SUPPORTING INFORMATION

Multicomponent Hosomi-Sakurai Reaction on Chiral, Bio-based, Alcohols

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Summary

EXPERIMENTAL PROCEDURES

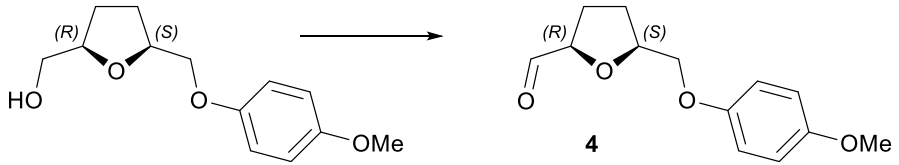
General methods

NMR spectra were taken at rt in $CDCl_3$ at 300 or 400 MHz (^1H), and 75 or 100 MHz (^{13}C), using, as internal standard, TMS (^1H NMR: 0.000 ppm) or the central peak of $CDCl_3$ (^{13}C: 77.02 ppm). Chemical shifts are reported in ppm (δ scale). Peak assignments were made with the aid of gCOSY, and gHSQC experiments. I.R. were recorded with the ATR methodology. TLC analyses were carried out on silica gel plates and viewed at UV (254 nm) and developed with Hanessian stain (dipping into a solution of $(NH_4)_4MoO_4 \cdot 4\ H_2O$ (21 g) and $Ce(SO_4)_2 \cdot 4\ H_2O$ (1 g) in H_2SO_4 (31 ml) and H_2O (469 ml) and warming) or with $KMnO_4$. R_f were measured after an elution of 7-9 cm. Column chromatographies were done with the "flash" methodology using 220-400 mesh silica. Petroleum ether (40-60 °C) is abbreviated as PE. In extractive work-up, aqueous solutions were always reextracted three times with the appropriate organic solvent. Organic extracts were always dried over Na_2SO_4 and filtered, before evaporation of the solvent under reduced pressure. All reactions using dry solvents were carried out under a nitrogen or argon atmosphere.

Preparation of trimethylsilyl ethers[1]

To a solution of alcohol (3.00 mmol) in dry CH_2Cl_2 (10 mL) iodine (60.0 µmol, 2 mol%) and hexamethyldisilazane (2.40 mmol) were added at rt. The initially colorless solution turned brown and the color faded over 10 min. Then, solid $Na_2S_2O_3 \bullet 5H_2O$ (968 mg, 3.90 mmol) was added and the reaction mixture turned colorless. The mixture was stirred for 30 min and then filtered quickly through a silica plug (1 cm) washing with CH_2Cl_2 (30 mL). The solvent was removed, and the silyl ether was used as such without further purification.

Synthesis of aldehyde 4[2]

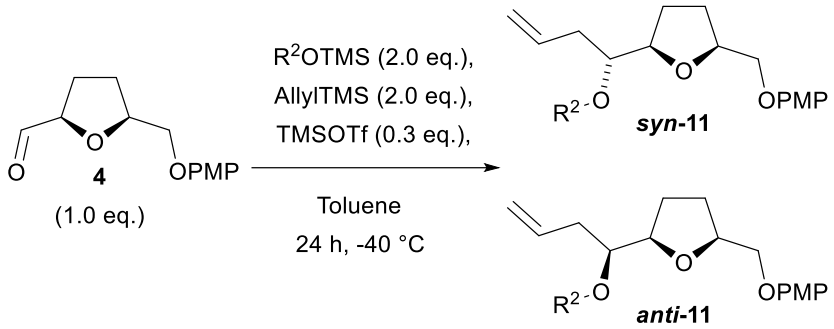


4

A two-neck flask under Ar containing dry CH_2Cl_2 (2.4 mL) and dry DMSO (150 µL, 2.10 mmol) was cooled to –78 °C. Then oxalyl chloride (1.43 M in CH_2Cl_2, 1.2 mL, 1.76 mmol) was added dropwise. After 10 min, a solution of ((*2R*,5*S*)-5-((4-methoxyphenoxy)methyl)tetrahydrofuran-2-yl)methanol[2] (200 mg, 0.839 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise and, after further 15 min, Et_3N (550 µL, 3.94 mmol) was slowly added. The mixture was stirred at –78 °C for 1 h and at –60 °C for 1.5 h. After quenching with 5% aqueous $(NH_4)H_2PO_4$ (10 mL), 2N HCl was added until pH = 4. The reaction mixture was extracted with 10:1 Et_2O/CH_2Cl_2 (3×15 mL), and the organic layer was washed with brine and dried over Na_2SO_4. After filtration and evaporation of the solvent, the crude was purified by chromatography (PE/EtOAc 6:4) to give the desired product as colorless oil (188 mg, 95%). The aldehyde was suddenly dissolved in dry toluene in order to obtain a 0.2 M solution, and treated with freshly activated 3 Å molecular sieves in rods (200 mg). The resulting suspension was kept under Ar overnight to further dry the aldehyde. This solution was used for all multiconponent Hosomi-Sakurai

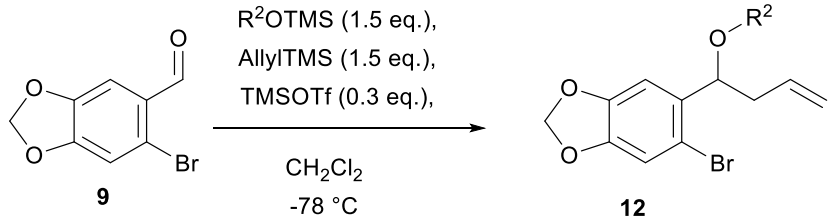
reactions. **R_f** 0.47 (PE/EtOAc 1:1). **GC-MS** (column HP-1, 12 m, Ø = 0.2 mm; flow: 1.0 ml/min (He); initial temp.: 70°C for 2 min, then increase of 20°C/min)**:** t_R = 9.04 min, *m/z* (%): 236 (29) $[M]^+$, 207 (12), 163 (43), 137 (17), 135 (7.5), 125 (14), 124 (100), 123 (30), 113 (24), 109 (42), 107 (8.2), 105 (5.3), 95 (15), 92 (12), 85 (13), 83 (39). Other data were in accordance with the literature.[2]

General procedure for the Hosomi-Sakurai MCR with aldehyde 4



In a flame-dried two-neck flask under Ar containing $CaCO_3$ (0.40 mmol) freshly prepared aldehyde **4** (0.40 mmol, 0.2 M solution in dry toluene) and the silyl ether (0.80 mmol) were added in short sequence. The solution was cooled at –40 °C (or 0 °C) and TMSOTf (0.12 mmol, 0.3 M solution in dry CH_2Cl_2) was added. After 1 h, AllylTMS (0.80 mmol) was added and the reaction mixture was stirred at –40 °C for 24 h. After quenching with aqueous saturated $NaHCO_3$ (10 mL), the mixture was extracted with Et_2O (3×15 mL) and the organic layer was washed with brine and evaporated to dryness. The crude product was purified by chromatography to give the desired products.

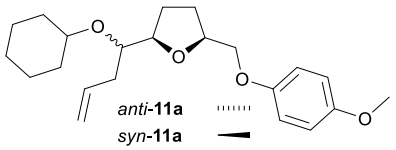
General procedure for the Hosomi-Sakurai MCR with aldehyde 9



A solution of 6-bromopiperonal (0.40 mmol) in dry CH_2Cl_2 (2 mL) under Ar was cooled at –78 °C, then the TMS ether (0.60 mmol), AllylTMS (0.60 mmol) and TMSOTf (0.12 mmol, 0.3 M solution in dry CH_2Cl_2) were added in this order. The mixture was stirred until completion (see Table 4 of the manuscript

for reaction times) and then quenched with aqueous saturated $NaHCO_3$ (10 mL). After extraction with Et_2O (3×15 mL) and washing of the organic layers with brine, evaporation and chromatography gave the desired products.

(2*R*,5*S*)-2-(1-(Cyclohexyloxy)but-3-en-1-yl)-5-((4-methoxyphenoxy)methyl)tetrahydrofuran 11a



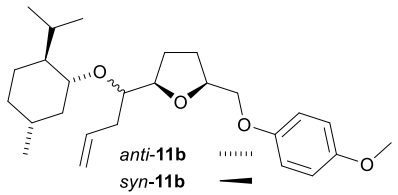
Following the general procedure, $CaCO_3$ (0.40 mmol, 40 mg), **4** (0.40 mmol, 2.0 mL, 0.2 M in dry toluene), (cyclohexyloxy)trimethylsilane **13b** (0.80 mmol, 138 mg, 160 µL), TMSOTf (0.12 mmol, 400 µL, 0.3 M in dry CH_2Cl_2) and AllylTMS (0.80 mmol, 140 µL) were reacted at –40 °C for 24 h. After workup, the crude was purified by chromatography (PE/Et_2O 9:1 to 8:2) to give *anti*-**11a** (minor, R_f 0.37, PE/Et_2O 8:2) and *syn*-**11a** (major, R_f 0.27) in 70% overall yield (102 mg) (d.r. 36:64 by HPLC).

Anti-**11a** (minor). Colorless oil. $\boldsymbol{R_f}$ 0.37 (PE/Et_2O 8:2). $\boldsymbol{[\alpha]_D}$ = +1.67 (c 1.1, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.95 – 6.74 (4 H, m, aromatic CH), 5.86 (1 H, ddt, *J* 17.2, 10.1, 7.1, C*H*=CH_2), 5.15 – 4.96 (2 H, m, CH=C*H*$_2$), 4.34 – 4.17 (1 H, m, C*H*CH_2OPMP), 4.02 – 3.81 (3 H, m, C*H*$_2$OPMP + C*H*CHOCy), 3.76 (3 H, s, OCH_3), 3.55 (1 H, td, *J* 6.0, 4.9, C*H*$CH_2CH=CH_2$), 3.46 – 3.31 (1 H, m, CH of Cy), 2.25 (2 H, ddt, *J* 7.2, 6.0, 1.2, CHC*H*$_2CH=CH_2$), 2.08 – 1.79 (6 H, m, 2×CH_2 THF part + Cy), 1.74 – 1.64 (2 H, m, Cy), 1.55 – 1.45 (1 H, m, Cy), 1.32 – 1.04 (5 H, m, Cy). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 154.0 (C-O), 153.3 (C-O), 135.4 (*C*H=CH_2), 116.8 (CH=*C*H_2), 115.6 (aromatic CH), 114.7 (aromatic CH), 82.2 (*C*HCHOCy), 77.6 (*C*HCH_2OPMP), 77.44 (*C*$HCH_2CH=CH_2$), 77.38 (CH of Cy), 71.4 (*C*H_2OPMP), 55.9 (OCH_3), 37.4 (CH*C*$H_2CH=CH_2$), 33.4 (CH_2), 33.1 (CH_2), 28.4 (CH_2), 26.1 (CH_2), 25.9 (CH_2), 24.51 (CH_2), 24.50 (CH_2). **IR** ν_{max} (cm^{-1}) 3074, 2930, 2855, 1734, 1640, 1592, 1507, 1464, 1451, 1359, 1340, 1288, 1229, 1180, 1153, 1080, 1041, 996, 911, 888, 822, 746, 713, 647. **HRMS** (ESI+): calcd. for $C_{22}H_{33}O_4^+$ $[M+H]^+$ 361.2372, found 361.2382.

Syn-**11a** (major). Colorless oil. $\boldsymbol{R_f}$ 0.27 (PE/Et_2O 8:2). $\boldsymbol{[\alpha]_D}$ = +2.12 (1.1, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.93 – 6.77 (4 H, m, aromatic CH), 5.89 (1 H, ddt, *J* 17.2, 10.1, 7.1, C*H*=CH_2), 5.14 – 4.96 (2 H, m, CH=C*H*$_2$), 4.34 – 4.19 (1 H, m, C*H*CH_2OPMP), 4.05 – 3.91 (2 H, m, C*H*CHOCy + part A of ABX C*H*$_2$OPMP), 3.86 (1 H, dd, J_{AB} 9.6, J_{BX} 5.3, part B of ABX of C*H*$_2$OPMP), 3.76 (3 H, s, OCH_3), 3.42 (1 H, dt, *J* 7.6, 4.9, C*H*$CH_2CH=CH_2$), 3.38 – 3.27 (1 H, m, CH of Cy), 2.42 – 2.26 (1 H, m, part A of C*H*$_2CH=CH_2$), 2.26 – 2.09 (1 H, m, part B of C*H*$_2CH=CH_2$), 2.08 – 1.77 (6 H, m, 2×CH_2 THF part + Cy), 1.76 – 1.62 (2 H, m, Cy), 1.60 – 1.45 (1 H, m, Cy), 1.35 – 1.07 (5 H, m, Cy). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 153.9 (C-O), 153.3 (C-O.), 135.8 (*C*H=CH_2), 116.6 (CH=*C*H_2), 115.7 (aromatic CH), 114.7 (aromatic CH), 81.6 (*C*HCHOCy), 78.8 (*C*$HCH_2CH=CH_2$), 77.6 (*C*HCH_2OPMP), 77.4 (CH of Cy), 71.3 (*C*H_2OPMP), 55.8 (OCH_3), 36.0 (*C*$H_2CH=CH_2$), 33.2 (CH_2), 33.0 (CH_2), 28.6 (CH_2), 26.9 (CH_2), 25.9 (CH_2), 24.5 (CH_2), 24.5 (CH_2). **IR** ν_{max} (cm^{-1}) 3074, 2930, 2855, 1734, 1640, 1592, 1507, 1464, 1452, 1358, 1288, 1229, 1180, 1079, 1041, 911, 888, 822, 746, 718, 639, 746, 713, 647. **HRMS** (ESI+): calcd. for $C_{22}H_{33}O_4^+$ $[M+H]+$ 361. 361.2372, found 361.2369.

(2*R*,5*S*)-2-(1-(((1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl)oxy)but-3-en-1-yl)-5-((4-methoxyphenoxy)methyl)tetrahydrofuran 11b

Following the general procedure, $CaCO_3$ (0.50 mmol, 50 mg), **4** (0.50 mmol, 2.5 mL, 0.2 M in dry toluene), (–)-menthol TMS ether **14b** (1.00 mmol, 228 mg, 263 µL), TMSOTf (0.15 mmol, 500 µL, 0.3 M in dry CH_2Cl_2) and AllylTMS (1.00 mmol, 160 µL) were reacted at –40 °C for 48 h. After workup, the

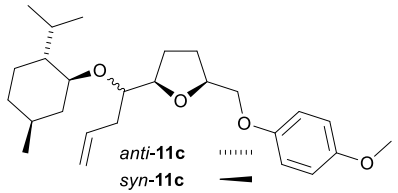


crude was purified by chromatography (PE/Et_2O 9:1) to give *anti*-**11b** (minor, R_f 0.35, PE/Et_2O 9:1) and *syn*-**11b** (major, R_f 0.30) in 65% overall yield (135 mg) (d.r. 8:92 by HPLC).

Anti-**11b** (minor). Colorless oil. $\boldsymbol{R_f}$ 0.35 (PE/Et_2O 9:1). $\boldsymbol{[\alpha]_D}$ = –47.9 (c 0.31, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$, 25 °C) δ 6.92 – 6.75 (4 H, m, aromatic CH), 5.87 (1 H, ddt, *J* 17.2, 10.1, 7.1, C*H*=CH_2), 5.14 – 4.95 (2 H, m, CH=C*H*$_2$), 4.18 (1 H, quintuplet, *J* 6.8, C*H*CH_2OPMP), 3.97 (1 H, dd, *J* 9.6, 5.9, part A of ABX C*H*$_2$OPMP), 3.95 – 3.88 (1 H, m, C*H*CHOR), 3.86 (1 H, dd, *J* 9.6, 5.1, part B of ABX C*H*$_2$OPMP), 3.76 (3 H, s, OCH_3), 3.61 (1 H, q, *J* 5.5, C*H*CH_2CH=CH_2), 3.22 (1 H, td, *J* 10.3, 4.2, CH-O menthol), 2.48 – 2.19 (3 H, m, C*H*$_2$CH=CH_2 + CH menthol), 2.09 – 1.57 (8 H, m, CH_2), 1.35 – 1.23 (1 H, m, CH menthol), 1.23 – 1.11 (1 H, m, CH menthol), 0.94 – 0.82 (8 H, m, 2×CH_3 menthol + CH_2), 0.76 (3 H, d, *J* 6.9, CH_3 menthol). **^{13}C NMR** (75 MHz, $CDCl_3$, 25 °C) δ 154.0 (C-O), 153.3 (C-O), 135.5 (*C*H=CH_2), 116.7 (CH=*C*H_2), 115.6 (aromatic CH), 114.7 (aromatic CH), 81.9 (*C*HCHOR), 78.8 (CH-O menthol), 77.6 (*C*HCH_2CH=CH_2), 77.5 (*C*HCH_2OPMP), 71.3 (*C*H_2OPMP), 55.9 (OCH_3), 49.3 (CH menthol), 42.6 (CH_2 menthol), 38.0 (*C*H_2CH=CH_2), 34.6 (CH_2 menthol), 31.7 (CH menthol), 28.4 (CH_2 THF), 25.7 (CH_2 THF), 24.8 (CH menthol), 23.0 (CH_2 menthol), 22.6 (CH_3), 21.6 (CH_3), 16.6 (CH_3). **HRMS** (ESI+): calcd. for $C_{26}H_{41}O_4^+$ $[M+H]^+$ 417.29994, found 417.3007.

Syn-**11b** (major). White solid. **M.p.** 31.9–33.1 °C (PE/Et_2O). $\boldsymbol{R_f}$ 0.30 (PE/Et_2O 9:1). $\boldsymbol{[\alpha]_D}$ = –84.0 (c 0.43, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$, 25 °C) δ 6.89 – 6.78 (4 H, m, aromatic CH), 5.89 (1 H, ddt, *J* 17.0, 10.1, 7.1, C*H*=CH_2), 5.15 – 4.97 (2 H, m, CH=C*H*$_2$), 4.35 – 4.21 (1 H, m, C*H*CH_2OPMP), 4.04 (1 H, td, *J* 6.8, 5.3, C*H*CHOR), 3.95 (1 H, dd, *J* 9.5, 5.3, part A of ABX C*H*$_2$OPMP), 3.84 (1 H, dd, *J* 9.5, 5.5, part B of ABX C*H*$_2$OPMP), 3.76 (3 H, s, OCH_3), 3.44 (1 H, q, *J* 5.3, C*H*CH_2CH=CH_2), 3.13 (1 H, td, *J* 10.4, 4.1, CH-O menthol), 2.51 – 2.39 (1 H, m. part A of C*H*$_2$CH=CH_2), 2.38 – 2.27 (1 H, m, CH menthol), 2.25 – 2.14 (1 H, m, part B of C*H*$_2$CH=CH_2), 2.12 – 1.59 (7 H, m, CH_2), 1.36 – 1.13 (2 H, m, CH menthol), 1.03 – 0.79 (9 H, m, 2×CH_3 menthol + CH_2), 0.74 (3 H, d, *J* 6.9, CH_3 menthol). **^{13}C NMR** (75 MHz, $CDCl_3$, 25 °C) δ 153.9 (C-O), 153.4 (C-O), 135.5 (*C*H=CH_2), 116.8 (CH=*C*H_2), 115.6 (aromatic CH), 114.7 (aromatic CH), 80.9 (*C*HCHOR), 77.9 (*C*HCH_2OPMP), 77.7 (*C*HCH_2CH=CH_2), 76.9 (CH-O menthol), 71.4 (*C*H_2OPMP), 55.9 (OCH_3), 48.8 (CH menthol), 41.3 (CH_2 menthol), 35.4 (*C*H_2CH=CH_2), 34.7 (CH_2 menthol), 31.7 (CH menthol), 28.9 (CH_2 THF), 27.1 (CH_2 THF), 24.9 (CH menthol), 23.2 (CH_2 menthol), 22.6 (CH_3), 21.5 (CH_3), 16.2 (CH_3). **IR** ν_{max} (cm^{-1}) 3075, 2952, 2920, 2868, 1733, 1640, 1592, 1507, 1455, 1385, 1369, 1332, 1288, 1230, 1180, 1080, 1065, 1043, 999, 912, 885, 822, 790, 747, 718, 639. **HRMS** (ESI+): calcd. for $C_{26}H_{41}O_4^+$ $[M+H]^+$ 417.29994, found 417.2998.

(2*R*,5*S*)-2-(1-(((1*S*,2*R*,5*S*)-2-Isopropyl-5-methylcyclohexyl)oxy)but-3-en-1-yl)-5-((4-methoxyphenoxy)methyl)tetrahydrofuran 11c



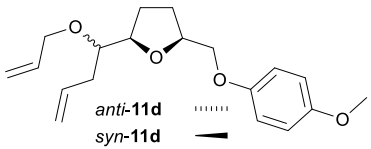
Following the general procedure, $CaCO_3$ (0.50 mmol, 50 mg), **4** (0.50 mmol, 2.5 mL, 0.2 M in dry toluene), (+)-menthol TMS ether ***ent*-14b** (1.0 mmol, 263 µL), TMSOTf (0.15 mmol, 500 µL, 0.3 M in dry CH_2Cl_2) and AllylTMS (1.0 mmol, 160 µL) were reacted at –40 °C for 48 h. After workup, the crude was purified by chromatography (PE/Et_2O 95:5 to 9:1) to give *syn*-**11c** (minor, R_f 0.32, PE/Et_2O 9:1) and *anti*-**11c** (major, R_f 0.25) in 70% overall yield (123 mg) (d.r. 43:57 by HPLC).

Syn-**11c** (minor). White foam. $\boldsymbol{R_f}$ 0.32 (PE/Et_2O 9:1). $\boldsymbol{[\alpha]_D}$ = +83.0 (c 1.4, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$, 25 °C) δ 6.91 – 6.77 (4 H, m, aromatic CH), 5.90 (1 H, ddt, *J* 17.1, 10.1, 7.0, C*H*=CH_2), 5.13 – 4.96 (2 H, m, CH=C*H*$_2$), 4.28 – 4.17 (1 H, m, C*H*CH_2OPMP), 4.04 (1 H, td, *J* 6.9, 5.4, C*H*CHOR), 3.95 (1 H, dd, *J* 9.6, 5.4, part A of ABX C*H*$_2$OPMP), 3.88 (1 H, dd, *J* 9.6, 4.9, part B of ABX

C*H*$_2$OPMP), 3.76 (3 H, s, OCH_3), 3.53 (1 H, ddd, *J* 8.1, 5.3, 4.0, C*H*$CH_2CH=CH_2$), 3.21 (1 H, td, *J* 10.4, 4.2, CH-O menthol), 2.42 – 2.22 (2 H, m, part A of C*H*$_2$$CH=CH_2$, CH menthol), 2.20 – 2.06 (1 H, m, part B of C*H*$_2$$CH=CH_2$), 2.06 – 1.69 (5 H, m, 2×CH_2 THF, part A of CH_2 menthol), 1.68 – 1.56 (2 H, m, 2×part A of CH_2 menthol), 1.36 – 1.09 (2 H, m, 2×CH menthol), 1.03 – 0.77 (9 H, m, 3×part A of CH_2 menthol, 3× CH_3 menthol), 0.76 (3 H, d, *J* 6.9, CH_3 menthol). **^{13}C NMR** (75 MHz, $CDCl_3$, 25 °C) δ 154.0 (C-O), 153.3 (C-O), 136.1 (*C*$H=CH_2$), 116.4 ($CH=CH_2$), 115.6 (aromatic CH), 114.7 (aromatic CH), 81.1 (*C*HCHOR), 78.0 (*C*$HCH_2CH=CH_2$), 77.9 (CH-O menthol), 77.6 (*C*HCH_2OPMP), 71.2 (*C*H_2OPMP), 55.9 (OCH_3), 48.9 (CH menthol), 41.9 (CH_2 menthol), 35.3 (*C*$H_2CH=CH_2$), 34.7 (CH_2 menthol), 31.7 (CH menthol), 28.6 (CH_2 THF), 26.3 (CH_2 THF), 24.9 (CH menthol), 23.1 (CH_2 menthol), 22.6 (CH_3), 21.6 (CH_3), 16.1 (CH_3). **IR** ν_{max} (cm^{-1}) 3085, 3020, 2957, 2922, 2867, 2845, 1730, 1643, 1593, 1513, 1456, 1385, 1372, 1330, 1317, 1298, 1229, 1178, 1148, 1121, 1094, 1069, 1032, 1021, 998, 974, 921, 886, 871, 836, 809, 751, 706, 646. **HRMS** (ESI+): calcd. for $C_{26}H_{41}O_4^+$ $[M+H]^+$ 417.29994, found 417.2997.

Anti-**11c** (major). Colorless oil. R_f 0.25 (PE/Et_2O 9:1). **[α]$_D$** = +69.9 (c 1.5, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$, 25 °C) δ 6.91 – 6.74 (4 H, m, aromatic CH), 5.85 (1 H, ddt, *J* 17.3, 10.2, 7.1, C*H*=CH_2), 5.13 – 4.96 (2 H, m, CH=C*H*$_2$), 4.26 (1 H, quintuplet, *J* 6.2, C*H*CH_2OPMP), 4.02 – 3.92 (2 H, m, part A of ABX C*H*$_2$OPMP, C*H*CHOR), 3.84 (1 H, dd, *J* 9.5, 5.1, part B of ABX C*H*$_2$OPMP), 3.76 (3 H, s, OCH_3), 3.56 (1 H, dt, *J* 6.8, 4.6, C*H*$CH_2CH=CH_2$), 3.14 (1 H, td, *J* 10.4, 4.1, CH-O menthol), 2.45 – 2.16 (3 H, m, C*H*$_2$$CH=CH_2$ + CH menthol), 2.16 – 2.06 (1 H, m, part A CH_2 menthol), 2.05 – 1.73 (4 H, m 2×CH_2 THF), 1.67 – 1.56 (2 H, m, 2×part A of CH_2 menthol), 1.32 – 1.24 (1 H, m, CH menthol), 1.19 – 1.10 (1 H, m, CH menthol), 0.93 – 0.83 (7 H, m, 2×CH_3 menthol, part B of CH_2 menthol), 0.83 – 0.65 (5 H, m CH_3 menthol, 2×part B of CH_2 menthol). **^{13}C NMR** (75 MHz, $CDCl_3$, 25 °C) δ 153.9 (C-O), 153.3 (C-O), 135.0 (*C*$H=CH_2$), 117.0 ($CH=CH_2$), 115.6 (aromatic CH), 114.7 (aromatic CH), 81.1 (*C*HCHOR), 77.7 (*C*HCH_2OPMP), 76.5 (CH-O menthol), 76.3 (*C*$HCH_2CH=CH_2$), 71.5 (*C*H_2OPMP), 55.9 (OCH_3), 48.9 (CH menthol), 41.2 (CH_2 menthol), 36.1 (*C*$H_2CH=CH_2$), 34.7 (CH_2 menthol), 31.6 (CH menthol), 28.5 (CH_2 THF), 26.2 (CH_2 THF), 25.0 (CH menthol), 23.2 (CH_2 menthol), 22.5 (CH_3), 21.5 (CH_3), 16.2 (CH_3). **IR** ν_{max} (cm^{-1}) 3085, 3020, 2957, 2922, 2867, 2845, 1730, 1643, 1593, 1513, 1456, 1385, 1372, 1330, 1317, 1298, 1229, 1178, 1148, 1121, 1094, 1069, 1032, 1021, 998, 974, 921, 886, 871, 836, 809, 751, 706, 646. **HRMS** (ESI+): calcd. for $C_{26}H_{41}O_4^+$ $[M+H]^+$ 417.29994, found 417.3003.

(2*R*,5*S*)-2-(1-(Allyloxy)but-3-en-1-yl)-5-((4-methoxyphenoxy)methyl)tetrahydrofuran 11d



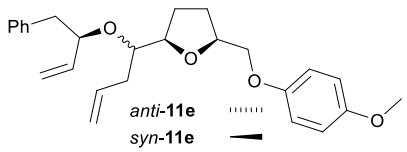
Following the general procedure, $CaCO_3$ (0.34 mmol, 34 mg), aldehyde **4** (0.34 mmol, 1.7 mL, 0.2 M in dry toluene), (allyloxy)trimethylsilane **15b** (0.68 mmol, 115 µL), TMSOTf (0.10 mmol, 340 µL, 0.3 M in dry CH_2Cl_2) and AllylTMS (0.68 mmol, 118 µL) were reacted at 0 °C for 24 h. After workup, the crude was purified by chromatography (PE/Et_2O 85:15) to give *anti*-**11d** (major, R_f 0.38, PE/Et_2O 8:2) and *syn*-**11d** (minor, R_f 0.25) in 55% overall yield (59 mg) (d.r. 52:48 by ^{1}H NMR).

Anti-**11d** (major). Colorless oil. R_f 0.38 (PE/Et_2O 8:2). **[α]$_D$** = +9.20 (c 1.22, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.92 – 6.75 (4 H, m, aromatic CH), 6.00 – 5.72 (2 H, m, 2×C*H*=CH_2), 5.23 (1 H, dq, *J* 17.2, 1.7, CH=C*H*H), 5.16 – 5.00 (3 H, m, CH=CH*H* + CH=C*H*$_2$), 4.26 (1 H, quintuplet,, *J* 6.2, C*H*CH_2OPMP), 4.15 – 4.06 (2 H, m, OC*H*$_2$$CH=CH_2$), 4.03 – 3.96 (1 H, m, C*H*CHOR), 3.93 (1 H, dd, *J* 9.6, 5.8, part A of ABX C*H*$_2$OPMP), 3.88 (1 H, dd, *J* 9.6, 5.0, part B of ABX C*H*$_2$OPMP), 3.76 (3 H, s, OCH_3), 3.52 (1 H, td, *J* 6.1, 4.4, C*H*$CH_2CH=CH_2$), 2.39 – 2.18 (2 H, m, CHC*H*$_2$$CH=CH_2$), 2.06 – 1.75 (4 H, m, 2×CH_2 THF part). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 153.9 (C-O), 153.2 (C-O), 135.5 (*C*$H=CH_2$), 135.0 (*C*$H=CH_2$), 117.0 ($CH=CH_2$), 116.6 ($CH=CH_2$), 115.5 (aromatic CH), 114.7 (aromatic

CH), 82.0 (*C*HCHOR), 79.8 (*C*HCH$_2$CH=CH$_2$), 77.7 (*C*HCH$_2$OPMP), 72.2 (O*C*H$_2$CH=CH$_2$), 71.2 (*C*H$_2$OPMP), 55.8 (OCH$_3$), 36.6 (CH*C*H$_2$CH=CH$_2$), 28.4 (CH$_2$), 25.8 (CH$_2$). **HRMS** (ESI+): calcd. for $C_{19}H_{27}O_4^+$ [M+H]$^+$ 319.19039, found 319.1921.

Syn-**11d** (minor). Colorless oil. R_f 0.25 (PE/Et$_2$O 8:2). **[α]$_D$** = –0.923 (0.93, CHCl$_3$). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 6.91 – 6.77 (4 H, m, aromatic CH), 6.01 – 5.79 (2 H, m, 2×C*H*=CH$_2$), 5.24 (1 H, dq, *J* 17.2, 1.6, CH=C*H*H), 5.18 – 4.99 (3 H, m, CH=CH*H* + CH=C*H*$_2$), 4.35 – 4.21 (1 H, m, C*H*CH$_2$OPMP), 4.17 – 4.06 (2 H, m, OC*H*$_2$CH=CH$_2$), 4.06 – 3.99 (1 H, m, C*H*CHOR), 3.96 (1 H, dd, *J* 9.6, 5.2, part A of ABX C*H*$_2$OPMP), 3.87 (1 H, dd, *J* 9.6, 5.3, part B of ABX C*H*$_2$OPMP), 3.76 (3 H, s, OCH$_3$), 3.37 (1 H, ddd, *J* 7.2, 5.8, 4.7, C*H*CH$_2$CH=CH$_2$), 2.45 – 2.28 (1 H, m, part A of CHC*H*$_2$CH=CH$_2$), 2.31 – 2.14 (1 H, m, part A of CHC*H*$_2$CH=CH$_2$), 2.08 – 1.70 (4 H, m, 2×CH$_2$ THF part). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 153.9 (C-O), 153.2 (C-O), 135.5 (*C*H=CH$_2$), 135.3 (*C*H=CH$_2$), 116.9 (CH=*C*H$_2$), 116.7 (CH=*C*H$_2$), 115.6 (aromatic CH), 114.7 (aromatic CH), 81.9 (*C*HCHOR), 81.0 (*C*HCH$_2$CH=CH$_2$), 77.6 (*C*HCH$_2$OPMP), 71.8 (O*C*H$_2$CH=CH$_2$), 71.2 (*C*H$_2$OPMP), 55.8 (OCH$_3$), 35.6 (CH*C*H$_2$CH=CH$_2$), 28.5 (CH$_2$), 27.3 (CH$_2$). **HRMS** (ESI+): calcd. for calcd. for $C_{19}H_{27}O_4^+$ [M+H]$^+$ 319.19039, found 319.1902.

(2*S*,5*R*)-2-((4-Methoxyphenoxy)methyl)-5-(1-(((*R*)-1-phenylbut-3-en-2-yl)oxy)but-3-en-1-yl)tetrahydrofuran 11e



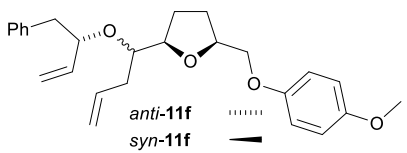
Following the general procedure, CaCO$_3$ (0.50 mmol, 50 mg), aldehyde **4** (0.50 mmol, 2.5 mL, 0.2 M in dry toluene), (*R*)-1-phenylbut-3-en-2-ol TMS ether **16b** (1.00 mmol, 220 mg, 250 µL), TMSOTf (0.15 mmol, 500 µL, 0.3 M in dry CH$_2$Cl$_2$) and AllylTMS (1.00 mmol, 172 µL) were reacted at –40 °C for 48 h. After workup, the crude was purified by chromatography (PE/Et$_2$O 9:1) to give *anti*-**11e** (minor, R_f 0.26, PE/Et$_2$O 9:1) and *syn*-**11e** (major, R_f 0.21) in 66% overall yield (d.r. 43:57 by HPLC).

