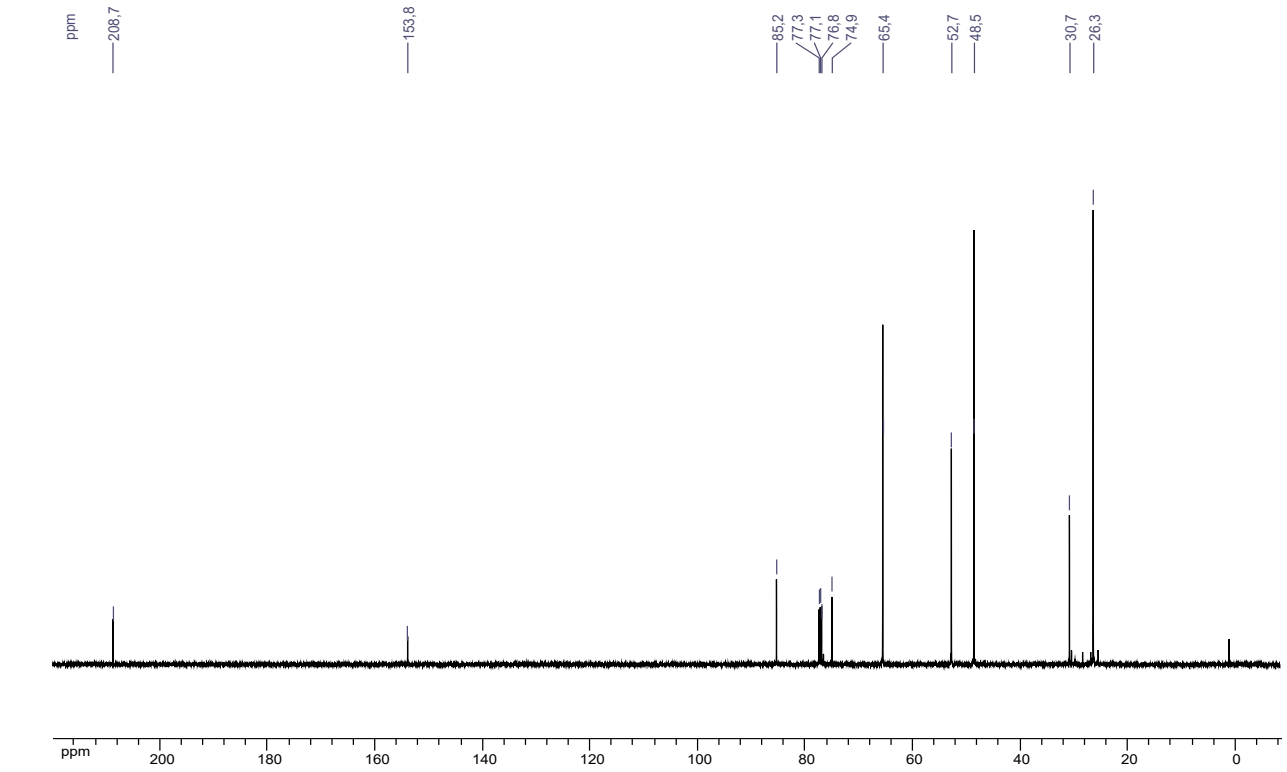
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 11



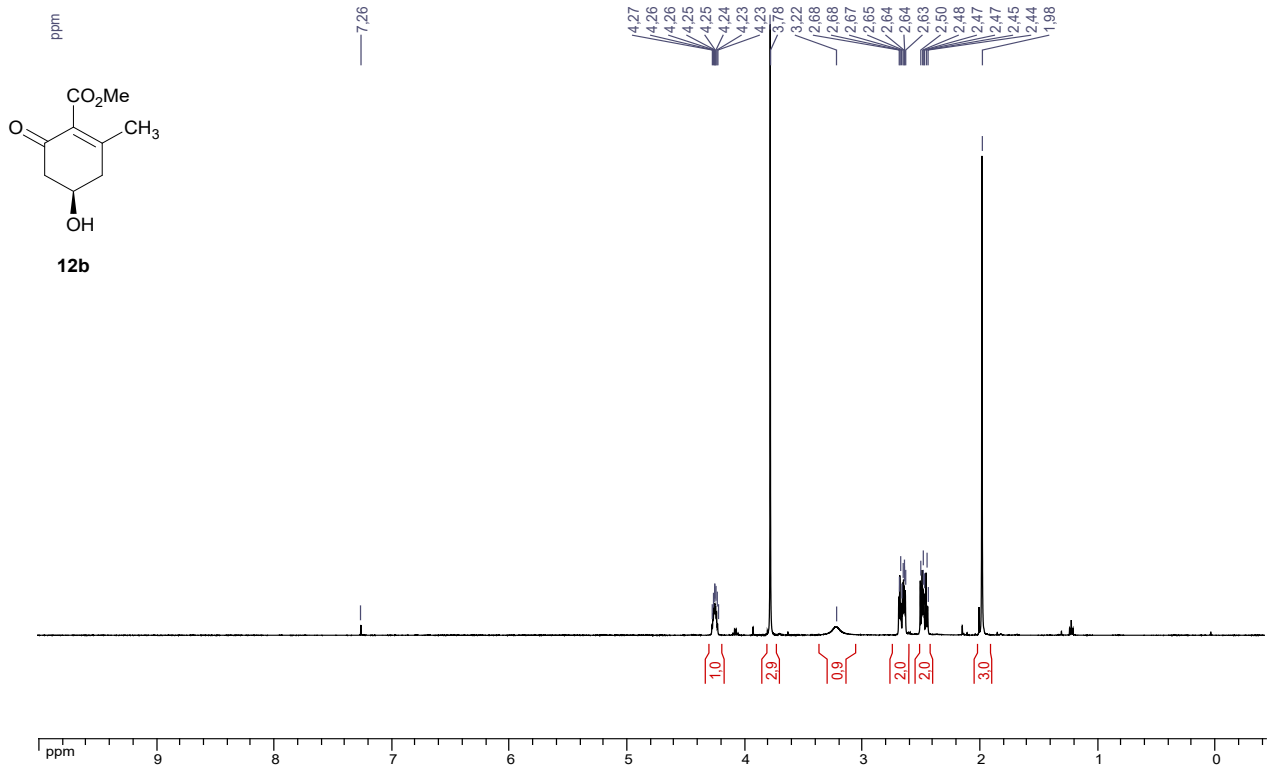
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 12



^{13}C NMR ($CDCl_3$, 125.8 MHz) of 12

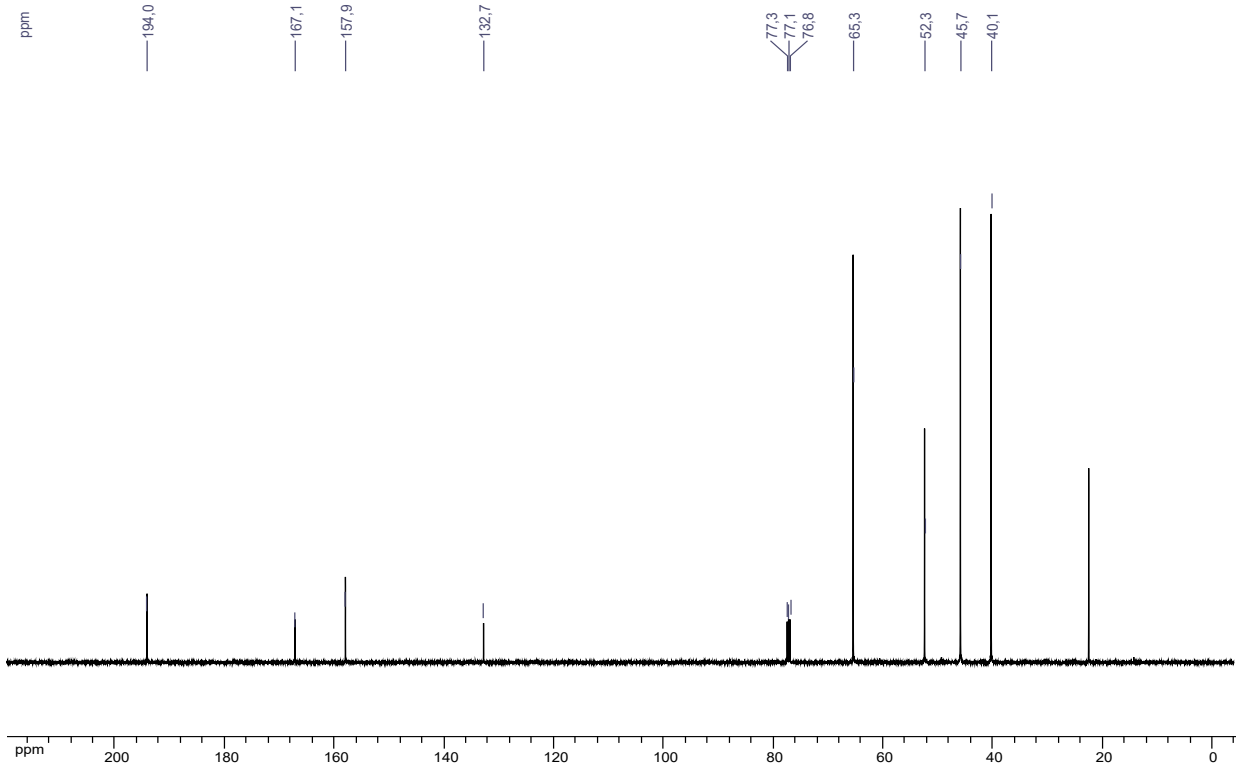


^{1}H NMR ($CDCl_3$, 500.1 MHz) of 12b

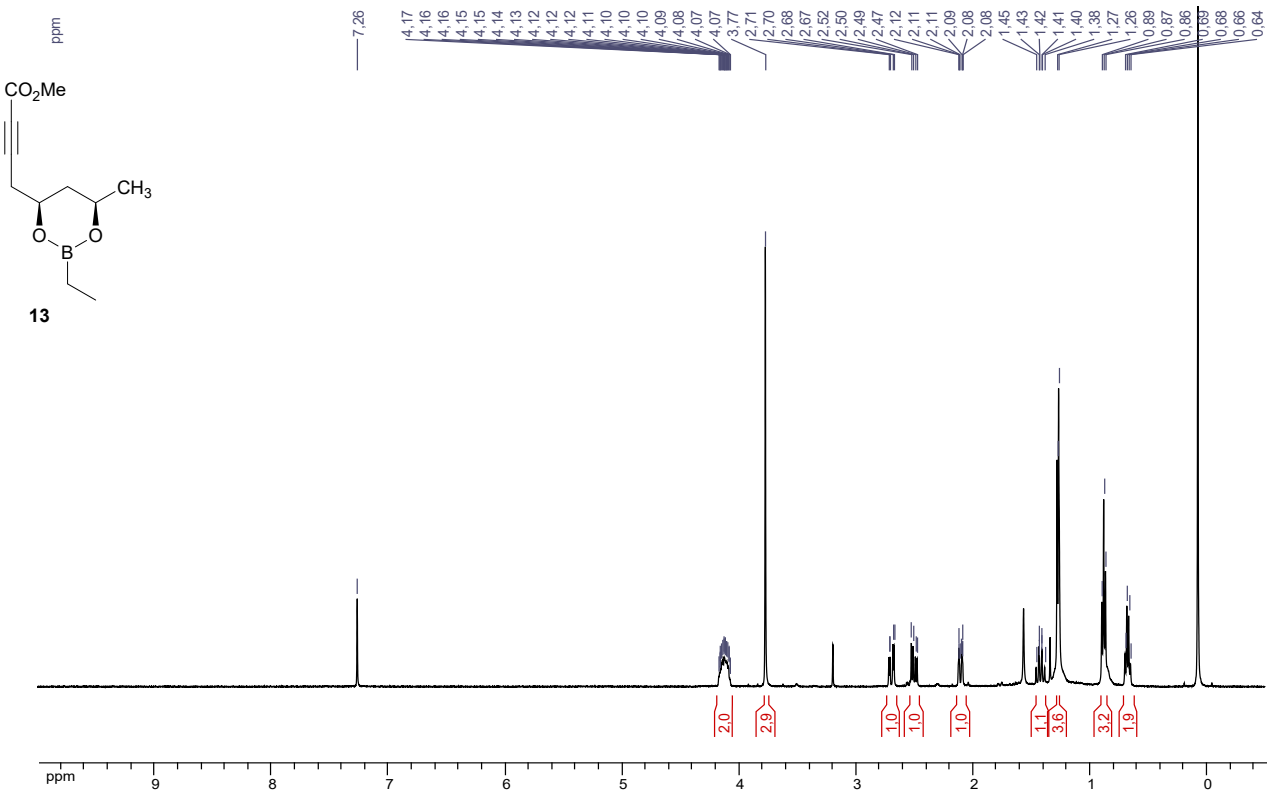


12b

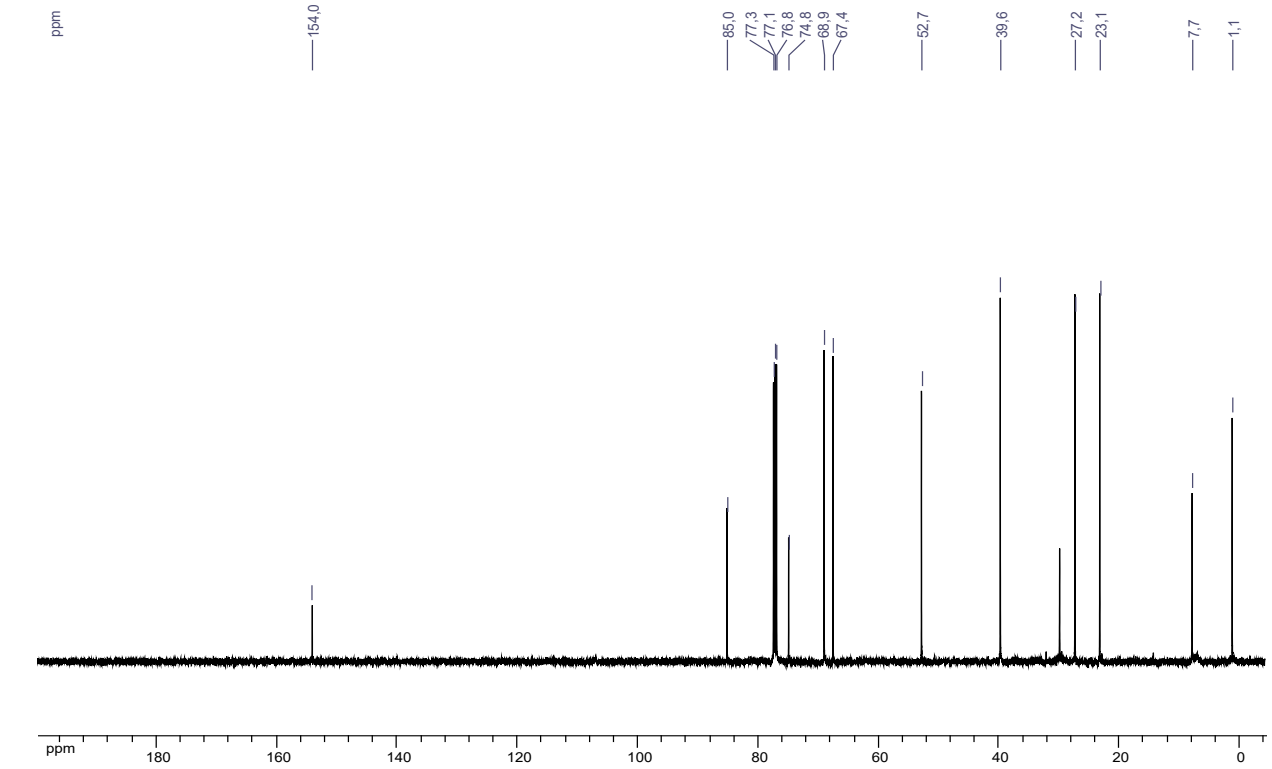
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 12b



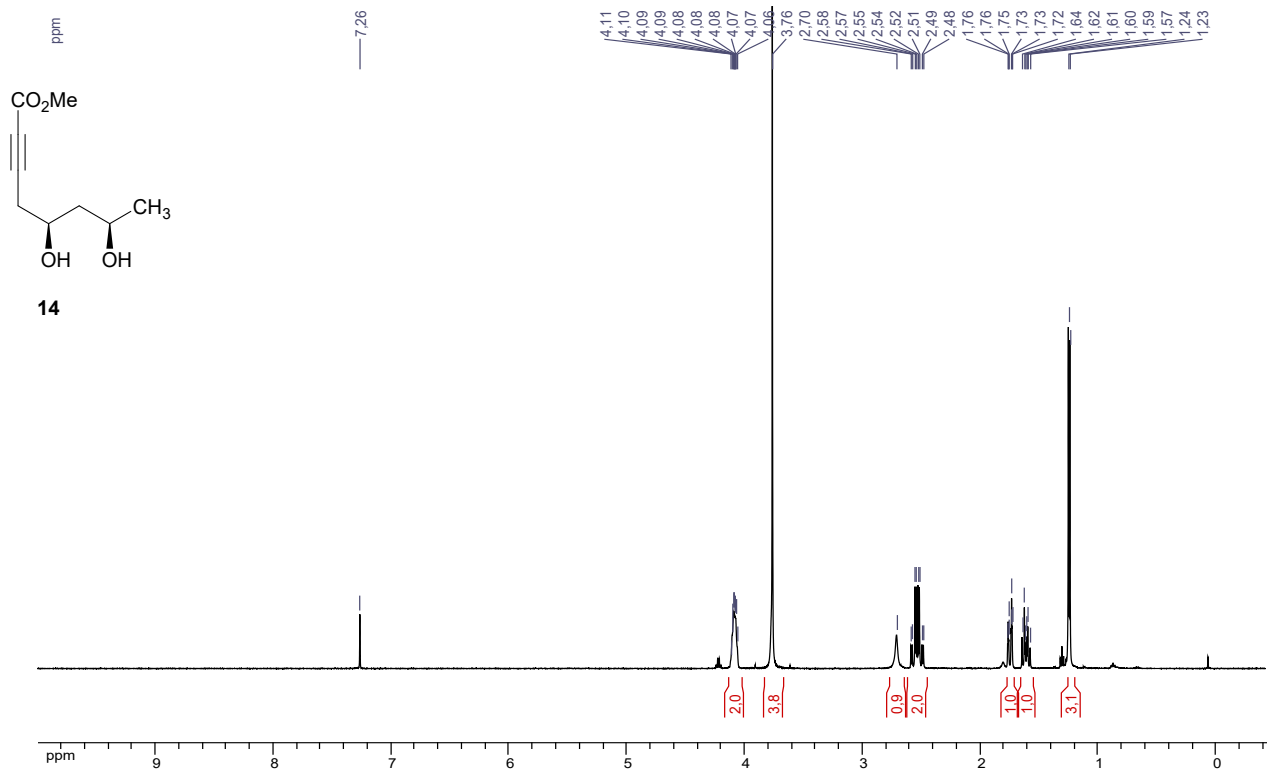
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 13



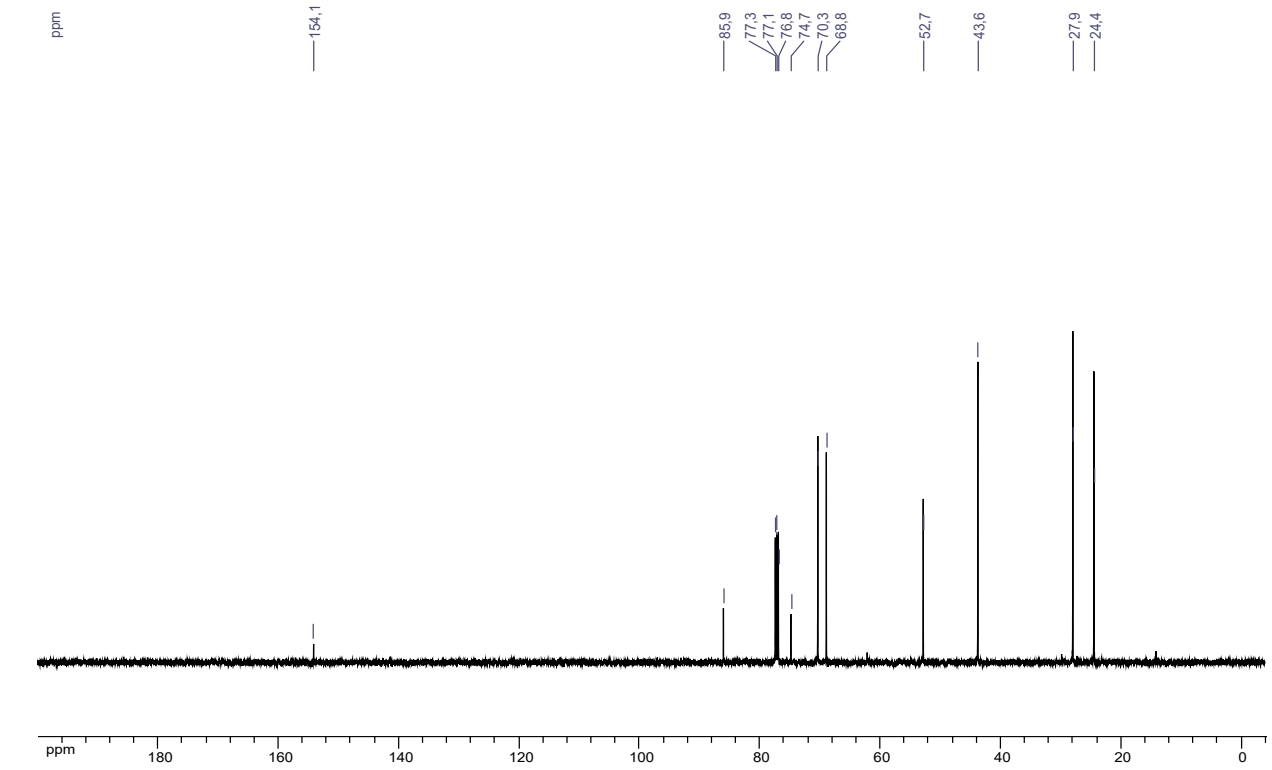
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 13