Anti-**11e** (minor). Colorless oil. R_f 0.26 (PE/Et$_2$O 9:1). **[α]$_D$** = –10.3 (c 0.51, CHCl$_3$). **^{1}H NMR** (400 MHz, CDCl$_3$, 25 °C) δ.22 – 7.13 (5 H, m, aromatic CH of Ph), 6.90 – 6.78 (4 H, m, aromatic CH of PMP), 5.79 (1 H, ddt, *J* 17.1, 10.2, 7.1, C*H*=CH$_2$), 5.66 (1 H, ddd, *J* 17.1, 10.4, 8.1, C*H*=CH$_2$), 5.12 – 4.96 (4 H, m, 2×CH=C*H*$_2$), 4.25 – 4.17 (1 H, m, PhCH$_2$C*H*), 4.16 – 4.08 (1 H, m, C*H*CH$_2$OPMP), 3.89 (1 H, td, *J* 7.4, 3.3, C*H*CHOR), 3.83 – 3.74 (5 H, m, C*H*$_2$OPMP + OCH$_3$), 3.69 (1 H, td, *J* 6.4, 3.4, C*H*CH$_2$CH=CH$_2$), 2.92 (1 H, dd, *J* 13.4, 6.8, part A of PhC*H*$_2$), 2.68 (1 H, dd, *J* 13.4, 6.6, part B of PhC*H*$_2$), 2.28 – 2.09 (2 H, m, C*H*$_2$CH=CH$_2$), 1.91 – 1.67 (3 H, m, CH$_2$ THF + part A of CH$_2$ THF), 1.50 – 1.43 (1 H, m, part B of CH$_2$ THF). **^{13}C NMR** (101 MHz, CDCl$_3$, 25 °C) δ 154.0 (C-O), 153.3 (C-O), 139.4 (*C*H=CH$_2$), 138.6 (C quat. of Ph), 135.4 (*C*H=CH$_2$), 130.0 (2×CH of Ph), 128.1 (2×CH of Ph), 126.1 (CH of Ph), 117.4 (CH=*C*H$_2$), 116.7 (CH=*C*H$_2$), 115.7 (2×CH of PMP), 114.7 (2×CH of PMP), 82.72 and 82.70 (PhCH$_2$*C*H and *C*HCHOR), 77.4 (*C*HCH$_2$OPMP), 76.2 (*C*HCH$_2$CH=CH$_2$), 71.4 (*C*H$_2$OPMP), 55.9 (OCH$_3$), 42.9 (CH$_2$Ph), 37.8 (*C*H$_2$CH=CH$_2$), 28.1 (CH$_2$ THF), 24.7 (CH$_2$ THF). **HRMS** (ESI+): calcd. for $C_{26}H_{33}O_4^+$ [M+H]$^+$ 409.23734, found 409.2374.

Syn-**11e** (major). Colorless oil. R_f 0.26 (PE/Et$_2$O 9:1). **[α]$_D$** = +13.1 (c 1.02, CHCl$_3$). **^{1}H NMR** (400 MHz, CDCl$_3$, 25 °C) δ 7.25 – 7.13 (5 H, m, aromatic CH of Ph), 6.88 – 6.76 (4 H, m, aromatic CH of PMP), 5.83 (1 H, ddt, *J* 17.1, 10.2, 7.0, C*H*=CH$_2$), 5.68 (1 H, ddd, *J* 17.2, 10.3, 7.9, C*H*=CH$_2$), 5.12 – 4.93 (4 H, m, 2×CH=C*H*$_2$), 4.23 – 4.10 (2 H, m, C*H*CH$_2$OPMP + PhCH$_2$C*H*), 3.91 (1 H, dd, *J* 9.6, 5.6, part A of C*H*$_2$OPMP), 3.87 – 3.82 (2 H, m, part B of C*H*$_2$OPMP + C*H*CHOR), 3.76 (3 H, s, OCH$_3$), 3.43 (1 H, ddd, *J* 8.0, 5.6, 4.3, C*H*CH$_2$CH=CH$_2$), 2.94 (1 H, dd, *J* 13.5, 7.0, part A of PhC*H*$_2$), 2.73 (1 H, dd, *J* 13.5, 6.5, part B of PhC*H*$_2$), 2.33 – 2.23 (1 H, m, part A of C*H*$_2$CH=CH$_2$), 2.18 – 2.09 (1 H, m, part B of C*H*$_2$CH=CH$_2$), 1.97 – 1.86 (1 H, m, part A of of CH$_2$ THF), 1.73 – 1.58 (3 H, m, part B of of CH$_2$ THF + CH$_2$ THF). **^{13}C NMR** (101 MHz, CDCl$_3$, 25 °C) δ 154.0 (C-O), 153.3 (C-O), 139.3 (*C*H=CH$_2$), 138.7 (C quat. of Ph), 135.8

(*C*H=CH$_2$), 129.9 (2×CH of Ph), 128.1 (2×CH of Ph), 126.1 (CH of Ph), 117.0 (CH=*C*H$_2$), 116.5 (CH=*C*H$_2$), 115.6 (2×CH of PMP), 114.7 (2×CH of PMP), 82.2 (C*H*CH$_2$OPMP or PhCH$_2$C*H*), 81.5 (C*H*CHOR), 78.4 (*C*HCH$_2$CH=CH$_2$), 77.6 (C*H*CH$_2$OPMP or PhCH$_2$C*H*), 71.3 (*C*H$_2$OPMP), 55.9 (OCH$_3$), 42.6 (CH$_2$Ph), 35.7 (*C*H$_2$CH=CH$_2$), 28.4 (CH$_2$ THF), 26.6 (CH$_2$ THF). **HRMS** (ESI+): calcd. for $C_{26}H_{33}O_4^+$ $[M+H]^+$ 409.23734, found 409.2369.

(2*S*,5*R*)-2-((4-Methoxyphenoxy)methyl)-5-(1-(((*S*)-1-phenylbut-3-en-2-yl)oxy)but-3-en-1-yl)tetrahydrofuran 11f

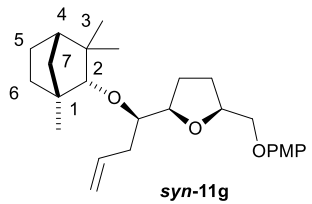


Following the general procedure, $CaCO_3$ (0.36 mmol, 36 mg), aldehyde **4** (0.36 mmol, 1.8 mL, 0.2 M in dry toluene), (*S*)-1-phenylbut-3-en-2-ol TMS ether ***ent*-16b** (0.72 mmol, 159 mg, 180 µL), TMSOTf (0.108 mmol, 360 µL, 0.3 M in dry CH_2Cl_2) and AllylTMS (0.72 mmol, 125 µL) were reacted at –40 °C for 48 h. After workup, the crude was purified by chromatography (PE/Et$_2$O 9:1) to give *anti*-**11f** (major, R_f 0.41, PE/Et$_2$O 8:2) and *syn*-**11f** (minor, R_f 0.34) in 57% overall yield (83 mg) (d.r. 68:32 by HPLC).

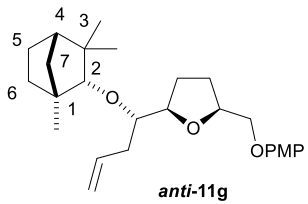
Anti-**11f** (major). Colorless oil. $\boldsymbol{R_f}$ 0.41 (PE/Et$_2$O 8:2). $\boldsymbol{[\alpha]_D}$ = –16.9 (c 1.61, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$, 25 °C) δ (300 MHz, Chloroform-*d*) 7.23 – 7.09 (5 H, m, aromatic CH of Ph), 6.90 – 6.76 (4 H, m, aromatic CH of PMP), 5.89 – 5.57 (2 H, m, 2×C*H*=CH$_2$), 5.15 – 4.94 (4 H, m, 2×CH=C*H*$_2$), 4.26 – 4.16 (1 H, m, PhCH$_2$C*H*), 4.16 – 4.05 (1 H, m, C*H*CH$_2$OPMP), 3.89 (1 H, td, *J* 7.3, 3.2, C*H*CHOR), 3.83 – 3.74 (5 H, m, C*H*$_2$OPMP + OCH$_3$), 3.70 (1 H, td, *J* 6.4, 3.1, C*H*CH$_2$CH=CH$_2$), 2.92 (1 H, dd, *J* 13.4, 6.8, part A of PhC*H*$_2$), 2.68 (1 H, dd, *J* 13.4, 6.6, part B of PhC*H*$_2$), 2.30 – 2.08 (2 H, m, C*H*$_2$CH=CH$_2$), 1.95 – 1.65 (3 H, m, CH$_2$ THF + part A of CH$_2$ THF), 1.50 – 1.36 (1 H, m, part B of CH$_2$ THF). **^{13}C NMR** (75 MHz, $CDCl_3$, 25 °C) δ 153.9 (C-O), 153.2 (C-O), 139.3 (*C*H=CH$_2$), 138.6 (C quat. of Ph), 135.3 (*C*H=CH$_2$), 130.0 (2×CH of Ph), 128.1 (2×CH of Ph), 126.1 (CH of Ph), 117.5 (CH=*C*H$_2$), 116.7 (CH=*C*H$_2$), 115.6 (2×CH of PMP), 114.7 (2×CH of PMP), 82.7 (PhCH$_2$*C*H), 82.7 (*C*HCHOR), 77.4 (*C*HCH$_2$OPMP), 76.1 (*C*HCH$_2$CH=CH$_2$), 71.3 (*C*H$_2$OPMP), 55.8 (OCH$_3$), 42.8 (CH$_2$Ph), 37.8 (*C*H$_2$CH=CH$_2$), 28.1 (CH$_2$ THF), 24.6 (CH$_2$ THF). **HRMS** (ESI+): calcd. for $C_{26}H_{33}O_4^+$ $[M+H]^+$ 409.23734, found 409.2383.

Syn-**11f** (minor). Colorless oil. $\boldsymbol{R_f}$ 0.34 (PE/Et$_2$O 8:2). $\boldsymbol{[\alpha]_D}$ = –26.0 (c 0.66, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$, 25 °C) δ 7.25 – 7.14 (5 H, m, aromatic CH of Ph), 6.89 – 6.78 (4 H, m, aromatic CH of PMP), 5.78 – 5.53 (2 H, m, 2×C*H*=CH$_2$), 5.13 – 5.02 (2 H, m, CH=C*H*$_2$), 5.02 – 4.88 (2 H, m, CH=C*H*$_2$), 4.34 – 4.20 (1 H, m, C*H*CH$_2$OPMP), 4.08 – 3.96 (2 H, m, PhCH$_2$C*H* + C*H*CHOR), 3.95 (1 H, dd, *J* 9.5, 5.5, part A of C*H*$_2$OPMP), 3.83 (1 H, dd, *J* 9.5, 5.4, part B of C*H*$_2$OPMP), 3.76 (3 H, s, OCH$_3$), 3.40 (1 H, q, *J* 5.3, C*H*CH$_2$CH=CH$_2$), 2.92 (1 H, dd, *J* 13.5, 7.1, part A of PhC*H*$_2$), 2.72 (1 H, dd, *J* 13.5, 6.2, part B of PhC*H*$_2$), 2.35 – 2.19 (1 H, m, part A of C*H*$_2$CH=CH$_2$), 2.12 – 1.93 (2 H, m, part B of C*H*$_2$CH=CH$_2$ + part A of of CH$_2$ THF), 1.93 – 1.69 (3 H, m, part B of of CH$_2$ THF + CH$_2$ THF). **^{13}C NMR** (75 MHz, $CDCl_3$, 25 °C) δ 153.9 (C-O), 153.3 (C-O), 139.1 (C quat. of Ph), 138.6 (*C*H=CH$_2$), 135.3 (*C*H=CH$_2$), 129.9 (2×CH of Ph), 128.1 (2×CH of Ph), 126.2 (CH of Ph), 117.1 (CH=*C*H$_2$), 116.7 (CH=*C*H$_2$), 115.6 (2×CH of PMP), 114.7 (2×CH of PMP), 81.2 and 81.1 (*C*HCHOR and PhCH$_2$*C*H), 78.3 (*C*HCH$_2$CH=CH$_2$), 77.7 (*C*HCH$_2$OPMP), 71.3 (*C*H$_2$OPMP), 55.9 (OCH$_3$), 42.6 (CH$_2$Ph), 35.0 (*C*H$_2$CH=CH$_2$), 28.7 (CH$_2$ THF), 27.0 (CH$_2$ THF). **HRMS** (ESI+): calcd. for $C_{26}H_{33}O_4^+$ $[M+H]^+$ 409.23734, found 409.2389.

(2*S*,5*R*)-2-((4-Methoxyphenoxy)methyl)-5-((*R*)-1-(((1*R*,2*R*,4*S*)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)but-3-en-1-yl)tetrahydrofuran 11g



***syn*-11g**



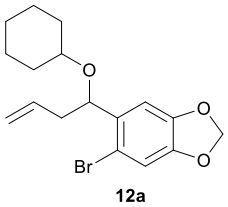
***anti*-11g**

Following the general procedure, $CaCO_3$ (0.40 mmol, 40 mg), aldehyde **4** (0.40 mmol, 2.0 mL, 0.2 M in dry toluene), (1*R*)-endo-(+)-fenchyl alcohol TMS ether **17b** (0.80 mmol, 181 mg, 215 µL), TMSOTf (0.12 mmol, 400 µL, 0.3 M in dry CH_2Cl_2) and AllylTMS (0.80 mmol, 140 µL) were reacted at –40 °C for 48 h. After workup, the crude was purified by chromatography (PE/Et_2O 20:1) to give a mixture of *syn* and *anti* products in 66% overall yield. In this case, due to the high d.r., we were not able to obtain a pure sample of *anti*-**11g**, and thus we report only the full characterization of *syn*-**11g** and some selected ^{1}HNMR peaks of *anti*-**11g**. The diastereomeric ratio was determined on the crude by ^{1}H NMR and was 90:10 (*syn*:*anti*).

Syn-**11g** (major). Colorless oil. R_f 0.26 (PE/Et_2O 9:1). $[\alpha]_D$ = –10.3 (c 0.51, $CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.88 – 6.79 (4 H, m), 5.89 (1 H, ddt, *J* 17.2, 10.2, 7.2, C*H*=CH_2), 5.08 (1 H, dq, *J* 17.2, 1.4, CH=C*H*H), 5.04 – 4.98 (1 H, m, CH=C*H*H), 4.27 (1 H, pent, *J* 6.0, C*H*CH_2OPMP), 4.14 (1 H, td, *J* 6.9, 4.3, C*H*-$CH_2CH=CH_2$), 3.96 (1 H, dd, *J* 9.5, 5.7, C*H*HOPMP), 3.87 (1 H, dd, *J* 9.5, 5.3, C*H*HOPMP), 3.77 (3 H, s, OCH_3), 3.37 (1 H, dt, *J* 6.7, 5.2, C*H*CHOR), 3.10 (1 H, d, *J* 1.8, *H*-2), 2.45 (1 H, dtt, *J* 6.8, 0.4, C*H*H-CH=CH_2), 2.27 – 2.17 (1 H, m, mc = 2.22, C*H*H-CH=CH_2), 2.07 – 1.81 (4 H, m), 1.80 – 1.71 (1 H, m), 1.70 – 1.62 (1 H, m), 1.62 – 1.59 (1 H, m), 1.47 – 1.41 (1 H, m), 1.36 (1 H, tdd, *J* 12.3, 5.8, 4.0), 1.09 (3 H, s), 1.07 – 1.01 (1 H, m), 1.00 (3 H, s), 0.99 – 0.89 (1 H, m), 0.85 (3 H, s). **^{13}C NMR** (100 MHz, $CDCl_3$, 25 °C) δ 153.8 (C-O), 153.2 (C-O), 139.3 (*C*H=CH_2), 135.6 (*C*H=CH_2), 117.5 (CH=*C*H_2), 116.6 (CH=*C*H_2), 115.4 (2×CH of PMP), 114.5 (2×CH of PMP), 90.67 (*C*-2), 80.8 (*C*HCHOR), 80.1(*C*$HCH_2CH=CH_2$), 77.6(*C*HCH_2OPMP), 71.2 (*C*H_2OPMP), 55.7 (OCH_3), 49.6 (*C*-1), 48.4 (*C*-4), 41.4 (*C*-7), 39.6 (*C*-3), 35.8 (*C*$H_2CH=CH_2$) 31.0 (*C*H_3), 28.7 (CH_2 THF), 26.4, 26.2, 26.1 (*C*-5, *C*-6, *C*H_2 THF), 21.9, 20.3 (*C*H_3). **HRMS** (ESI+): calcd. for $C_{26}H_{39}O_4$ $[M+H]^+$ 415.28429, found 415.2855.

Anti-**11g** (minor). Colorless oil. R_f 0.21 (PE/Et_2O 9:1). **^{1}H NMR** (400 MHz, Chloroform-*d*)(selected peaks) δ 5.83 (1 H, ddt, *J* 17.2, 10.2, 7.2, C*H*=CH_2), 4.22 (1 H, pent, *J* 6.0, C*H*-$CH_2CH=CH_2$), 4.07 (1 H, td, *J* 6.9, 4.3, C*H*CH_2OPMP), 3.16 (1 H, d, *J* 1.6, *H*-2).

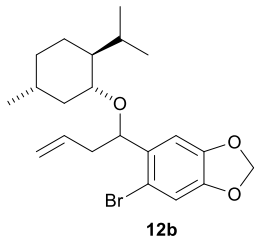
***racemic* 5-Bromo-6-(1-(cyclohexyloxy)but-3-en-1-yl)benzo[d][1,3]dioxole 12a**



12a

Following the general procedure, 6-bromopiperonal **9** (0.438 mmol, 100 mg), (cyclohexyloxy)trimethylsilane **13b** (0.657 mmol, 113 mg, 130 µL), AllylTMS (0.657 mmol, 104 µL), TMSOTf (0.131 mmol, 438 µL, 0.3 M in dry CH_2Cl_2) were reacted in dry CH_2Cl_2 (2.2 mL) at –78 °C for 2 h. After workup, the crude was purified by chromatography (PE/CH_2Cl_2 6:4) to give **12a** in 93% yield (145 mg) as colorless oil. R_f 0.35 (PE/CH_2Cl_2 6:4). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.02 (1 H, s, aromatic CH), 6.94 (1 H, s, aromatic CH), 5.98 (1 H, d, *J* 1.4, part A of AB of OCH_2O), 5.96 (1 H, d, *J* 1.4, part B of AB of OCH_2O), 5.88 (1 H, ddt, *J* 17.1, 10.2, 6.9, C*H*=CH_2), 5.11 – 4.99 (2 H, m, CH=C*H*$_2$), 4.78 (1 H, dd, *J* 7.1, 5.7, C*H*$CH_2CH=CH_2$), 3.11 (1 H, tt, *J* 9.4, 3.6, CH of Cy), 2.38 – 2.30 (2 H, m, C*H*$_2$CH=CH_2), 1.99 – 1.89 (1 H, m, Cy), 1.76 – 1.62 (3 H, m, Cy), 1.53 – 1.43 (1 H, m, Cy), 1.35 – 1.24 (2 H, m, Cy), 1.23 – 1.13 (3 H, m, Cy). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.8 (C-O), 147.5 (C-O), 136.3 (C quat.), 135.2 (*C*H=CH_2), 116.9 (CH=*C*H_2), 112.8 (C-Br), 112.3 (aromatic CH), 107.8 (aromatic CH), 101.8 (OCH_2O), 77.0 (*C*$HCH_2CH=CH_2$), 75.6 (CH of Cy), 41.9 (*C*$H_2CH=CH_2$), 33.6 (CH_2 Cy), 31.7 (CH_2 Cy), 25.9 (CH_2 Cy), 24.4 (CH_2 Cy), 24.2 (CH_2 Cy). **HRMS** (ESI+): calcd. for $C_{17}H_{22}BrO_3^+$ $[M+H]^+$ 353.07468, found 353.0745 (only the lighter isotope is reported).

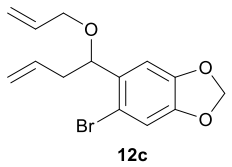
5-Bromo-6-(1-(((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)but-3-en-1-yl)benzo[d][1,3]dioxole 12b



12b

Following the general procedure, 6-bromopiperonal **9** (0.445 mmol, 102 mg), (–)-menthol TMS ether **14b** (0.667 mmol, 153 mg, 173 µL), AllylTMS (0.667 mmol, 106 µL), TMSOTf (0.133 mmol, 445 µL, 0.3 M in dry CH_2Cl_2) were reacted in dry CH_2Cl_2 (2.2 mL) at –78 °C for 4 h. After workup, the crude was purified by chromatography (PE/CH_2Cl_2 8:2) to give **12b** in 87% yield (159 mg) as colorless oil (inseparable epimers, d.r. 55:45 by ^{1}H NMR). ***R*****$_f$** 0.46 (PE/CH_2Cl_2 8:2). **^{1}H NMR** (400 MHz, $CDCl_3$, **mixture of epimers**) δ 7.01 (1 H, s, aromatic CH epimer A), 6.95 (1 H, s, aromatic CH epimer B), 6.94 (1 H, s, aromatic CH epimer B), 6.93 (1 H, s, aromatic CH epimer A), 6.01 – 5.93 (4 H, m, 2×OCH_2O epimer A+B), 5.86 – 5.72 (2 H, m, 2×C*H*=CH_2 epimer A+B), 5.07 – 4.97 (4 H, m, 2×CH=C*H*$_2$ epimer A+B), 4.94 (1 H, dd, *J* 7.3, 6.2, C*H*CH_2CH=CH_2 epimer B), 4.72 (1 H, dd, *J* 7.1, 5.3, C*H*CH_2CH=CH_2 epimer A), 3.18 (1 H, td, *J* 10.5, 4.2, CH-O menthol epimer A), 2.89 (1 H, td, *J* 10.4, 4.1, CH-O menthol epimer B), 2.52 – 2.18 (7 H, m, 2×C*H*$_2$CH=CH_2 epimer A+B, 2×CH menthol epimer A+B, part A of CH_2 menthol epimer A,), 1.70 – 1.53 (5 H, m, 2×CH_2 menthol epimer A+B, 3× part A of CH_2 menthol epimer A+B,), 1.35 – 1.14 (4 H, m, 4×CH menthol epimer A+B), 1.00 – 0.63 (19 H, m, 5×CH_3 epimer A+B, 4×part B of CH_2 menthol epimer A+B,), 0.36 (3 H, d, *J* 6.9, CH_3 epimer B). **^{13}C NMR** (101 MHz, $CDCl_3$, **mixture of epimers**) δ 147.8 (C-O), 147.6(C-O), 147.5(C-O), 147.3(C-O), 137.2 (C quat.), 135.3 (C quat.), 134.73 (*C*H=CH_2), 134.68 (*C*H=CH_2), 117.3 (CH=*C*H_2), 117.1 (CH=*C*H_2), 113.9 (C-Br), 112.0 (aromatic CH epimer A), 112.0 (C-Br), 112.0 (aromatic CH epimer B), 108.6 (aromatic CH epimer A), 108.5 (aromatic CH epimer B), 101.8 (OCH_2O epimer B), 101.7 (OCH_2O epimer A), 80.1 (CH-O menthol epimer A), 79.5 (*C*HCH_2CH=CH_2 epimer A), 75.4 (*C*HCH_2CH=CH_2 epimer B), 75.3 (CH-O menthol epimer B), 49.2 (CH menthol), 48.5 (CH menthol), 42.2 (CH_2 menthol), 42.0 (2×*C*H_2CH=CH_2), 40.5 (CH_2 menthol), 34.6 (CH_2 menthol), 34.5 (CH_2 menthol), 31.7 (CH menthol), 31.6 (CH menthol), 25.2 (CH menthol), 25.0 (CH menthol), 23.1 (CH_2 menthol), 22.8 (CH_2 menthol), 22.6 (CH_3), 22.5 (CH_3), 21.5 (CH_3), 21.4 (CH_3), 16.2 (CH_3 epimer A), 15.4 (CH_3 epimer B). **HRMS** (ESI+): calcd. for $C_{21}H_{30}BrO_3^+$ $[M+H]^+$ 409.13728, found 409.1382(only the lighter isotope is reported).

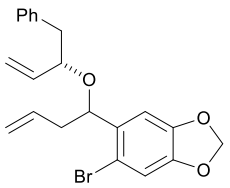
racemic 6-(1-(Allyloxy)but-3-en-1-yl)-5-bromobenzo[d][1,3]dioxole 12c



12c

Following the general procedure, 6-bromopiperonal **9** (0.438 mmol, 100 mg), (allyloxy)trimethylsilane **15b** (0.657 mmol, 110 µL), AllylTMS (0.657 mmol, 104 µL), TMSOTf (0.131 mmol, 438 µL, 0.3 M in dry CH_2Cl_2) were reacted in dry CH_2Cl_2 (2.2 mL) at –78 °C for 2 h. After workup, the crude was purified by chromatography (PE/CH_2Cl_2 65:35) to give **12c** in 82% yield (111 mg) as colorless oil. ***R*****$_f$** 0.28 (PE/CH_2Cl_2 6:4). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.96 (2 H, s, aromatic CH), 5.99 (1 H, d, *J* 1.4, part A of AB of OCH_2O), 5.97 (1 H, d, *J* 1.4, part B of AB of OCH_2O), 5.94 – 5.79 (2 H, m, 2×C*H*=CH_2), 5.31 – 5.21 (1 H, m, CH=C*H*H), 5.20 – 5.14 (1 H, m, CH=C*H*H), 5.11 – 5.01 (2 H, m, CH=C*H*$_2$), 4.73 (1 H, dd, *J* 7.0, 5.7, C*H*CH_2CH=CH_2), 3.91 (1 H, ddt, *J* 12.8, 5.1, 1.5, part A of OC*H*$_2$CH=CH_2), 3.77 (1 H, ddt, *J* 12.8, 6.0, 1.4, part A of OC*H*$_2$CH=CH_2), 2.51 – 2.33 (2 H, m, CHC*H*$_2$CH=CH_2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.0 (C-O), 147.7 (C-O), 134.7 (C quat.), 134.6 (2×*C*H=CH_2), 117.2 (2×CH=*C*H_2), 113.3 (C-Br), 112.5 (aromatic CH), 107.6 (aromatic CH), 101.8 (OCH_2O), 79.3 (*C*HCH_2CH=CH_2), 69.9 (O*C*H_2CH=CH_2), 41.4 (CH*C*H_2CH=CH_2). **HRMS** (ESI+): calcd. for $C_{14}H_{16}BrO_3^+$ $[M+H]^+$ 311.02773, found 311.0288 (only the lighter isotope is reported).

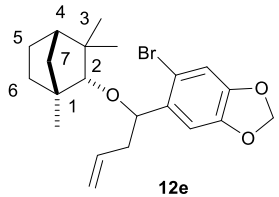
5-Bromo-6-(1-(((*S*)-1-phenylbut-3-en-2-yl)oxy)but-3-en-1-yl)benzo[d][1,3]dioxole 12d



12d

Following the general procedure, 6-bromopiperonal **9** (0.441 mmol, 101 mg), (*S*)-1-phenylbut-3-en-2-ol TMS ether ***ent*-16b** (0.661 mmol, 146 mg, 166 µL), AllylTMS (0.661 mmol, 114 µL), TMSOTf (0.132 mmol, 440 µL, 0.3 M in dry CH_2Cl_2) were reacted in dry CH_2Cl_2 (2.2 mL) at –78 °C for 1 h. After workup, the crude was purified by chromatography (PE/Et_2O 50:1) to give **12d** in 89% yield as colorless oil (nearly inseparable epimers, 157 mg), d.r. 18:82 by ^{1}H NMR). R_f 0.22 (major), 0.26 (minor) (PE/Et_2O 100:2) **^{1}H NMR** (400 MHz, $CDCl_3$, measured on enriched **major epimer**) δ 7.31 – 7.26 (2 H, m, aromatic CH of Ph), 7.24 – 7.18 (3 H, m, aromatic CH of Ph), 6.96 (1 H, s, aromatic CH of piperonyl), 6.91 (1 H, s, aromatic CH of piperonyl), 5.97 (1 H, d, *J* 1.0, part A of AB of OCH_2O), 5.95 (1 H, d, *J* 0.9, part B of AB of OCH_2O), 5.69 – 5.54 (2 H, m, 2×C*H*=CH_2), 5.06 – 4.91 (4 H, m, 2×CH=CH_2), 4.75 – 4.70 (1 H, m, C*H*CH_2CH=CH_2), 3.93 (1 H, q, *J* 6.7, PhCH_2C*H*), 2.98 (1 H, dd, *J* 13.5, 6.6, part A of PhCH_2), 2.77 (1 H, dd, *J* 13.5, 6.5, part B of PhCH_2), 2.35 – 2.28 (2 H, m, CH_2CH=CH_2). **^{13}C NMR** (101 MHz, $CDCl_3$, measured on enriched **major epimer**) δ 147.6 (C-O), 147.5 (C-O), 138.5 (*C*H=CH_2), 138.3 (C quat.), 135.8 (C quat.), 134.4 (*C*H=CH_2), 129.9 (2×CH of Ph), 128.2 (2×CH of Ph), 126.3 (CH of Ph), 117.2 (CH=*C*H_2), 116.2 (CH=*C*H_2), 112.7 (C-Br), 112.1 (CH of piperonyl), 108.4 (CH of piperonyl), 101.7 (OCH_2O), 81.2 (PhCH_2*C*H), 78.2 (*C*HCH_2CH=CH_2), 41.9 (Ph*C*H_2), 41.2 (*C*H_2CH=CH_2). **HRMS** (ESI+): calcd. for $C_{21}H_{22}BrO_3^+$ $[M+H]^+$ 401.07468, found 401.0741 (only the lighter isotope is reported).

5-Bromo-6-(1-(((1*R*,2*R*,4*S*)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-yl)oxy)but-3-en-1-yl)benzo[d][1,3]dioxole 12e



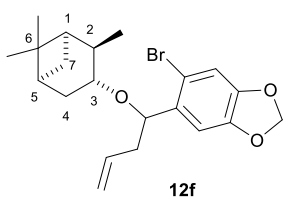
12e

Following the general procedure, 6-bromopiperonal **9** (0.480 mmol, 110 mg), (1*R*)-*endo*-(+)-fenchyl alcohol TMS ether **17b** (0.72 mmol, 194 µL), AllylTMS (0.72 mmol, 124 µL), TMSOTf (0.144 mmol, 480 µL, 0.3 M in dry CH_2Cl_2) were reacted in dry CH_2Cl_2 (2.4 mL) at –78 °C for 1.5 h. After workup, the crude was purified by chromatography (PE/CH_2Cl_2 9:1) to give **12e** in 60% overall yield as colorless oil, d.r. 52:48 (A:B) by ^{1}H NMR. R_f 0.33 and 0.28 (PE/CH_2Cl_2 9:1). Although the two epimers are difficult to separate, we could obtain fractions enriched in epimer **A** (faster running) or **B** (slower running).

Epimer A: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.97 (1 H, s, aromatic CH of piperonyl), 6.93 (1 H, s, aromatic CH of piperonyl), 5.98 (1 H, d, *J* 1.4, part A of AB of OCH_2O), 5.96 (1 H, d, *J* 1.4, part B of AB of OCH_2O), 5.86 (1 H, ddt, *J* 16.4, 10.7, 7.1, C*H*=CH_2), 5.07-4.94 (2 H, m, CH=CH_2), 4.79 (1 H, dd, *J* 7.0, 5.3, C*H*-CH_2C=), 2.95 (1 H, d, *J* 2.0, *H*-2), 2.50-2.31 (2 H, m, CH_2C=CH_2), 1.85 (1 H, ddt, *J* 11.9, 6.5, 3.2, 1 *H*-5), 1.71-1.61 (1 H, m, 1 *H*-6), 1.60-1.53 (1 H, m, *H*-4), 1.43-1.30 (2 H, m), 1.04 (3 H, s, CH_3), 1.05-0.95 (2 H, m), 0.792, 0.786 (2x3 H, 2s, CH_3). **^{13}C NMR** (101 MHz, CDCl3) δ 147.4 (C-O), 147.3 (C-O), 136.0 (C quat.), 134.7 (*C*H=CH_2), 117.1 (CH=*C*H_2), 112.8 (C-Br), 111.9 (CH of piperonyl), 108.4 (CH of piperonyl), 101.6 (OCH_2O), 90.1 (*C*-2), 79.5 (*C*HCH_2CH=CH_2), 49.5 (*C*-1), 48.3 (*C*-4), 41.6 (*C*-7), 41.2 (*C*H_2CH=CH_2), 39.5 (*C*-3), 30.9 (*C*H_3), 26.3 (*C*-6), 26.1 (*C*-5), 21.7 (*C*H_3), 20.9 (*C*H_3).

Epimer B: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.96 (1 H, s, aromatic CH of piperonyl), 6.93 (1 H, s, aromatic CH of piperonyl), 5.98 (1 H, d, *J* 0.8, part A of AB of OCH_2O), 5.96 (1 H, d, *J* 0.8, part B of AB of OCH_2O), 5.82 (1 H, mc, C*H*=CH_2), 5.05-4.93 (2 H, m, CH=CH_2), 4.75 (1 H, t, *J* 6.6, C*H*-CH_2C=), 2.80 (1 H, d, *J* 1.2, *H*-2), 2.52-2.30 (2 H, m, CH_2C=CH_2), 1.90-1.60 (m, 1 *H*-6 and 1 *H*-5), 1.60-1.53 (1 H, m, *H*-4), 1.45-1.30 (2 H, m), 1.04 (6 H, s, CH_3), 1.05-0.95 (2 H, m), 0.91 (3 H, s, CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.5 (x2)(C-O), 135.2 (C quat.), 134.4 (*C*H=CH_2), 117.0 (CH=*C*H_2), 113.5 (C-Br), 111.9 (CH of piperonyl), 108.5 (CH of piperonyl), 101.6 (OCH_2O), 89.2(*C*-2), 78.5 (*C*HCH_2CH=CH_2), 49.1 (*C*-1), 48.3 (*C*-4), 42.1 (*C*-7), 41.3 (*C*H_2CH=CH_2), 39.4 (*C*-3), 31.7 (*C*H_3), 26.2 (*C*-6), 25.9 (*C*-5), 21.4 (*C*H_3), 20.2 (*C*H_3). **HRMS** (on the mixture) (ESI+): calcd. for $C_{21}H_{28}BrO_3^+$ $[M+H]^+$ 407.12163, found 407.1214 (only the lighter isotope is reported).

5-Bromo-6-(1-(((1*R*,2*R*,3*R*,5*S*)-2,6,6-trimethylbicyclo[3.1.1]heptan-3-yl)oxy)but-3-en-1-yl)benzo[d][1,3]dioxole 12f



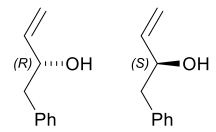
12f

Following the general procedure, 6-bromopiperonal **9** (107 mg, 0.47 mmol), (–) isopinocampheol TMS ether **18b** (0.70 mmol, 159 mg), AllylTMS (0.70 mmol, 111 µL), TMSOTf (140 µmol, 466 µL, 0.3 M in dry CH_2Cl_2) were reacted in dry CH_2Cl_2 (2.3 mL) at –78 °C for 6 h. After workup, the crude was purified by chromatography (PE/CH_2Cl_2 9:1) to give **12e** (94 mg, 49% overall yield) as colorless oil. Although the two epimers are difficult to separate, we could obtain fractions enriched in epimer **A** (faster running) or **B** (slower running). D.r. 52:48 (A:B) by ^{1}H NMR. R_f 0.27 and 0.20 (PE/CH_2Cl_2 9:1).

Epimer A: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.00 (1 H, s, aromatic CH of piperonyl), 6.96 (1 H, s, aromatic CH of piperonyl), 5.99 (1 H, d, *J* 1.5, part A of AB of OCH_2O), 5.97 (1 H, d, *J* 1.5, part B of AB of OCH_2O), 5.92 (1 H, ddt, *J* 17.2, 10.4, 7.0, C*H*=CH_2), 5.12-5.00 (2 H, m, CH=CH_2), 4.79 (1 H, dd, *J* 7.8, 4.7, C*H*-CH_2C=), 3.55 (1 H, dt, *J* 9.0, 3.8, *H*-3), 2.40-2.20 (4 H, m, CH_2CH=CH_2, 1 *H*-7,1 *H*-4, 1 *H*-6), 2.13 (1 H, qdd, *J* 7.2, 4.0, 2.4, *H*-2), 1.84 (1 H, tt, *J* 5.7, 3.1, *H*-1 or *H*-5), 1.81-1.71 (2 H, m, *H*-1 or *H*-5 + 1 *H*-4 or *H*-6), 1.15-1.10 (1 H, m, *H*-4 or *H*-6), 1.18, 0.81 (2 s, 2 x 3 H, CH_3), 1.11 (3 H, d, *J* 7.2, CH_3CH). **^{13}C NMR** (101 MHz, CDCl3) δ 147.7 (C-O), 147.4 (C-O), 135.9 (C quat.), 135.1 (*C*H=CH_2), 116.9 (CH=*C*H_2), 112.7 (C-Br), 112.2 (CH of piperonyl), 107.9 (CH of piperonyl), 101.6 (OCH_2O), 78.1 (*C*HCH_2CH=CH_2), 76.8 (*C*-3), 47.8 (*C*-1 or *C*-5), 44.5 (*C*-2), 41.8 (*C*H_2CH=CH_2), 41.0 (*C*-1 or *C*-5), 38.2 (*C*-6), 36.3 (*C*-7 or *C*-4), 32.5 (*C*-7 or *C*-4), 27.4 (*C*H_3), 23.8 (*C*H_3), 21.9 (*C*H_3CH). **HRMS**: (ESI+): calcd. for $C_{21}H_{28}BrO_3^+$ $[M+H]^+$ 407.12163, found 407.1217 (only the lighter isotope is reported).

Epimer B: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.00 (1 H, s, aromatic CH of piperonyl), 6.96 (1 H, s, aromatic CH of piperonyl), 5.99 (1 H, d, *J* 1.5, part A of AB of OCH_2O), 5.97 (1 H, d, *J* 1.5, part B of AB of OCH_2O), 5.89 (1 H, ddt, *J* 17.2, 10.2, 7.0, C*H*=CH_2), 5.11-5.00 (2 H, m, CH=CH_2), 4.79 (1 H, dd, *J* 7.6, 5.5, C*H*-CH_2C=), 3.41 (1 H, dt, *J* 8.9, 4.3, *H*-3), 2.42-2.28 (4 H, m, CH_2CH=CH_2, 1 *H*-7,1 *H*-4, 1 *H*-6), 2.02 (1 H, qdd, *J* 7.2, 5.2, 2.0, *H*-2), 1.94 (1 H, tt, *J* 5.8, 3.1, *H*-1 or *H*-5), 1.84 (1 H, dt, *J* 13.4, 3.8, *H*-4 or *H*-6), 1.74 (1 H, td, *J* 5.9, 2.1, *H*-1 or *H*-5), 1.18-0.78 (2 s, 2 x 3 H, CH_3), 1.08 (1 H, d, *J* 9.6, *H*-4 or *H*-6), 0.91 (3 H, d, *J* 7.4, CH_3CH). **^{13}C NMR** (101 MHz, CDCl3) δ 147.7 (C-O), 147.5 (C-O), 135.4 (C quat.), 135.0 (*C*H=CH_2), 116.9 (CH=*C*H_2), 113.5 (C-Br), 112.1 (CH of piperonyl), 107.9 (CH of piperonyl), 101.7 (OCH_2O), 76.5 (*C*HCH_2CH=CH_2), 75.5 (*C*-3), 47.5 (*C*-1 or *C*-5), 44.6 (*C*-2), 42.0 (*C*H_2CH=CH_2), 41.6 (*C*-1 or *C*-5), 38.4 (*C*-6), 35.5 (*C*-7 or *C*-4), 33.4 (*C*-7 or *C*-4), 27.5 (*C*H_3), 23.7 (*C*H_3), 20.5 (*C*H_3CH). **HRMS** (ESI+): calcd. for $C_{21}H_{28}BrO_3$ $[M+H]^+$ 407.1221, found 407.1229 (only the lighter isotope is reported).

(2*R*)-Phenylbut-3-ene-2-ol 16a and (2*S*)-phenylbut-3-ene-2-ol *ent*-16a.



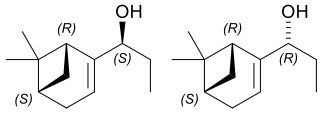
16a ***ent*-16a**

These alcohols are known in both enantiomeric forms.[3-5] However, we prepared them as follows. Freshly distilled phenylacetaldehyde (4.6 mL, 41.6 mmol) was dissolved in dry THF (165 mL) and cooled to −10 °C. Then, vinyl magnesium bromide (50 mL of a 1.0 M solution in MeOH, 50 mmol) was slowly added through a dropping funnel. At the end of addition, the mixture was stirred at 0 °C for 3 h and 35 min. The mixture was quenched with a saturated aqueous NH_4Cl solution (100 mL). After evaporation of most THF at the rotavapor, extraction with Et_2O and evaporation afforded a crude product that was purified by chromatography (PE/Et_2O 4:1) to give pure **racemic 16a** (5.05 g, 82%).[6] All analytical data were in agreement with those reported.[7]

A sample of this racemic alcohol (1.03 g, 6.95 mmol) was dissolved in diisopropyl ether (31 mL) in a thermostated bath at 20 °C. 3 Å powdered molecular sieves (0.35 g) were added, followed by vinyl butyrate (4.4 mL, 34.6 mmol) and by Amano PS lipase (0.51 g). The suspension was stirred for 7 h, and

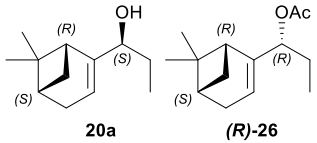
then filtered through a celite cake, washing with CH_2Cl_2. The filtrate was evaporated to dryness and the crude product controlled by ^1H NMR to determine conversion, that was 48.5%. Chromatography (PE/Et_2O from 15:1 to 4:1) afforded first butyrate (*S*)-**25** (666 mg, 44%) (e.e. > 98%), and then alcohol (*R*)-**16a** (388 mg, 38%) (e.e. 97%).
Butyrate (*S*)-**25** (0.56 g, 3.75 mmol) was directly dissolved in MeOH (15 mL) and treated with 1 M KOH in MeOH (5.8 mL, 5.8 mmol). The solution was stirred for 4 h at rt. After addition of saturated aqueous NH_4Cl (final pH = 7), extraction with Et_2O and evaporation gave pure (*S*)-***ent*-16a (**356 mg, 94%). Enantiomeric excess were measured on alcohols (*R*)-**16a** (recovered from enzymatic resolution) and (*S*)-***ent*-16a** (obtained from hydrolyisis of butyrate (*S*)-**25**), by HPLC on chiral stationary phase [Daicel ChiralPak AD (250×4.6 mm) with detector DAD (226 nm, 220 nm)]. Eluent: *n*-hexane/*i*PrOH 99:1, Flow: 0.8 mL/min. R_t = 21.7 (*R*) and 23.4 (*S*). The e.e. of **25** was deduced from the one of alcohol ***ent*-16a**.
All spectroscopic and polarimetric data were in agreement with those reported before.[3-5]

Epimeric mixture of (1*R*,5*S*)-2-((*S*)-1-hydroxypropyl))-6,6-dimethylbicyclo[3.1.1]hept-2-ene 20a and (1*R*,5*S*)-2-((*R*)-1-hydroxypropyl))-6,6-dimethylbicyclo[3.1.1]hept-2-ene 21a



A solution of (−)-myrtenal (1.974 g, 13.14 mmol) in dry Et_2O (130 mL), was cooled to −78 °C and treated with a 3 M EtMgBr solution in Et_2O (7.4 mL, 22.2 mmol). After stirring for 4 h, the mixture was quenched with saturated aqueous NH_4Cl and the phases separated. After washing with brine, the organic extracts were evaporated and chromatographed (PE/Et_2O 9:1) to give the pure mixture of epimers (2.079 g, 88%) as a colorless oil in a 57:43 ratio (**20a** major)(determined by ^1H NMR). With PE/Et_2O they coelute (R_f 0.16). Using PE/CH_2Cl_2/Et_2O 9:1:1 they were slightly separated. R_f of **20a** 0.31, R_f of **21a** 0.26.

(1*R*,5*S*)-2-((*S*)-1-Hydroxypropyl))-6,6-dimethylbicyclo[3.1.1]hept-2-ene 20a and (1*R*,5*S*)-2-((*R*)-1-acetoxypropyl))-6,6-dimethylbicyclo[3.1.1]hept-2-ene 26.

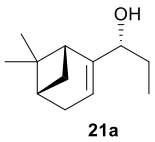


The 57:43 epimeric mixture of **20a** and **21a** (1.514 g, 8.40 mmol) was dissolved in vinyl acetate (84 mL), and treated with 3Å powder molecular sieves (420 mg) and with Amano AK lipase (605 mg). After stirring for 4 days at rt, the mixture was filtered, washing with CH_2Cl_2, and the filtrate was evaporated and chromatographed (PE/CH_2Cl_2/Et_2O 9:0.5:0.5 to give acetate (*R*)-**26** (d.r. 95:5) (805 mg, 43%) and alcohol (*S*)-**20a** (859 mg, 57%) (d.r. 97:3). R_f 0.72 (**26**) and 0.31 (**20a**) (PE / CH_2Cl_2 / Et_2O 9:1:1).

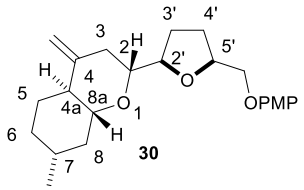
(*R*)-**26**. **$[\alpha]_D$** = +57.2 (c 1.0, $CHCl_3$). **^1H NMR** (300 MHz, $CDCl_3$) δ 5.48-5.44 (1 H, m, C*H*=C), 5.05 (1 H, t, *J* 6.6, C*H*OAc), 2.38 (1 H, dt, *J* 8.4, 5.7, *H*-7), 2.35-2.14 (3 H, m, 2 *H*-4 + *H*-1 or *H*-5), 2.12-2.04 (1 H, m, *H*-1 or*H*-5), 2.03 (3 H, s, C*H*$_3$C=O), 1.66-1.46 (2 H, m, C*H*$_2$CH$_3$), 1.28 and 0.82 (2 x 3H, (C*H*$_3$)$_2$C), 1.11 (1 H, d, *J* 8.6, *H*-7), 0.88 (3 H, t *J* 7.4, CH$_2$C*H*$_3$). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.5 (*C*=O), 146.3 (*C*-2) 119.5 (*C*-3), 77.9 (*C*HOAc), 42.4 (*C*-1 or *C*-5), 40.8 (*C*-1 or *C*-5), 37.8 (*C*-6), 31.5 (*C*-7), 31.1 (*C*-4), 26.2, 21.3, (*C*H$_3$)$_2$C, 25.4 (*C*H$_2$CH$_3$), 21.2 (*C*H$_3$C=O), 9.8 (*C*H$_3$CH$_2$). **HRMS** (ESI+): calcd. for $C_{14}H_{23}O_2^+$ $[M+H]^+$ 223.16926, found 223.1701.

(*S*)-**20a**. **[α]$_D$** = –48.3 (c 1.1, $CHCl_3$). ^{1}H and ^{13}C NMR were identical to those reported by Seebach *et al*.[8] In particular the ^{1}H signals most useful in order to recognize the epimers and to determine the d.r. are those of one of the methyl groups of the bridge, which falls at 0.85 for (*S*)-**20a** and at 0.82 for (*R*)-**21a**.

(1*R*,5*S*)-2-((*R*)-1-Hydroxypropyl))-6,6-dimethylbicyclo[3.1.1]hept-2-ene 21a



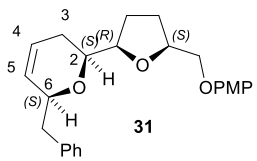
A solution of acetate (*R*)-**26** (833 mg, 3.75 mmol) in MeOH (9.4 mL) was treated with a 0.6 M solution of KOH in MeOH (9.4 mL, 5.72 mmol) and stirred at rt for 20 h. A saturated aqueous NH_4Cl solution was added, and most methanol was evaporated**.** Extraction with Et_2O, washing with brine, evaporation, and chromatography gave pure alcohol **21** (567 mg, 84%) with d.r. 95:5.
(*R*)-**21a**: **[α]$_D$** = –28.6 (c 1.0, $CHCl_3$). ^{1}H and ^{13}C NMR were identical to those reported by Seebach *et al*.[8]



^{1}H NMR of Prins adduct 30 ((2*R*,4a*S*,7*R*,8a*R*)-2-((2*R*,5*S*)-5-((4-methoxyphenoxy)methyl)tetrahydrofuran-2-yl)-7-methyl-4-methyleneoctahydro-2*H*-chromene

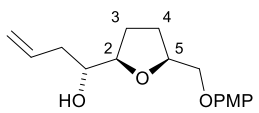
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88-6.78 (4 H, m, aromatic *H* of PMP), 4.73 (1 H, q, *J* 1.2, C*H*=C), 4.62 (1 H, q, *J* 1.2, C*H*=C), 4.30 (1 H, dt, *J* 7.3, 5.4, C*H*-CH_2OPMP), 4.01 (1 H, dd, *J* 9.6, 5.1, C*H*HOPMP), 3.93 (dt, *J* 7.8, 6.0, *H*-2'), 3.85 (1 H, dd, *J* 9.6, 5.7, *H*-5'), 3.76 (3 H, s, O*CH*$_3$), 3.37 (1 H, ddd, *J* 10.7, 5.9, 3.3, *H*-2), 2.95 (ddd, *J* 10.8, 9.9, 3.9, *H*-8a), 2.27-1.77 (7 H, m, CH_2), 1.77-1.61 (3 H, m, *H*-4a + 2H of CH_2), 1.55-1.32 (1 H, m, C*H*-CH_3), 1.30-0.90 (m, 3 H), 0.93 (3 H, d, *J* 6.6, CH_3CH). The configuration of C-*2* was assigned considering that the *J* of *H*-2 clearly indicate that this hydrogen is axial. On the other hand, the *trans* fusion of the bicyclic system makes it rigid and thus *H*-2 and *H*-8a must be in a *cis* relationship.

(2*R*,5*S*)-2-((2*S*,6*S*)-6-Benzyl-*2H*,*3H*,*6H*-dihydropyran-2-yl)-5-((4-methoxyphenoxy)methyl) tetrahydrofuran 31



A solution of *anti*-**11f** (31.4 mg, 76.9 µmol) in dry CH_2Cl_2 (20 mL), was treated under Ar with Grubbs 1st generation catalyst (Benzylidene-*bis*(tricyclohexylphosphine)dichlororuthenium) (8.0 mg, 9.2 µmol). The solution was refluxed for 3h. The solution was evaporated and chromatographed (PE/Et_2O 8:2) to give pure **31** as an oil (28.4 mg, 97%). ***R*$_f$** 0.09 (PE/Et_2O 90:10). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.32-7.15 (5 H, m, C*H* of Bn), 6.81 (4 H, s, C*H* of PMP), 5.81 (1 H, ddt, *J* 9.7, 4.5, 2.6, *H*-4 of DHP), 5.63 (1 H, dq, *J* 9.7, 1.2, *H*-5 of DHP), 4.39-4.29 (1 H, m, *H*-6 of DHP), 4.25 (1 H, quint, *J* 6.1, C*H*-CH_2OPMP), 3.96 (1 H, q, *J* 5.9, *H*-2 of THF), 3.82-3.71 (2 H, m, CH_2OPMP), 3.76 (3 H, s, O*CH*$_3$), 3.55 (dt, *J* 8.7, 5.2, *H*-2 of DHP), 2.89 (1 H, dd, *J* 13.6, 7.5, C*H*HPh), 2.72 (1 H, dd, *J* 13.6, 7.3, C*H*HPh), 2.10-1.90 (5 H, m), 1.87-1.71 (1 H, m). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 153.8, 153.1 (*C*-O), 138.5 (quat. Bn), 129.6 (x2)(ortho o meta Bn), 129.5 (*C*H=CH), 128.1 (x2)(ortho o meta Bn), 126.1 (para Bn), 124.8 (*C*H=CH), 115.5, 114.5 (*C* of PMP), 82.1 (*C*-2 of THF), 78.0 (*C*HCH_2OPMP), 76.0 (*C*-6 of DHP), 75.7 (*C*-2 of DHP), 71.2 (*C*H_2OPMP), 55.7 (O*C*H_3), 42.0 (*C*H_2Ph), 28.1, 27.8, 26.8 (*C*H_2 of DHP and THF). NOESY spectrum shows a nOe between *H*-2 and *H*-6 of the dihydropyran ring, whereas no nOe is observed betwen *H*-2 of DHP and the CH_2Ph signals, and no nOe between *H*-6 of DHP and *H*-2 of THF. **HRMS** (ESI+): calcd. for $C_{24}H_{29}O_4^+$ $[M+H]^+$ 381.20604, found 381.2070.

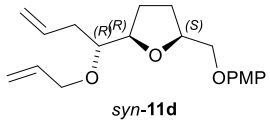
(2*R*,5*S*)-2-((*R*)-1-Hydroxybut-3-en-1-yl)-5-((4-methoxyphenoxy)methyl) tetrahydrofuran 32



32

$MgBr_2 \cdot Et_2O$ (568 mg, 2.20 mmol) was weighed in a flask, put under argon, and treated with a 0.1 M solution of aldehyde **8** in CH_2Cl_2 (10 mL, 1.0 mmol). The solution was cooled to –78 °C, and treated with allyltributyltin (620 µL, 2.00 mmol). After stirring for 5 h at this temperature, the mixture was quenched with saturated aqueous NH_4Cl. After warming to room temperature, the mixture was extracted with Et_2O (3 times), evaporated, and chromatographed (PE/CH_2Cl_2/Et_2O 5:5:1) to give a product that was not yet completely pure. A second chromatography PE/EtOAc 8:2) finally gave diastereomerically pure **32** as an oil (221 mg, 79%). R_f 0.27 (PE/EtOAc 80:20). **[α]$_D$** = −8.0 (c 0.8, $CHCl_3$). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.89-6.79 (4 H, m, aromatics), 5.89 (1 H, ddt, *J* 17.1, 10.2, 7.0, C*H*=CH_2), 5.18-5.05 (2 H, m, CH=C*H*$_2$), 4.37-4.26 (1 H, m, C*H*-CH_2OPMP), 4.01 (1 H, dd, *J* 9.9, 4.1, C*H*HOPMP), 3.97-3.89 (1 H, m (hidden by the signals of C*H*$_2$OPMP), *H*-2 of THF), 3.94 (1 H, dd, *J* 9.9, 4.5, C*H*HOPMP), 3.76 (3 H, s, OC*H*$_3$), 3.53 (1 H, dq, *J* 5.7, 6.9, C*H*OH), 2.62 (1 H, d *J* 5.9, O*H*), 2.36-2.19 (2 H, m, C*H*$_2$CH=CH_2), 2.13-1.79 (4 H, m, *H*-3 and *H*-4 of THF). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 154.1, 152.9 (aromatic quat.), 134.9 (*C*H=CH_2), 117.1 (CH=*C*H$_2$), 115.5, 114.7 (aromatic *C*H), 82.3 (*C*-2 of THF), 77.9 (*C*H-CH_2OPMP), 73.7 (*C*H-OH), 70.8 (*C*H$_2$OPMP), 55.7 (O*C*H$_3$), 38.8 (*C*H$_2$CH=CH_2), 28.1, 28.0 (*C*-3 and *C*-4 of THF). **HRMS** (ESI+): calcd. for $C_{16}H_{23}O_4$ $[M+H]^+$ 279.15909, found 279.1595.

(2*R*,5*S*)-2-((*R*)-1-(Allyloxy)but-3-en-1-yl)-5-((4-methoxyphenoxy)methyl)tetrahydrofuran *syn*-11d (*from* 32)



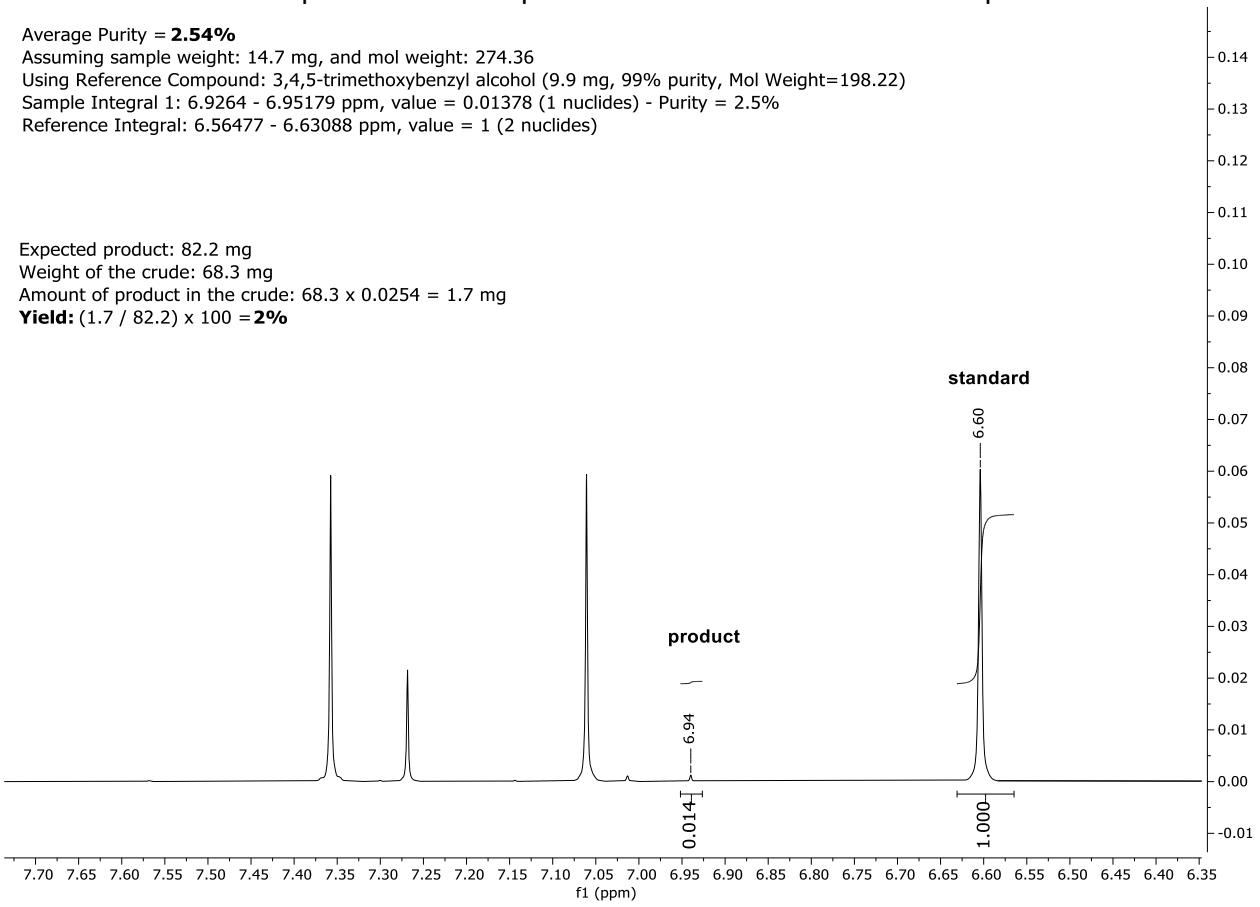
syn-**11d**

A solution of **32** (51.1 mg, 184 µmol) in dry DMF (2 mL), was treated with 60% NaH in mineral oil (11 mg, 275 µmol), and then, after 5 min, with allyl bromide (24 µL, 275 µmol). The mixture was stirred at 50 °C for 8 h. Then it was poured into saturated aqueous NH_4Cl and extracted three times with Et_2O. The organic extracts were washed with brine, evaporated, and chromatographed to give pure *syn*-**11d** (58 mg, 100%), identical to the one obtained by Hosomi-Sakurai reaction and described above.

OPTIMIZATION PROCEDURES

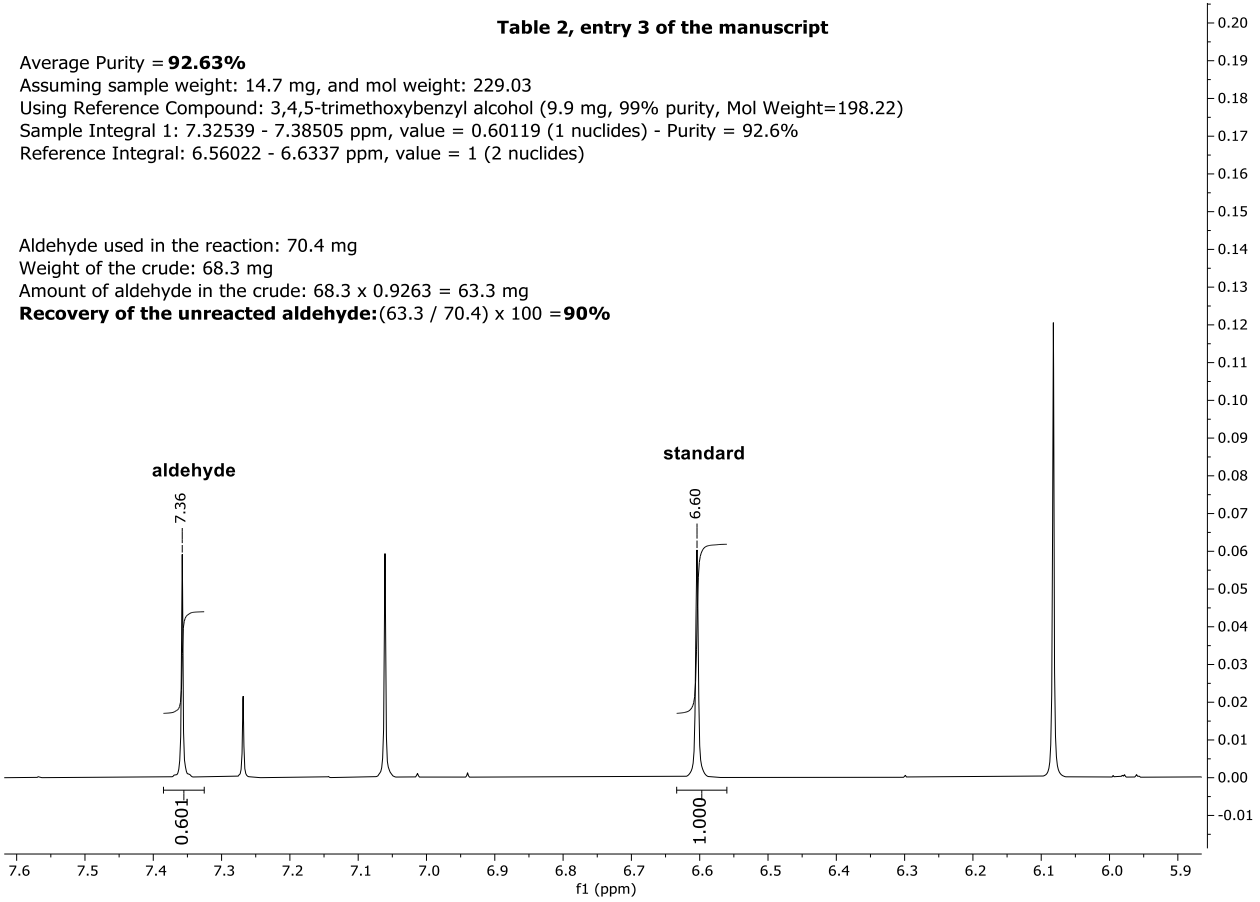
Protocol for the determination of the NMR yields reported in Table 1 of the manuscript

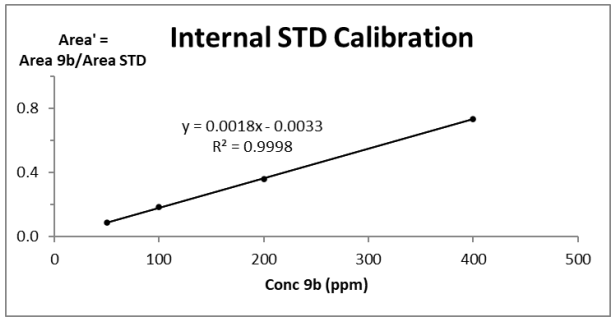
A sample of the crude (not less than 10 mg) and the internal standard 3,4,5-dimethoxybenzyl alcohol (not less than 10 mg, purity: 99%) were precisely weighted in a vial. Then $CDCl_3$ (750 µL) was added, and the resulting mixture was sonicated for 5 min. The solution was transferred into an NMR tube and a proton spectrum was registered (relaxation delay: 20 s, scans: 16). Using the "Purity calculator" script of the software MestReNova 14.0 the purity of 4-bromopiperonal and the product **12a** in the crude was determined. From those data, the yield of the reaction and the recovery of the starting material were determined. Below are reported ^1H NMR spectra and the calculations as examples.



Protocol for the determination of the yields reported in Table 2 of the manuscript

A calibration using 1,2-dimethoxybenzene as internal standard was carried out. A mother solution of compound *syn*-**11b** (only the major diastereoisomer) in *i*PrOH at 2000 ppm was prepared. A mother solution of the internal standard in hexane at 2000 ppm was prepared. A set of 4 calibration solutions of compound *syn*-**11b** was prepared at the following concentrations: 50 ppm, 100 ppm, 200 ppm, and 400 ppm (hexane was used for the final dilution). Each solution contains 250 ppm of the internal standard. The solutions were analyzed by chiral-HPLC (column Chiralpack AD 250x4.6 mm, eluent hexane/*i*PrOH 99:1, flow 0.8 mL/min, V inj = 20 µL, T = 25 °C, 226 nm) as triplicate.