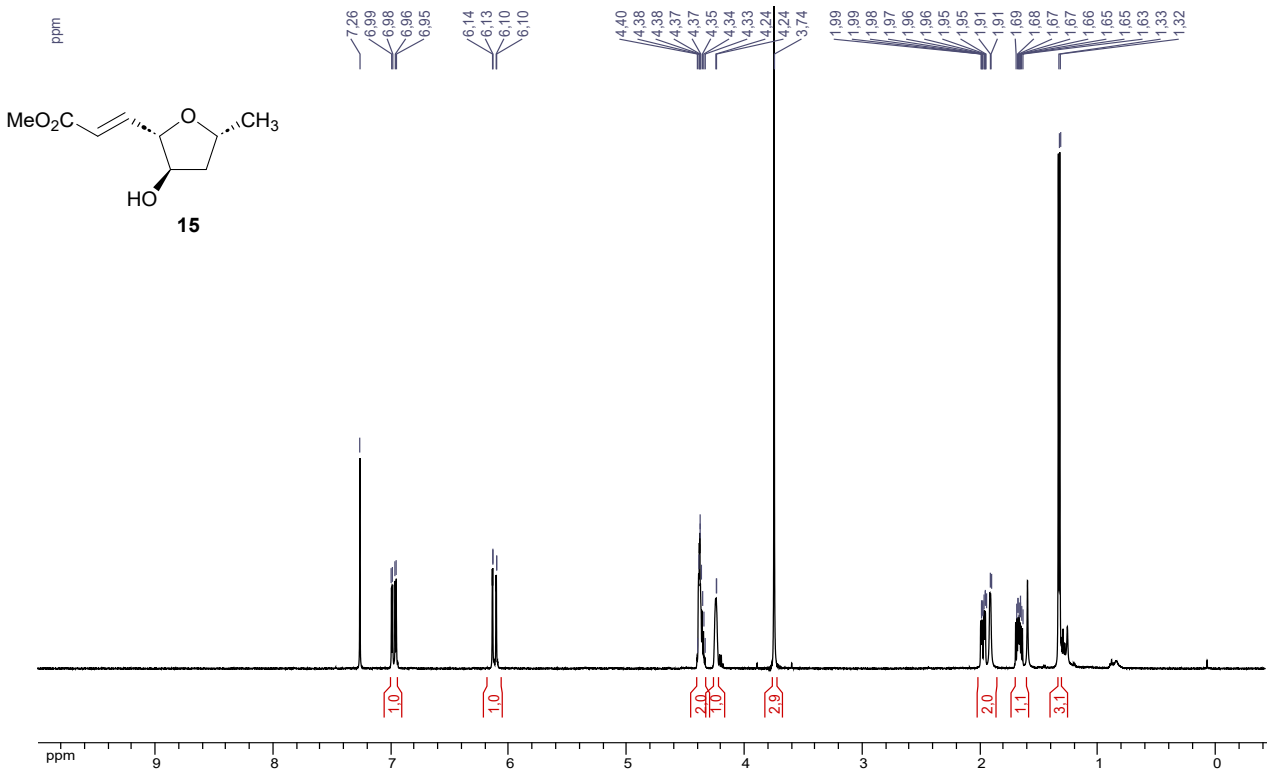
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 14



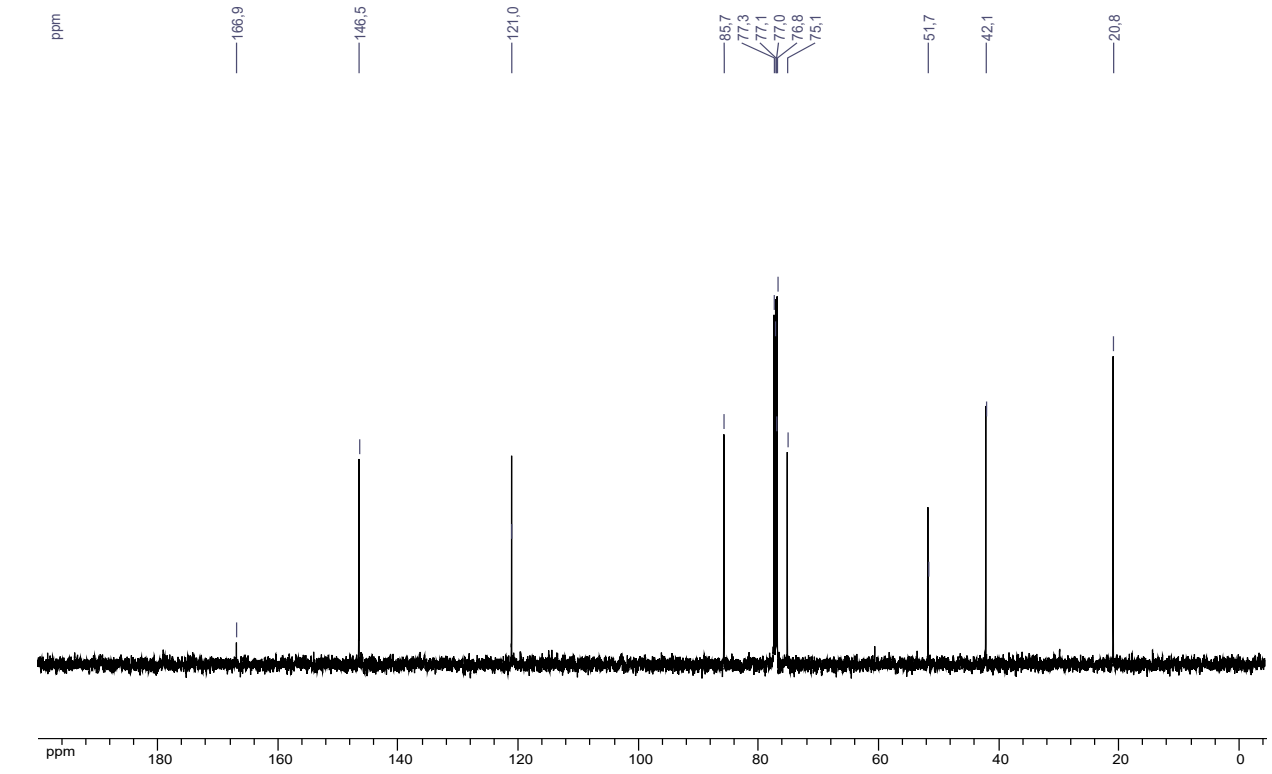
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 14



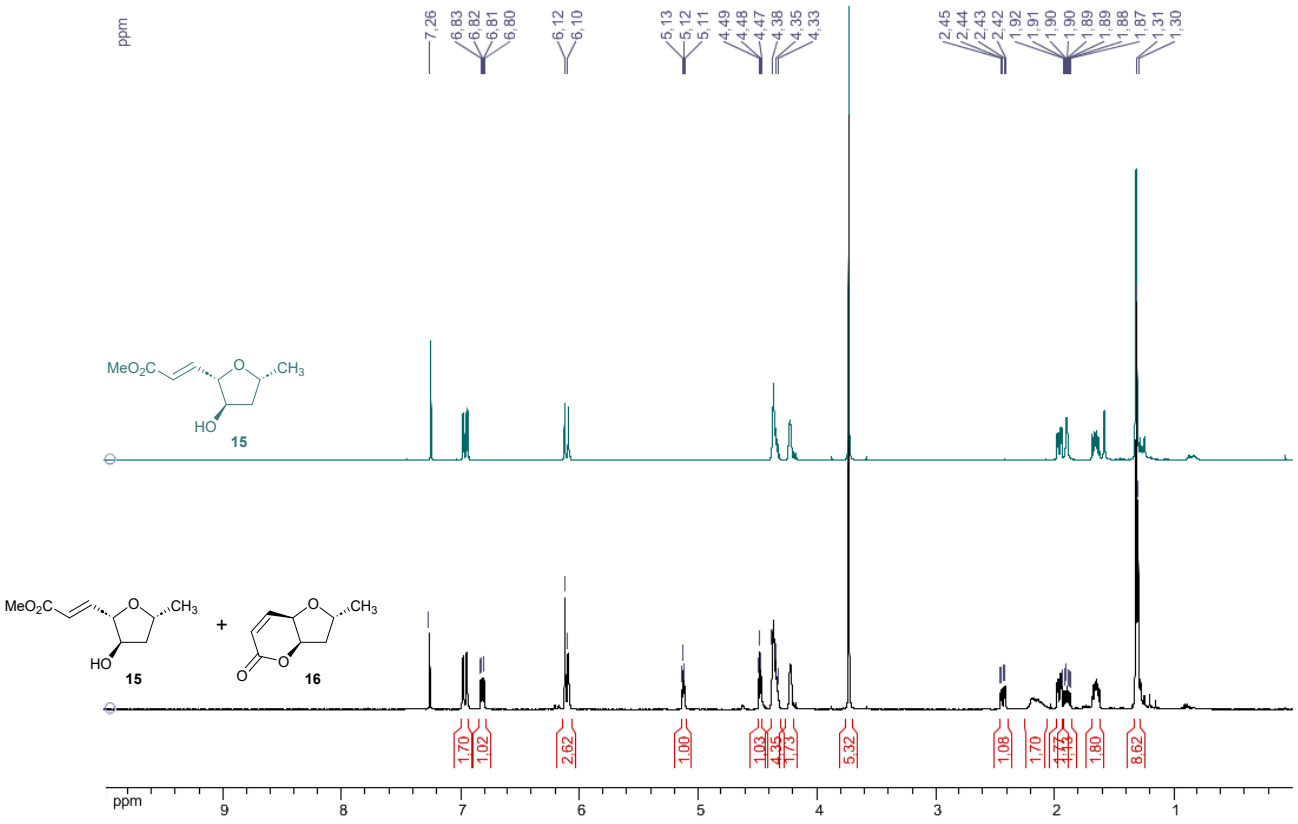
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 15



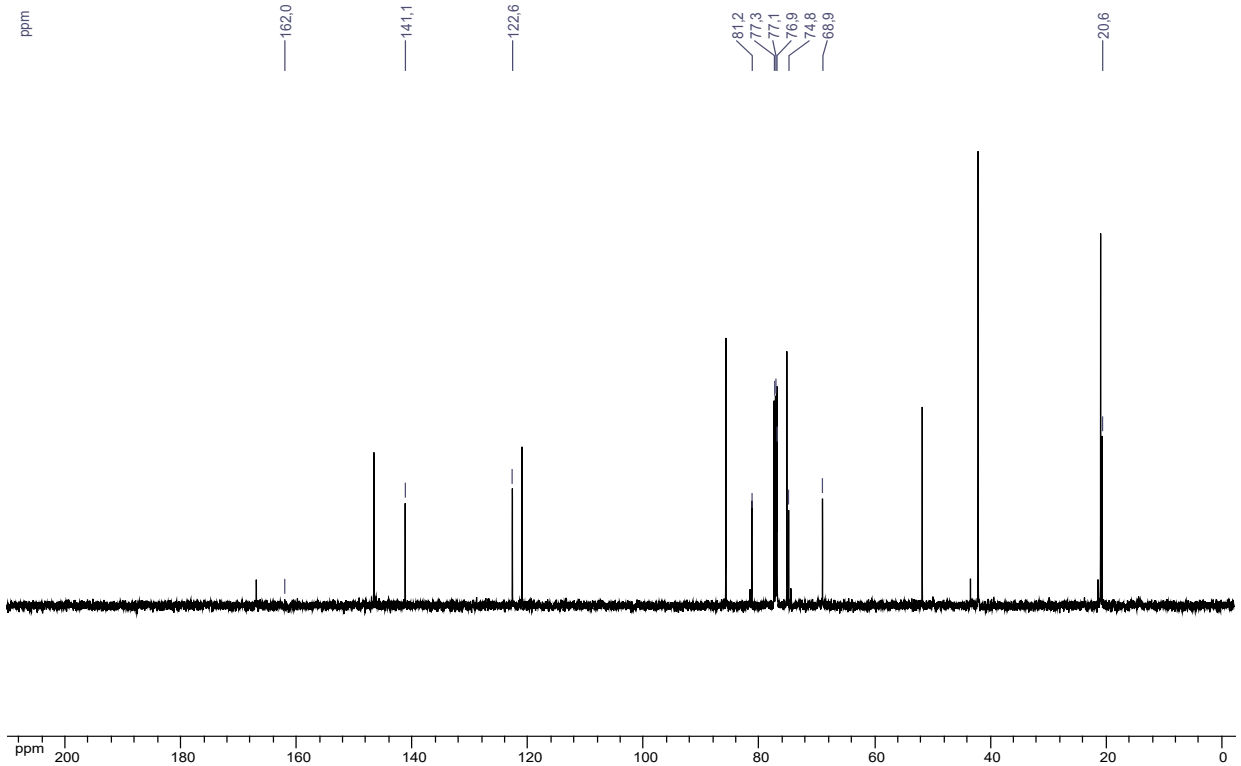
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 15



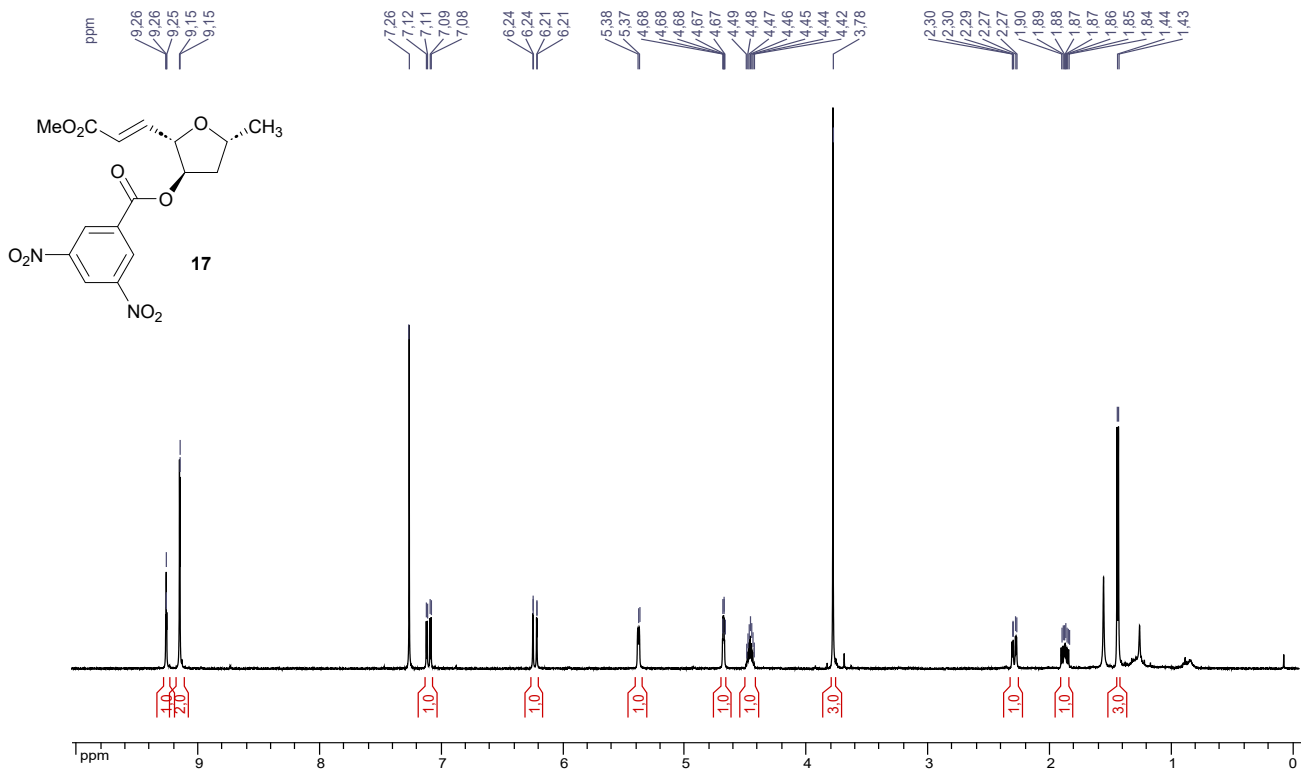
^{1}H NMR ($CDCl_3$, 500.1 MHz) of mixture 15 and 16



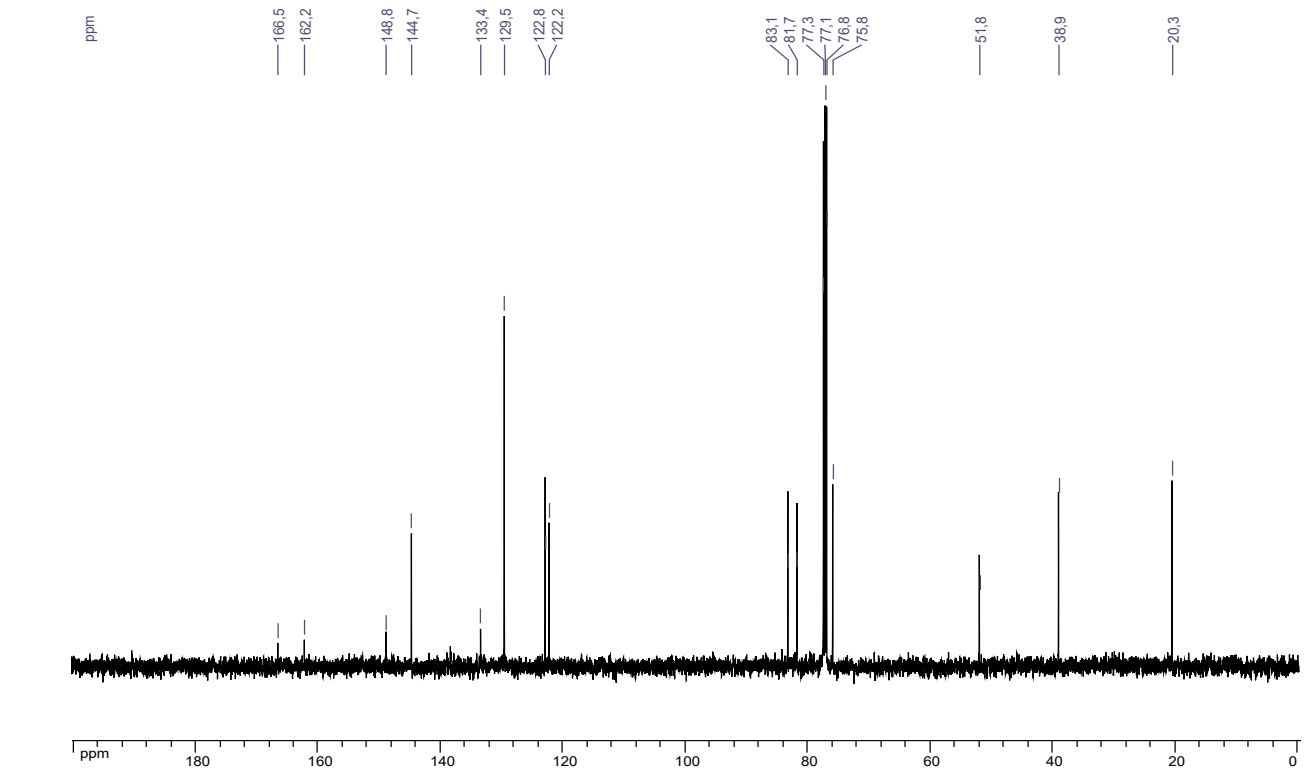
^{13}C NMR ($CDCl_3$, 125.8 MHz) of mixture 15 and 16