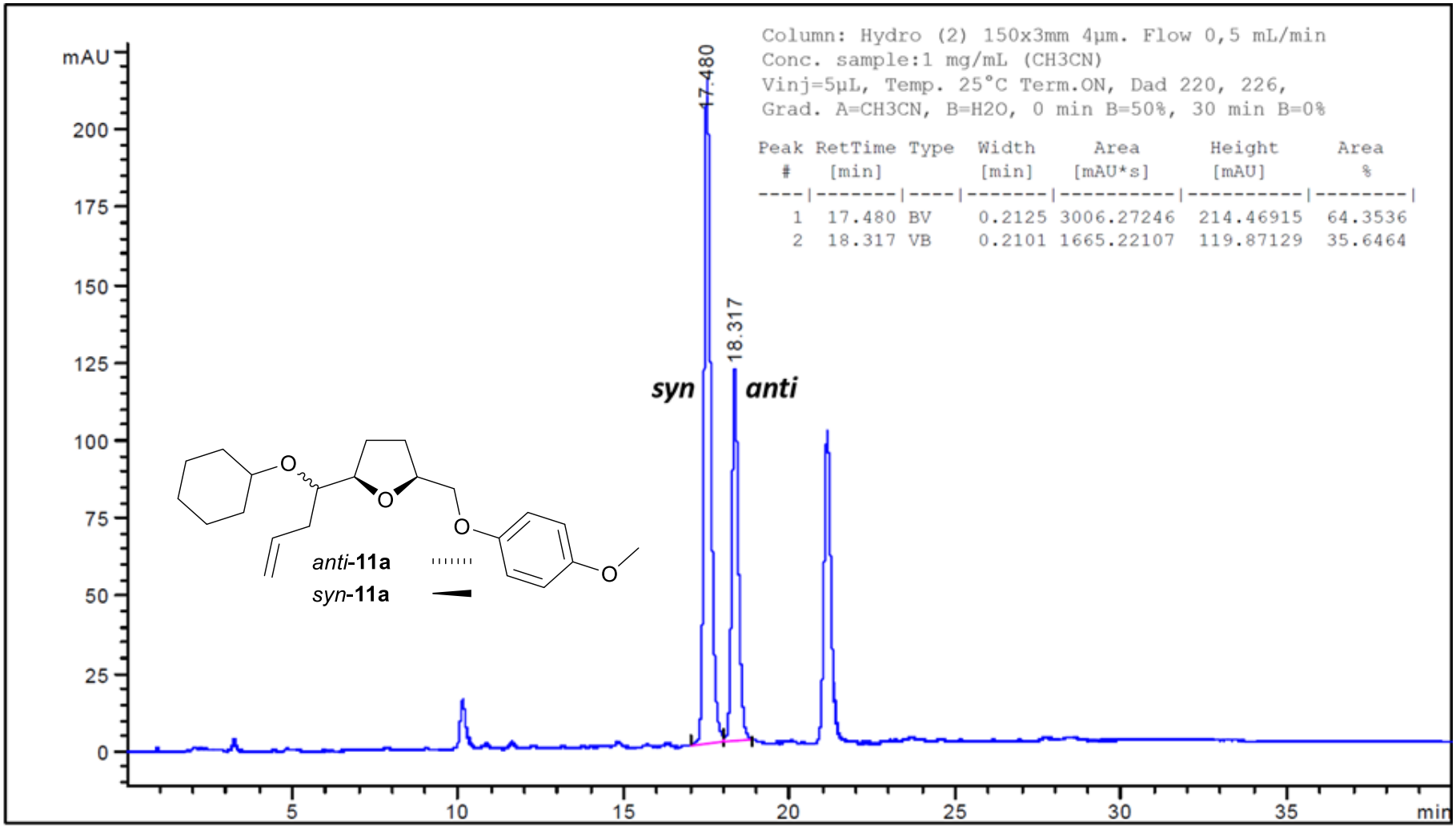


Optimization of enzymatic acetylation of 20a + 21a

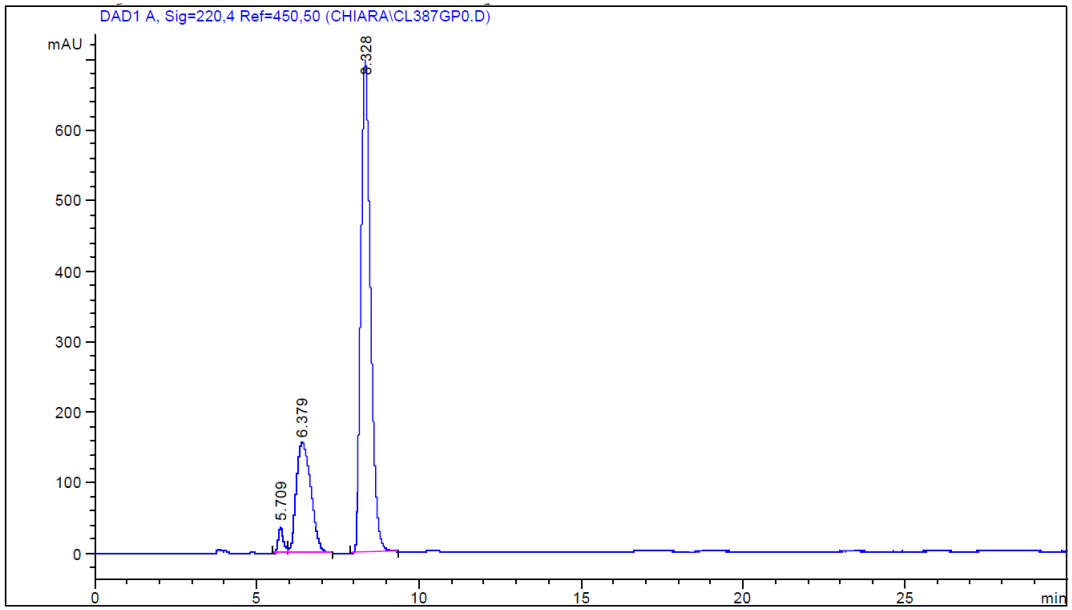
*Enzymes tested (initial ratio **20a** : **21a** = 57:43)*

- Amano AS: no conversion
- Amano AY: no conversion
- Novozym 435: sluggish reaction.
- Amano PS lipase supported on celite[11] (40 mg per 100 mg of substrate): after 8 days conversion = 43%. D.r. acetate: 97:3. D.r. alcohol (favouring **20a**) 97:3
- Amano AK lipase (40 mg per 100 mg of substrate): after 5 days conversion 44%%. D.r. acetate 95:5. D.r. alcohol (favouring **20a**) 97:3

ANALYSIS OF D.R. ratios

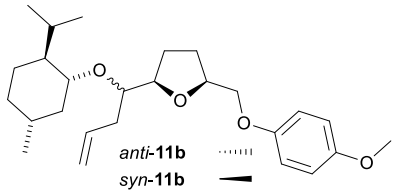


HPLC analysis of d.r. ratio of *anti* and *syn* 11a



Conditions: column ChiralPak AD,
Flow: 0.8 mL/min
Eluent: *n*-hexane/*i*PrOH 99:1 (isocratic)

Note: the peak at 8.328 minutes is 1,2-dimethoxybenzene, used as internal standard

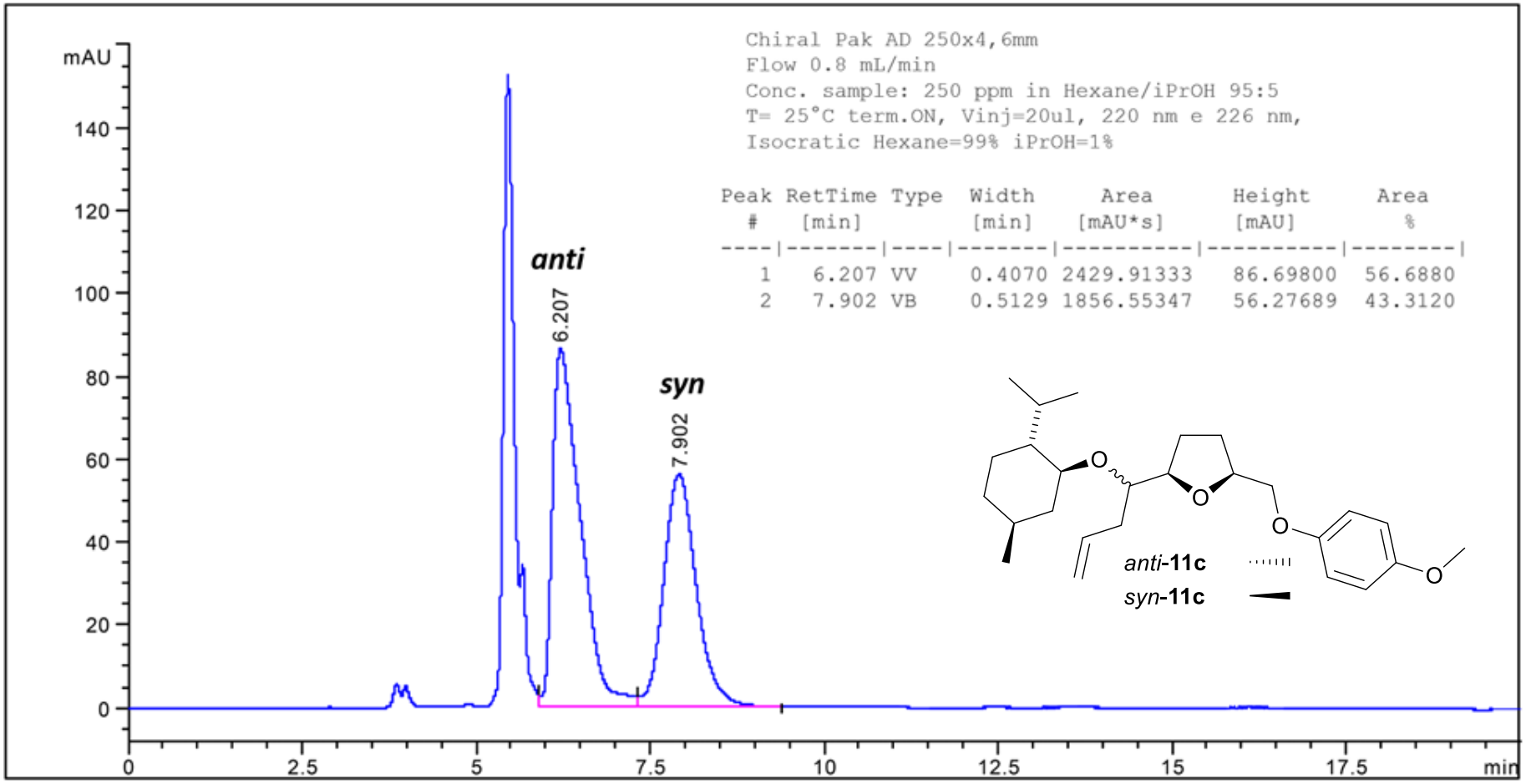


Signal 1: DAD1 A, Sig=220,4 Ref=450,50

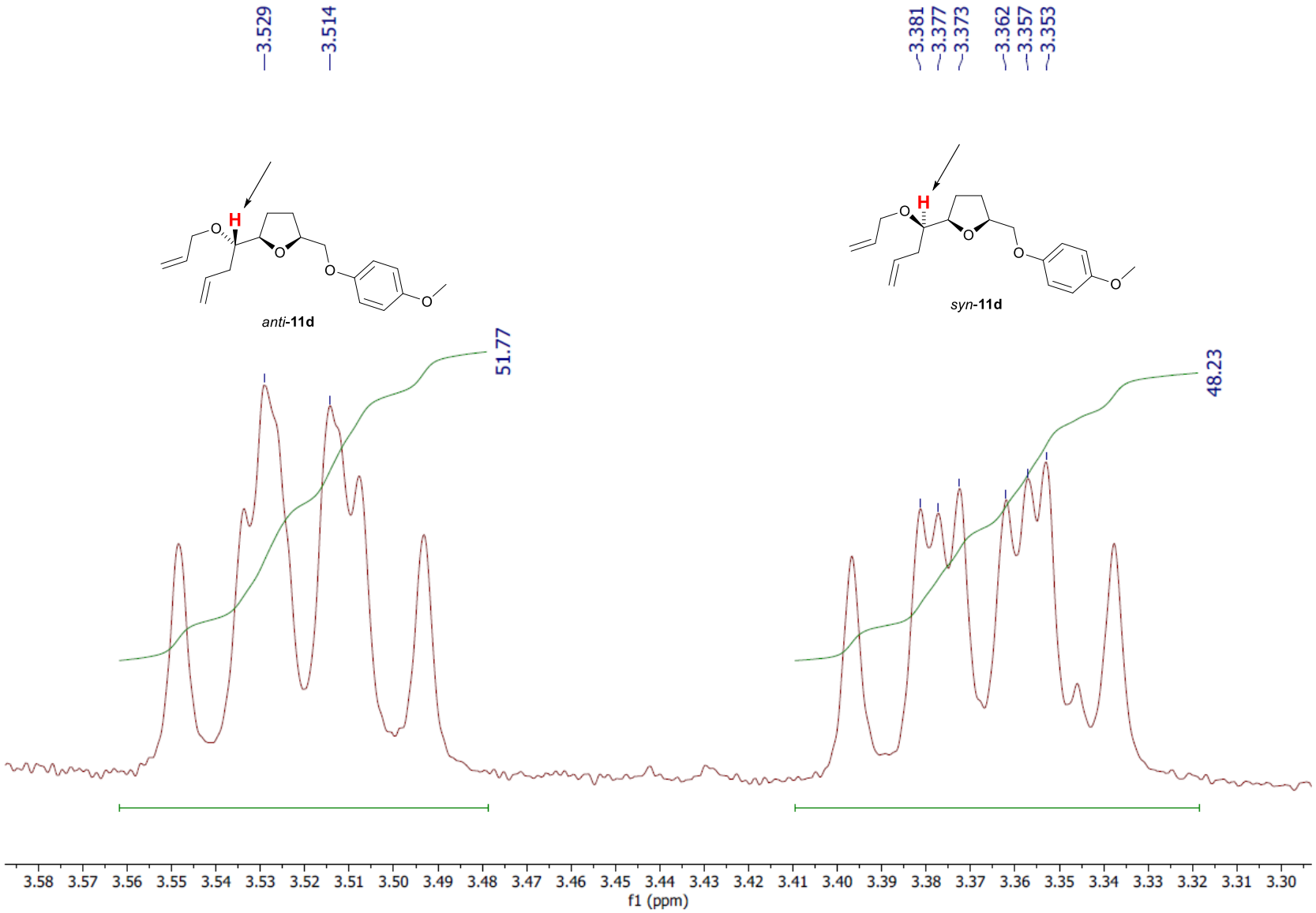
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.709	PV	0.1578	437.08508	37.81554	2.1861
2	6.379	VB	0.5082	4962.90723	157.66167	24.8219
3	8.328	PB	0.3314	1.45941e4	699.57666	72.9920

7

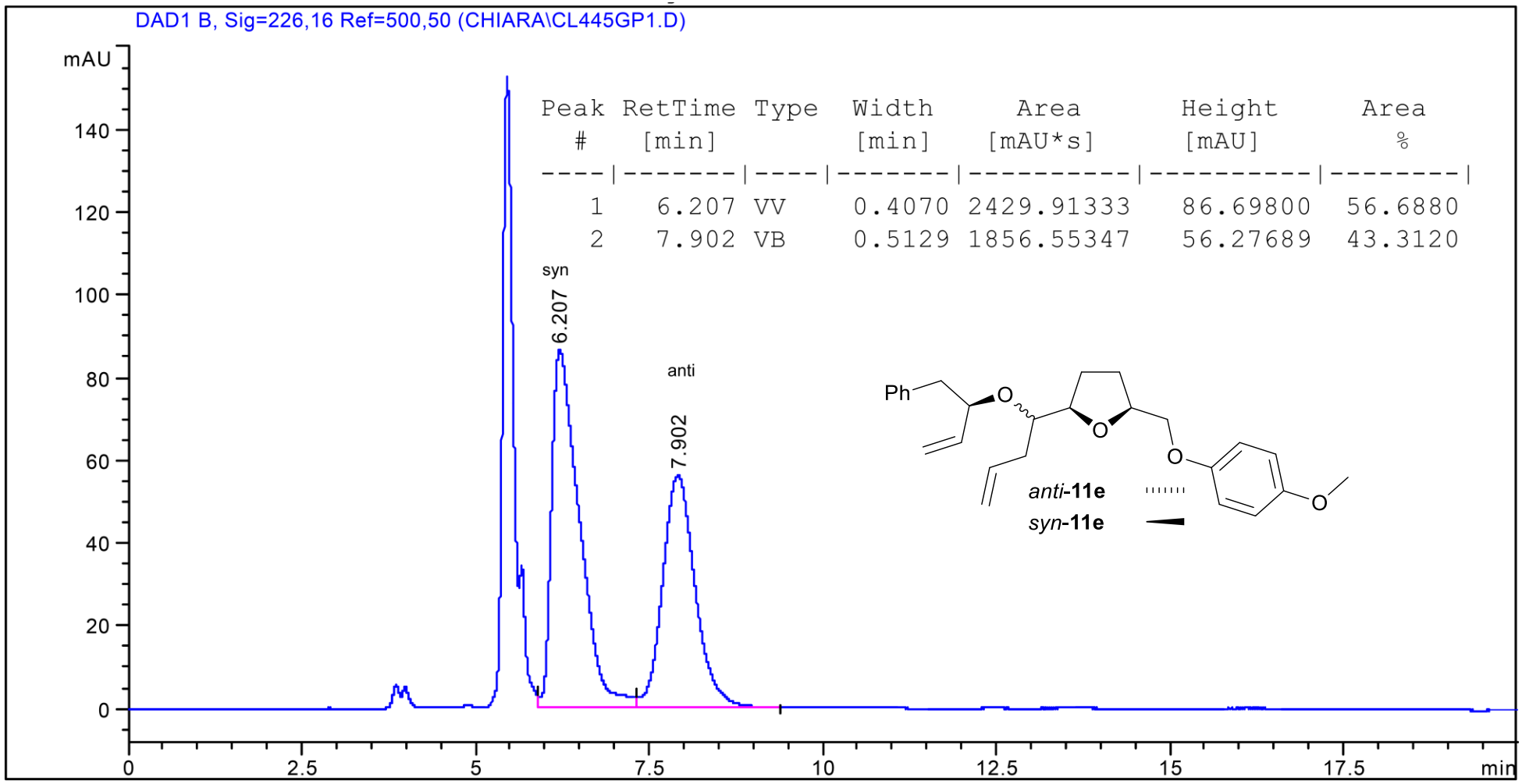
HPLC analysis of d.r. ratio of *anti* and *syn* 11b



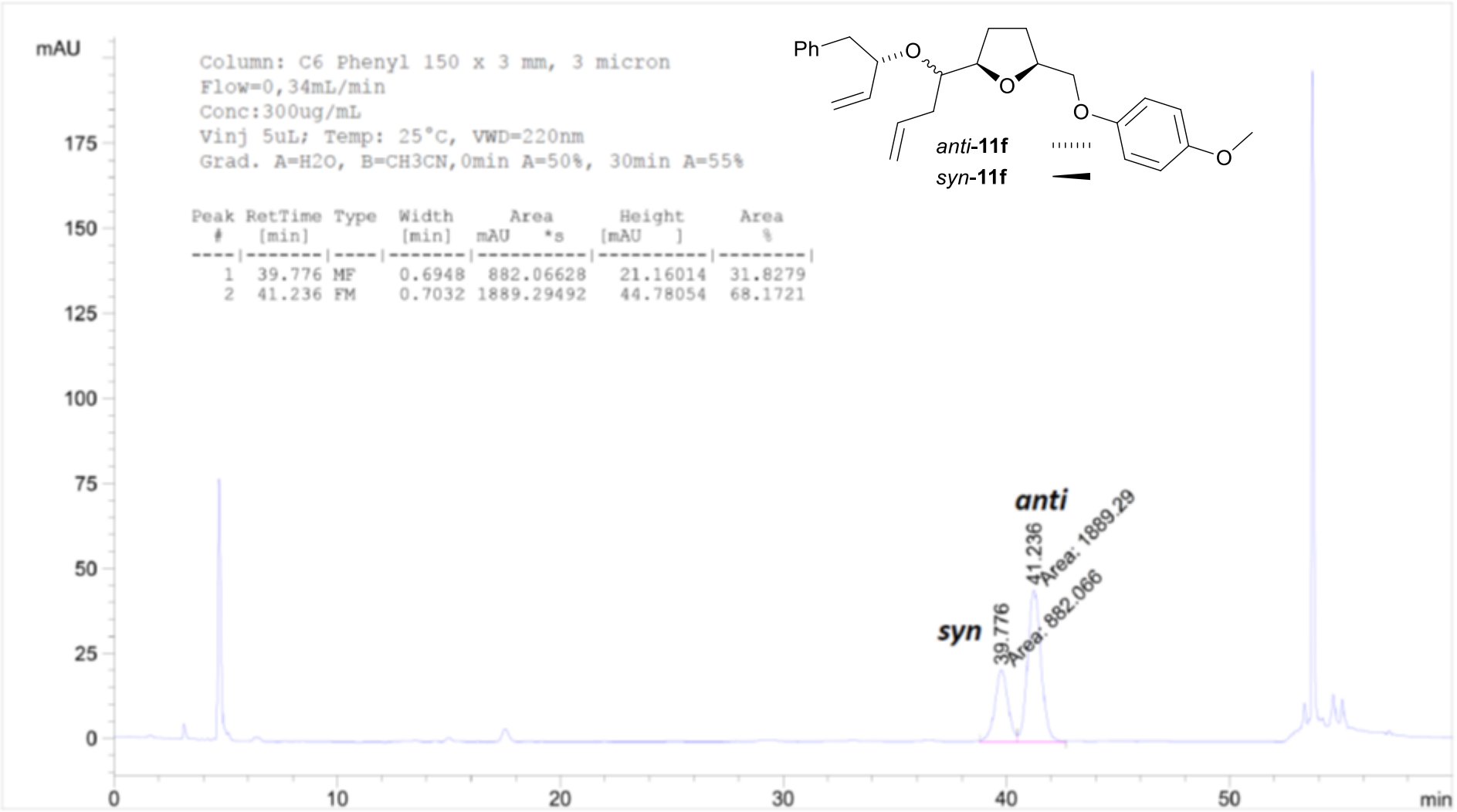
HPLC analysis of d.r. ratio of *anti* and *syn* 11c



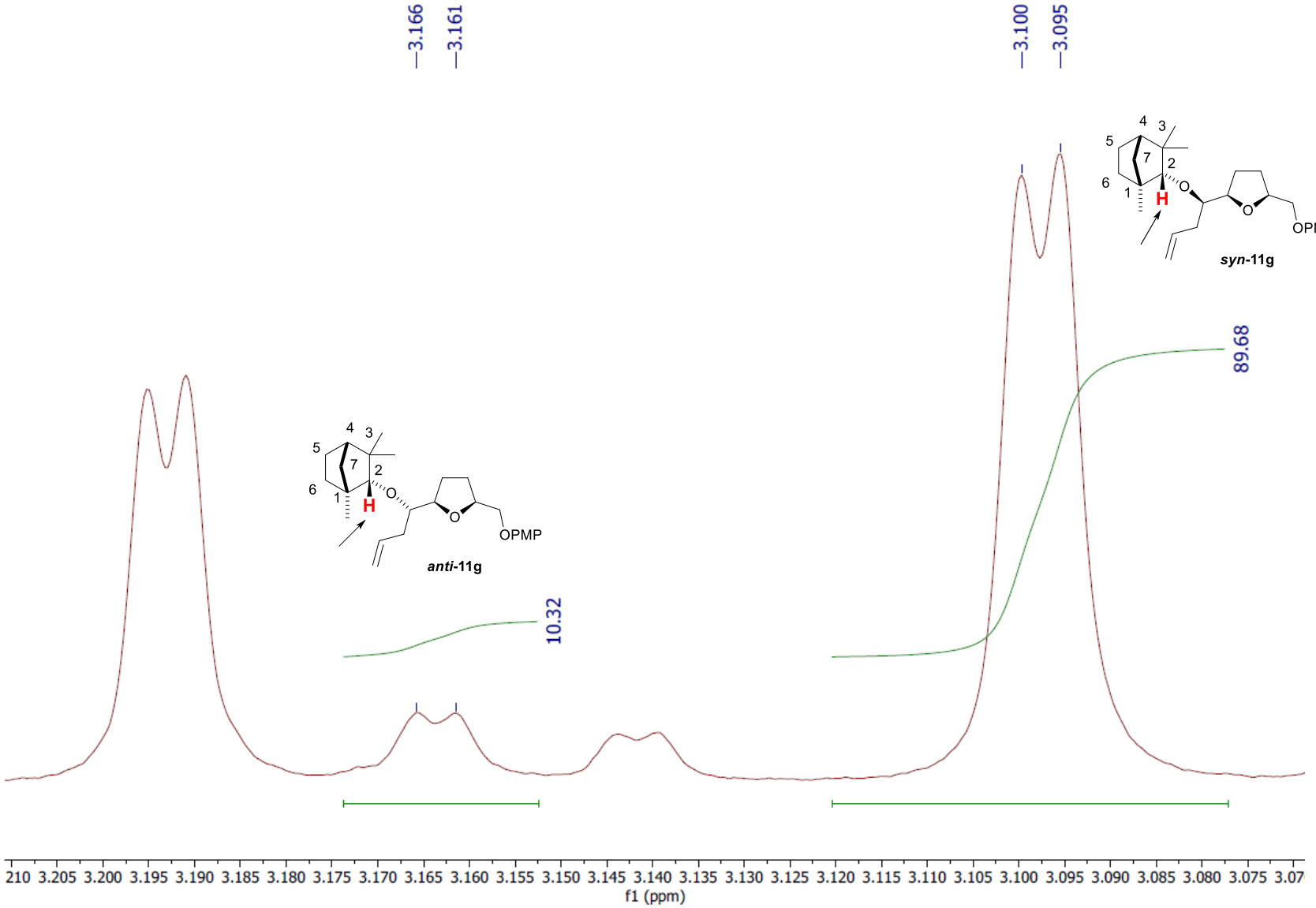
^{1}H NMR analysis of d.r. ratio of *anti* and *syn* 11d (made on crude product)



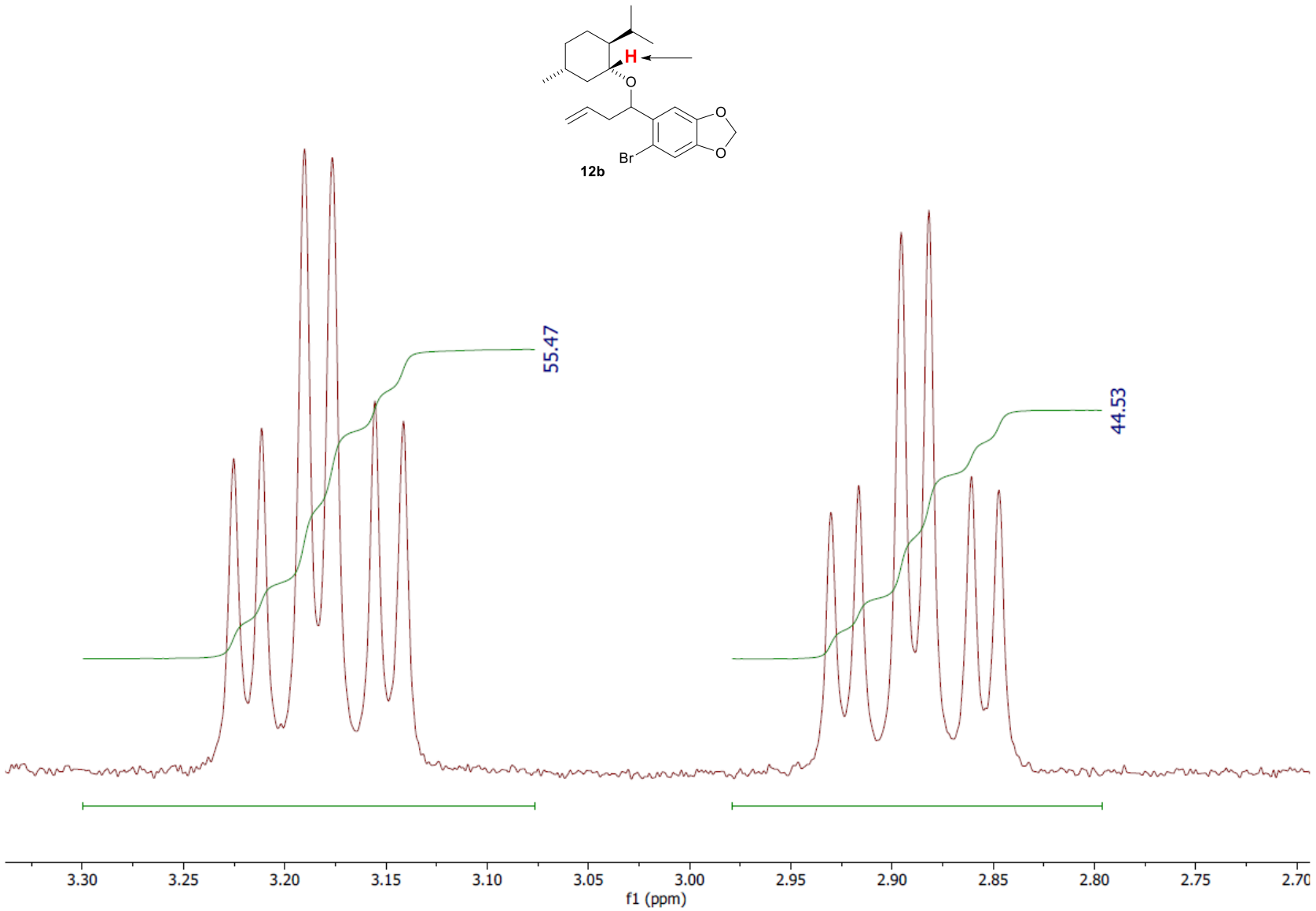
HPLC analysis of d.r. ratio of *anti* and *syn* 11e



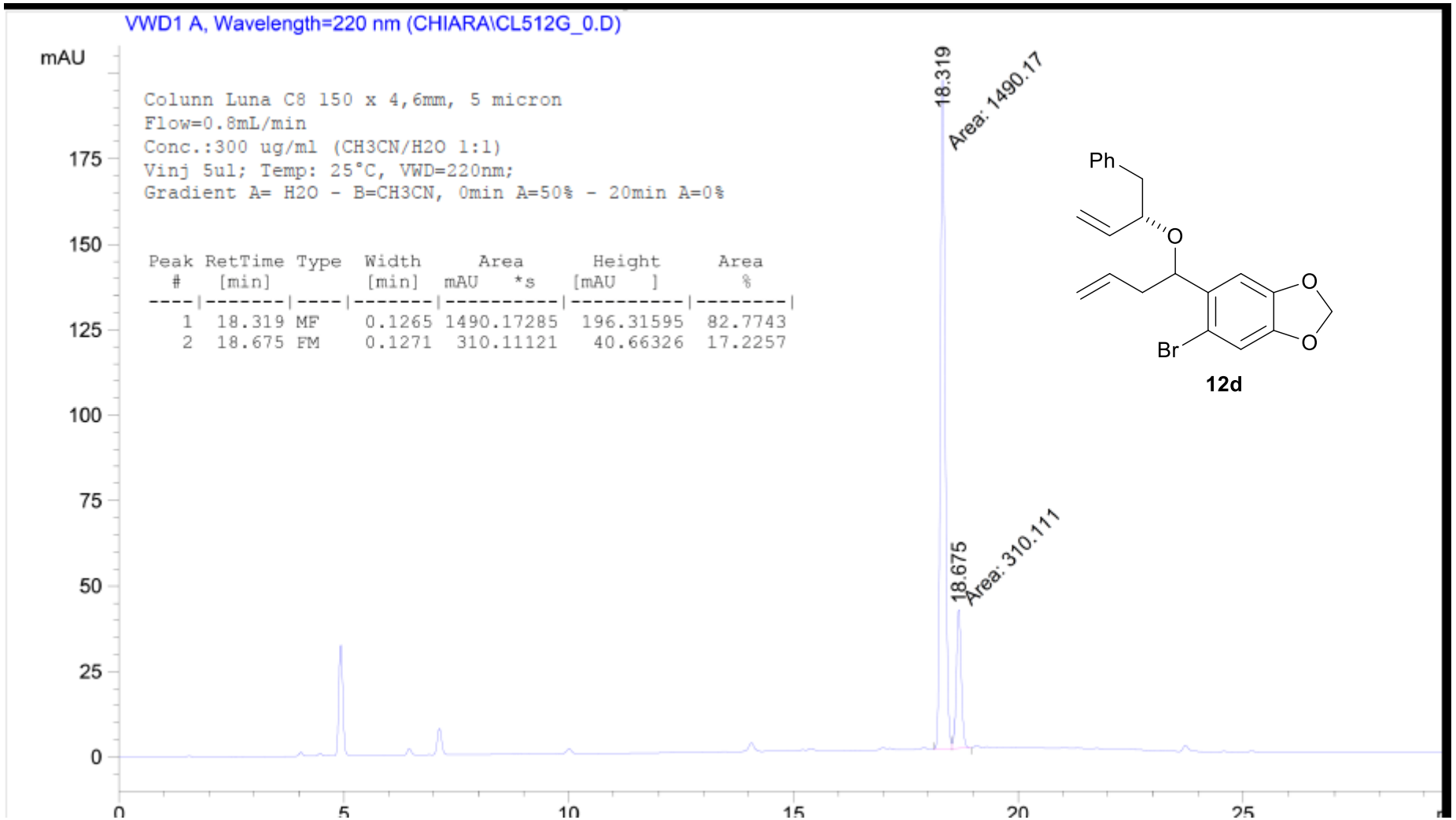
HPLC analysis of d.r. ratio of *anti* and *syn* 11f



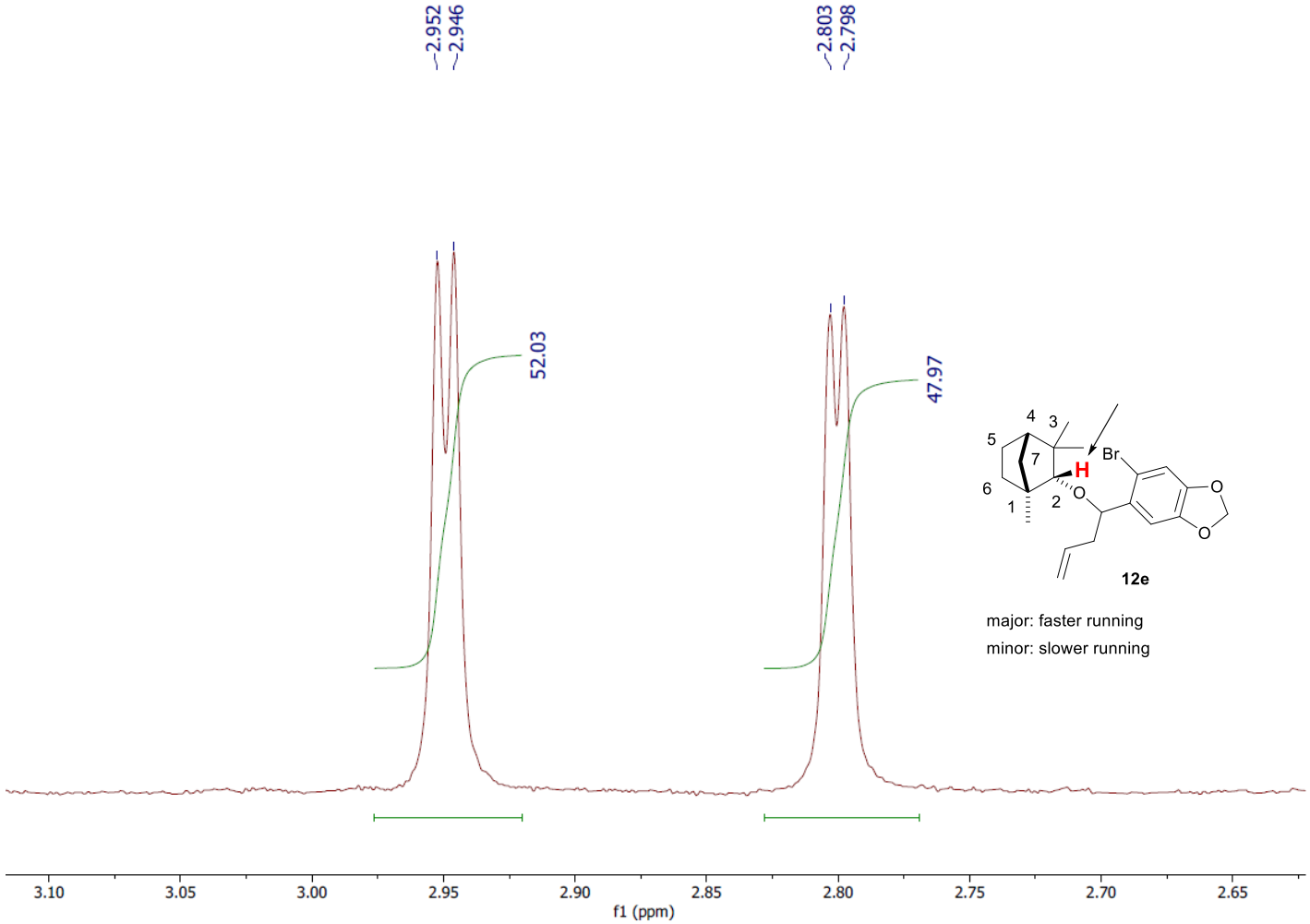
^{1}H NMR analysis of d.r. ratio of *anti* and *syn* 11g (made on crude product)