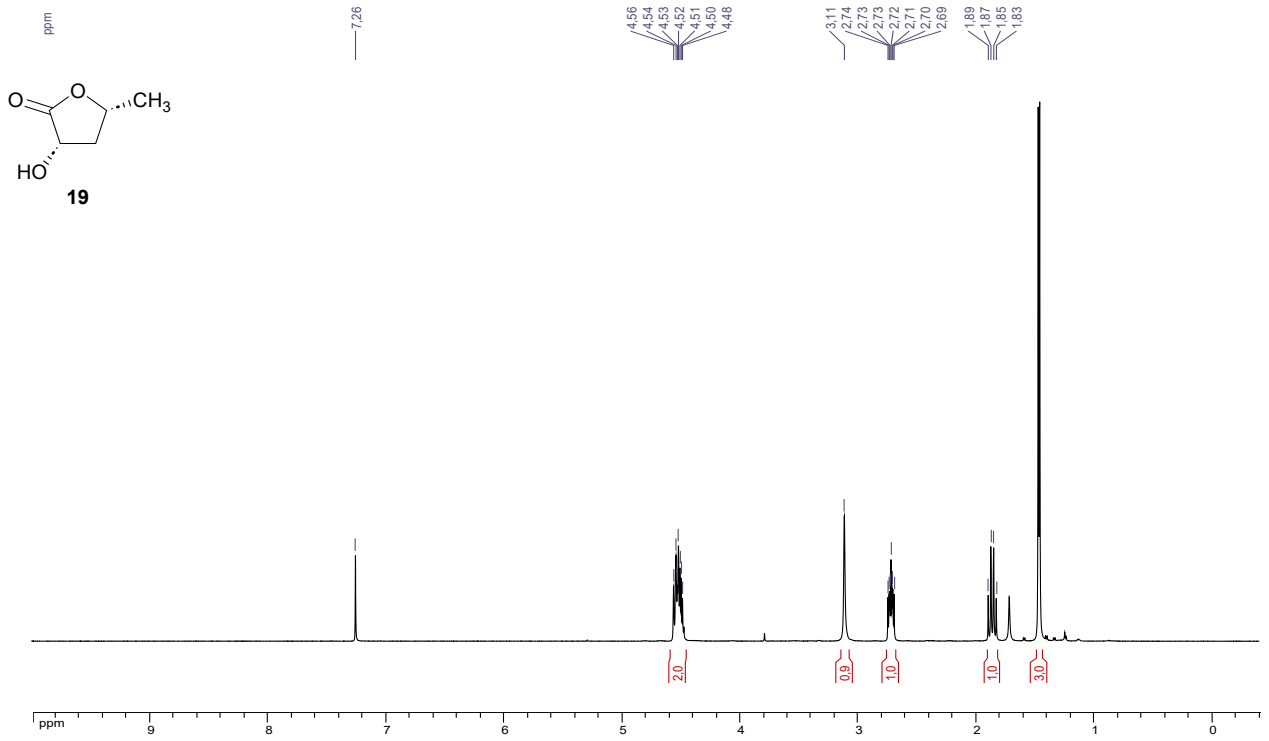
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 17



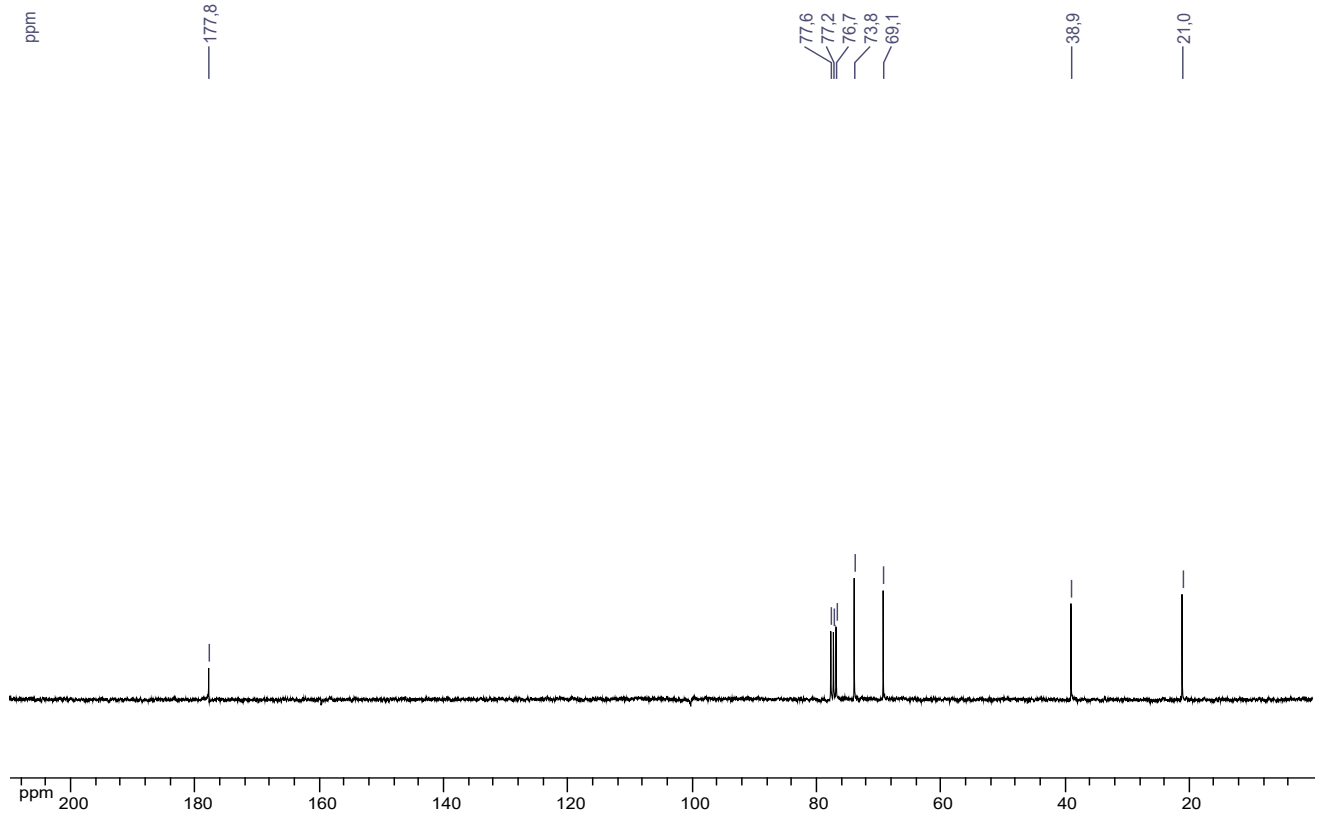
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 17



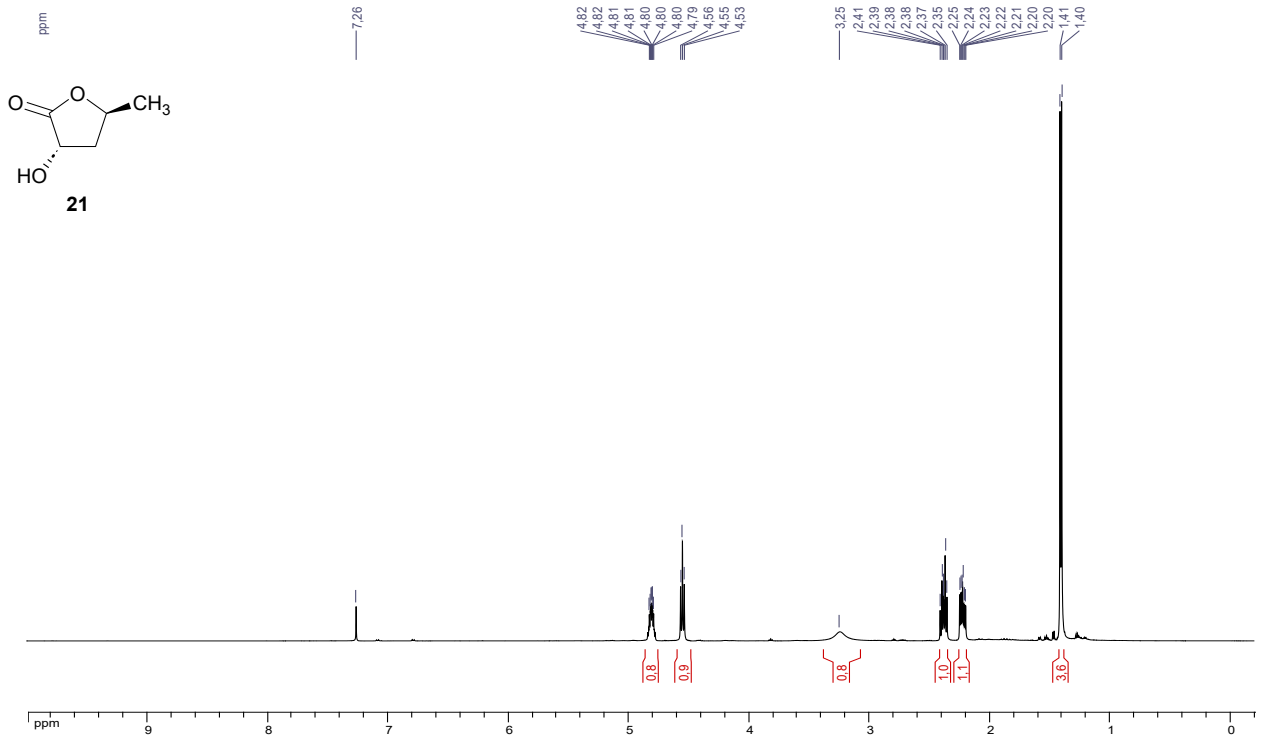
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 19



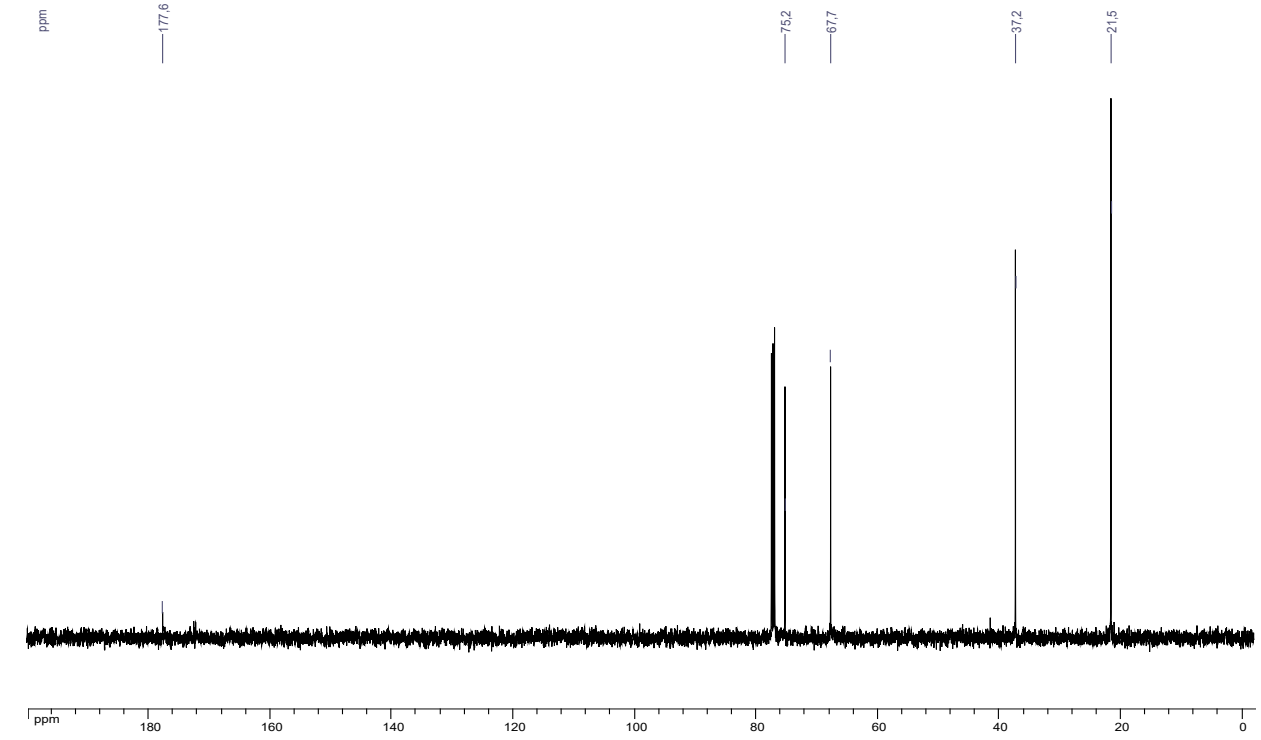
^{13}C NMR ($CDCl_3$, 75.5 MHz) of 19



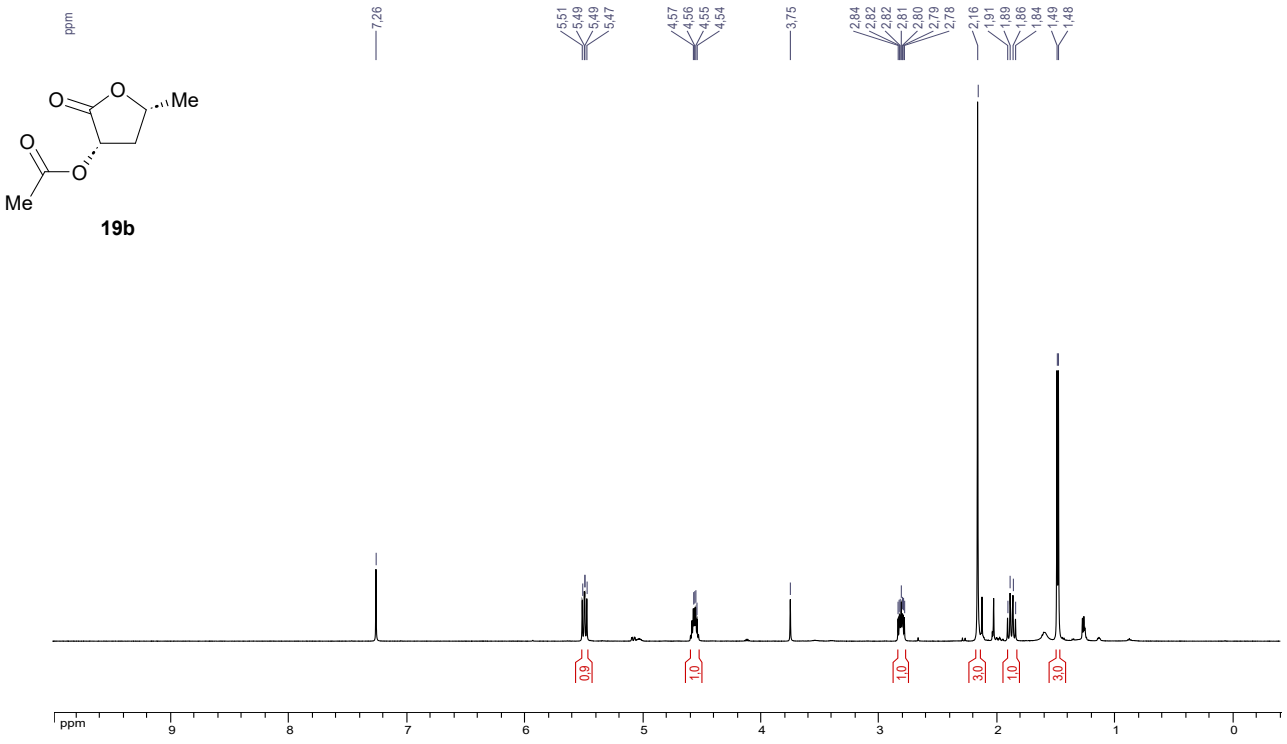
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 21



^{13}C NMR ($CDCl_3$, 125.8 MHz) of 21

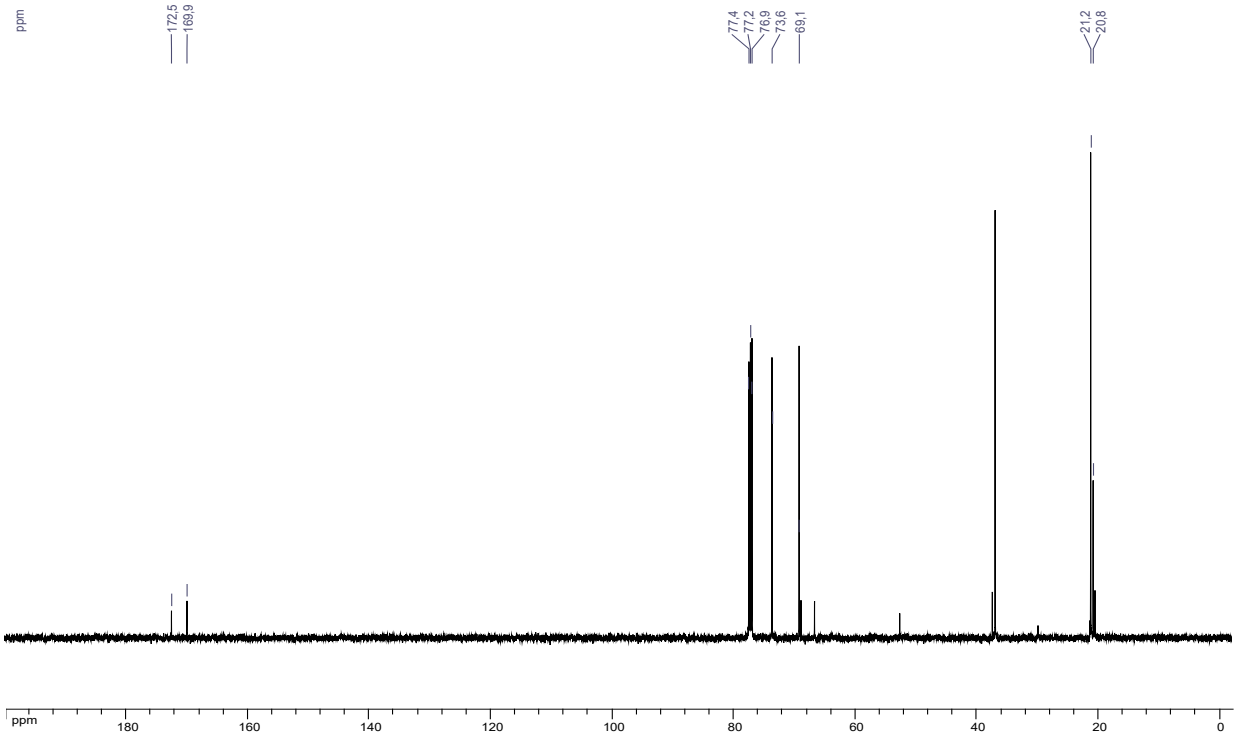


^{1}H NMR ($CDCl_3$, 500.1 MHz) of 19b

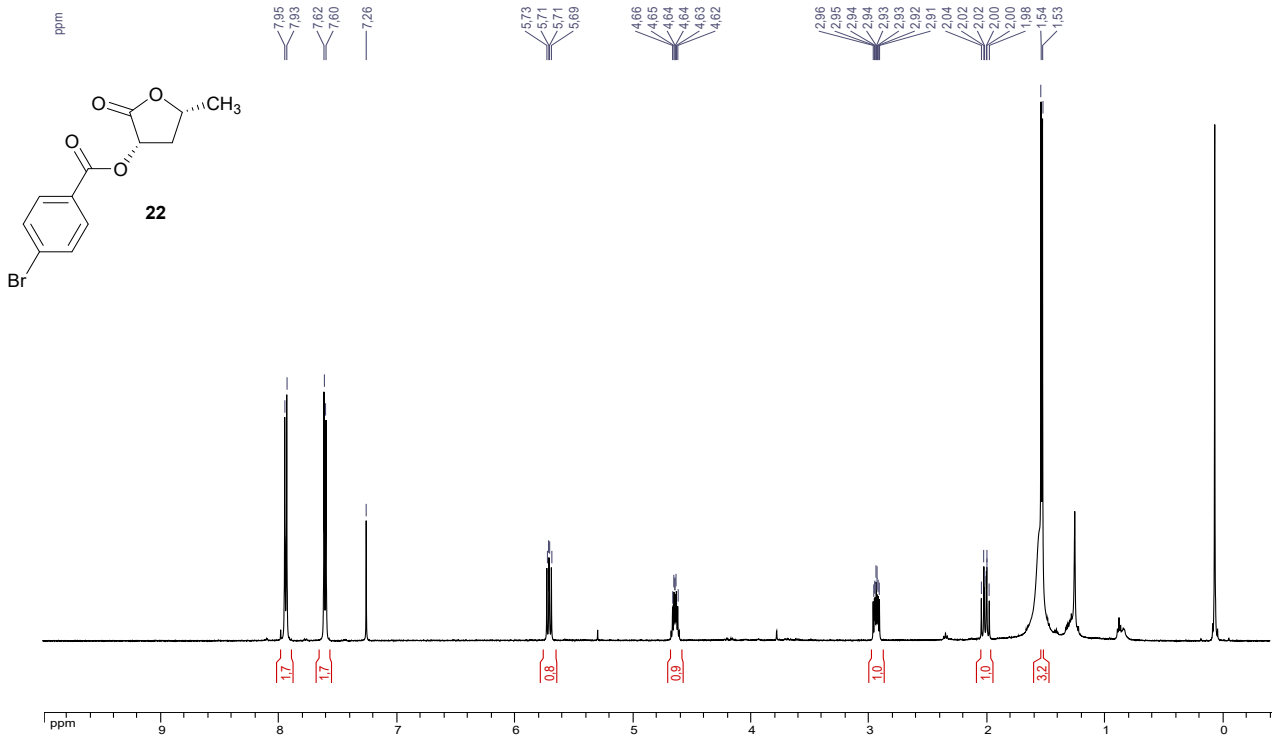


19b

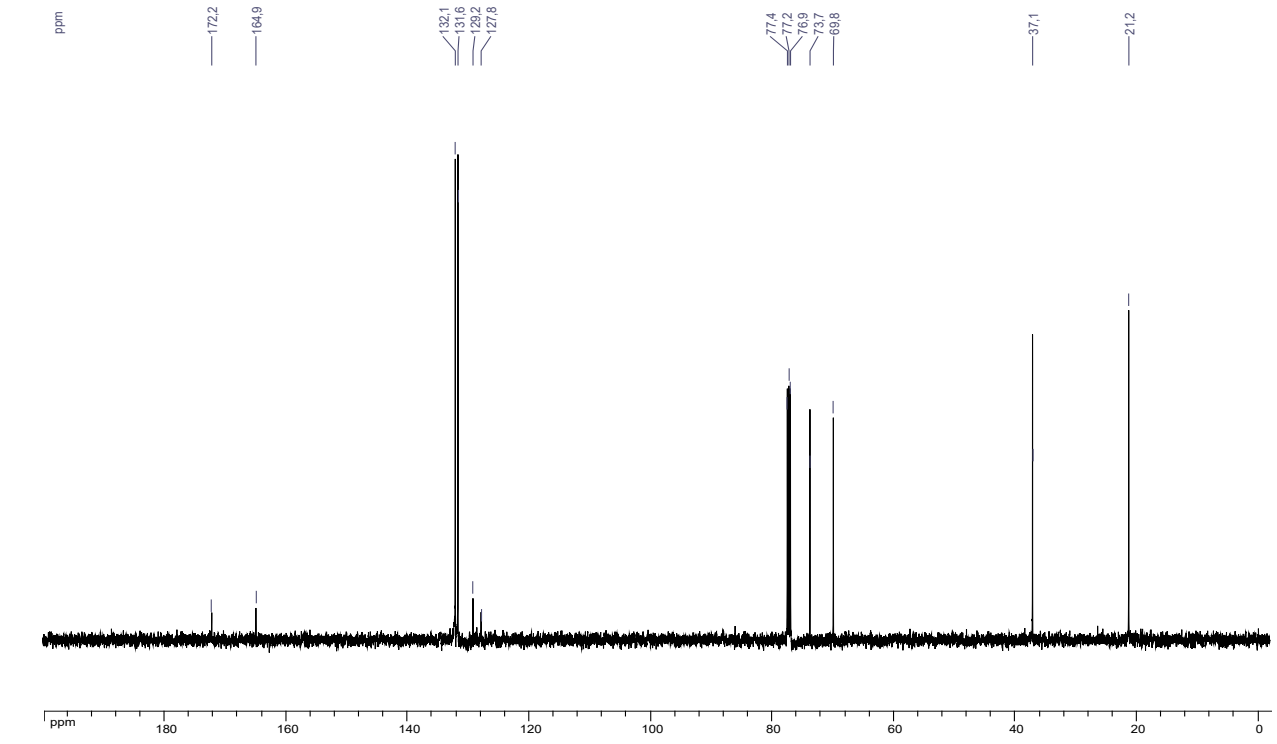
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 19b