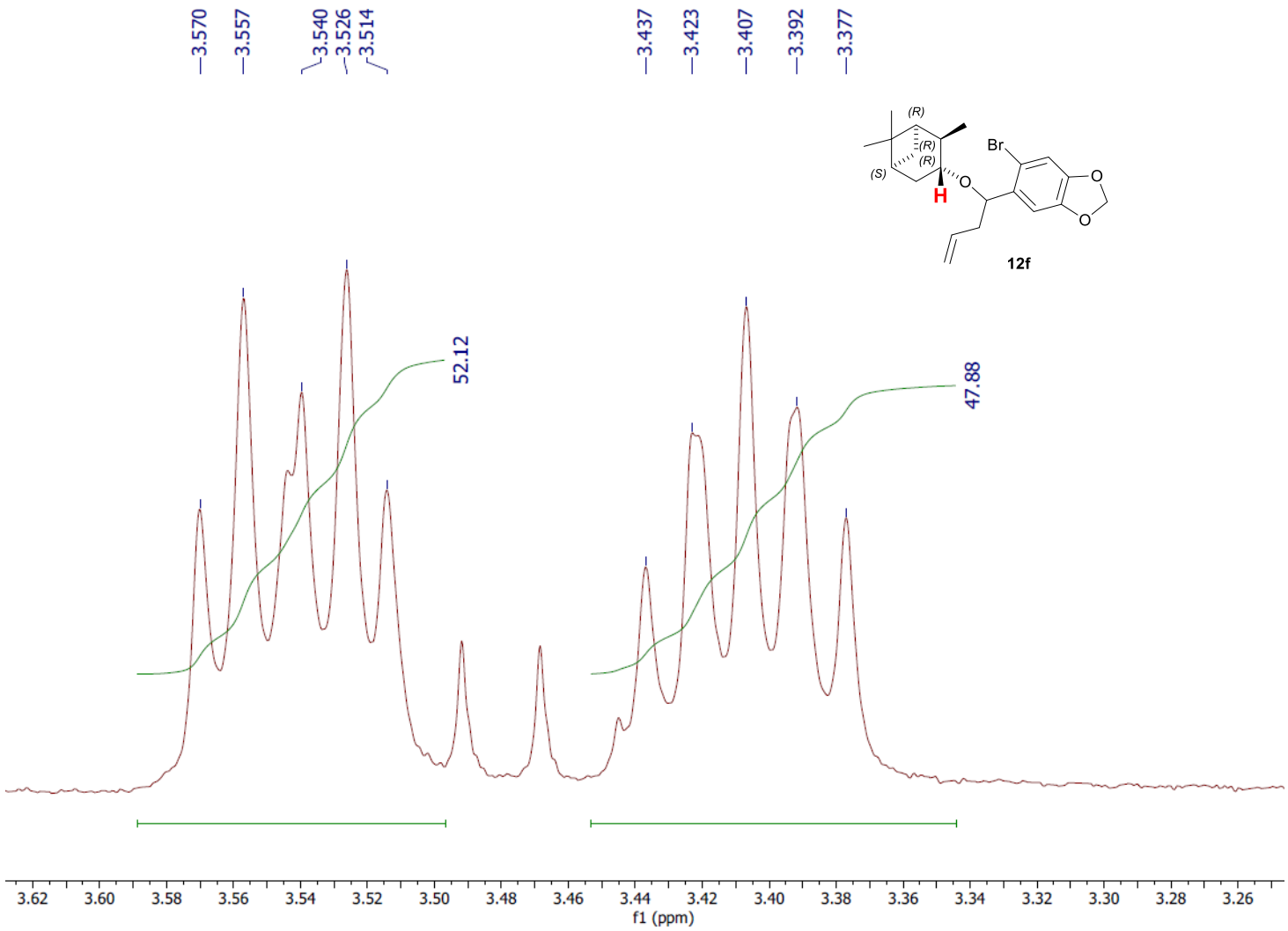
^{1}H NMR analysis of d.r. ratio of 12b



HPLC analysis of d.r. ratio of *anti* and *syn* 11f



^{1}H NMR analysis of d.r. ratio of 12e

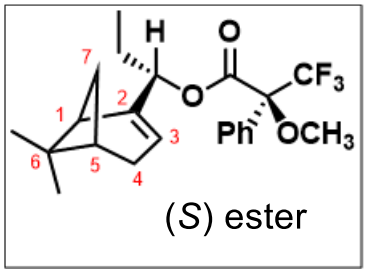


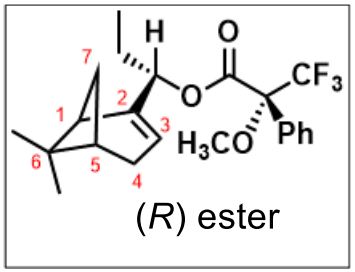
^{1}H NMR analysis of d.r. ratio of 12f (made on crude product at 300 MHz)

DETERMINATION OF CONFIGURATION

Assignment of configuration to alcohol 20a

Alcohols **20a** and **21a** were already reported by Seebach *et al*.[8] However, they did not prove the configuration, but assumed it only according to the known preference of their chiral catalyst. Thus, we preferred to corroborate their assignment in this way:
20a was converted into the two diastereomeric Mosher's esters, by reaction with the two enantiomeric acyl chlorides in CH_2Cl_2 in the presence of 4-*N*,*N*-dimethylaminopyridine. Analysis of the NMR spectra afforded the following results. Based on Mosher's rule, the configuration of **20a** was assessed as (*S*). This assignment corresponds to the one proposed by Seebach *et al.*



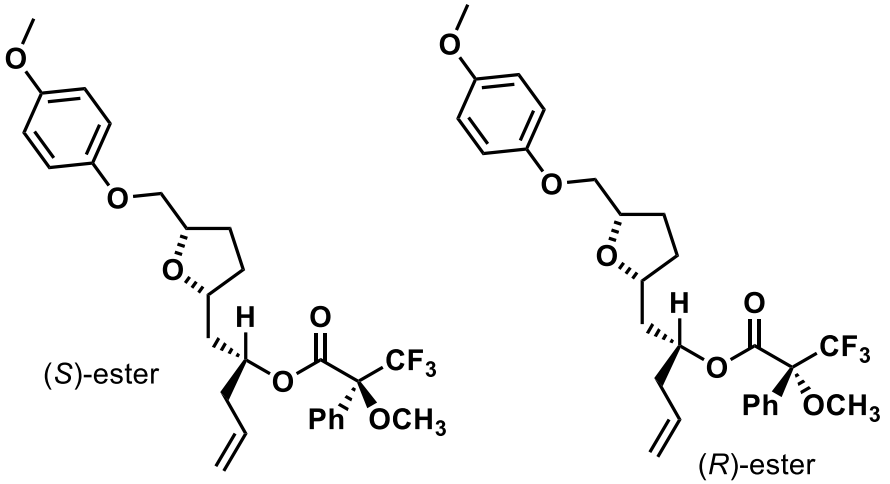


Peak	Δ (*S*) ester (ppm)	δ (*R*) ester (ppm)	Δ δ(*SR*)	
			ppm	Hz (300 MHz)
CH-O	5,27	5,27	0,00	0
CH_2 CH_3	1,64	1,70	-0,06	-18
CH_2**CH_3**	0,83	0,90	-0,07	-21
H_1	2,22	2,18	0,04	12
H_3	5,59	5,47	0,12	36
H_4 (they fall together)	2,28	2,23	0,05	15

H_5	2,09	2,06	0,03	9
6-CH_3a	1,25	1,23	0,02	6
6-CH_3b	0,75	0,68	0,07	21
7a	2,41	2,39	0,02	6
7b	1,12	1,10	0,02	6

Assignment of configuration to alcohol 32

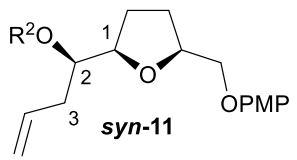
32 was converted into the two diastereomeric Mosher's esters, by reaction with the two enantiomeric acyl chlorides in CH_2Cl_2 in the presence of 4-*N*,*N*-dimethylaminopyridine. Analysis of the NMR spectra afforded the following results. Based on Mosher's rule, the configuration was assessed as (*R*)



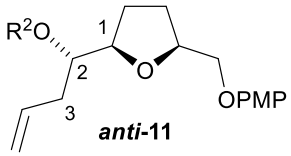
Peak	**δ (*S*) ester (ppm)**	**δ (*R*) ester (ppm)**	**Δ δ(*SR*)**	
			ppm	**Hz (300 MHz)**
CH-OC=O	5,14	5,15	-0,01	-3
OCH_3	3,77	3,76	0,01	3

aromatic C*H* para to OMe	6,83	6,81	0,02	6
CH**CH_2**OPMP (AB)	3,87	3,92	-0,05	-15
	3,72	3,82	-0,10	-30
CHCH_2OPMP	4,21	4,28	-0,07	-21
CH_2 ring	1,88	2,02	-0,14	-42
CH_2 ring	1,56	1,79	-0,23	-69
CH$CH_2CH=CH_2$	4,10	4,09	0,01	3
CH_2 $CH=CH_2$	2,52	2,38	0,14	42
CH_2**CH**$=CH_2$	5,80	5,66	0,14	42
$CH_2CH=$**CH_2**	5,14	5,02	0,13	38

NMR ANALOGIES



***syn*-11**



***anti*-11**

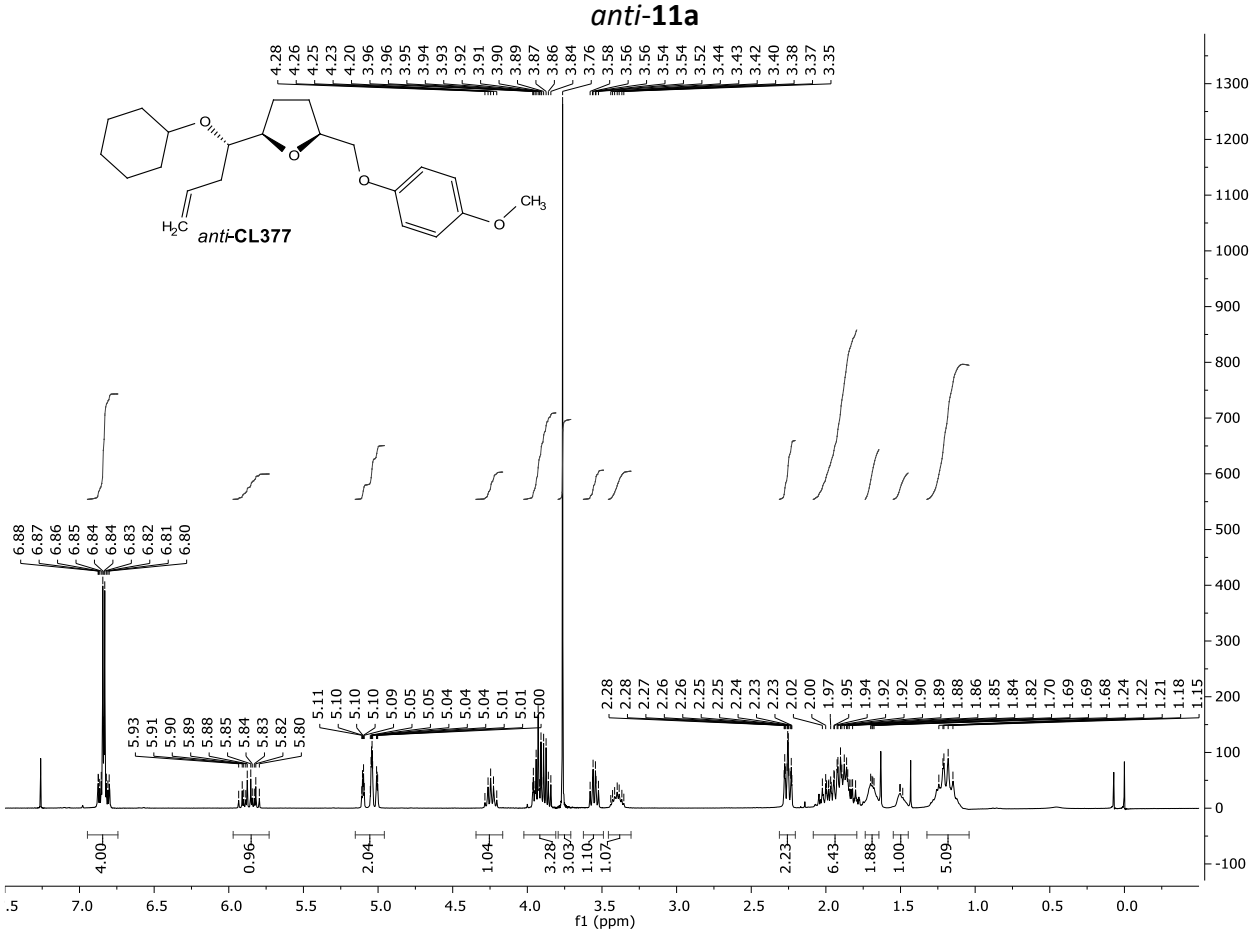
Analogies:

- For *H*-3, the *syn* diastereomers always have a higher difference in the chemical shifts of the two diastereotopic protons.
- For *H*-2, the chemical shift of *anti* isomer is always higher
- For *H*-1 the chemical shift of *syn* isomer is always higher (with the exception of **11e**)

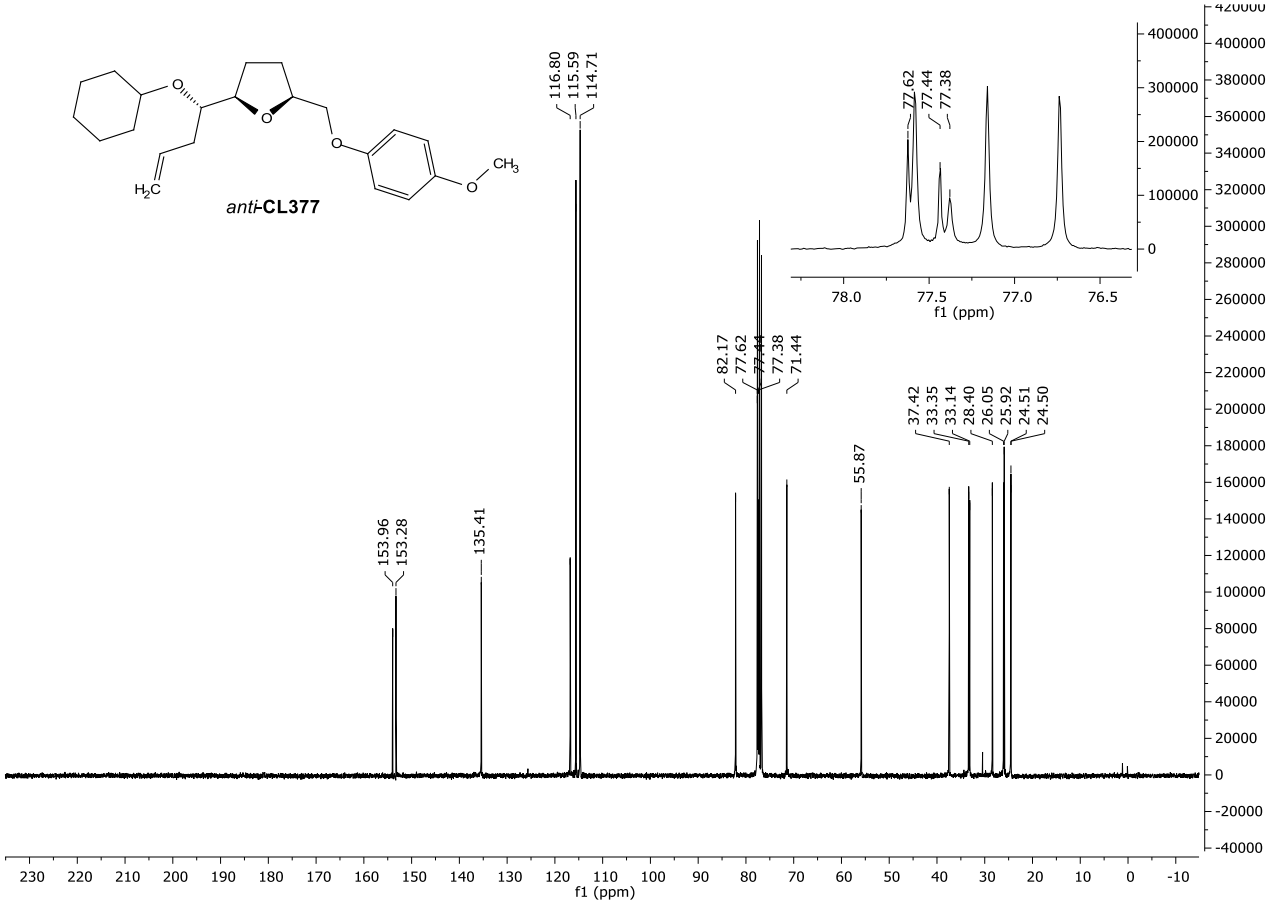
The configuration of the compounds highlighted in yellow was unambigously established.

R^2	Product	*H*-1		*H*-2		*H*-3	
		syn	*anti*	*syn*	*anti*	*syn*	*anti*
cy-Hex	**11a**	4.00 (td) J = 7.0, 5.3	3.92 (m)	3.42 (dt) J = 7.6, 4.9	3.55 (td) J = 6.0, 4.9	2.34 and 2.18	2.25
(-)-menthyl	**11b**	4.04 (td) J = 6.8, 5.3	3.92 (m)	3.44 (q) J = 5.3	3.61 (q) J = 5.5	2.44 and 2.19	2.32 and 2.26
(+)-menthyl	**11c**	4.04 (td) J = 6.9, 5.4	3.96 (m)	3.53 (ddd) J = 8.0, 5.3, 4.0	3.56 (dt) J = 6.8, 4.6	2.34 and 2.12	2.35 and 2.25
allyl	**11d**	4.02 (m)	3.98 (m)	3.37 (ddd) J = 7.2, 5.9, 4.7	3.52 (td) J = 6.1, 4.4	2.35 and 2.22	2.27
(*R*)-**16a**	**11e**	3.84 covered by other signals	3.89 (td) J = 7.4, 3.3	3.43 (ddd) J = 8.0, 5.6, 4.3	3.69 (td) J = 6.4, 3.4	2.26 and 2.15	2.18
(*S*)-**16a**	**11f**	3.99 (m)	3.89 (td) J= 7.3, 3.2	3.40 (q) J= 5.3	3.70 (td) J= 6.4, 3.1	2.27 and 2.06	2.19
17a	**11g**	4.14 (dt) J = 6.9, 4.3	4.07 (mc)	3.37 (td) J = 6.4, 5.2	3.56 (quint) J = 4.0	2.45 and 2.22	2.38

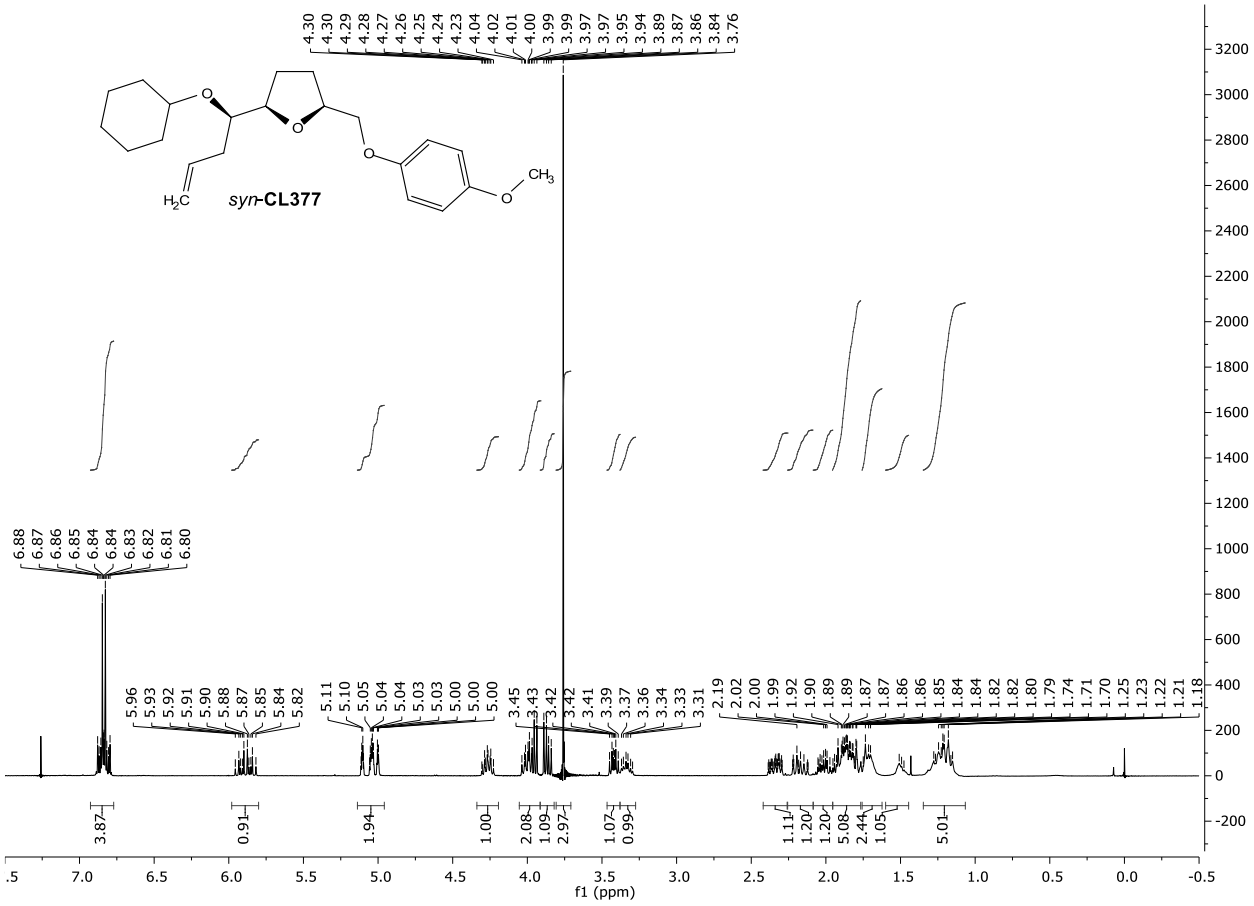
COPY OF NMR SPECTRA



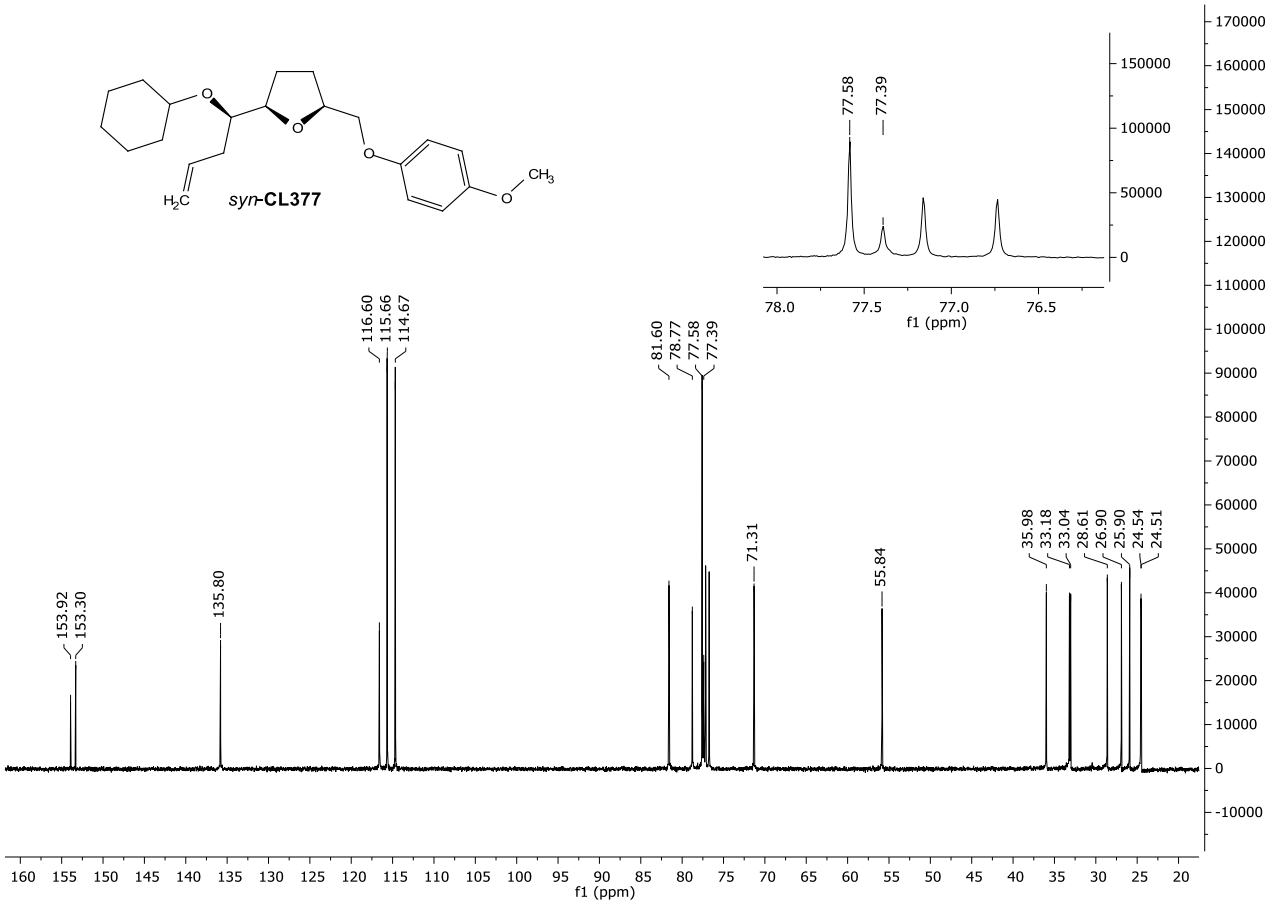
anti-**11a**


anti-CL377
153.96
153.28
135.41
116.80
115.59
114.71
82.17
77.62
77.44
77.38
71.44
55.87
37.42
33.35
33.14
28.40
26.05
25.92
24.51
24.50
f1 (ppm)

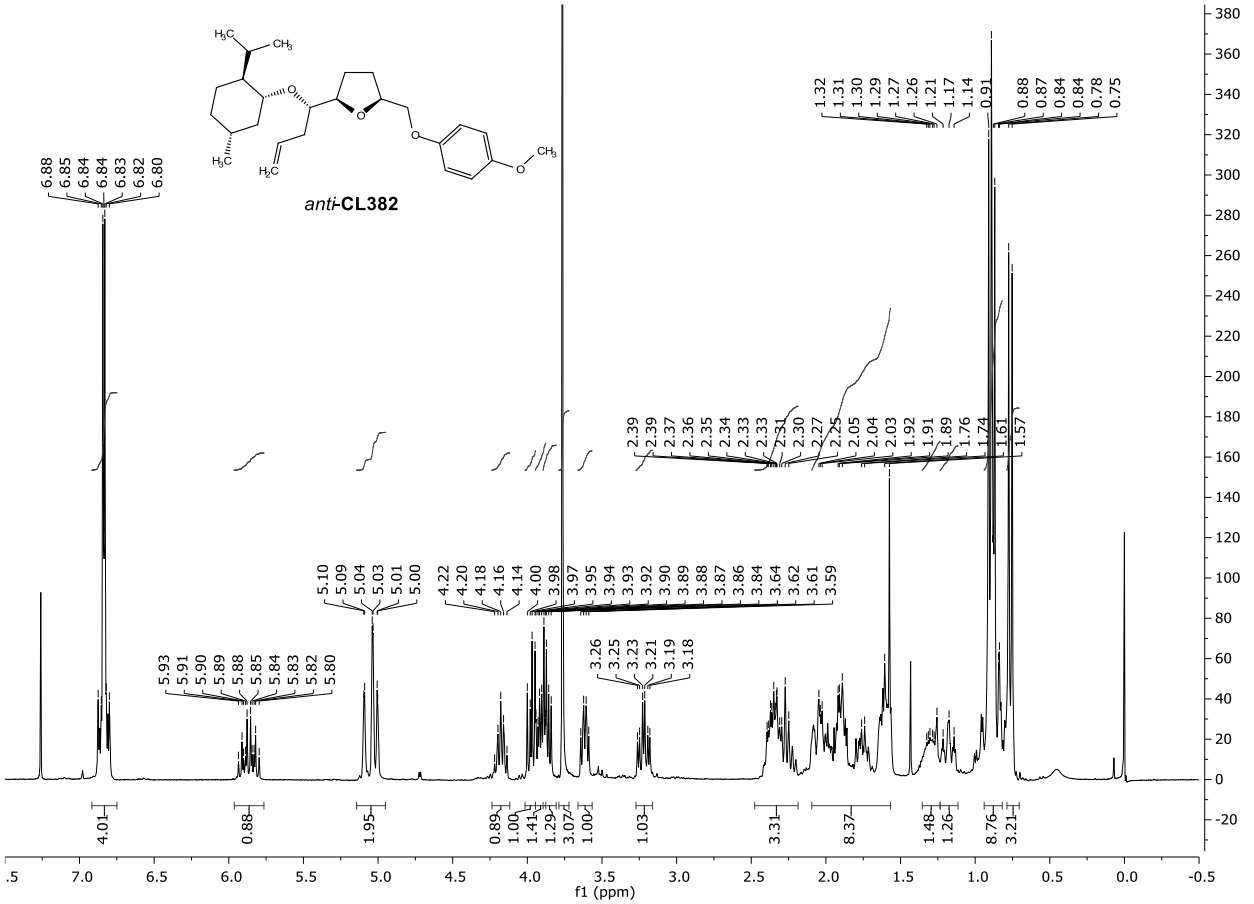
syn-11a



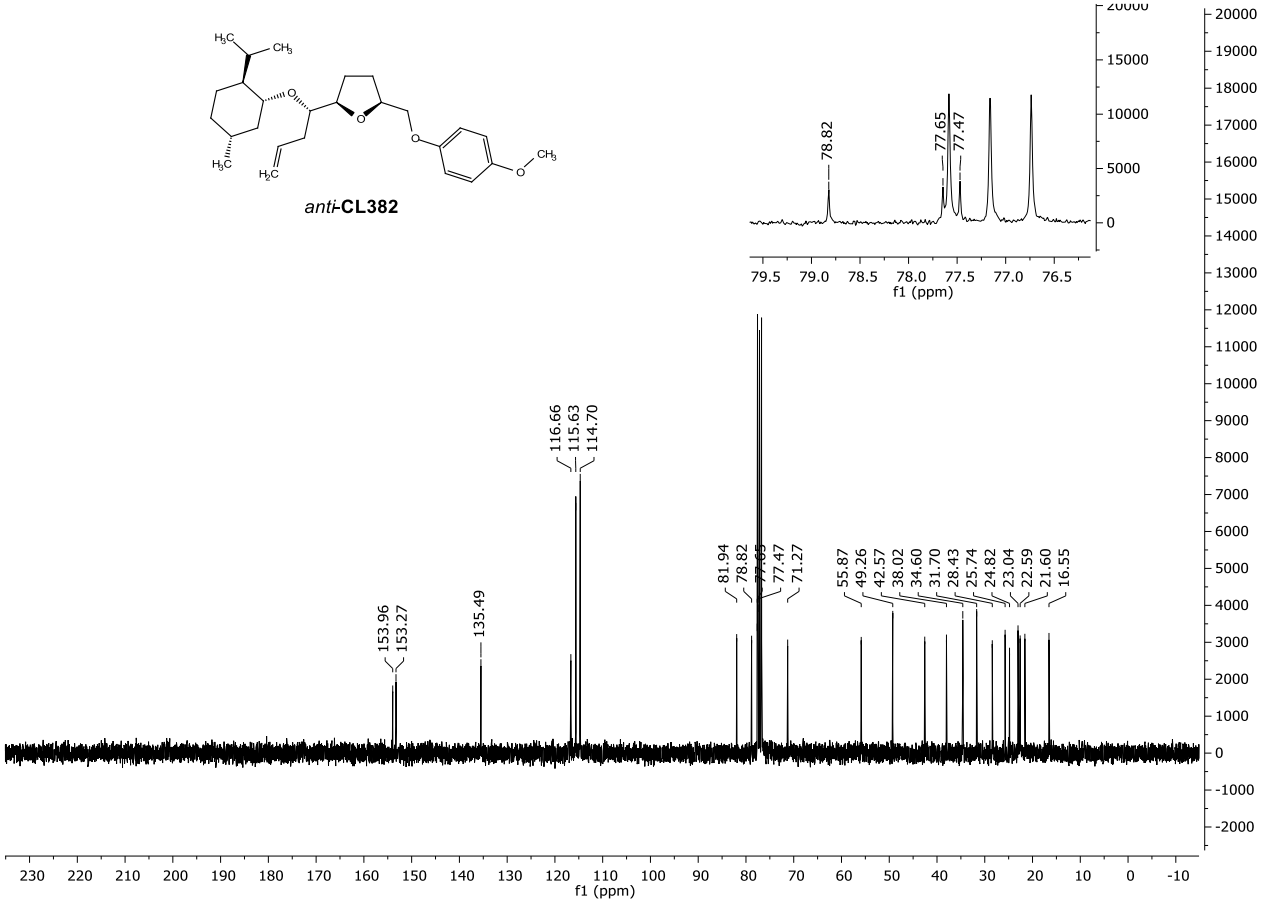
syn-11a


syn-CL377
153.92
153.30
135.80
116.60
115.66
114.67
81.60
78.77
77.58
77.39
71.31
55.84
35.98
33.18
33.04
28.61
26.90
25.90
24.54
24.51
f1 (ppm)