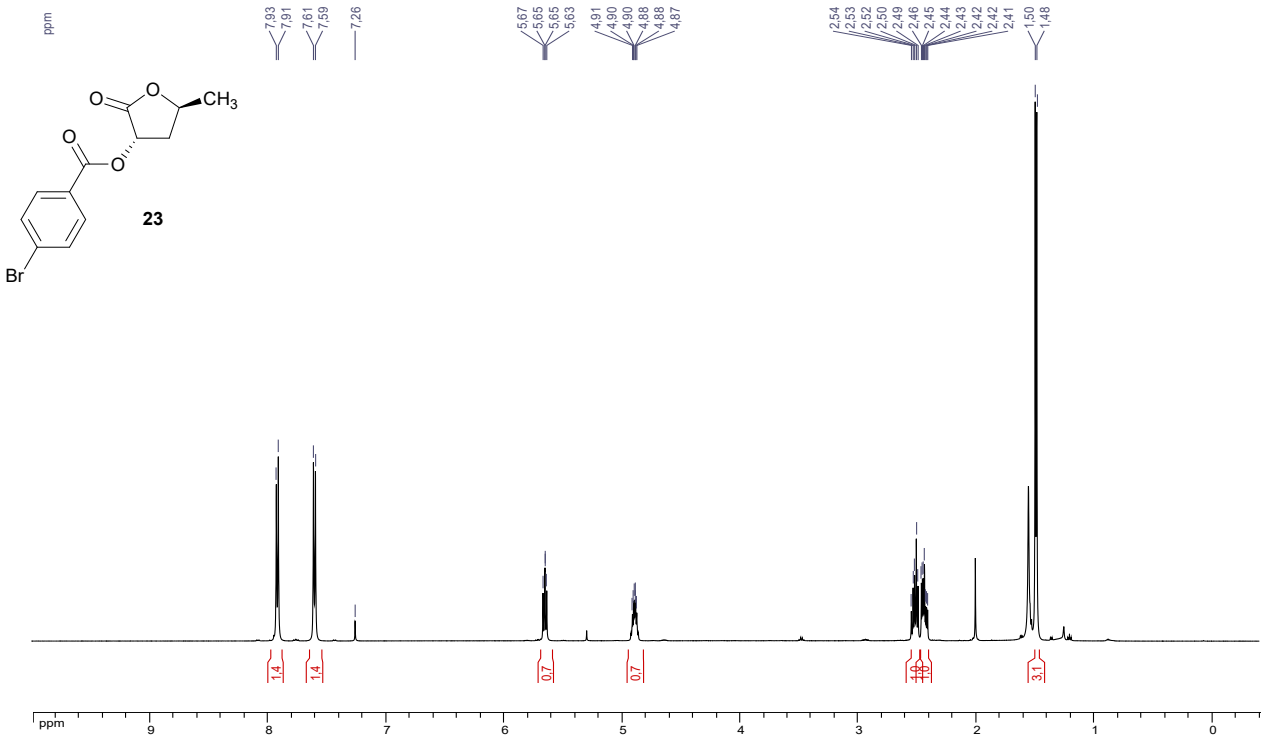
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 22



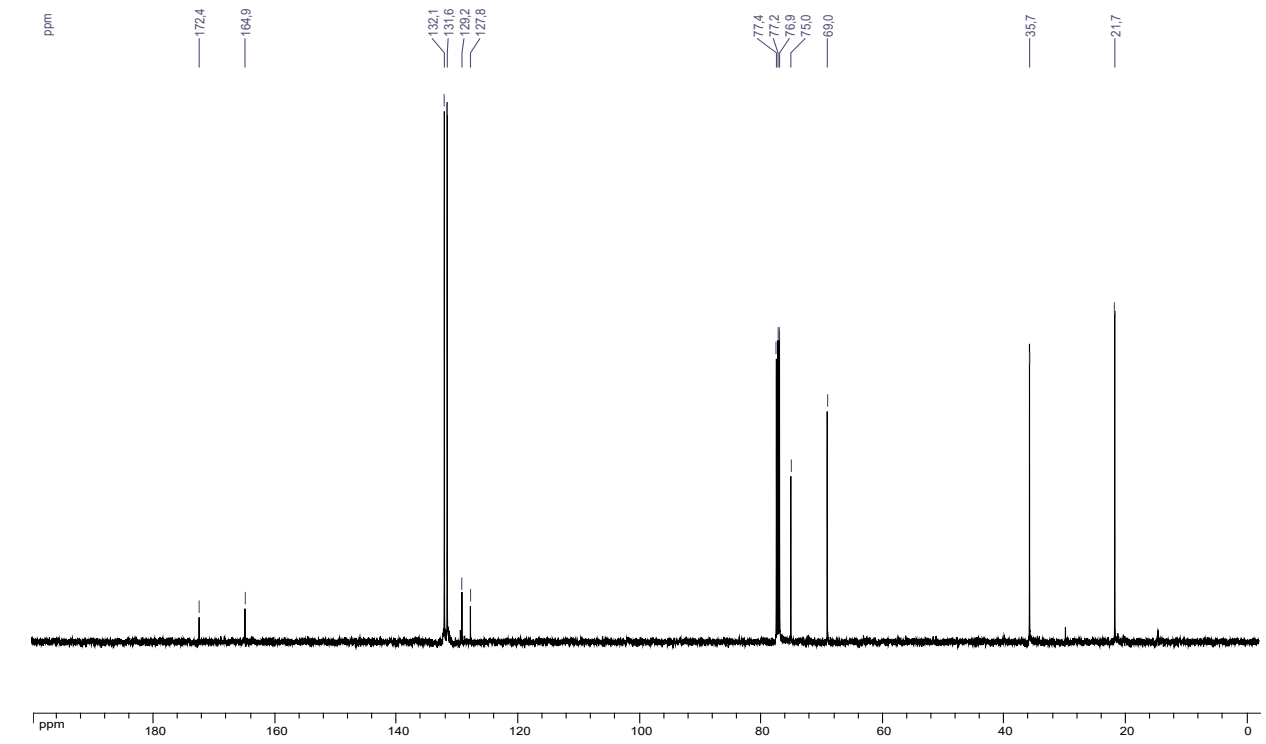
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 22



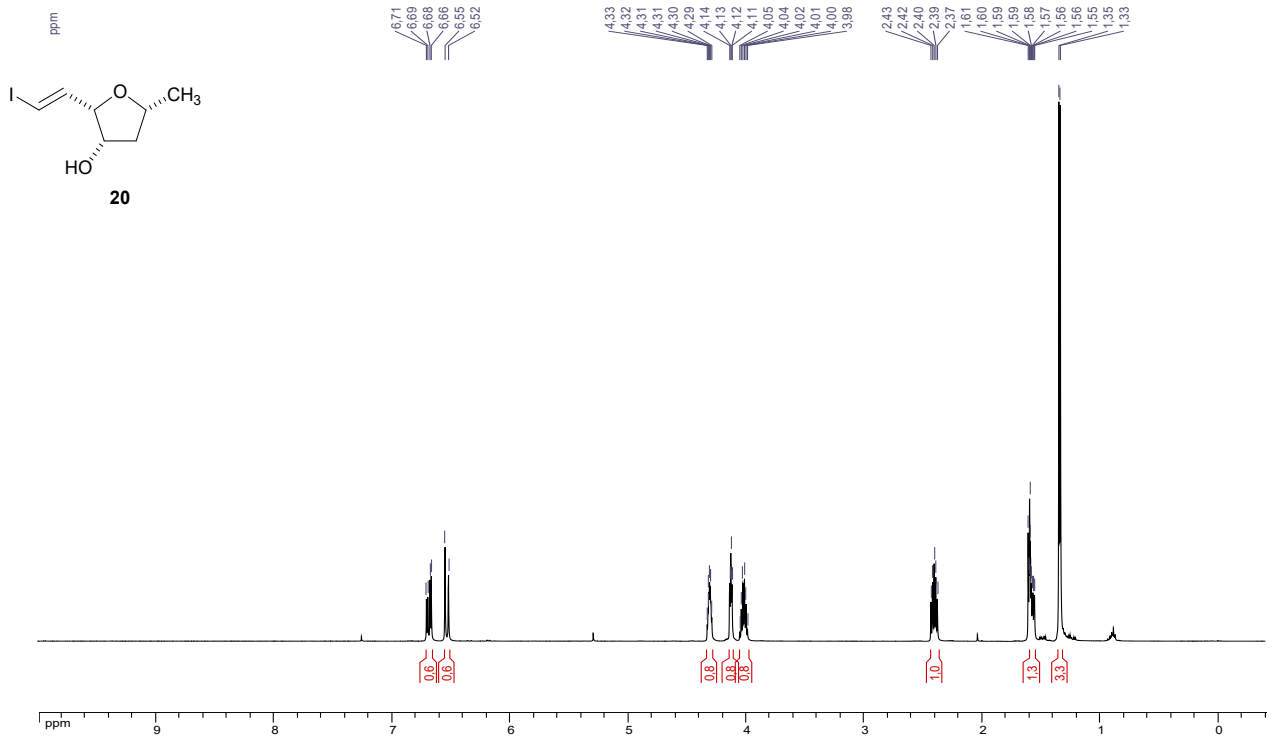
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 23



^{13}C NMR ($CDCl_3$, 125.8 MHz) of 23

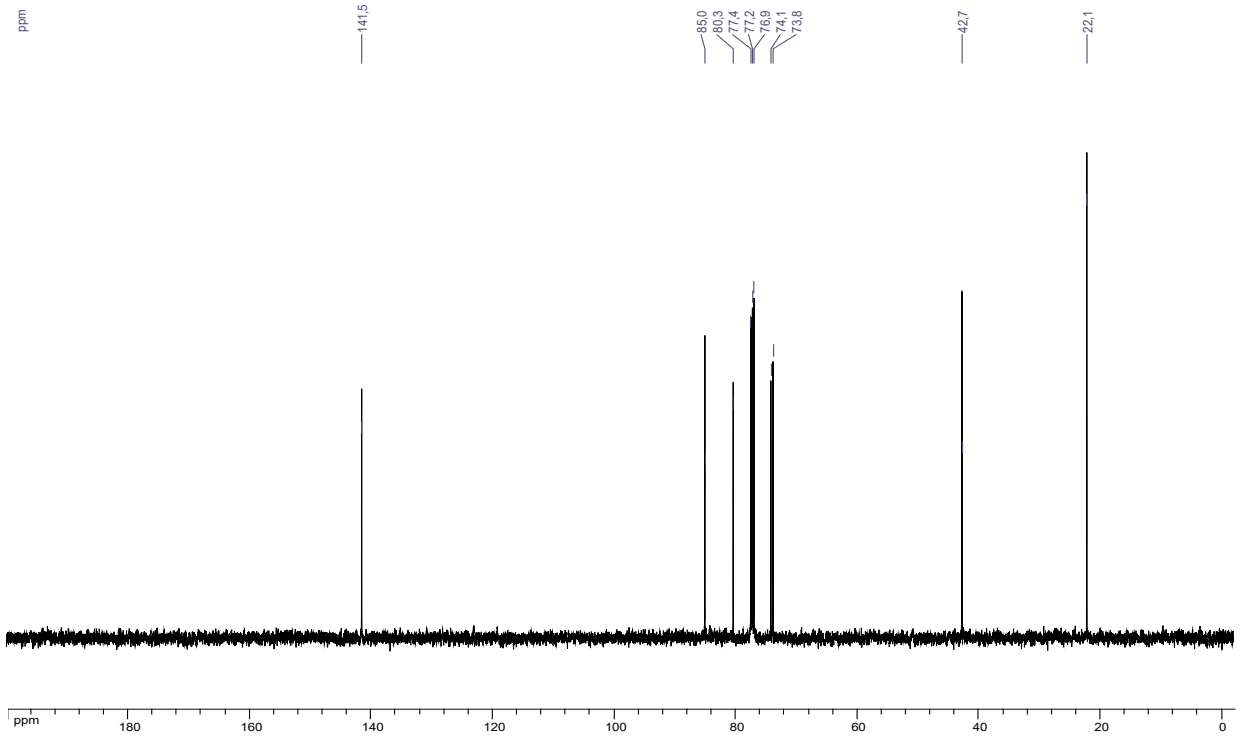


^{1}H NMR ($CDCl_3$, 500.1 MHz) of 20

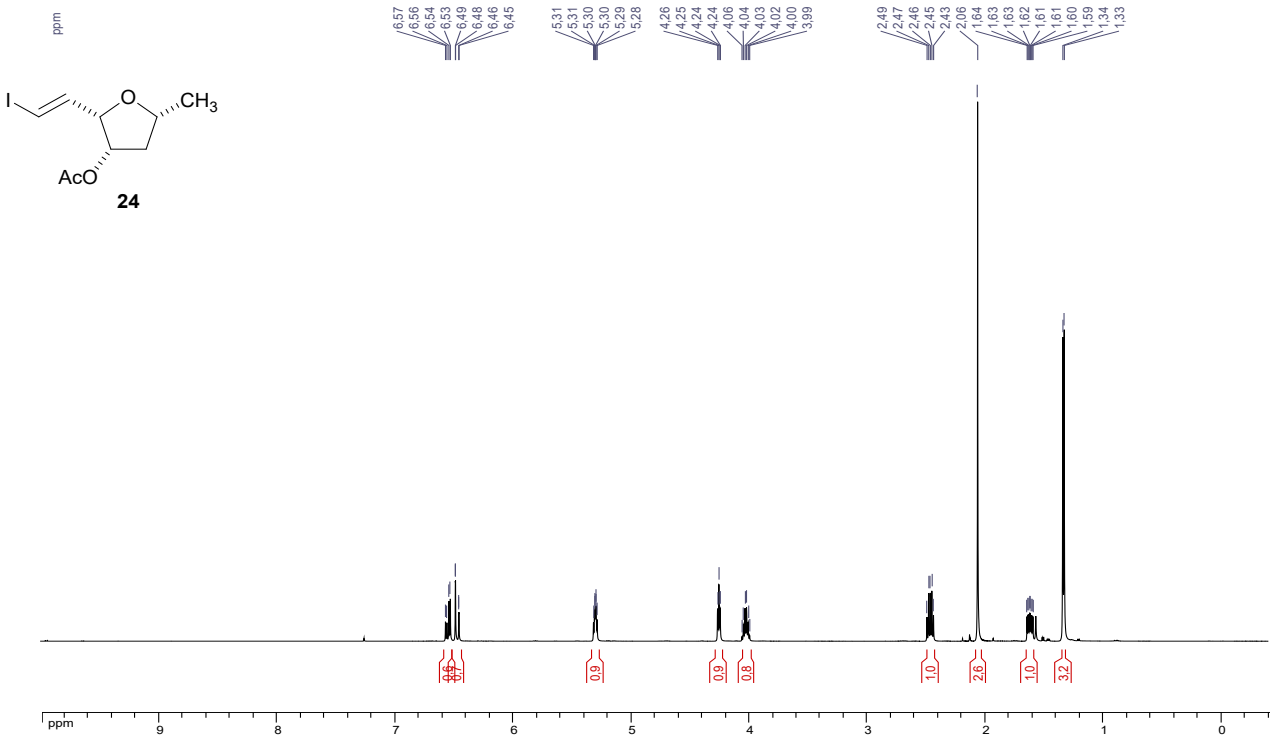


20

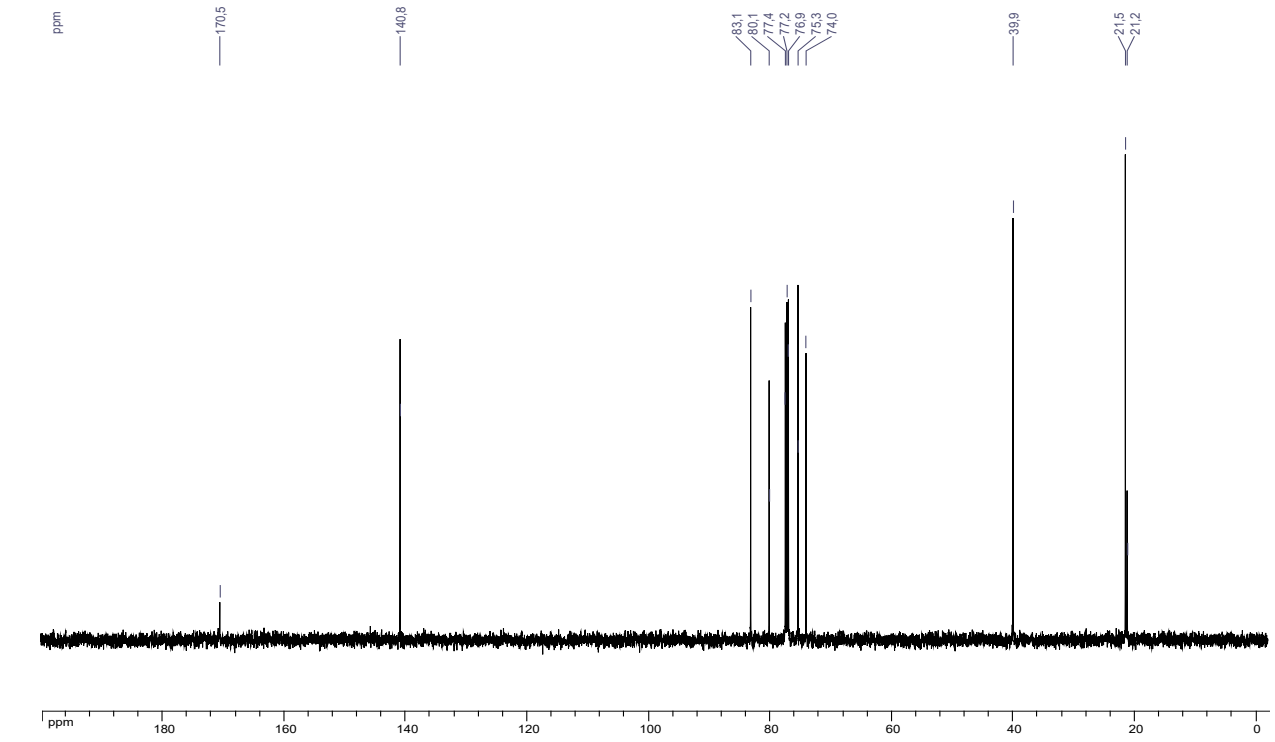
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 20