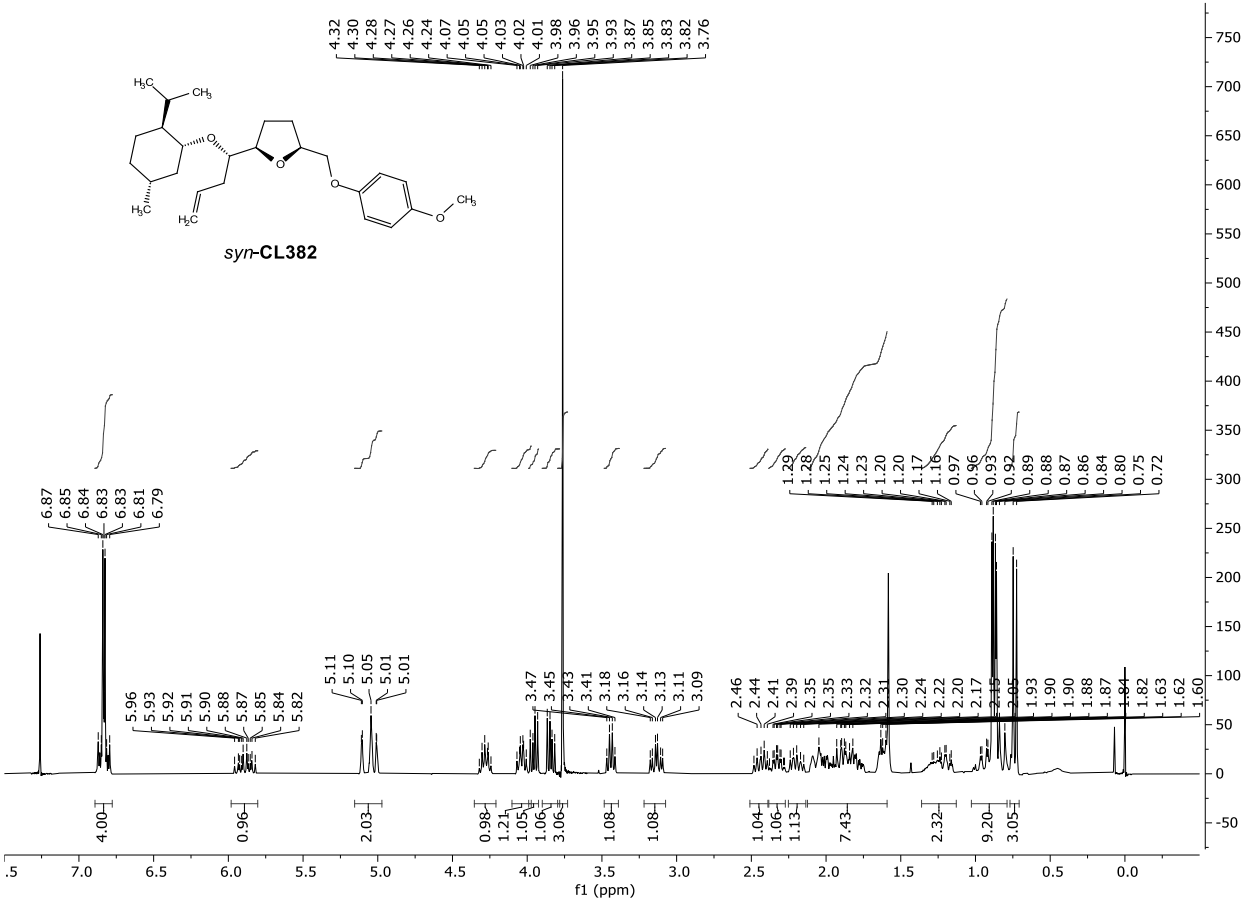
anti-**11b**



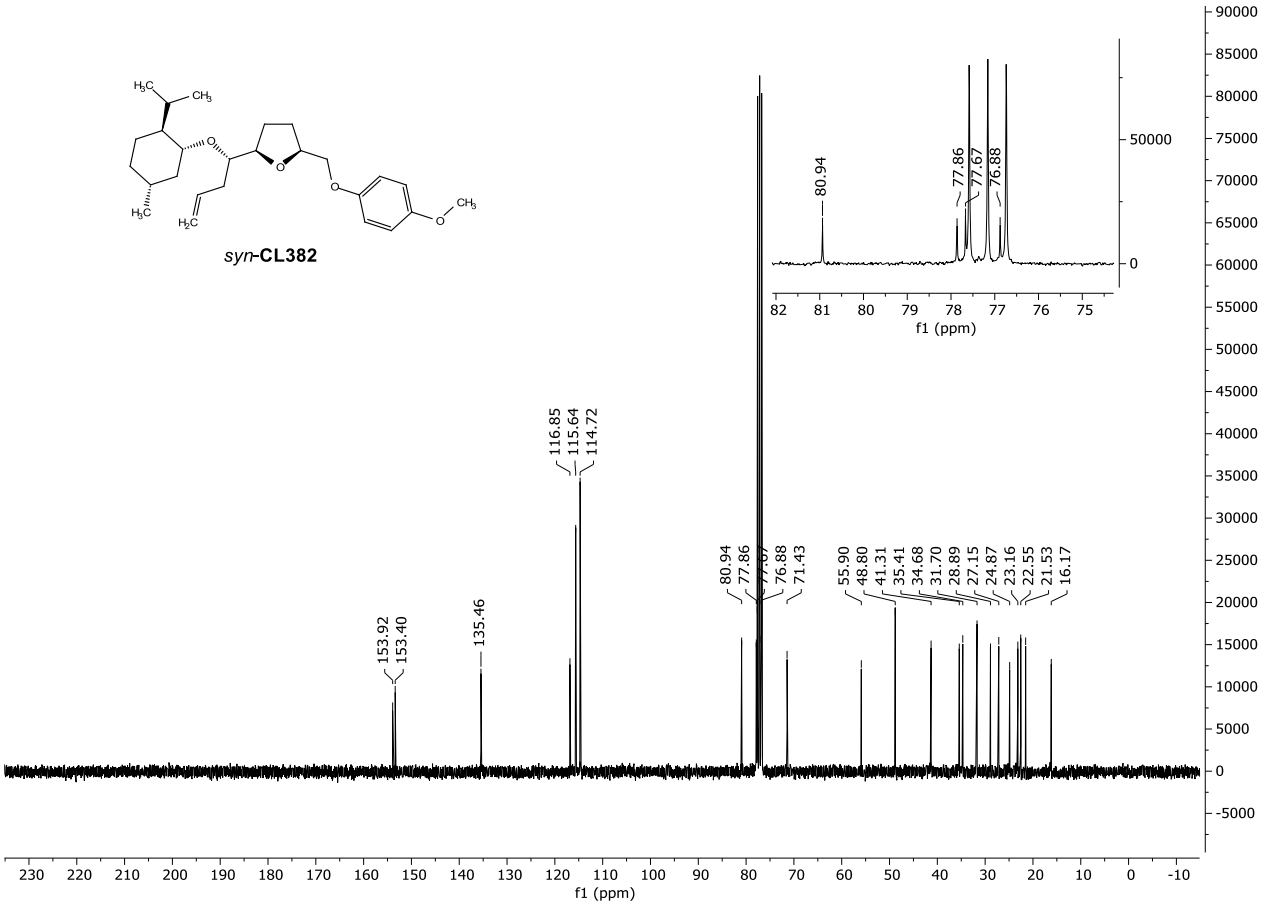
anti-**11b**


anti-CL382
78.82
77.65
77.47
79.5 79.0 78.5 78.0 77.5 77.0 76.5
f1 (ppm)
116.66
115.63
114.70
153.96
153.27
135.49
81.94
78.82
77.65
77.47
71.27
55.87
49.26
42.57
38.02
34.60
31.70
28.43
25.74
24.82
23.04
22.59
21.60
16.55
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

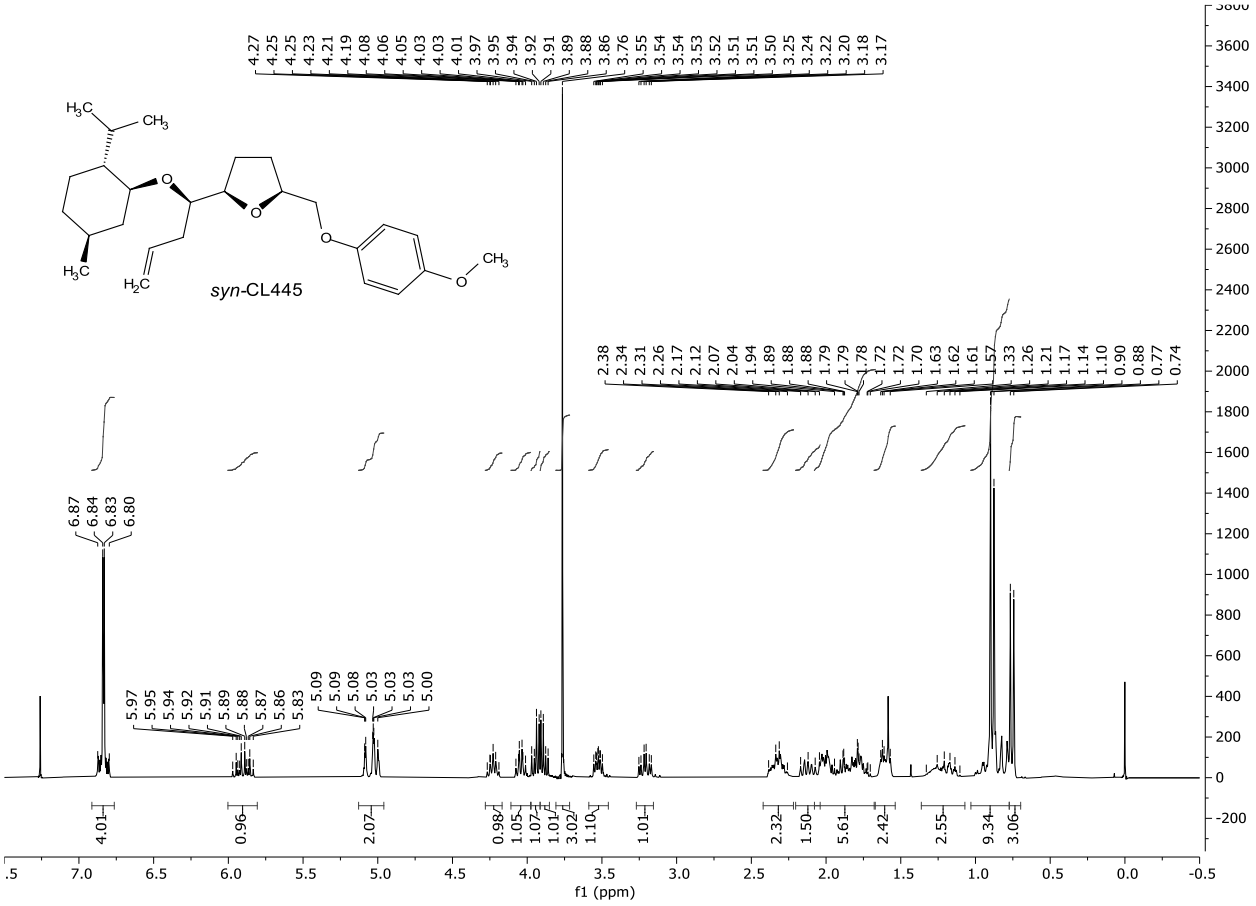
syn-11b



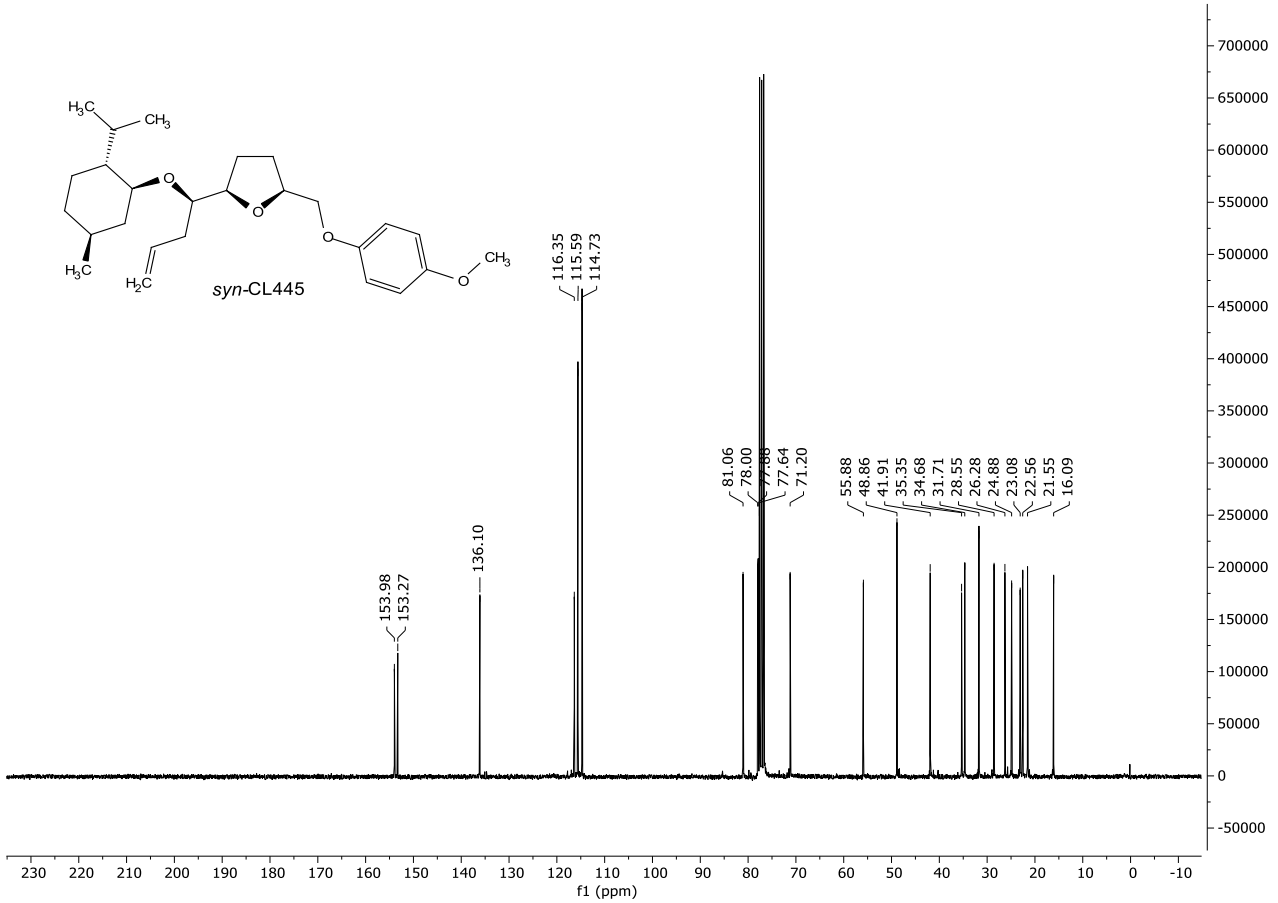
syn-11b


syn-CL382
80.94
77.86
77.67
76.88
f1 (ppm)
153.92
153.40
135.46
116.85
115.64
114.72
80.94
77.86
77.67
76.88
71.43
55.90
48.80
41.31
35.41
34.68
31.70
28.89
27.15
24.87
23.16
22.55
21.53
16.17
f1 (ppm)

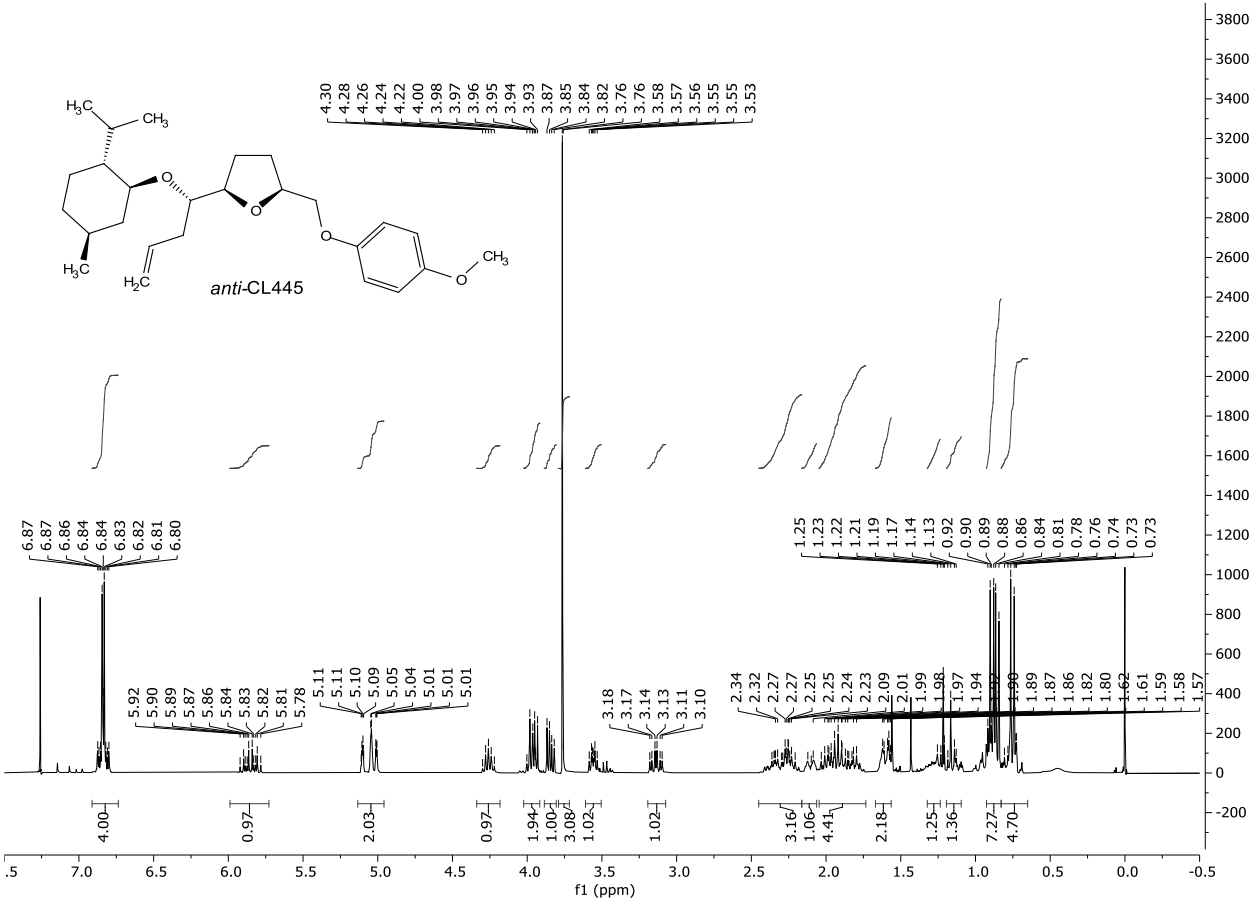
***syn*-11c**



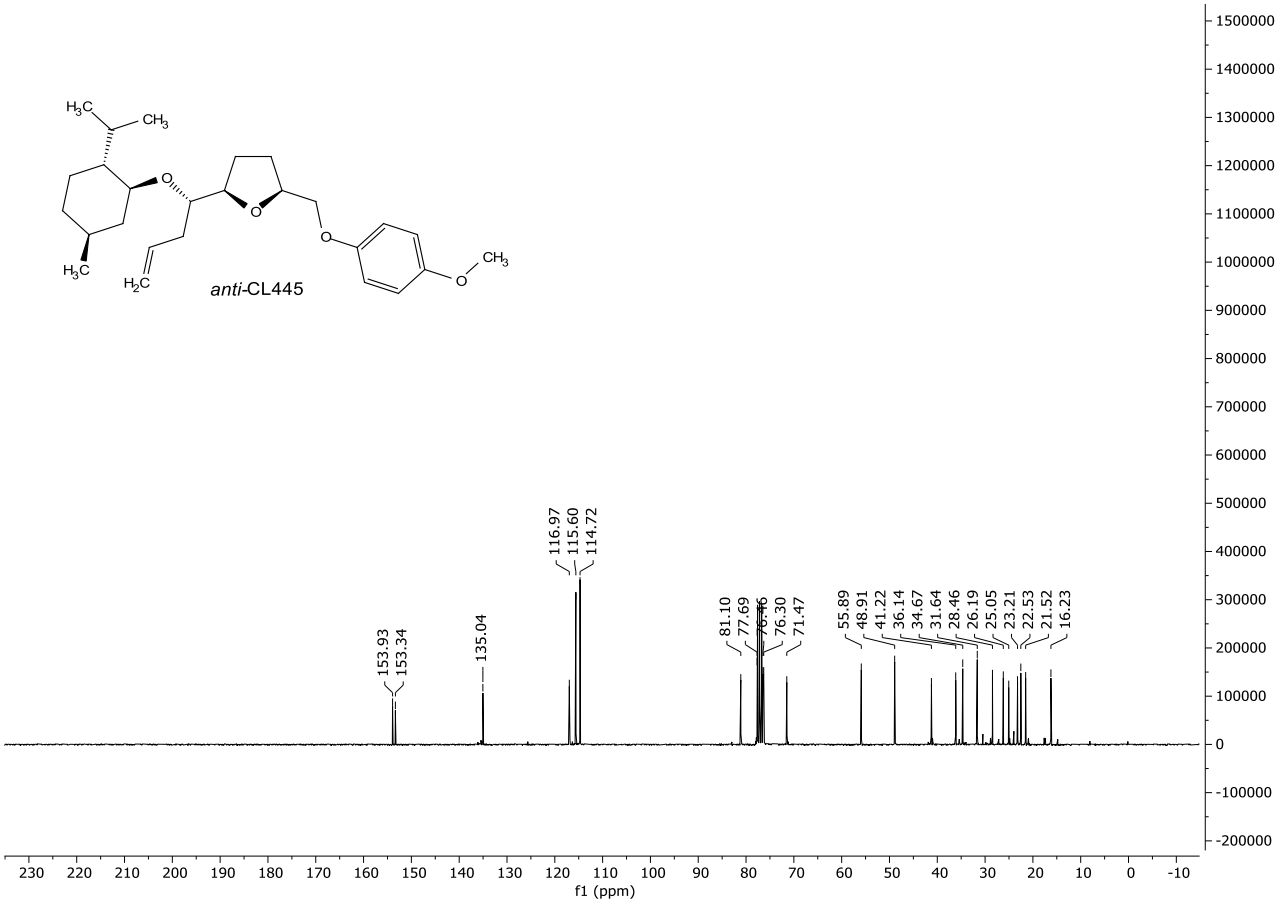
syn-11c

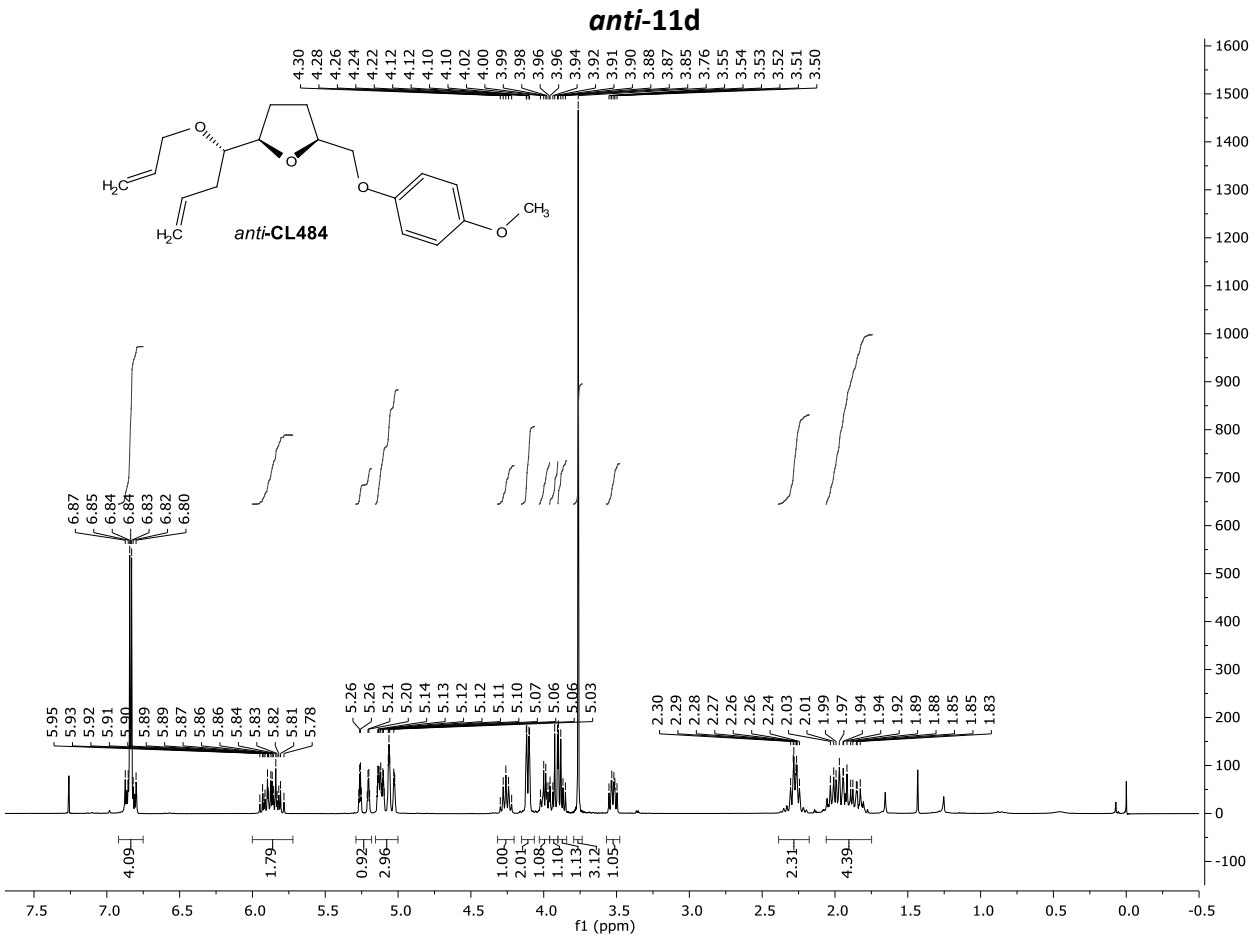

syn-CL445
153.98
153.27
136.10
116.35
115.59
114.73
81.06
78.00
77.86
77.64
71.20
55.88
48.86
41.91
35.35
34.68
31.71
28.55
26.28
24.88
23.08
22.56
21.55
16.09
f1 (ppm)

anti-11c

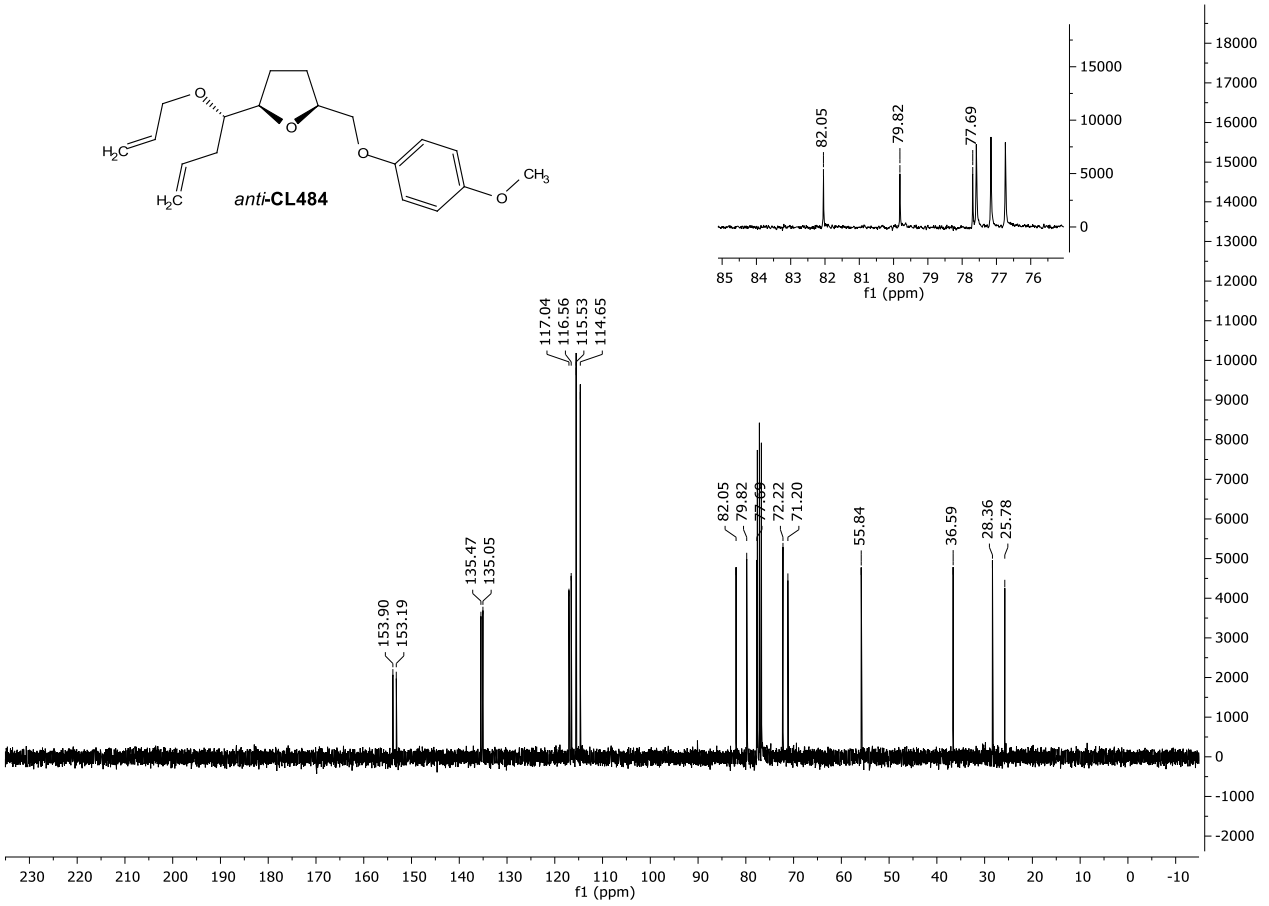


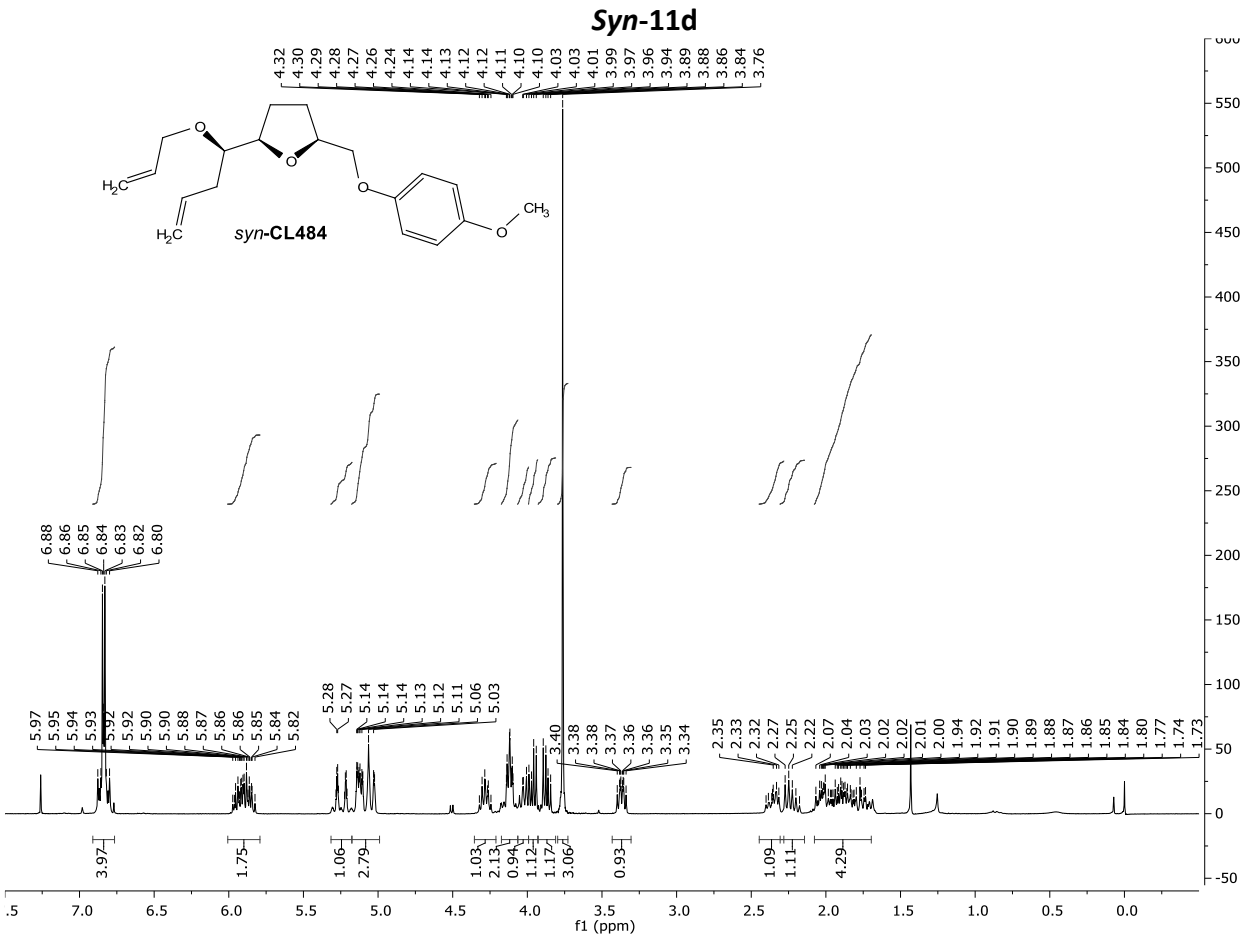
anti-11c


anti-CL445
153.93
153.34
135.04
116.97
115.60
114.72
81.10
77.69
76.46
76.30
71.47
55.89
48.91
41.22
36.14
34.67
31.64
28.46
26.19
25.05
23.21
22.53
21.52
16.23
f1 (ppm)