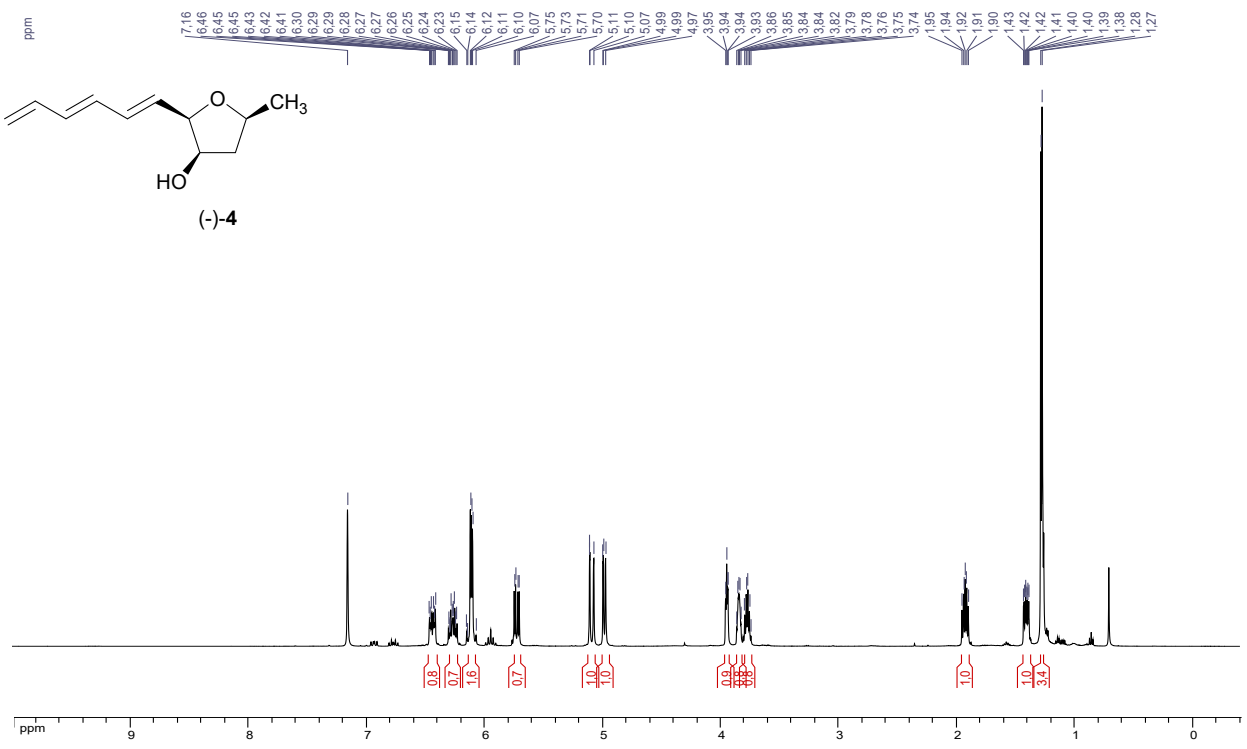
^{1}H NMR ($CDCl_3$, 500.1 MHz) of 24



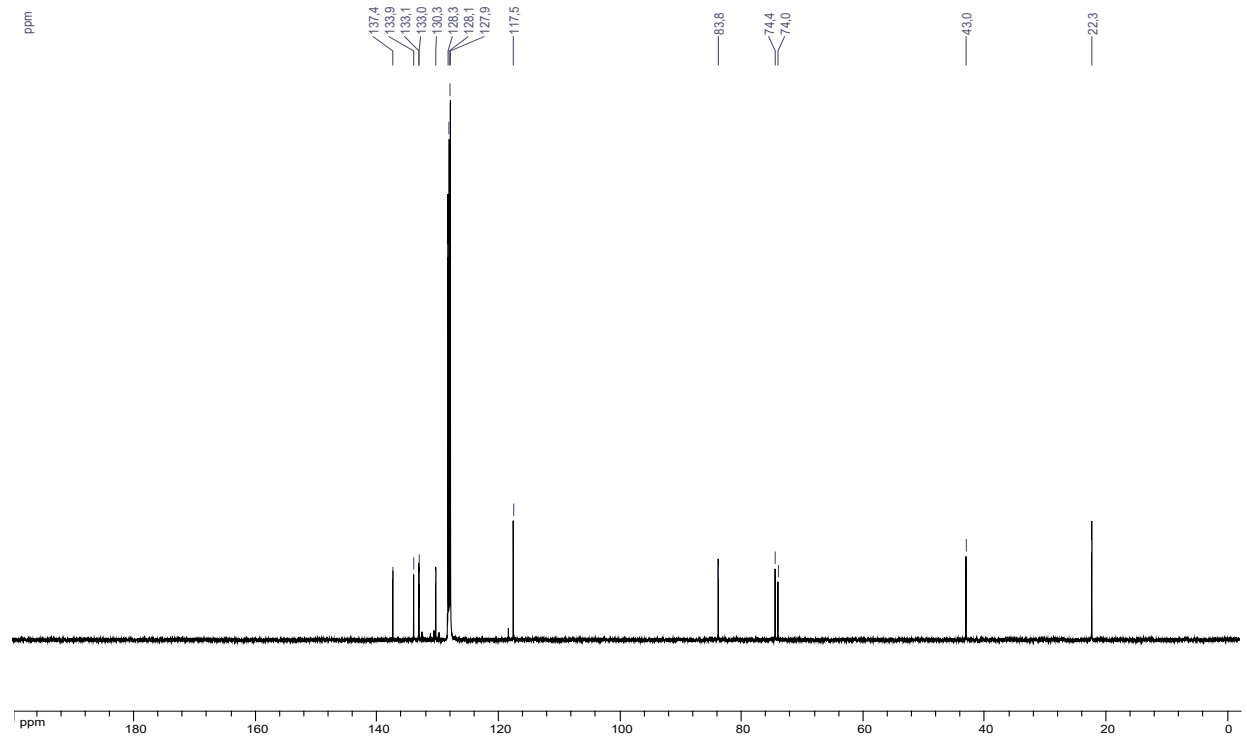
^{13}C NMR ($CDCl_3$, 125.8 MHz) of 24



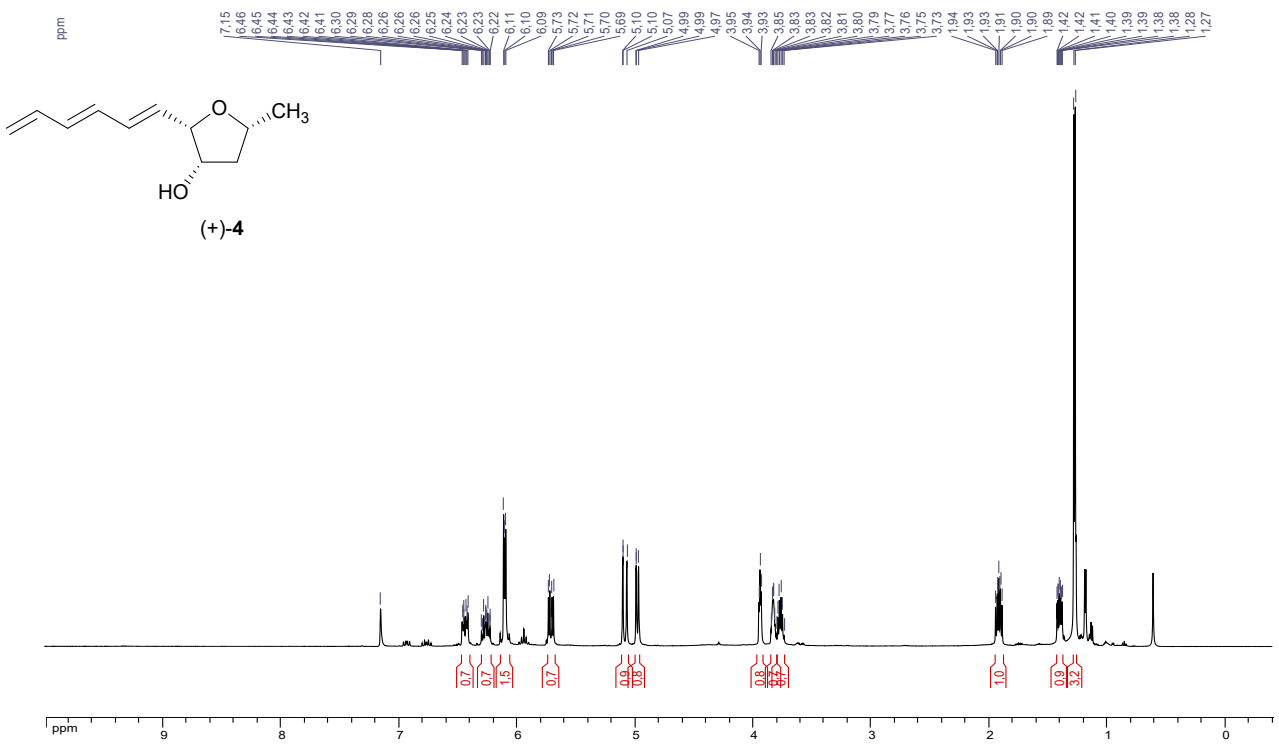
^{1}H NMR (C_6D_6, 500.1 MHz) of trienylfuranol A (-)-4



^{13}C NMR (C_6D_6, 125.8 MHz) of trienylfuranol A (-)-4

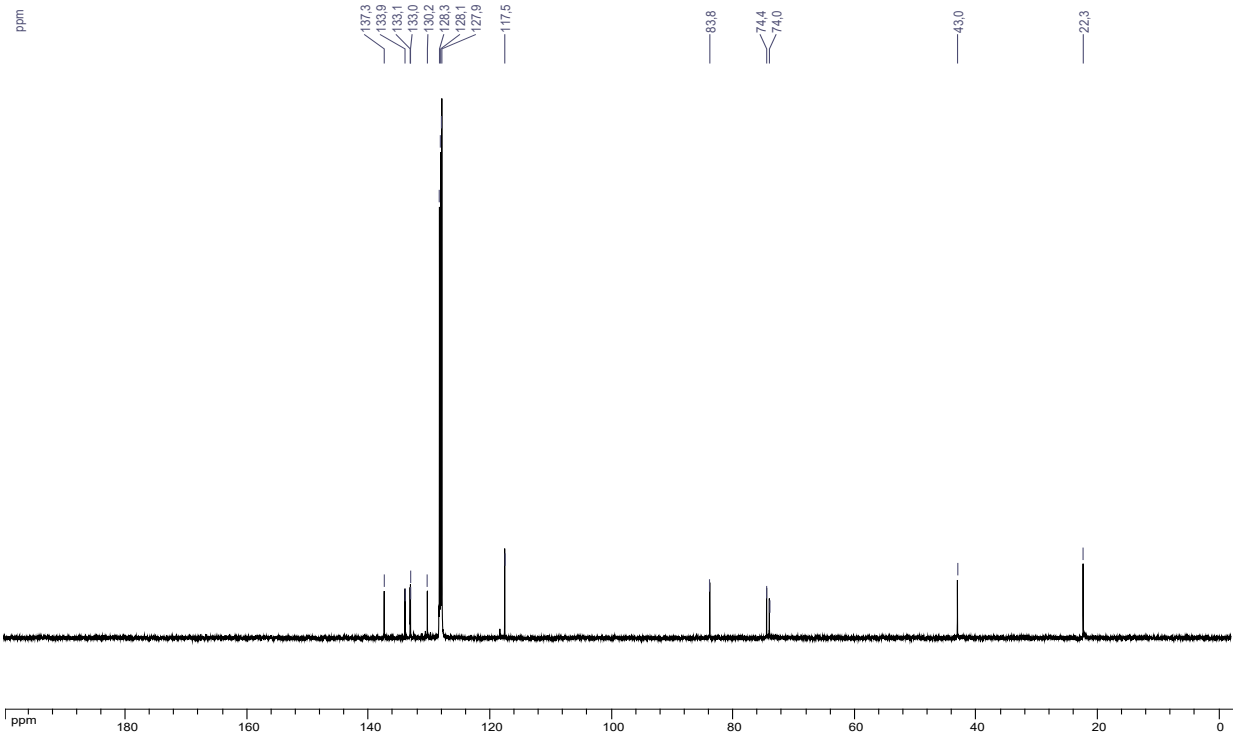


^{1}H NMR (C_6D_6, 500.1 MHz) of trienylfuranol A (+)-4

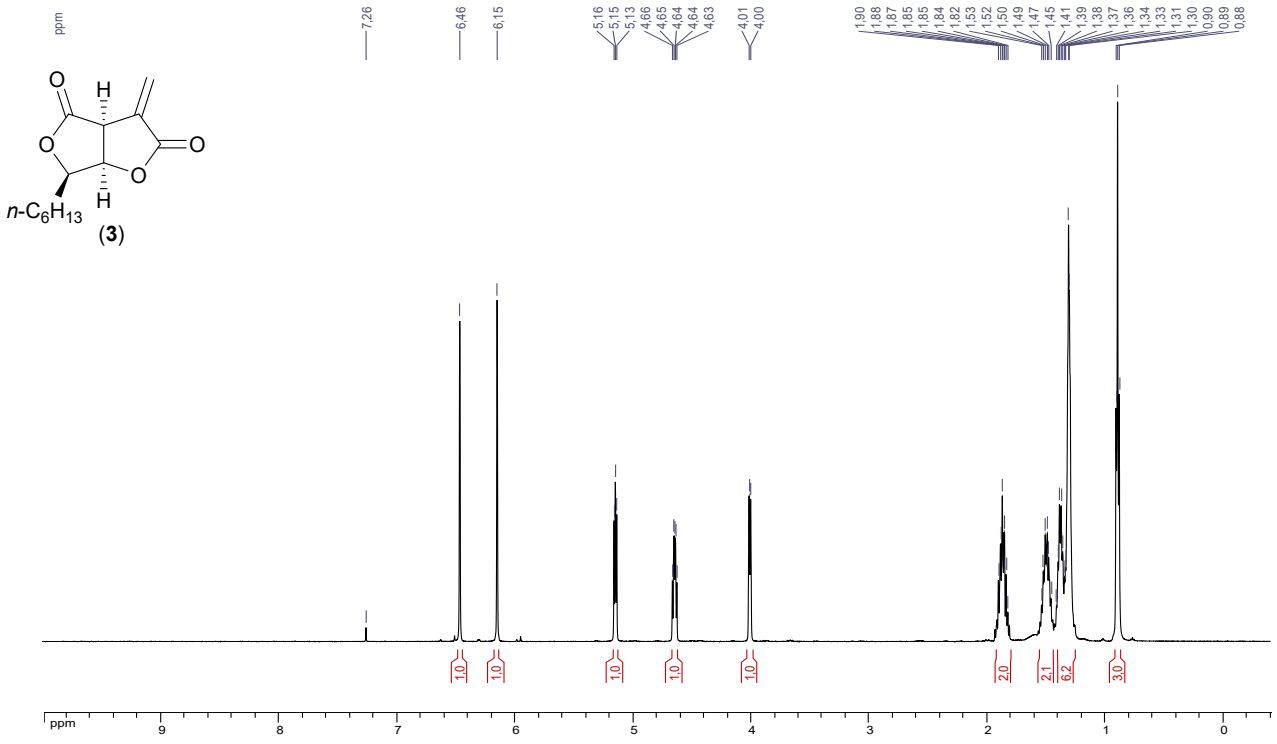


(+)-**4**

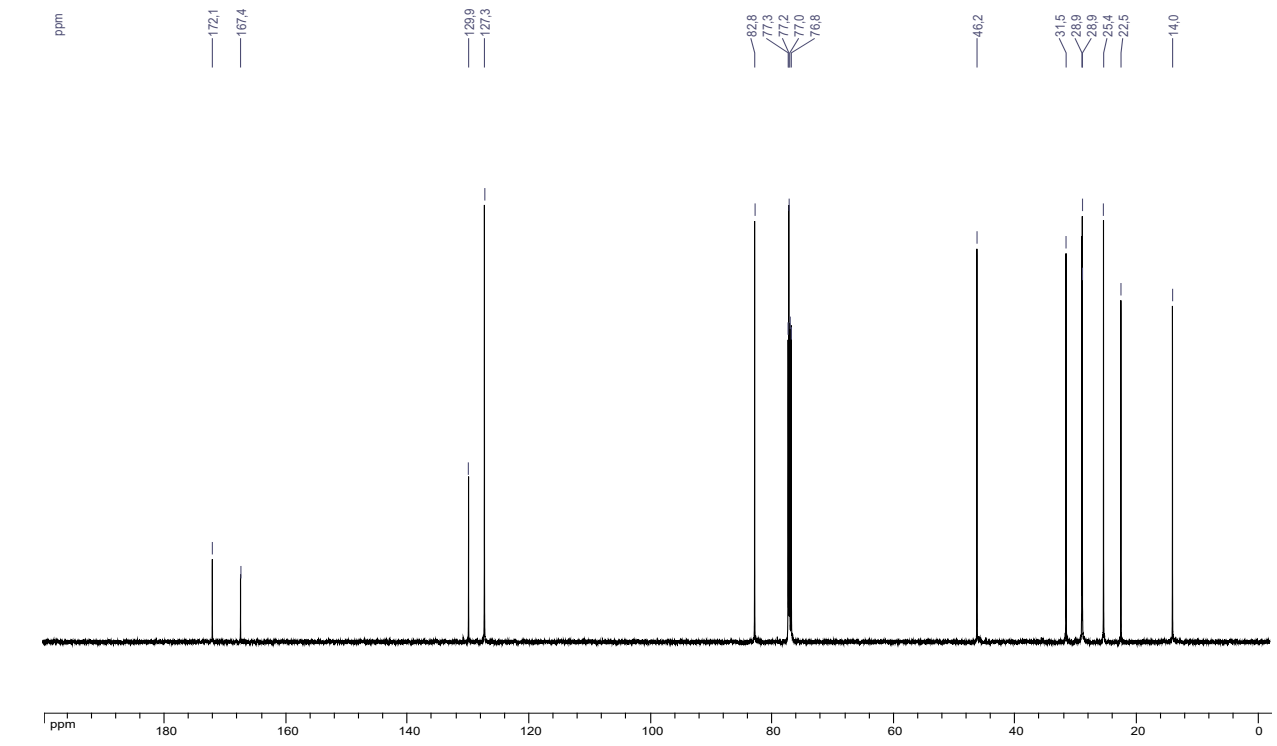
^{13}C NMR (C_6D_6, 125.8 MHz) of trienylfuranol A (+)-4



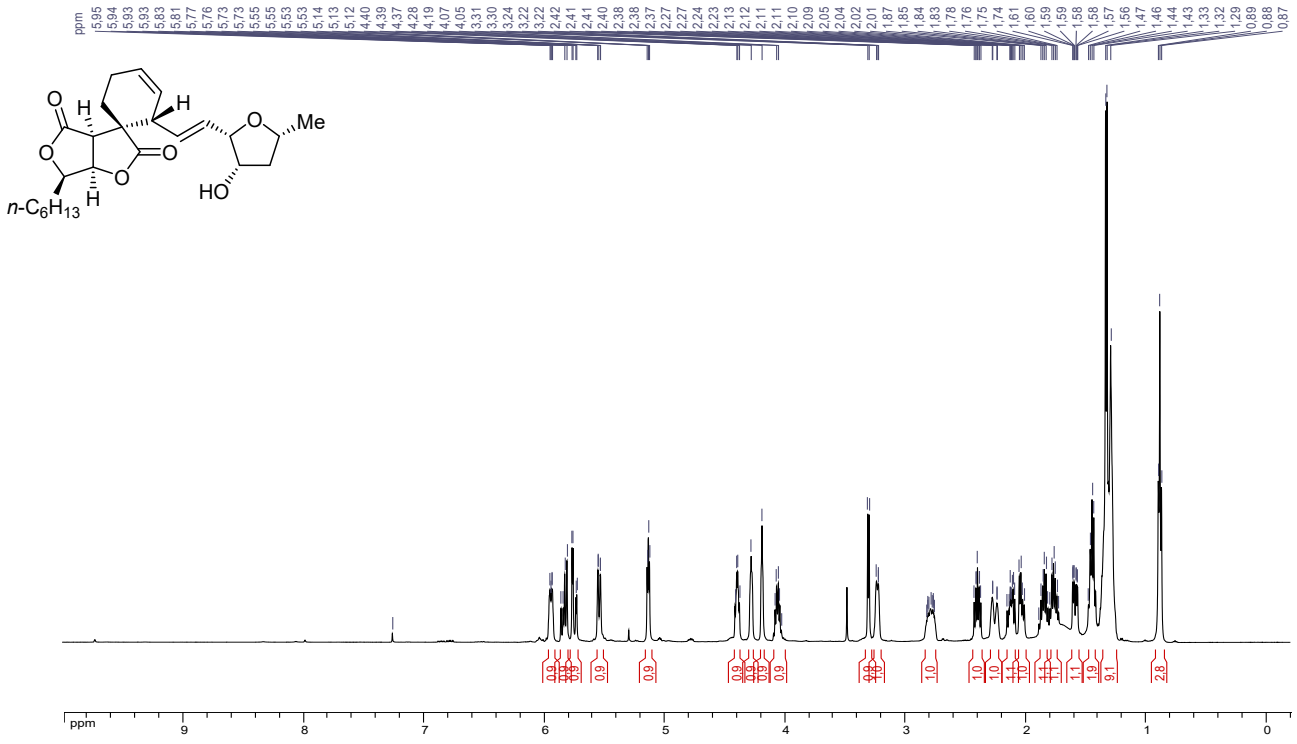
^{1}H NMR ($CDCl_3$, 500.1 MHz) of sporothriolide



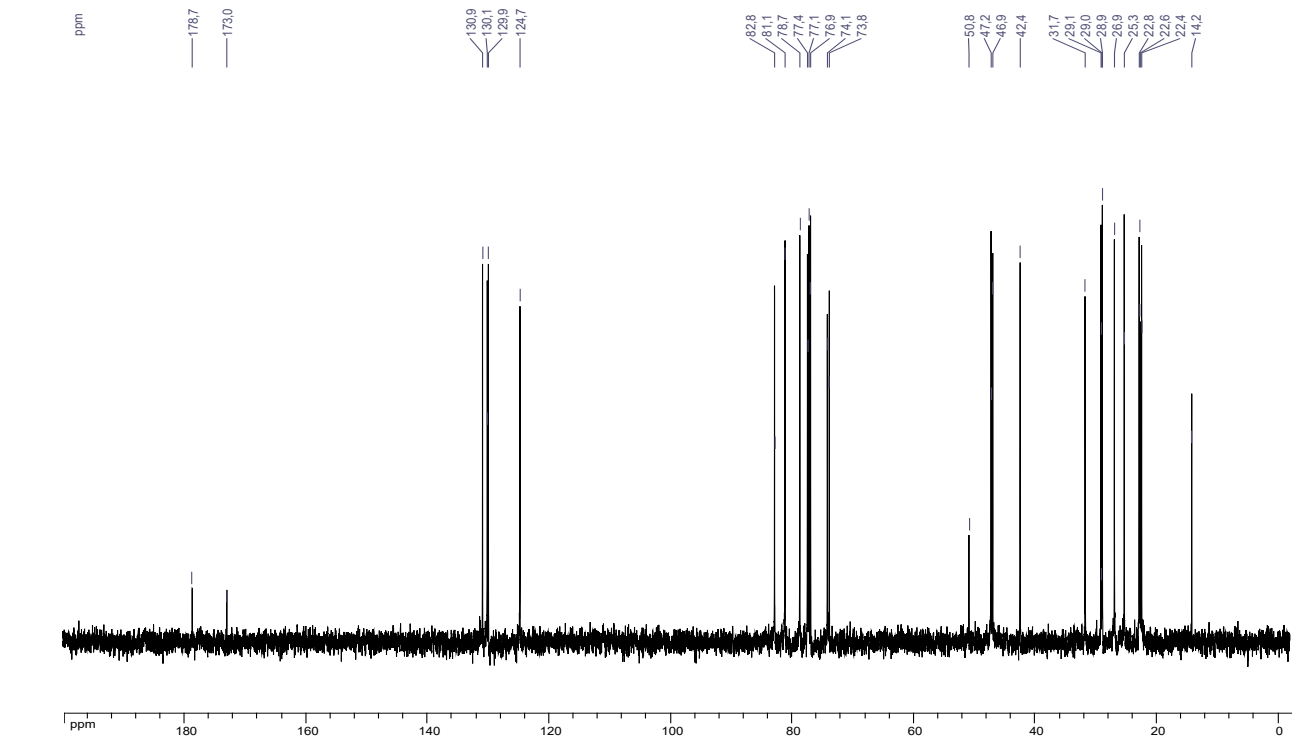
^{13}C NMR ($CDCl_3$, 125.8 MHz) of sporothriolide



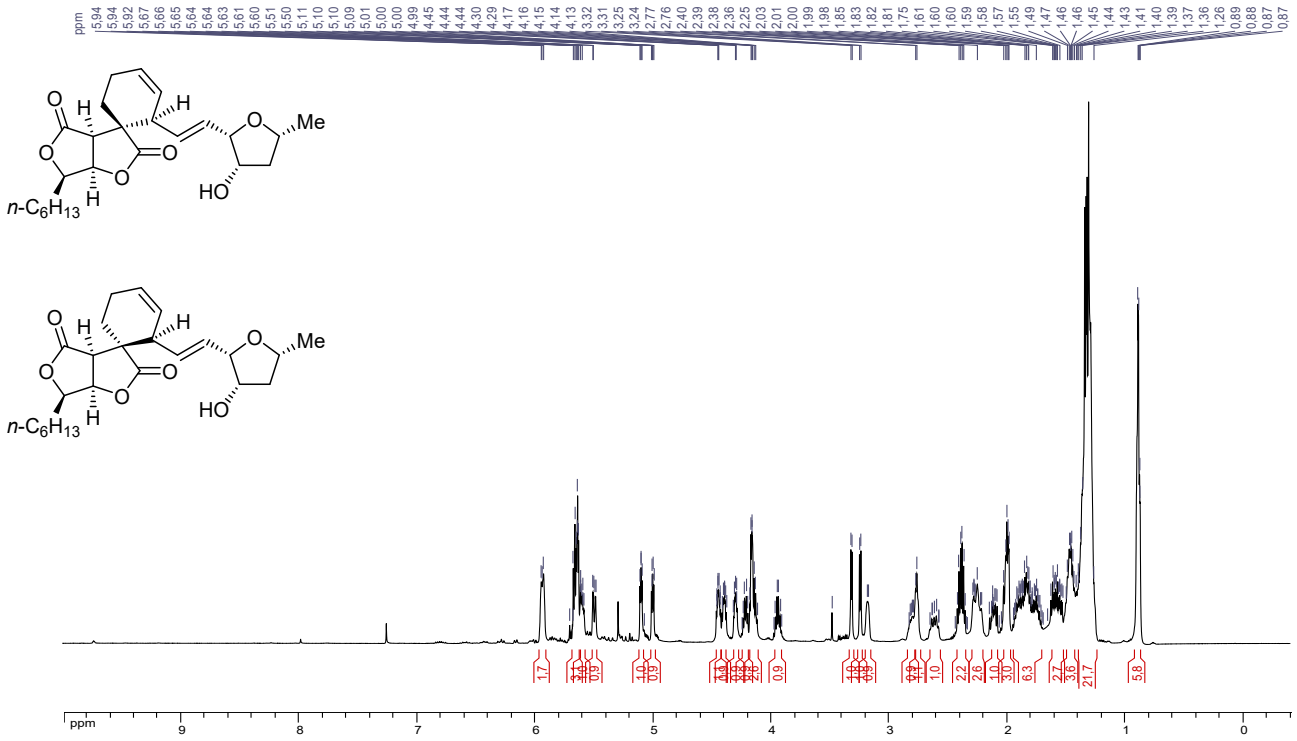
^{1}H NMR ($CDCl_3$, 500.1 MHz) of Sporochartine B



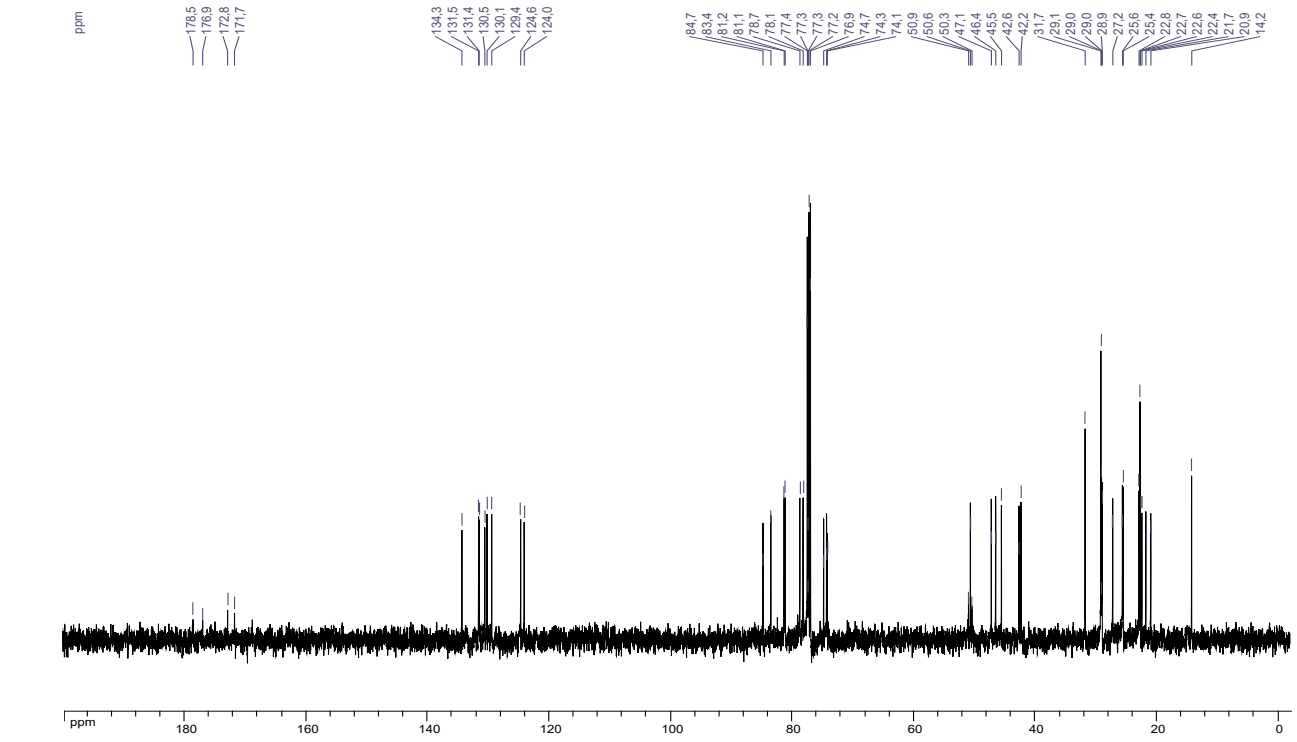
^{13}C NMR ($CDCl_3$, 125.8 MHz) of Sporochartine B



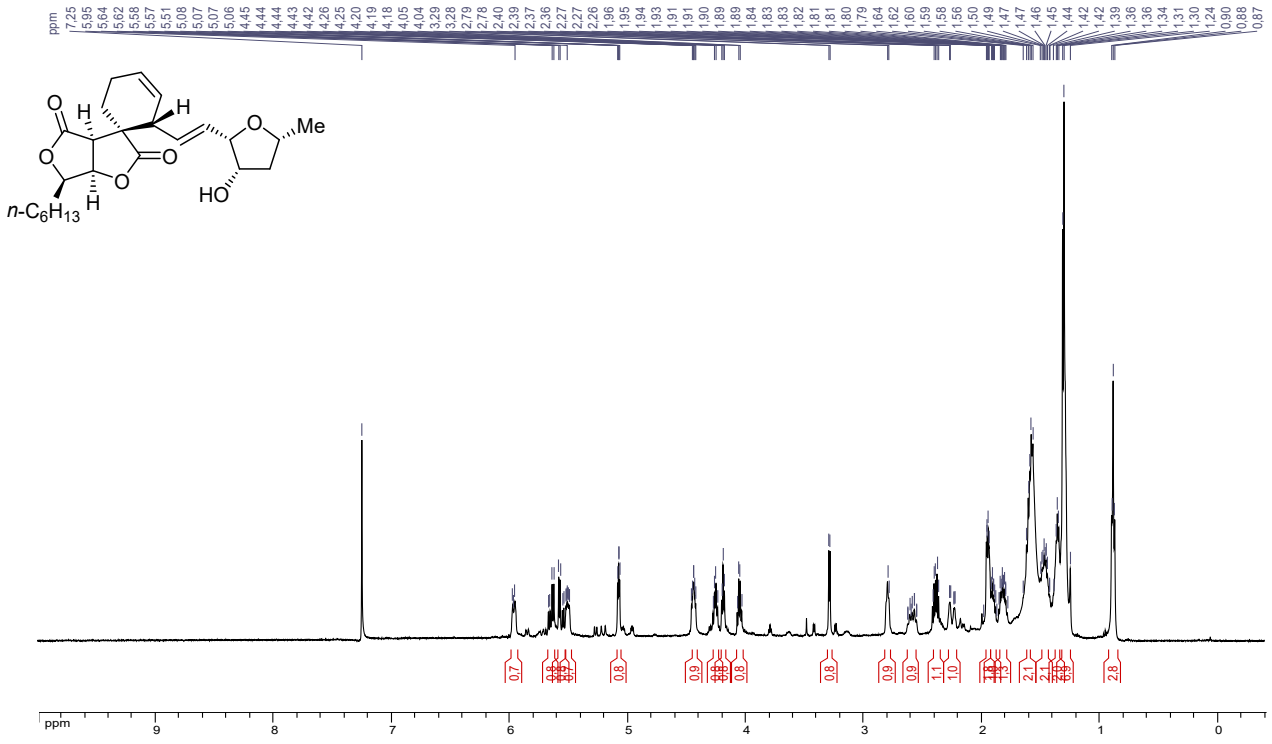
^{1}H NMR ($CDCl_3$, 500.1 MHz) of Sporochartines A/C mixture



^{13}C NMR ($CDCl_3$, 125.8 MHz) of Sporochartines A/C mixture

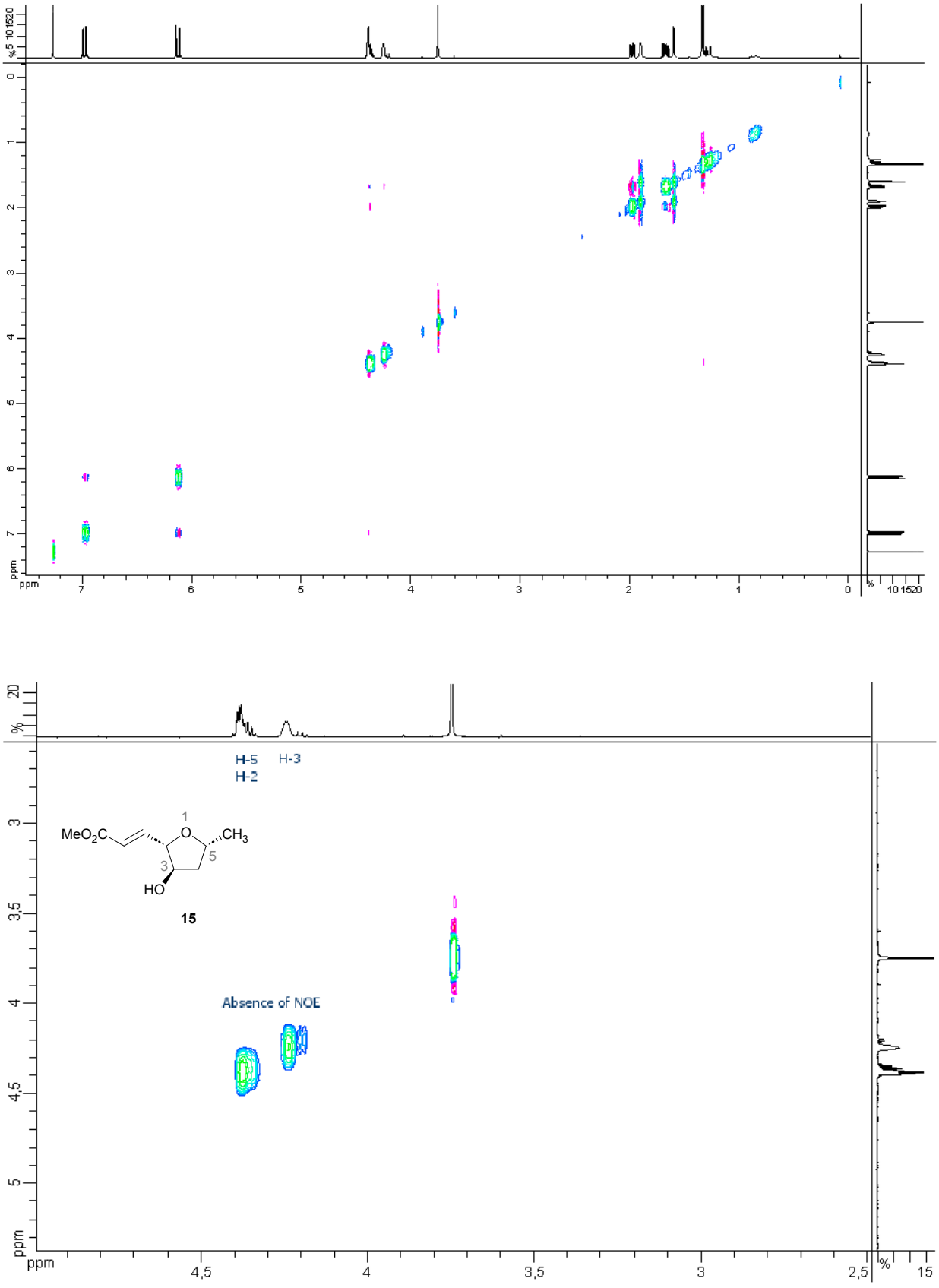


^{1}H NMR ($CDCl_3$, 500.1 MHz) of Sporochartine D

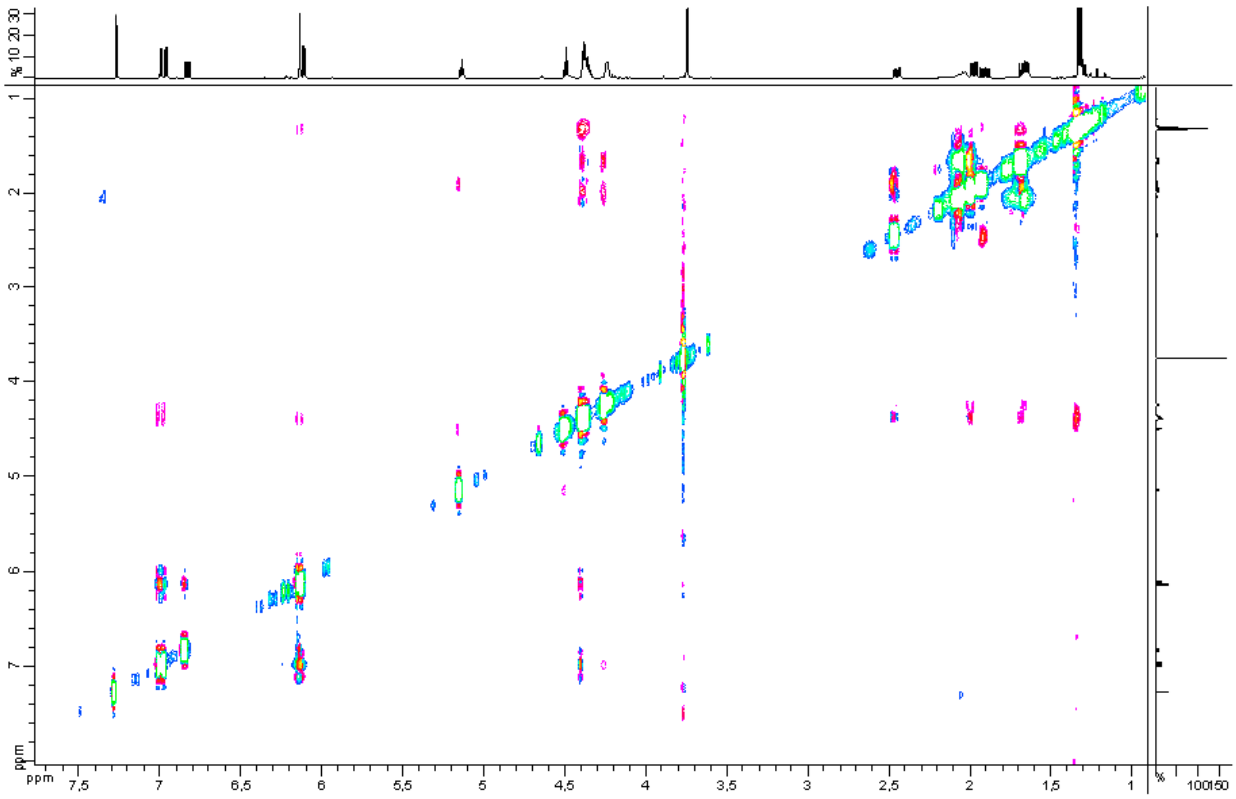


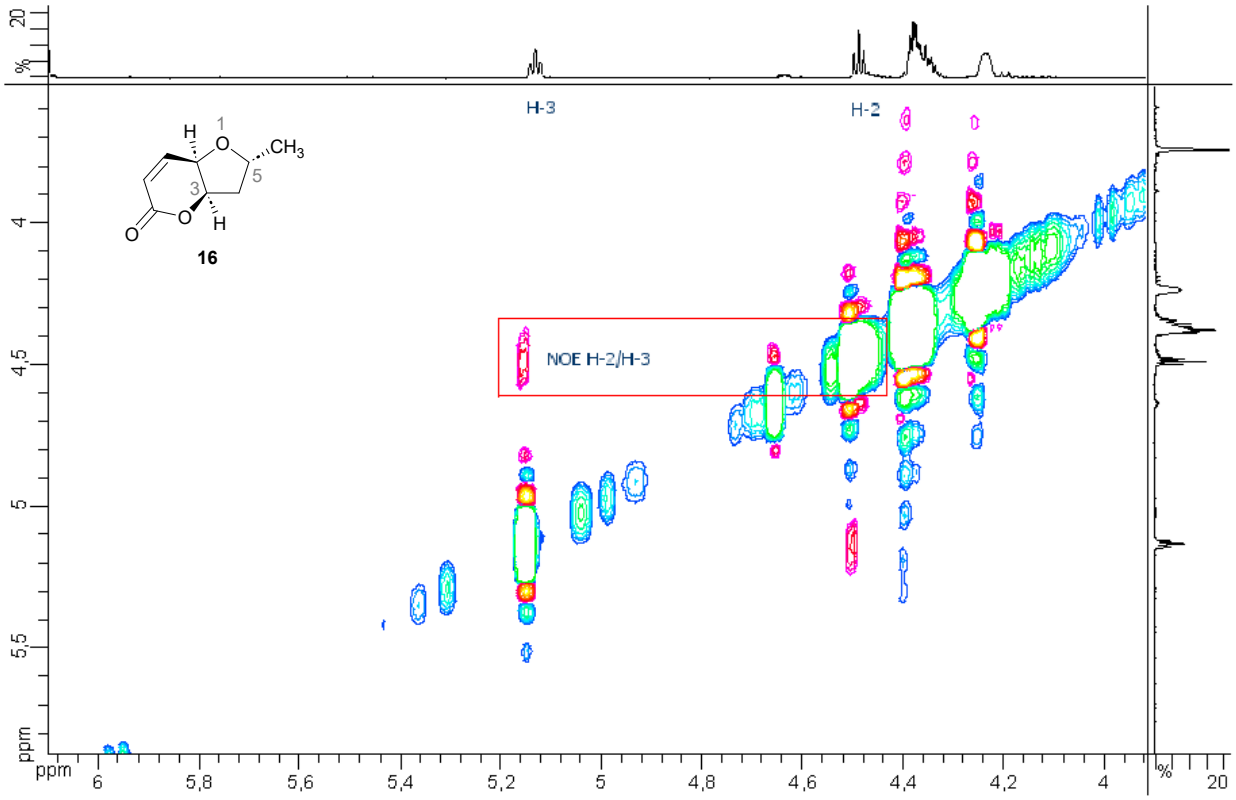
V - NMR 2D Experiments

NOESY Spectrum of compound 15 (500.1 MHz, $CDCl_3$)



NOESY Spectrum of the mixture of compounds 15 and 16 (500.1 MHz, $CDCl_3$)





VI - X-Ray crystal structure determination of compound 17

Experimental

Crystals of compound **17** were obtained by liquid-liquid diffusion dichloromethane/*n*-hexane.