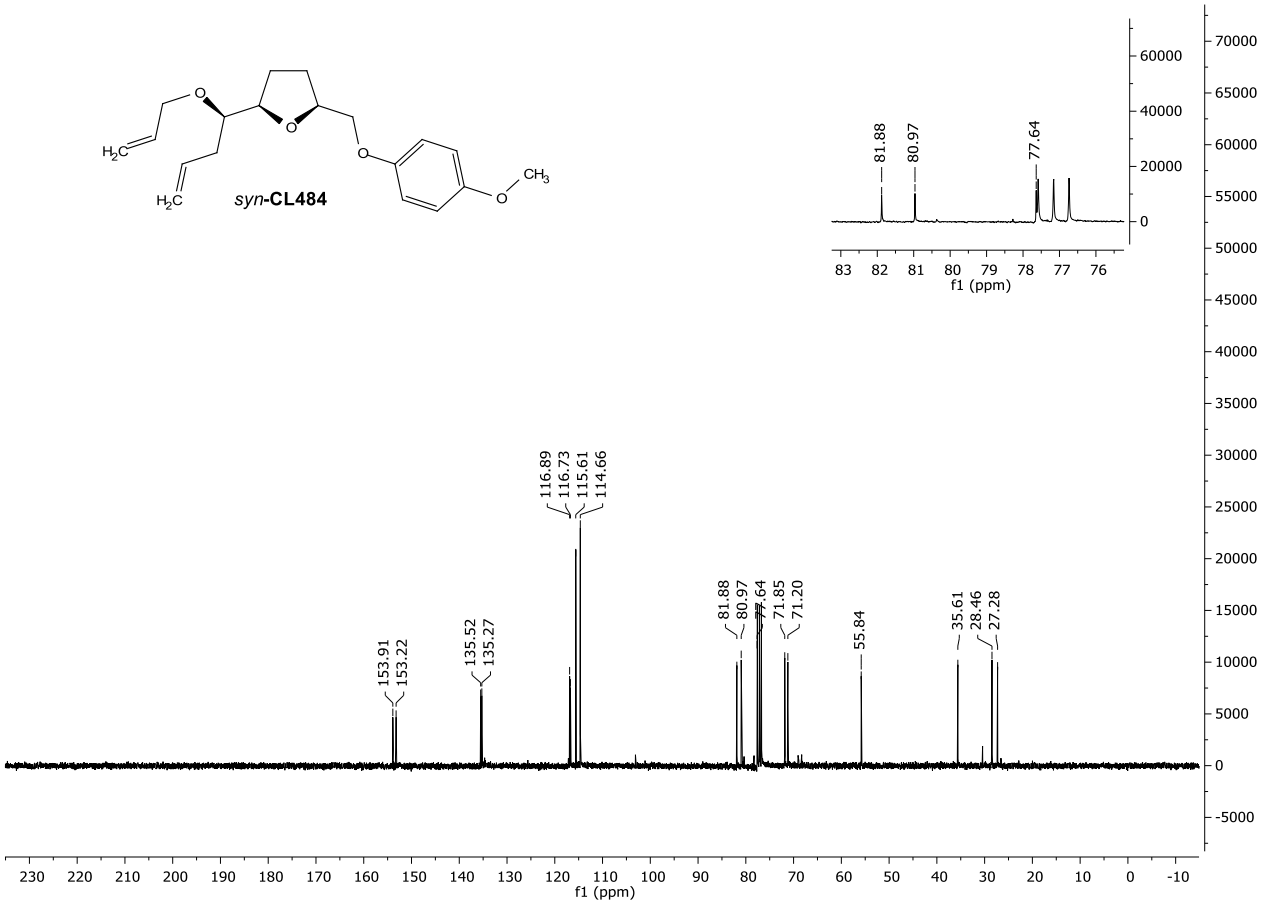

anti-11d
anti-CL484
f1 (ppm)

anti-11d

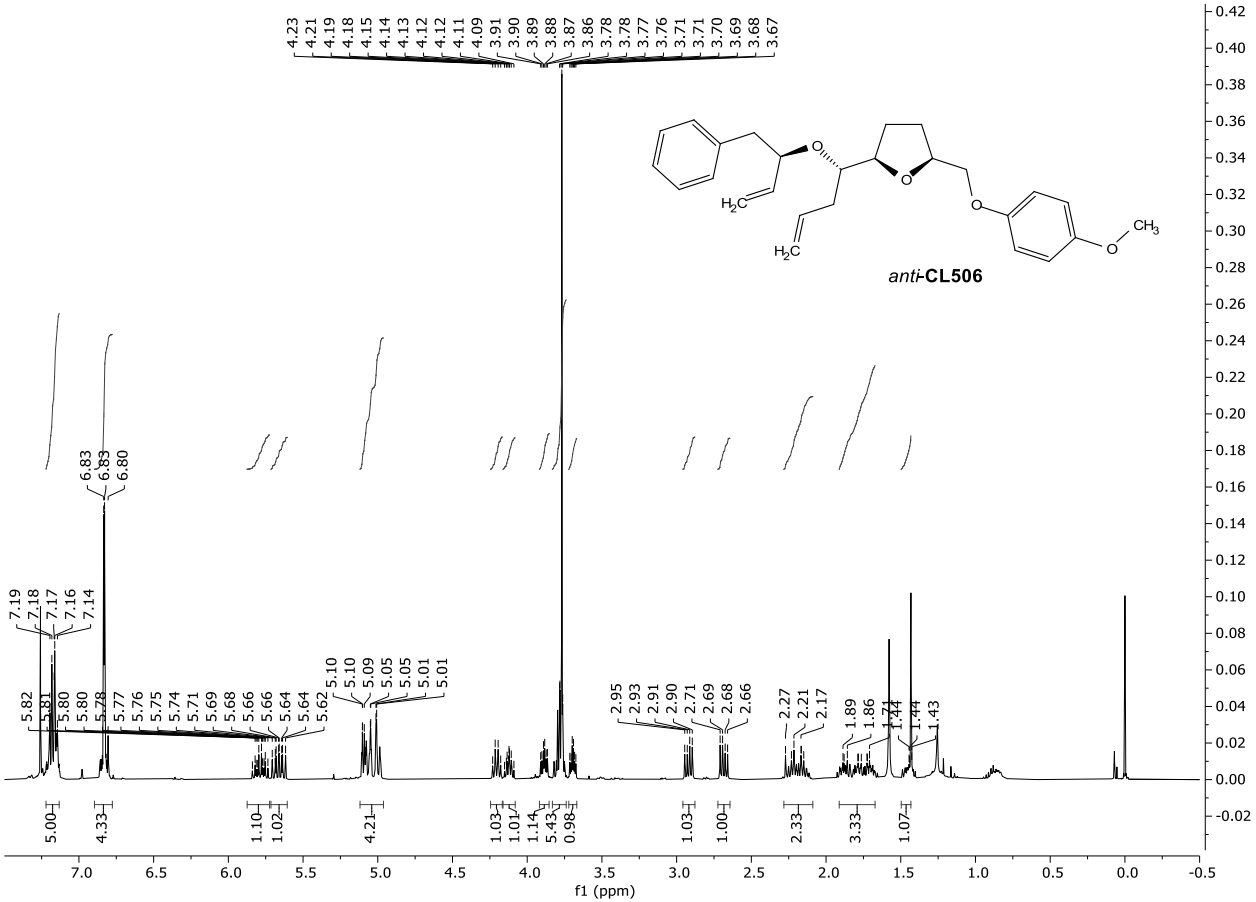

anti-CL484
82.05
79.82
77.69
f1 (ppm)
117.04
116.56
115.53
114.65
153.90
153.19
135.47
135.05
82.05
79.82
77.69
72.22
71.20
55.84
36.59
28.36
25.78
f1 (ppm)


Syn-11d
syn-CL484
f1 (ppm)

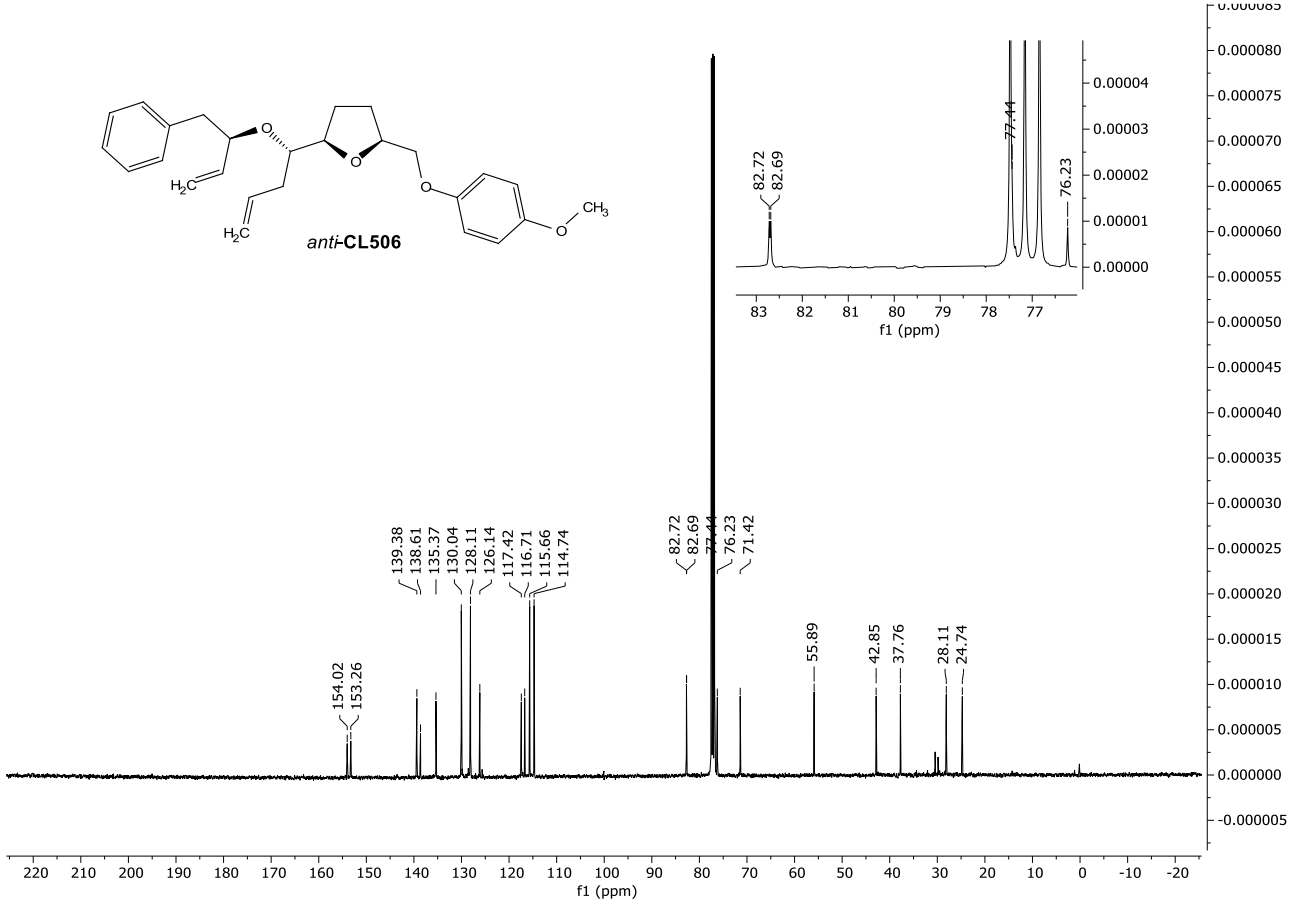
Syn-11d


syn-CL484
81.88
80.97
77.64
f1 (ppm)
116.89
116.73
115.61
114.66
153.91
153.22
135.52
135.27
81.88
80.97
77.64
71.85
71.20
55.84
35.61
28.46
27.28
f1 (ppm)

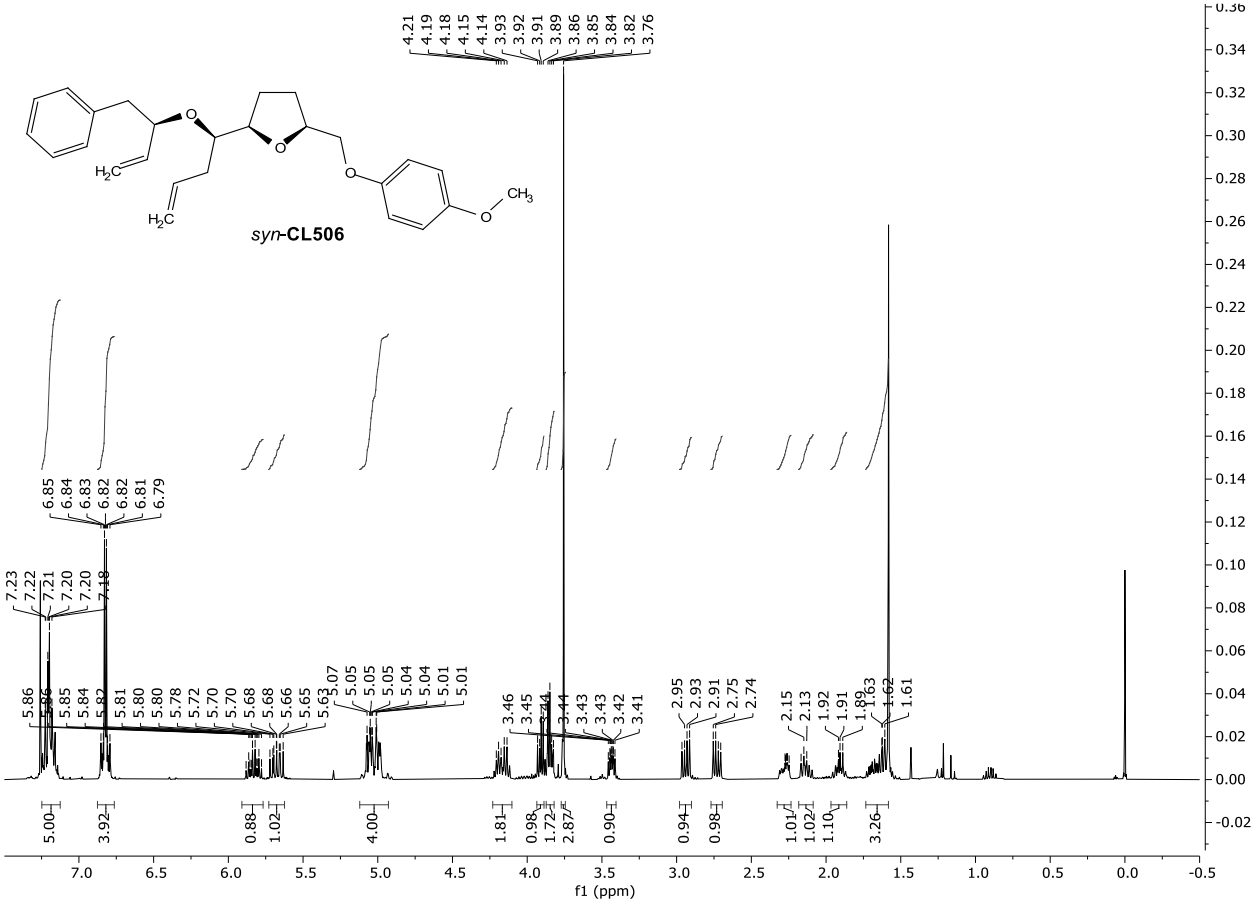
anti-11e



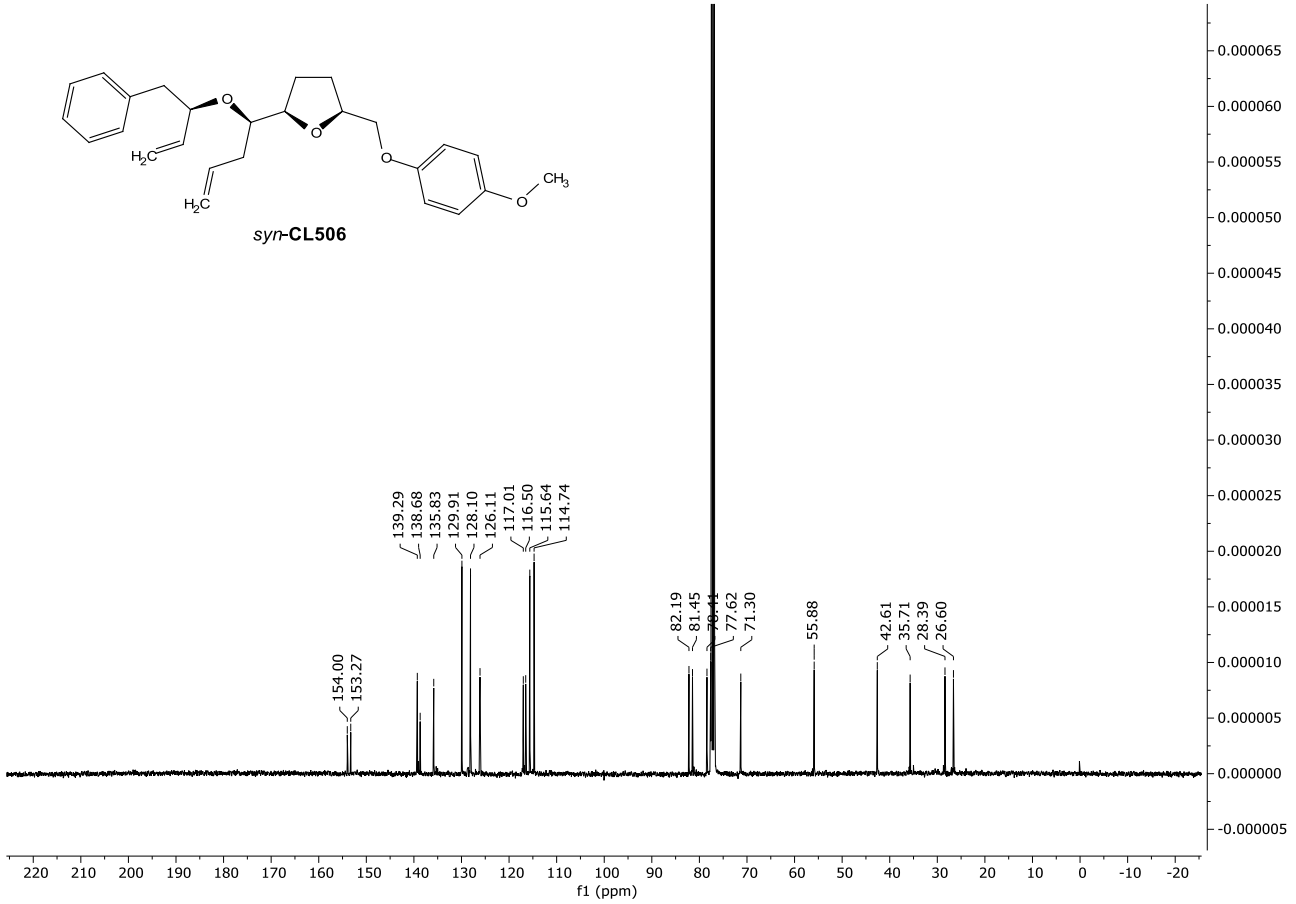
anti-11e


anti-CL506
82.72
82.69
77.44
76.23
f1 (ppm)
139.38
138.61
135.37
130.04
128.11
126.14
117.42
116.71
115.66
114.74
154.02
153.26
82.72
82.69
77.44
76.23
71.42
55.89
42.85
37.76
28.11
24.74
f1 (ppm)

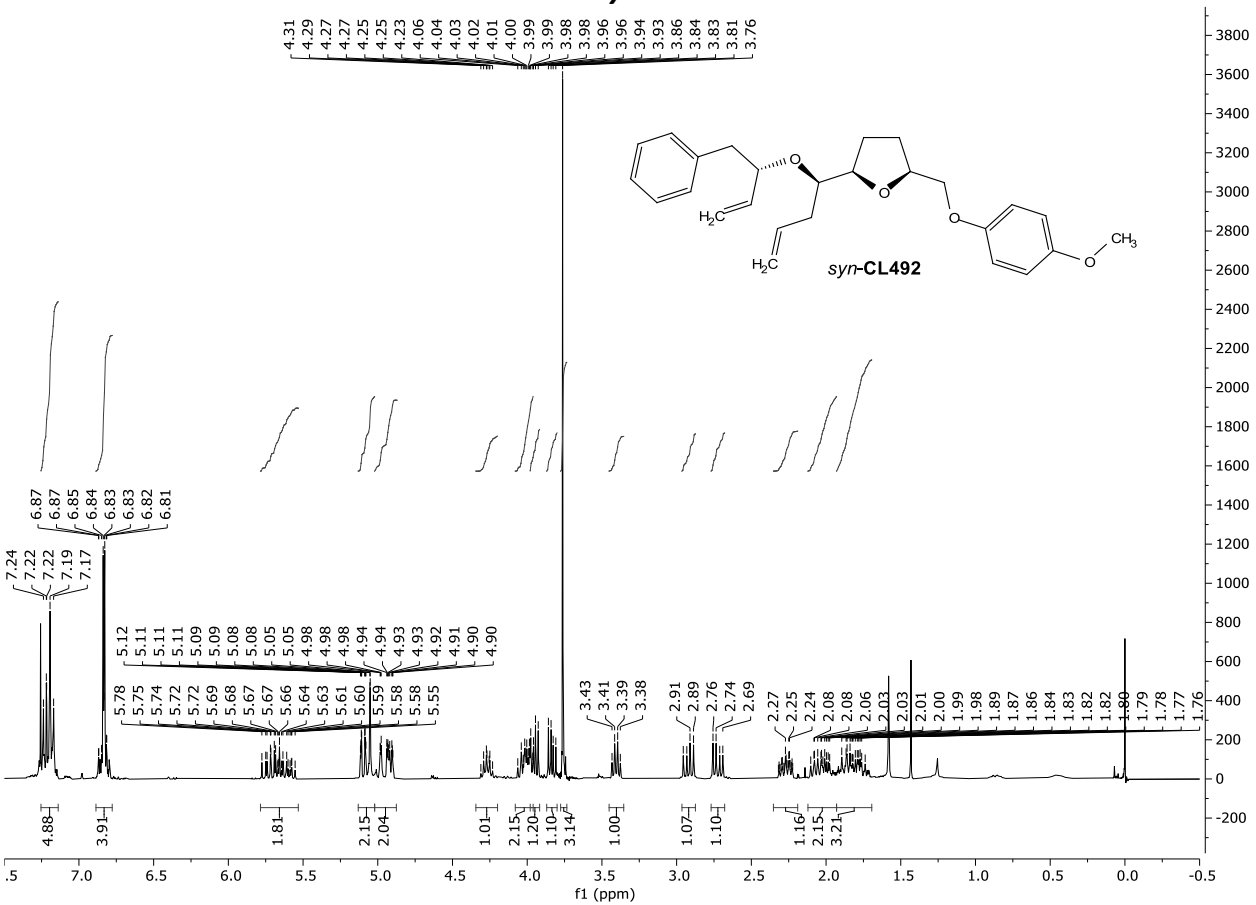
syn-11e



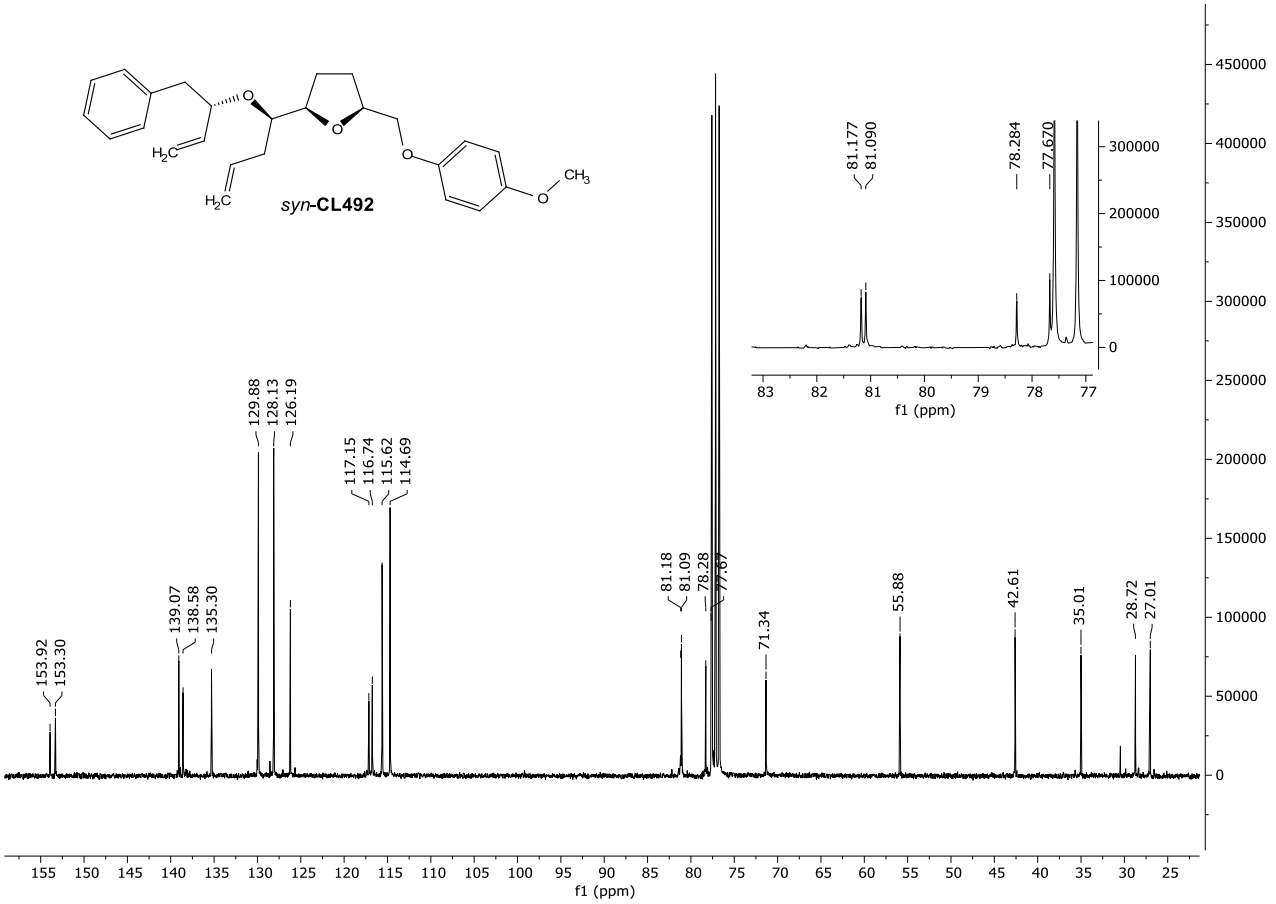
syn-11e


syn-CL506
154.00
153.27
139.29
138.68
135.83
129.91
128.10
126.11
117.01
116.50
115.64
114.74
82.19
81.45
77.62
71.30
55.88
42.61
35.71
28.39
26.60
f1 (ppm)

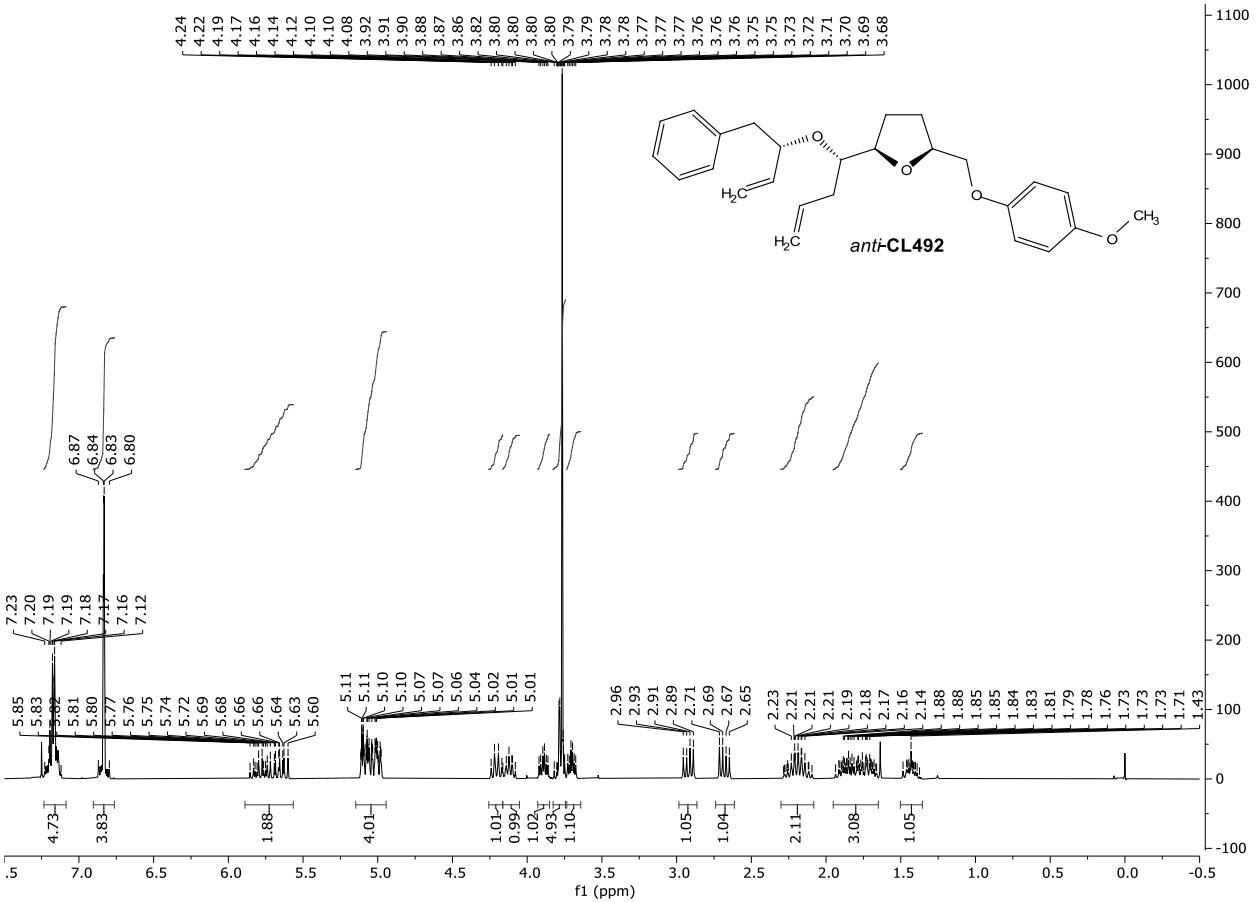
syn-11f


4.31 4.29 4.27 4.27 4.25 4.25 4.23 4.06 4.04 4.03 4.02 4.01 4.00 3.99 3.99 3.98 3.98 3.96 3.96 3.94 3.93 3.86 3.84 3.83 3.81 3.76
6.87 6.87 6.85 6.84 6.83 6.83 6.82 6.81
7.24 7.22 7.22 7.19 7.17
5.12 5.11 5.11 5.11 5.09 5.09 5.08 5.08 5.05 5.05 4.98 4.98 4.98 4.94 4.94 4.93 4.93 4.92 4.91 4.90 4.90
5.78 5.75 5.74 5.72 5.72 5.69 5.68 5.67 5.67 5.66 5.64 5.63 5.61 5.60 5.59 5.58 5.58 5.55
3.43 3.41 3.39 3.38
2.91 2.89 2.76 2.74 2.69
2.27 2.25 2.24 2.08 2.08 2.06 2.03 2.03 2.01 2.00 1.99 1.98 1.89 1.87 1.86 1.84 1.83 1.82 1.82 1.80 1.79 1.78 1.77 1.76
4.88 3.91 1.81 2.15 2.04 1.01 2.15 1.20 1.10 3.14 1.00 1.07 1.10 1.16 2.15 3.21
f1 (ppm)
H2C
H2C
O
O
O
O
CH3
syn-CL492

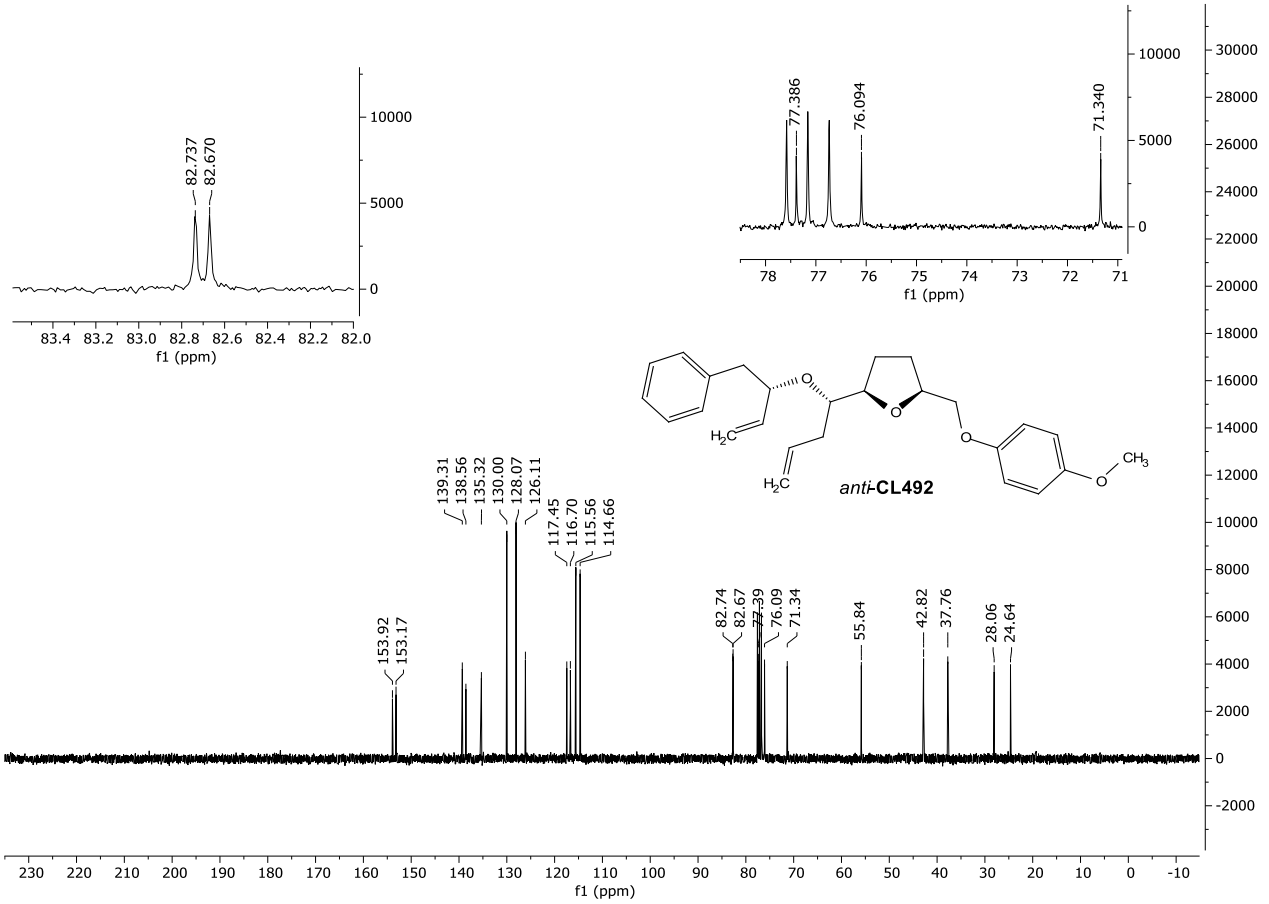
syn-11f


syn-CL492
153.92
153.30
139.07
138.58
135.30
129.88
128.13
126.19
117.15
116.74
115.62
114.69
81.18
81.09
78.28
77.67
71.34
55.88
42.61
35.01
28.72
27.01
81.177
81.090
78.284
77.670
f1 (ppm)