Single crystals suitable to X-ray diffraction structural analyses were transferred upon a microscope slide and one of them selected under a binocular, mounted on a nylon loop and fixed with Paratone® oil. Then, X-ray diffraction and crystallographic data were collected at 100 K using redundant ω scans on a Rigaku XtaLabPro single-crystal diffractometer using microfocus Mo Kα radiation and a HPAD PILATUS3 R 200K detector. CrysAlisPro 1.171.39.46[4] was employed for the data processing, with SCALE3 ABSPACK scaling algorithm implemented for the empirical absorption correction using spherical harmonics.

Using Olex2,[5] the structures was readily solved by intrinsic phasing methods (SHELXT[6]), and by full-matrix least-squares methods on F^2 using SHELXL.[6] The non-hydrogen atoms were refined anisotropically, and hydrogen atoms, most of them were identified in difference maps and were treated as riding on their parent atoms.

The Flack parameter[7] was also refined. The determination of the absolute structure was confirmed by using Bayesian statistics on Bijvoet differences[8] based on the Olex2 results and the characterized enantiopure compound **17** was confirmed by the use of enantiopure (*R*)-epichlorhydrine **7** as starting material.

The molecular graphics presented here were computed with Mercury 2020.3.0.[9]

Crystallographic data have been deposited in the Cambridge Crystallographic Data Centre database (the deposition number is 2269175). Copies of the data can be obtained free of charge from the CCDC at https://www.ccdc.cam.ac.uk/structures/

Crystal data for compound 17

$C_{16}H_{16}N_2O_9$, M_r =380.31, triclinic, $P2_1$ (No. 4), a = 10.3384(5) Å, b = 5.3232(2) Å, c = 16.2069(9) Å, β = 107.001(6)°, V = 852.95(8) Å^3, Z = 2, T = 100.15 K, μ(MoKα) = 0.123, 30178 reflections measured, 3502 unique (R_{int} = 0.0602) which were used in all calculations. The final wR_2 was 0.0672 (all data) and R_1 was 0.0283 (I > 2σ(I)) . The goodness of fit on F2 was 1.078. Flack parameter = -0.1(4). Hooft parameter = -0.1(3).

Figure S1. ORTEP drawing of 17

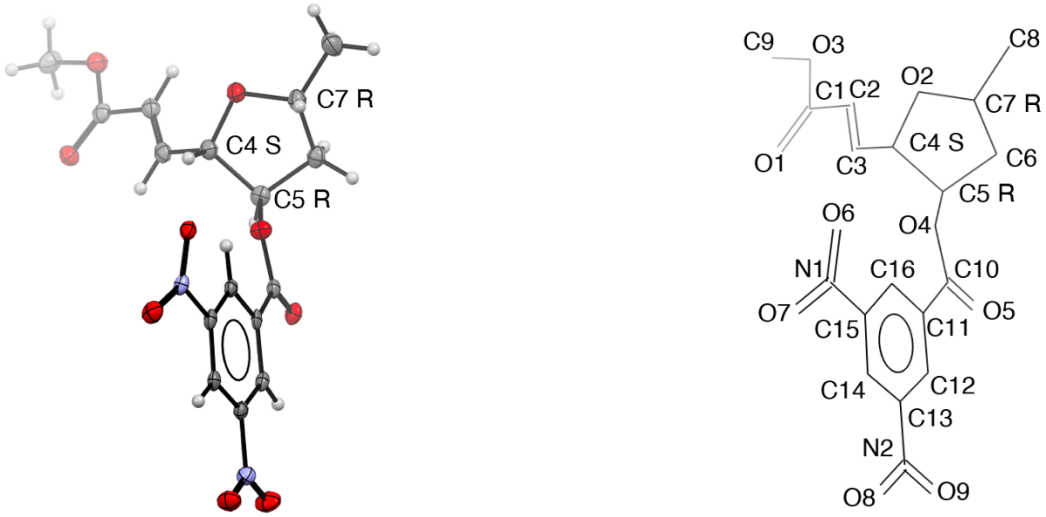


Figure S1: (left) ORTEP drawing of **17** with thermal ellipsoids drawn at the 50% probability level and (right) Labelling scheme of the structure.

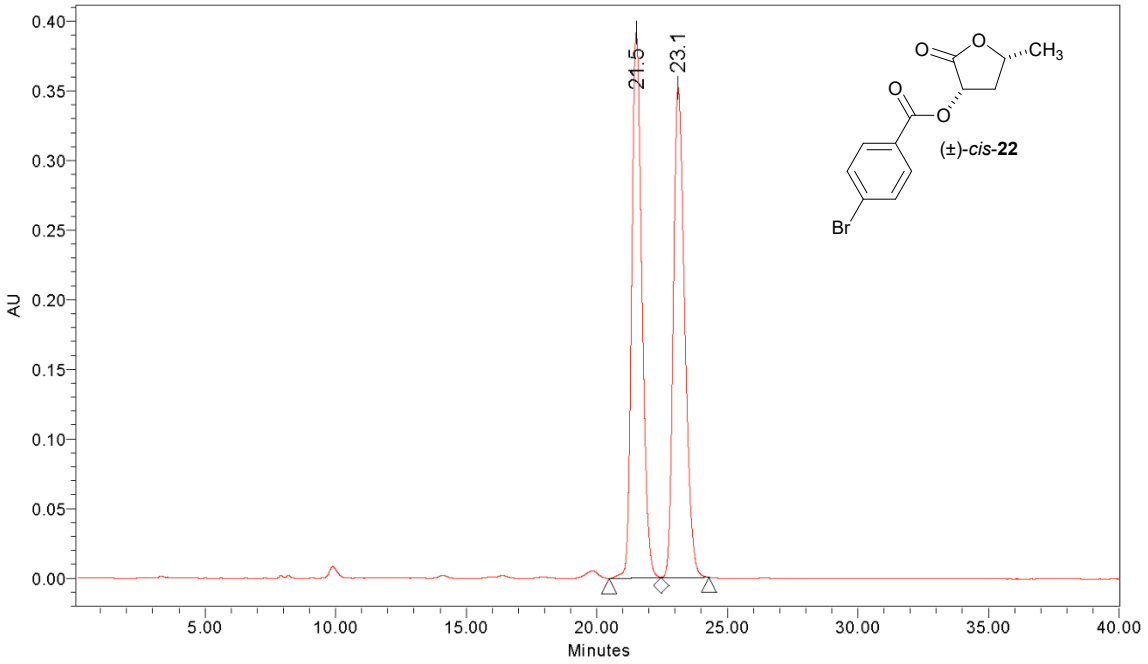
Table S3. Crystal data and structure refinement

Compound Identification code		**17**
Empirical Formula		$C_{16}H_{16}N_2O_9$
Formula Weight		380.31
Crystal Color, Habit		[clear light colourless, rect.Prism]
Crystal Dimensions (mm^3)		0.35 × 0.04 × 0.02
Crystal System		monoclinic
Space Group		$P2_1$
Unit cell dimensions	*a* (Å)	10.3384(5)
	b (Å)	5.3232(2)
	c (Å)	16.2069(9)
	α (°)	90
	β (°)	107.001(5)
	γ (°)	90
Volume (Å3)		852.94(7)
Z value		2
Calculated density $D_{calc.}$ (g.cm^{-3})		1.481
Absorption coefficient μ (mm^{-1})		0.123
F (000)		396.0
Diffractometer		Rigaku XtaLAB PRO
Radiation type		Mo K_α
Wavelength (Å)		0.71073
Voltage, Current (kV, mA)		(50, 0.6)
***T* (K)**		100.15
2θ range for data collection (°)		7.57 to 52.038
Limiting indices		-12 ≤ h ≤ 12, -6 ≤ k ≤ 6, -20 ≤ l ≤ 20
Reflections collected/unique		30178/3502
Completeness to θ full (%)		99.6
R_{int}		0.0602
Absorption correction		Semi-empirical from equivalents
Refinement method		Full-matrix least-squares on F^2
Data/restraints/parameters		3502/1/283
Goodness-of-fit on F^2		1.078
Final R indices [*I*>2σ(*I*)]	R_1 wR_2	0.0283 0.0658
R indices (all data)	R_1 wR_2	0.0311 0.0672
Absolute structure parameters **Flack Parameter** **Hooft Parameter**		 -0.1(4) -0.1(3)
Largest Δ peak and hole (e.Å^{-3})		0.17/-0.17
CCDC Deposit Number		2269175

VII - HPLC and SFC chromatograms

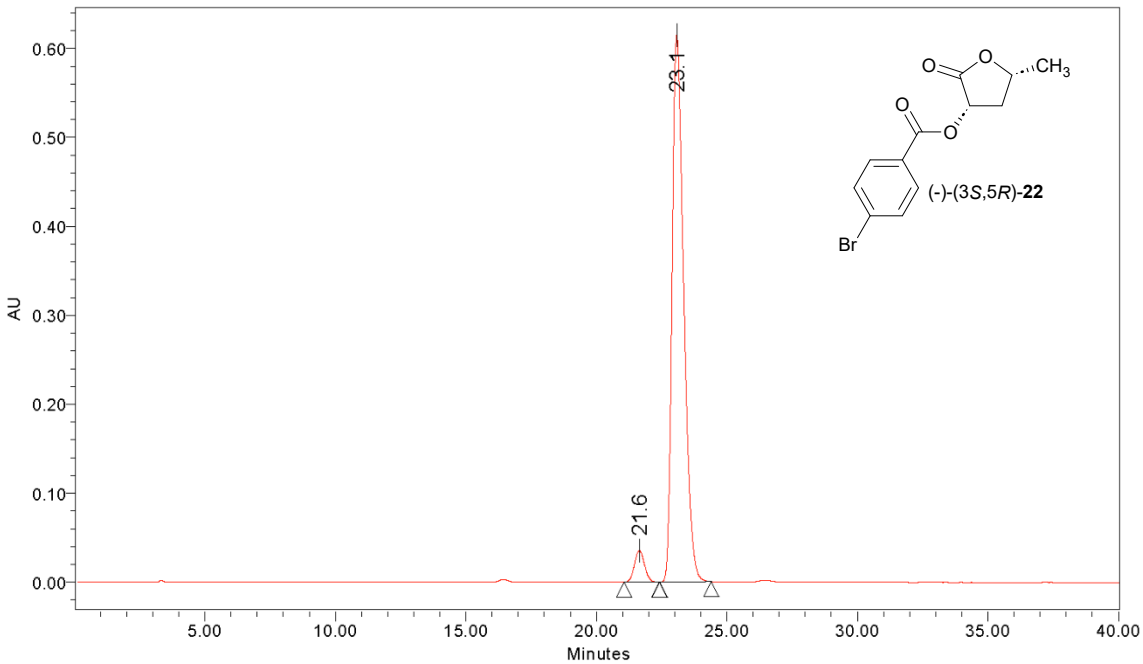
VII.1 - Chiral HPLC chromatograms of compounds (±)-*cis*-22 and (-)-(3*S*,5*R*)-22

Enantiomeric excess of compound **22** has been measured to 91% by HPLC analysis (Waters) equipped with a Chiralpak® ID column (5 µm, 10x250 mm) with *n*-heptane/*i*-propanol 85:15 as solvent at a flow rate of 1 mL.min^{-1}, a temperature of 25°C, and a detection at 250 nm.



Peak Results

	RT	Area	Height	% Area
1	21.512	10725852	392026	50.17
2	23.119	10651878	351824	49.83

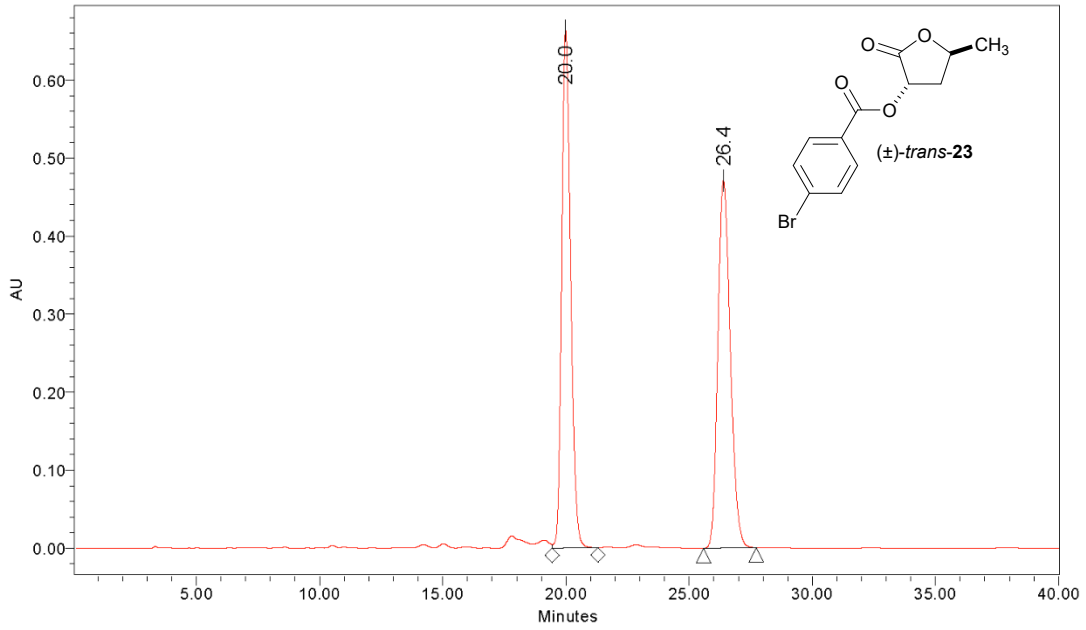


Peak Results

	RT	Area	Height	% Area
1	21.644	948279	35513	4.76
2	23.080	18963423	614892	95.24

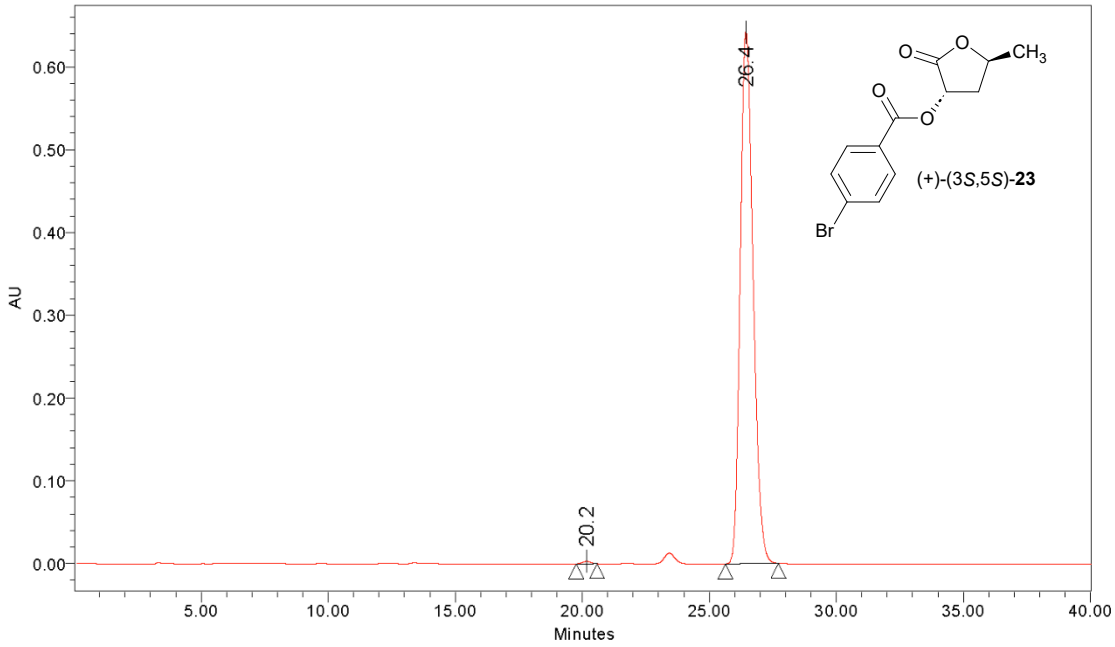
VII.2 - Chiral HPLC chromatograms of compounds (±)-*trans*-23 and (+)-(3*S*,5*S*)-23

Enantiomeric excess of compound **23** has been measured to 99% by HPLC analysis (Waters) equipped with a Chiralpak® ID column (5 µm, 10x250 mm) with *n*-heptane/*i*-propanol 85:15 as solvent at a flow rate of 1 mL.min^{-1}, a temperature of 25°C, and a detection at 250 nm.



Peak Results

	RT	Area	Height	% Area
1	19.987	16666606	663130	50.23
2	26.394	16514892	471269	49.77

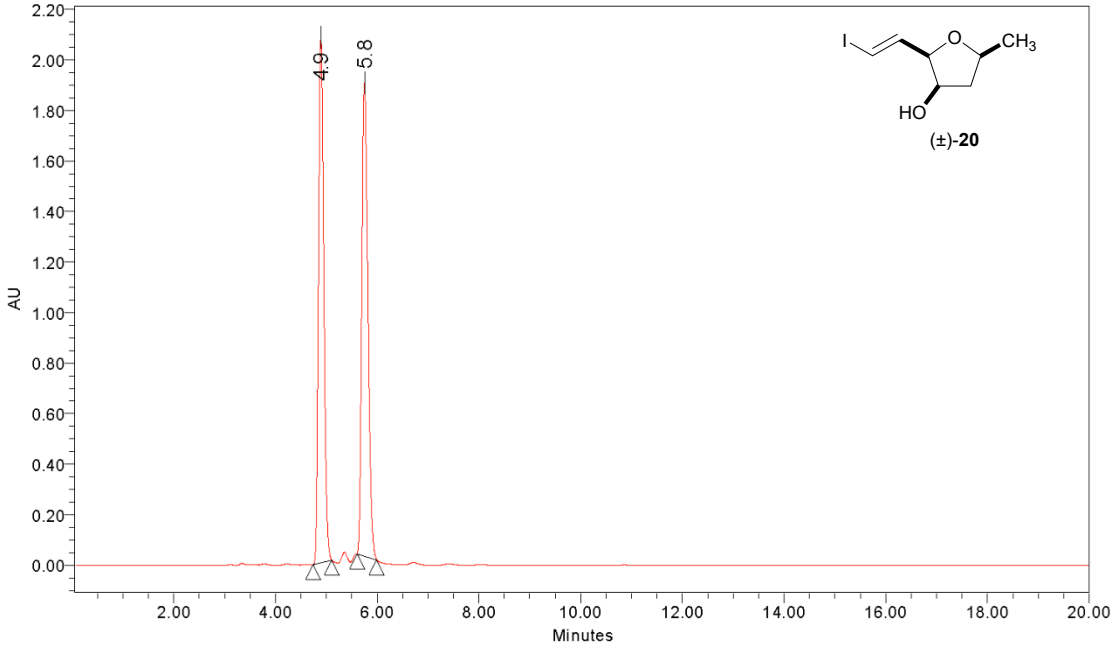


Peak Results

	RT	Area	Height	% Area
1	20.173	67232	2933	0.30
2	26.441	22532503	642765	99.70

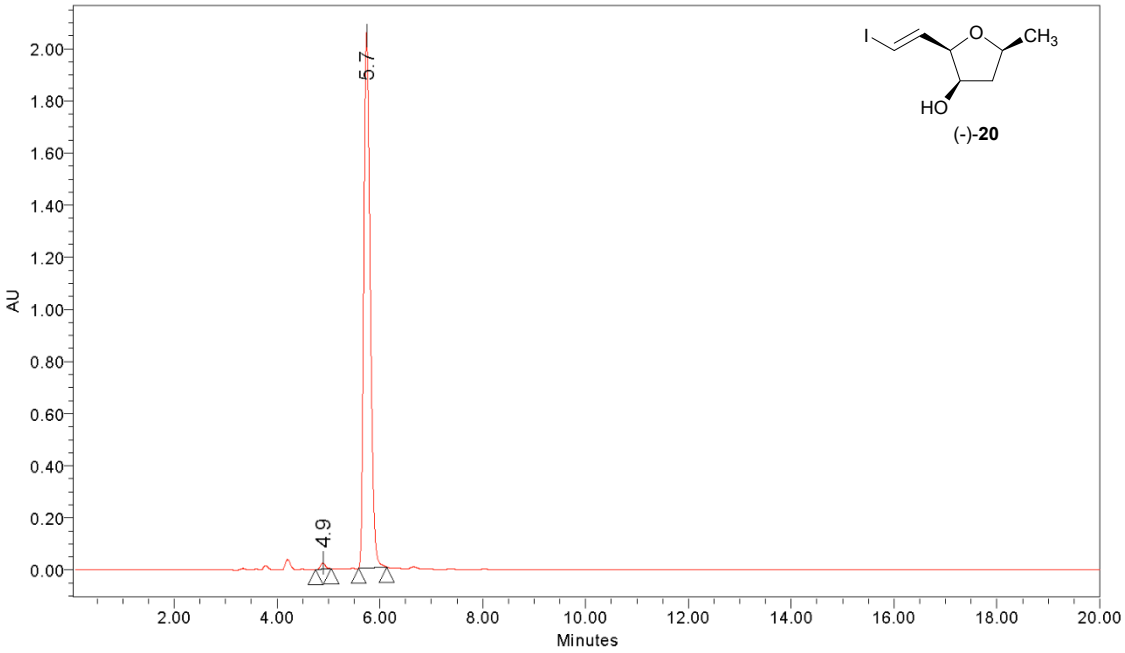
VII.3 - Chiral HPLC chromatograms of compounds (±)-20 and (-)-20

Enantiomeric excess of alcohol **20** has been measured to 99% by HPLC analysis (Waters) equipped with a Chiralpak® ID column (5 µm, 10x250 mm) with *n*-heptane/*i*-propanol 80:20 as solvent at a flow rate of 1 mL.min^{-1}, a temperature of 25°C, and a detection at 230 nm.



Peak Results

	RT	Area	Height	% Area
1	4.894	15137076	2100452	49.30
2	5.751	15565816	1883164	50.70

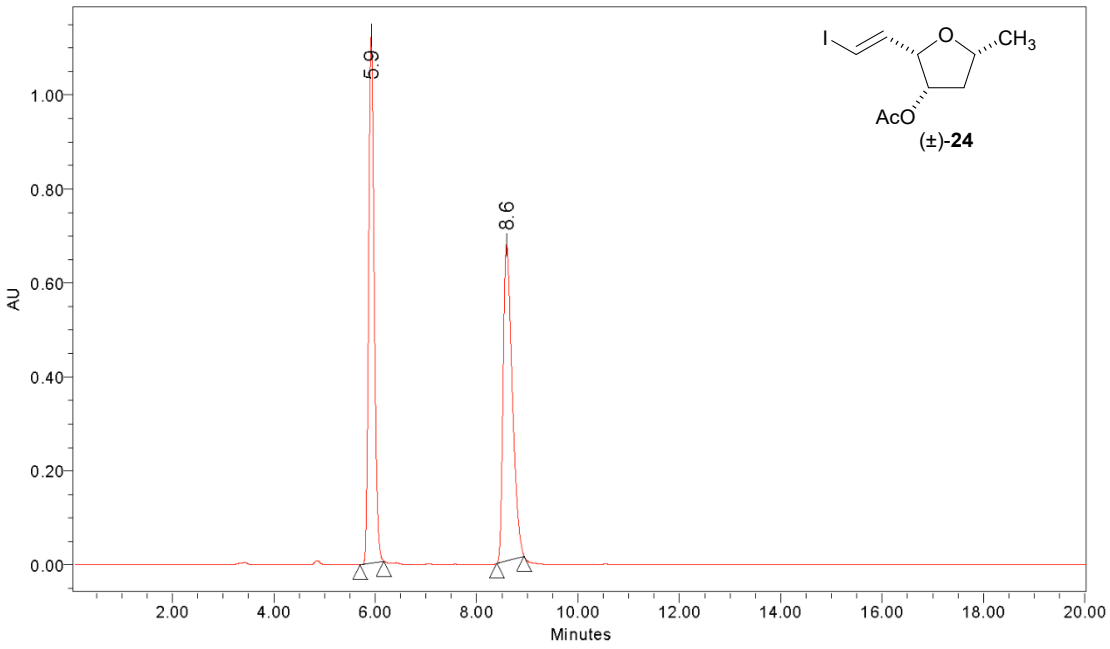


Peak Results

	RT	Area	Height	% Area
1	4.893	152623	24143	0.85
2	5.742	17850972	2063685	99.15

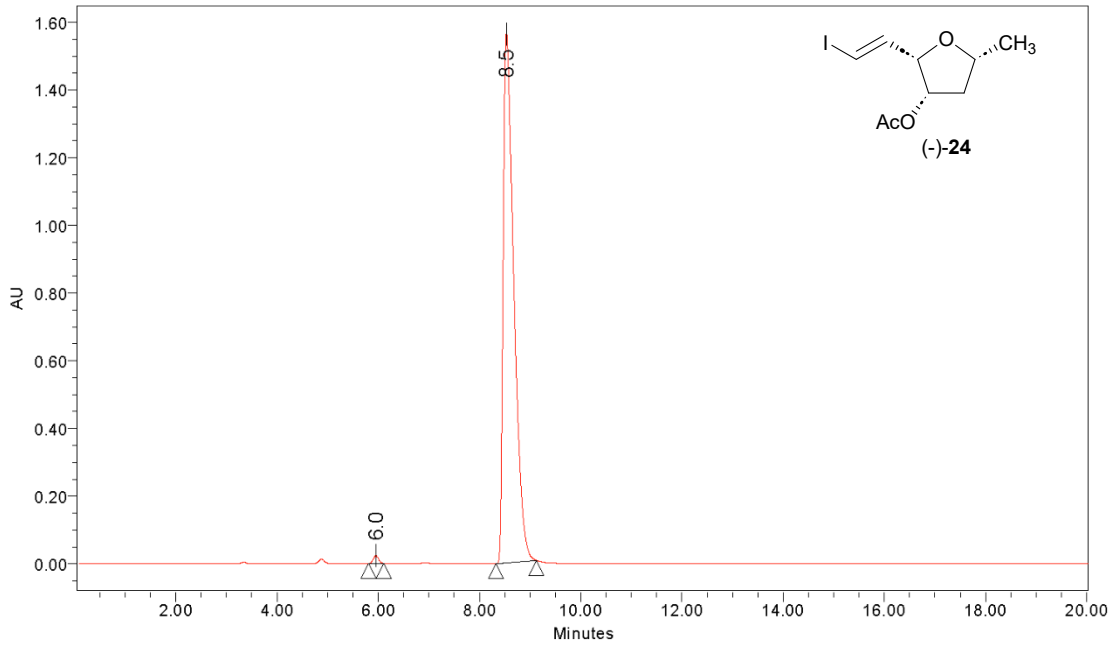
VII.4 - Chiral HPLC chromatograms of compounds (±)-24 and (-)-24

Enantiomeric excess of acetate **24** has been measured to 99% by HPLC analysis (Waters) equipped with a Chiralpak® ID column (5 µm, 10x250 mm) with *n*-heptane/*i*-propanol 95:5 as solvent at a flow rate of 1 mL.min^{-1}, a temperature of 25°C, and a detection at 230 nm.



Peak Results

	RT	Area	Height	% Area
1	5.922	8539015	1123600	50.53
2	8.594	8359841	675189	49.47



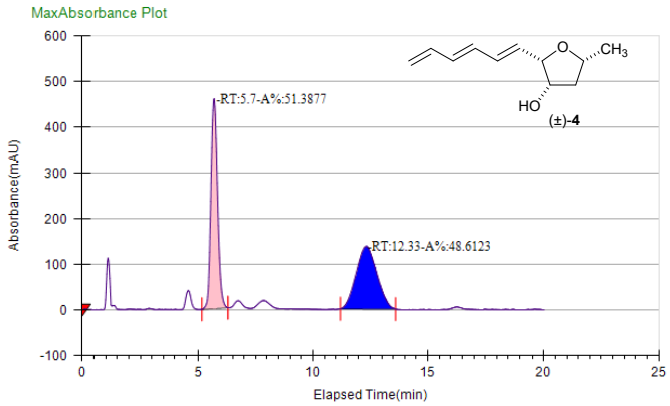
Peak Results

	RT	Area	Height	% Area
1	5.951	170159	23920	0.74
2	8.537	22726627	1576594	99.26

VII.5 - Chiral SFC chromatograms of (±)-, (-)- and (+)-trienylfuranol A 4

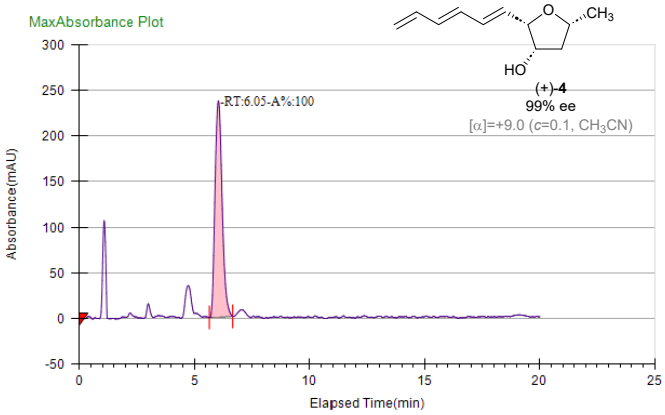
Enantiomeric excesses were determined by supercritical fluid chromatography (Thar SFC, Waters) equipped with a CHIRALPAK® IA column (5 µm, 4.6x250 mm), 25 °C, eluent: 5% *i*-PrOH in CO_2, 4 mL.min^{-1}, pressure of 100 bar, detection at UV max absorbance: retention times 5.7 and 12.3 min.

Chiral SFC chromatogram of (±)-trienylfuranol A



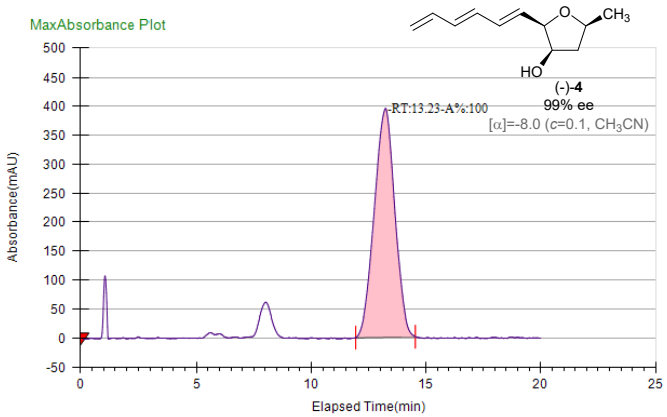
Ret. Time	Area Sum	Area %	Height
5.7 min		51.3877	458.9009
12.33 min	17553.5244	48.6123	137.1101

Chiral SFC chromatogram of (+)-trienylfuranol A



Ret. Time	Area Sum	Area %	Height
6.05 min	5043.1443	100	236.6988

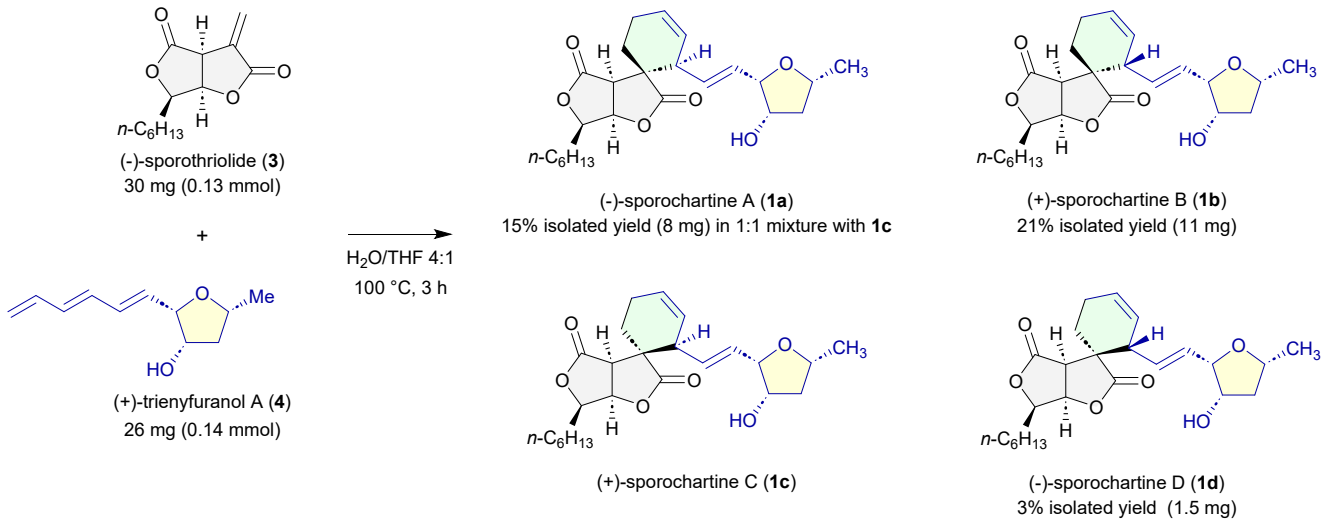
Chiral SFC chromatogram of (-)-trienylfuranol A



Ret. Time	Area Sum	Area %	Height
13.23 min	24253.2773	100	394.5088

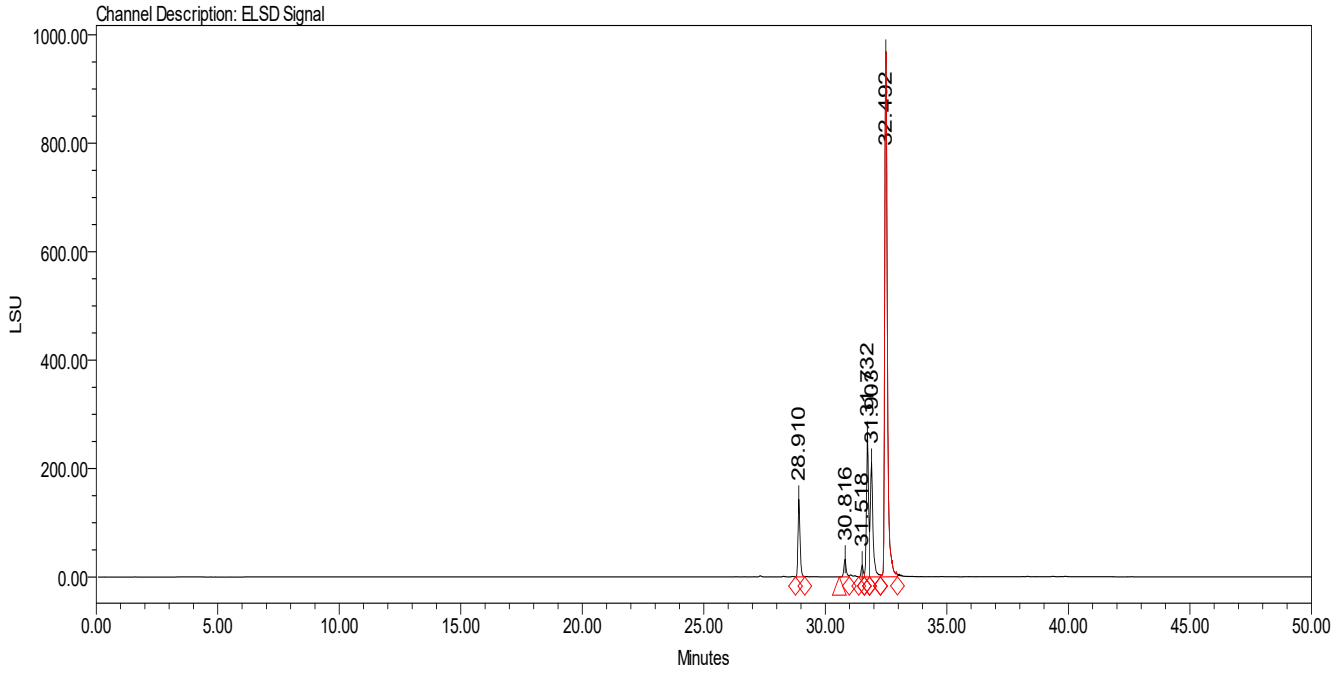
VII.6 - HPLC chromatograms analysis of Diels-Alder reaction

Diels-Alder reaction between (-)-sporothriolide and (+)-trienylfuranol A

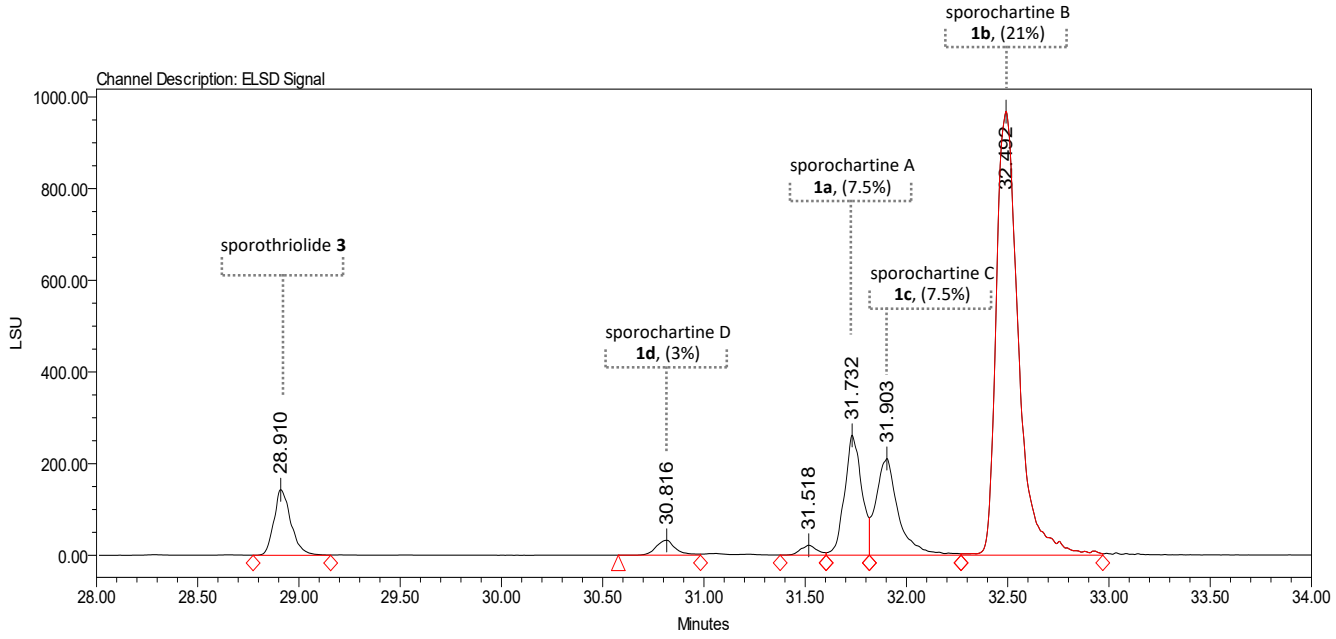


HPLC chromatogram of crude reaction mixture between (-)-sporothriolide 3 and (+)-trienylfuranol A 4

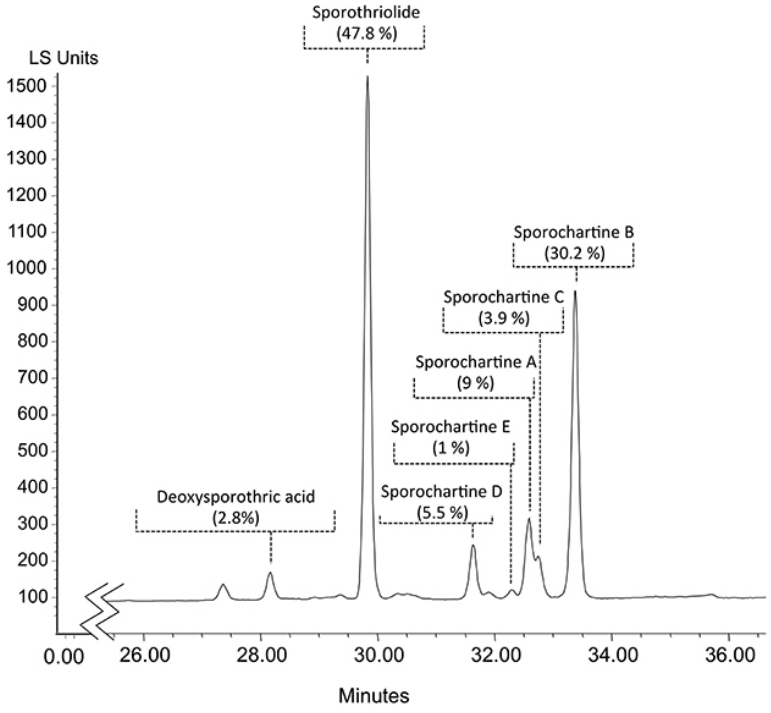
Samples were analyzed on a Waters Alliance HPLC system coupled with a photodiode array (PDA, Waters 2996), an evaporative light-scattering detector (ELSD, Waters 2424), and a mass detector (Waters, QDa). A Sunfire analytical C18 column (4.6 x 150 mm, 3.5 µm) was used with a flow rate of 0.7 mL/min. The elution gradient consisted of 100% water (+0.1% formic acid) to 100% acetonitrile (+0.1% formic acid) in 40 min, then 10 min at 100% acetonitrile (+0.1% formic acid).



Magnification of HPLC chromatogram of crude reaction mixture between (-)-sporothriolide 3 and (+)-trienylfuranol A 4



Magnification of HPLC chromatogram obtained from fermentation culture of *Hypoxylon monticulosum* CLL-205[3]



VIII - References

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