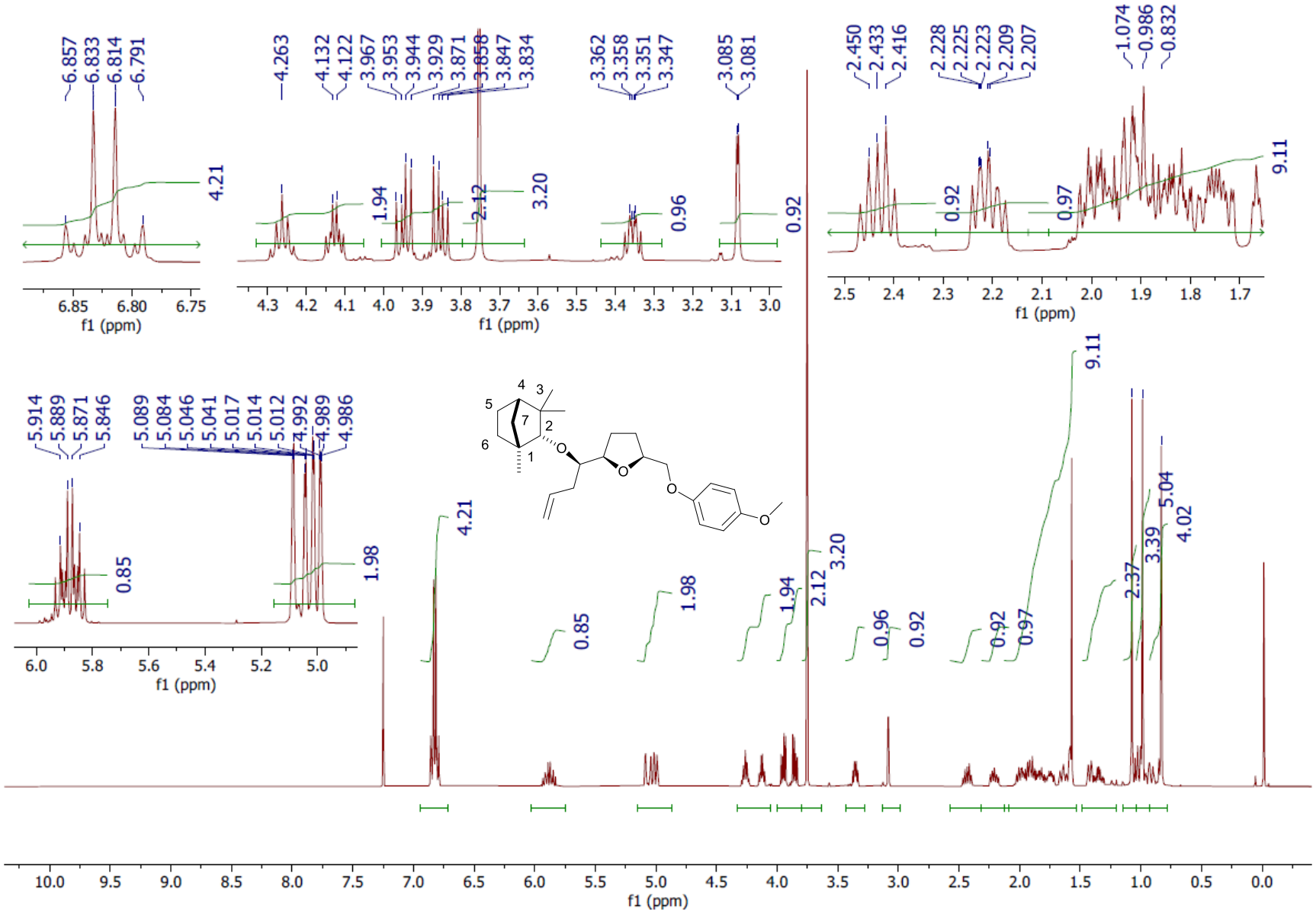
***anti*-11f**



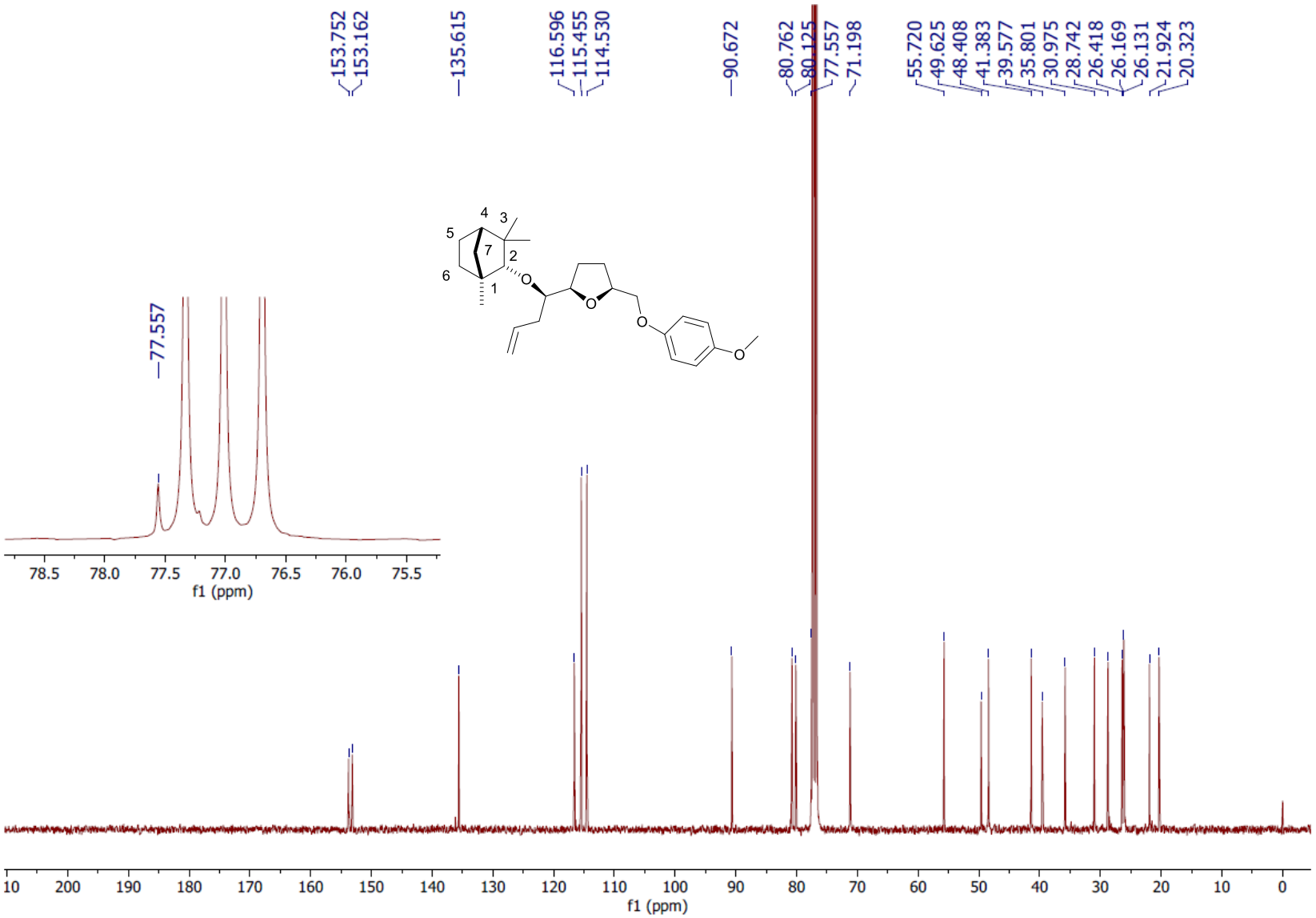
anti-11f


82.737
82.670
77.386
76.094
71.340
anti-CL492
153.92
153.17
139.31
138.56
135.32
130.00
128.07
126.11
117.45
116.70
115.56
114.66
82.74
82.67
77.39
76.09
71.34
55.84
42.82
37.76
28.06
24.64
f1 (ppm)

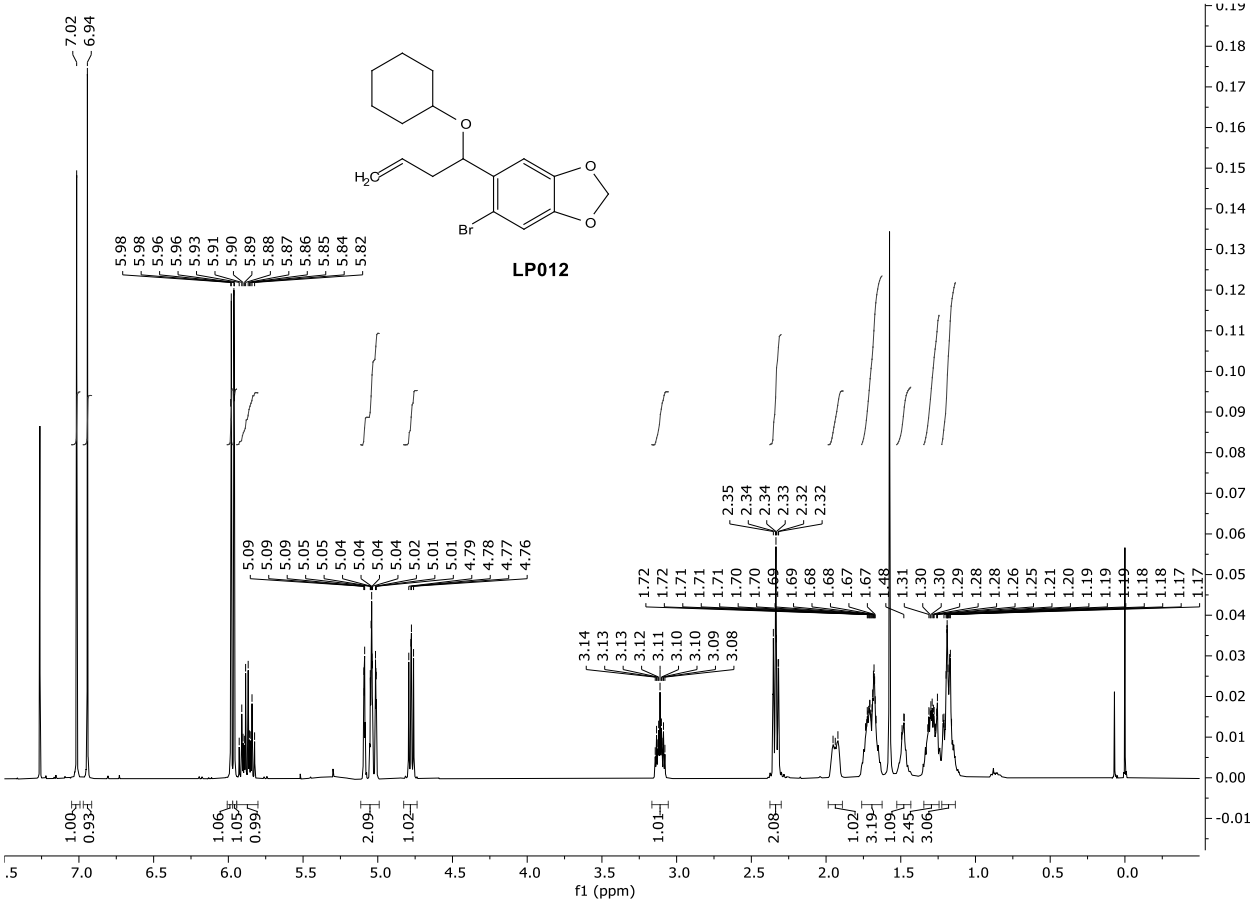
***syn*-11g**


6.857
6.833
6.814
6.791
4.21
6.85
6.80
6.75
f1 (ppm)
4.263
4.132
4.122
3.967
3.953
3.944
3.929
3.871
3.858
3.847
3.834
3.362
3.358
3.351
3.347
3.085
3.081
1.94
2.12
3.20
0.96
0.92
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
f1 (ppm)
2.450
2.433
2.416
2.228
2.225
2.223
2.209
2.207
1.074
0.986
0.832
0.92
0.97
9.11
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
f1 (ppm)
5.914
5.889
5.871
5.846
5.089
5.084
5.046
5.041
5.017
5.014
5.012
4.992
4.989
4.986
0.85
1.98
6.0
5.8
5.6
5.4
5.2
5.0
f1 (ppm)
4
3
5
7
2
6
1
O
O
O
O
4.21
0.85
1.98
1.94
2.12
3.20
0.96
0.92
0.92
0.97
9.11
2.37
3.39
5.04
4.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

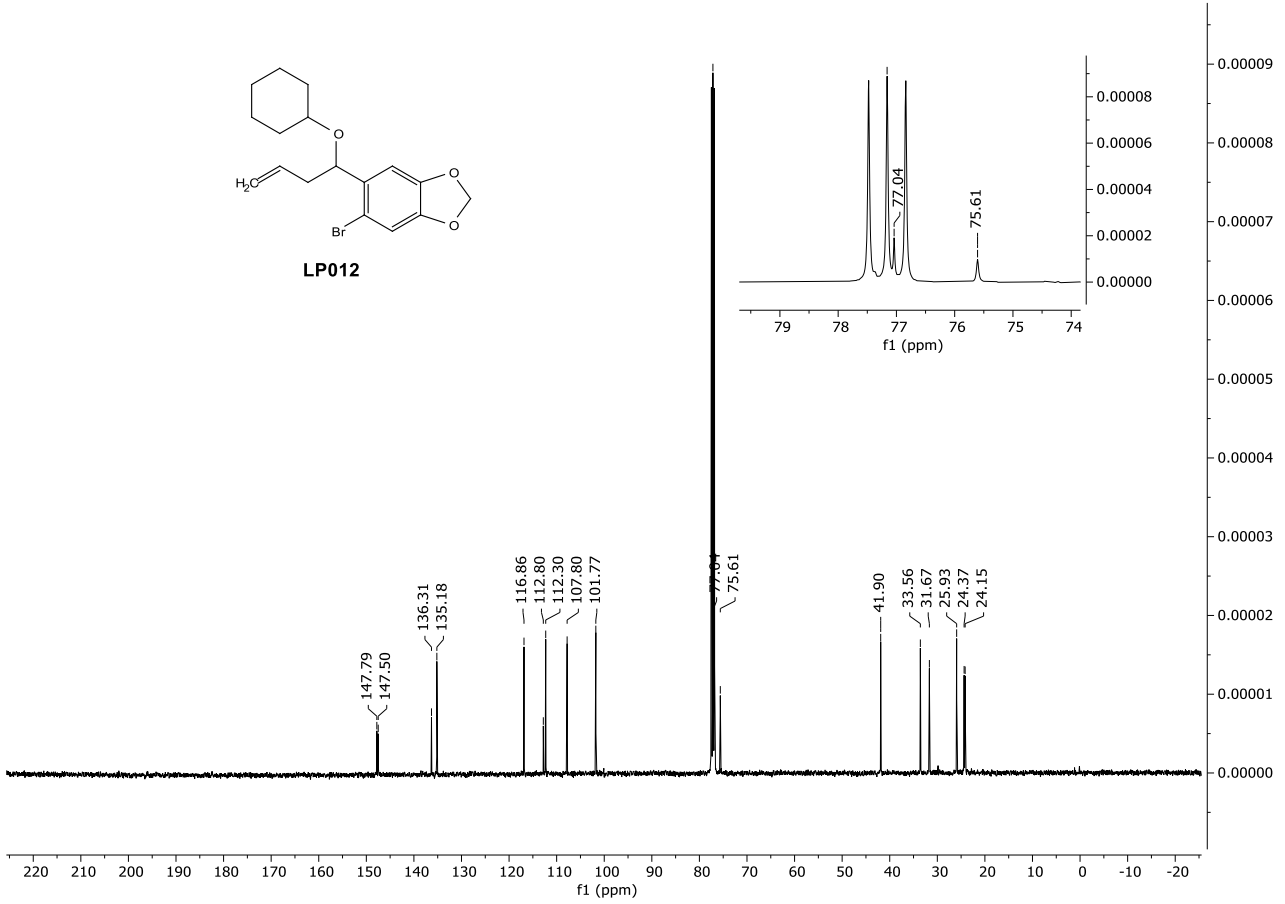
***syn*-11g**


153.752
153.162
135.615
116.596
115.455
114.530
90.672
80.762
80.125
77.557
71.198
55.720
49.625
48.408
41.383
39.577
35.801
30.975
28.742
26.418
26.169
26.131
21.924
20.323
77.557
78.5 78.0 77.5 77.0 76.5 76.0 75.5
f1 (ppm)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

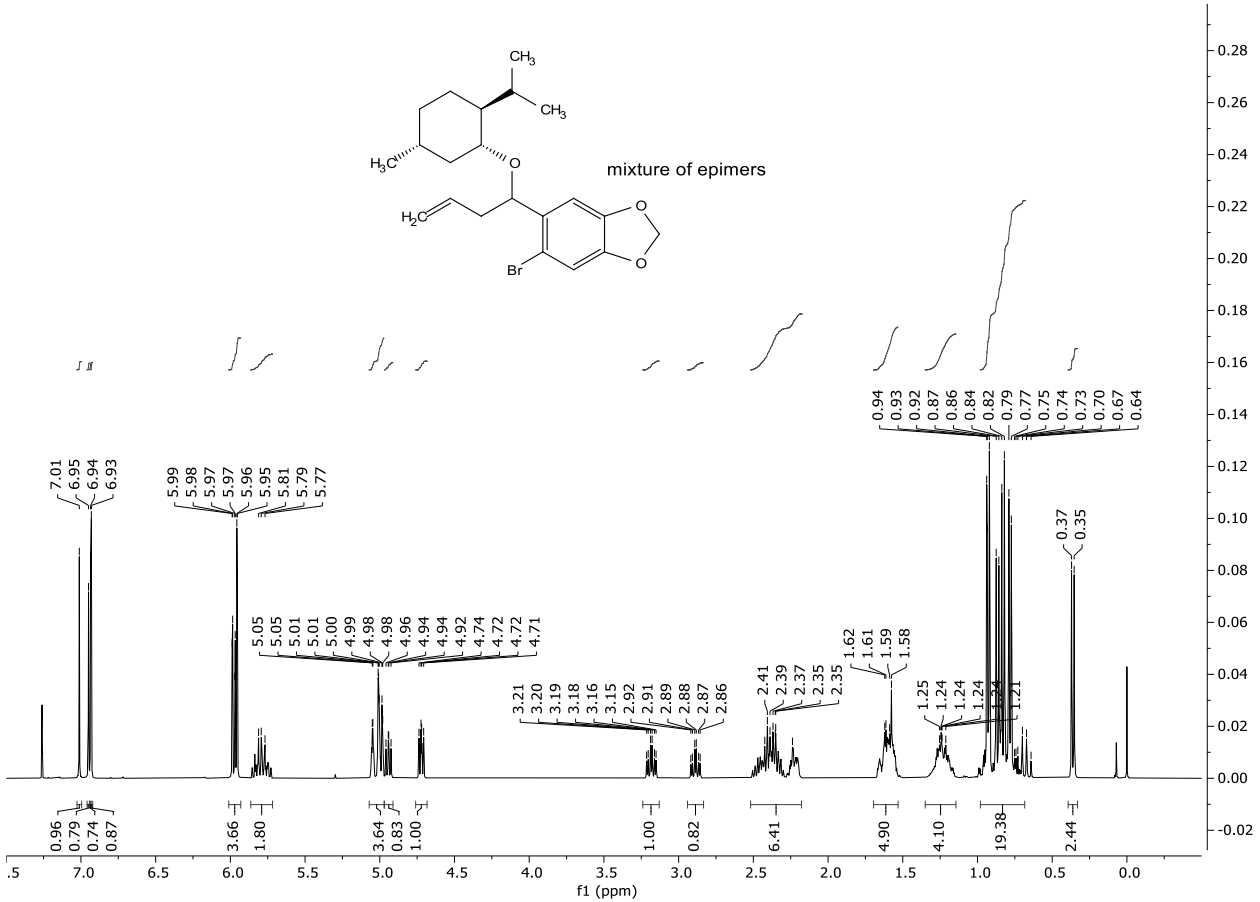
12a



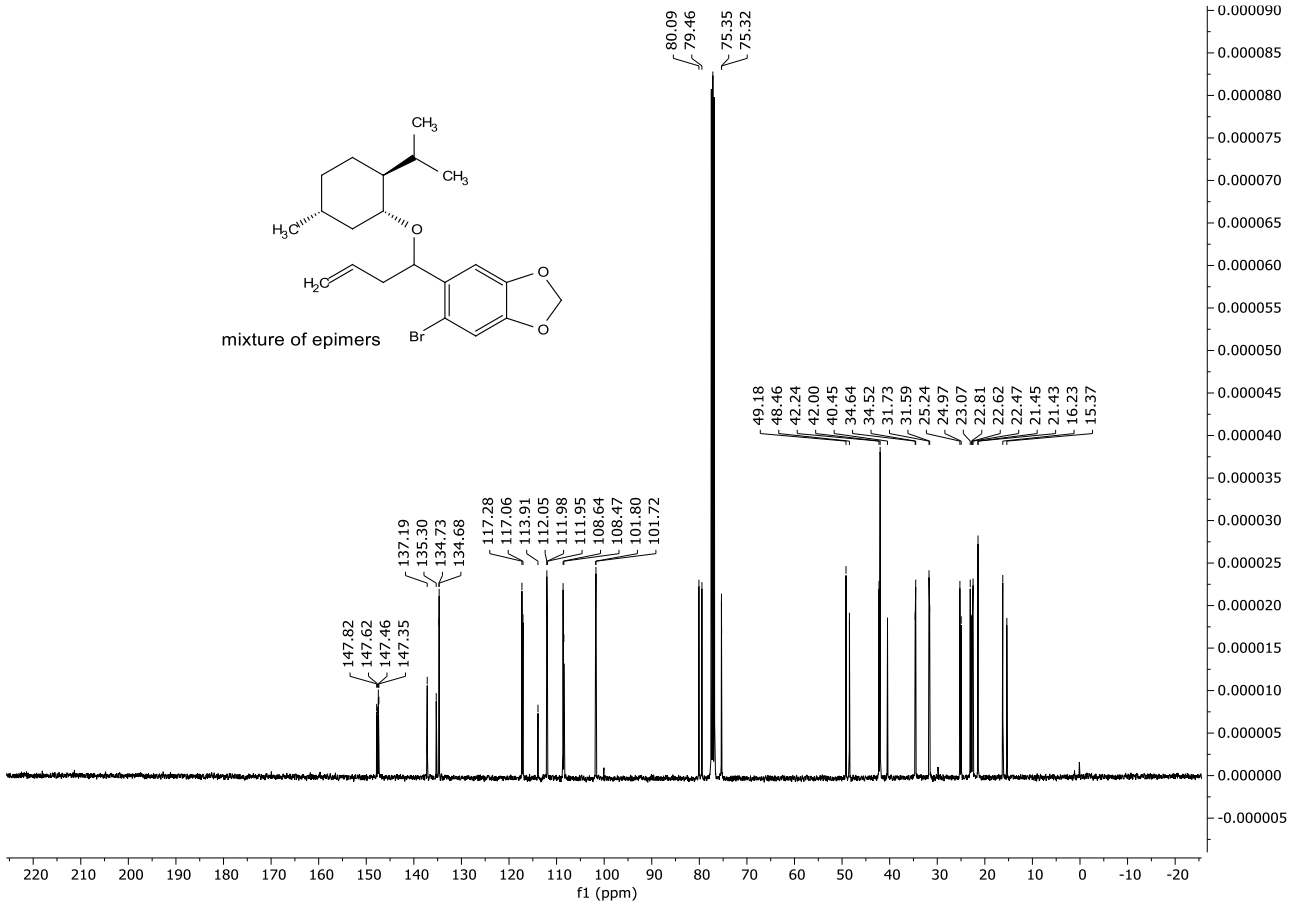
12a


LP012
147.79
147.50
136.31
135.18
116.86
112.80
112.30
107.80
101.77
77.04
75.61
41.90
33.56
31.67
25.93
24.37
24.15
f1 (ppm)

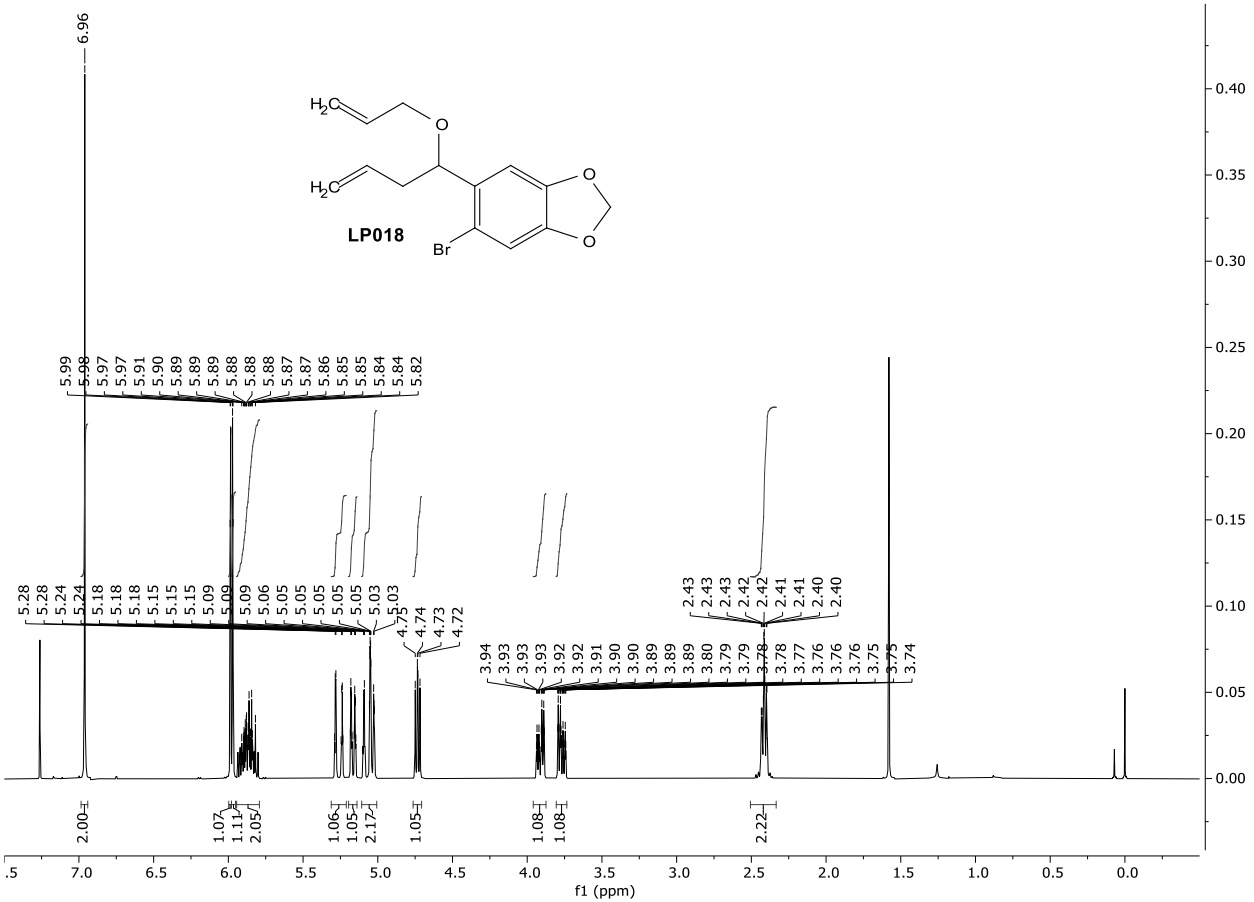
12b


CH3
CH3
H3C
O
H2C
Br
O
O
mixture of epimers
7.01
6.95
6.94
6.93
5.99
5.98
5.97
5.97
5.96
5.95
5.81
5.79
5.77
5.05
5.05
5.01
5.01
5.00
4.99
4.98
4.98
4.96
4.94
4.94
4.92
4.74
4.72
4.72
4.71
3.21
3.20
3.19
3.18
3.16
3.15
2.92
2.91
2.89
2.88
2.87
2.86
2.41
2.39
2.37
2.35
2.35
1.62
1.61
1.59
1.58
1.25
1.24
1.24
1.24
1.24
1.21
0.94
0.93
0.92
0.87
0.86
0.84
0.82
0.79
0.77
0.75
0.74
0.73
0.70
0.67
0.64
0.37
0.35
0.96
0.79
0.74
0.87
3.66
1.80
3.64
0.83
1.00
1.00
0.82
6.41
4.90
4.10
19.38
2.44
f1 (ppm)

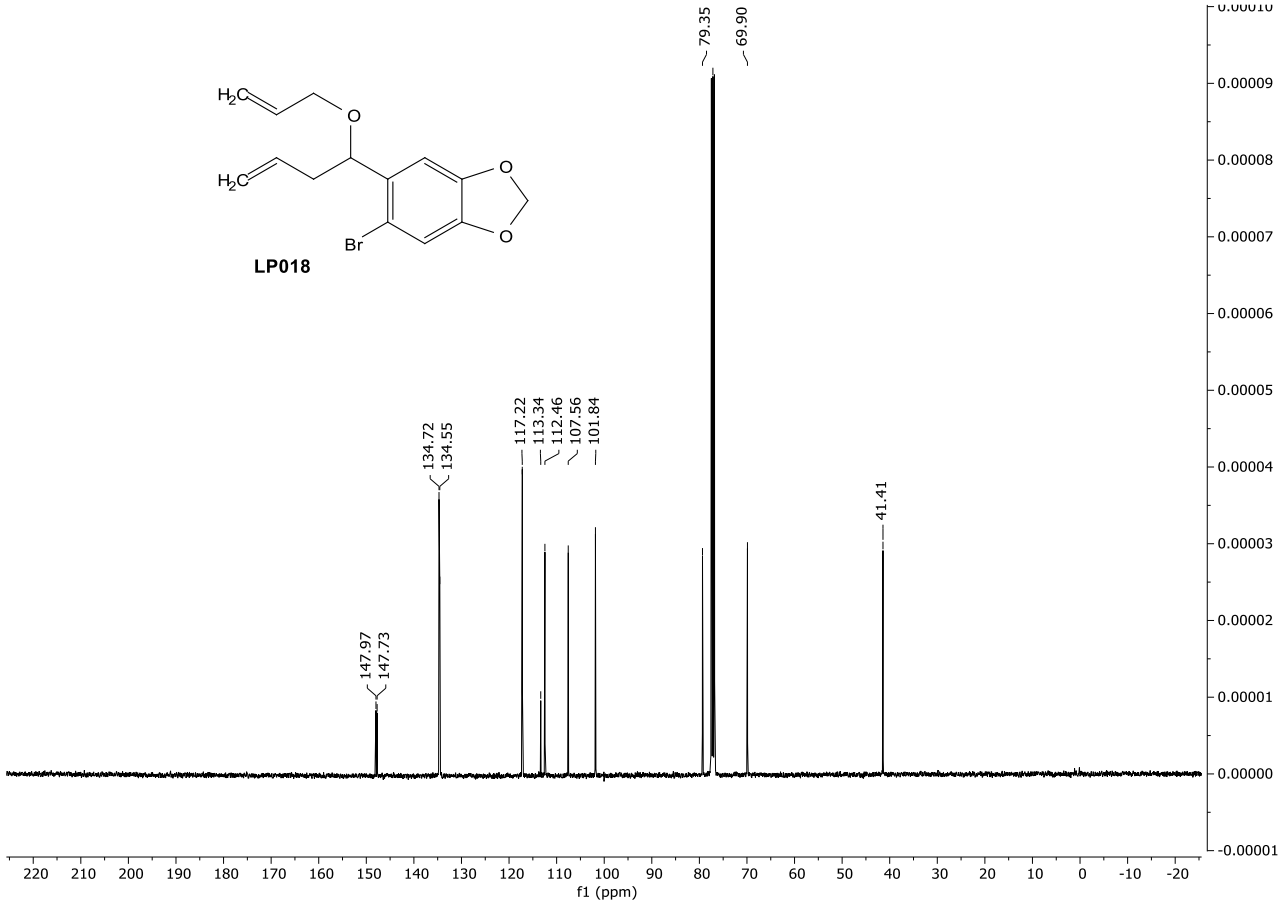
12b


mixture of epimers
80.09
79.46
75.35
75.32
49.18
48.46
42.24
42.00
40.45
34.64
34.52
31.73
31.59
25.24
24.97
23.07
22.81
22.62
22.47
21.45
21.43
16.23
15.37
137.19
135.30
134.73
134.68
117.28
117.06
113.91
112.05
111.98
111.95
108.64
108.47
101.80
101.72
147.82
147.62
147.46
147.35
f1 (ppm)

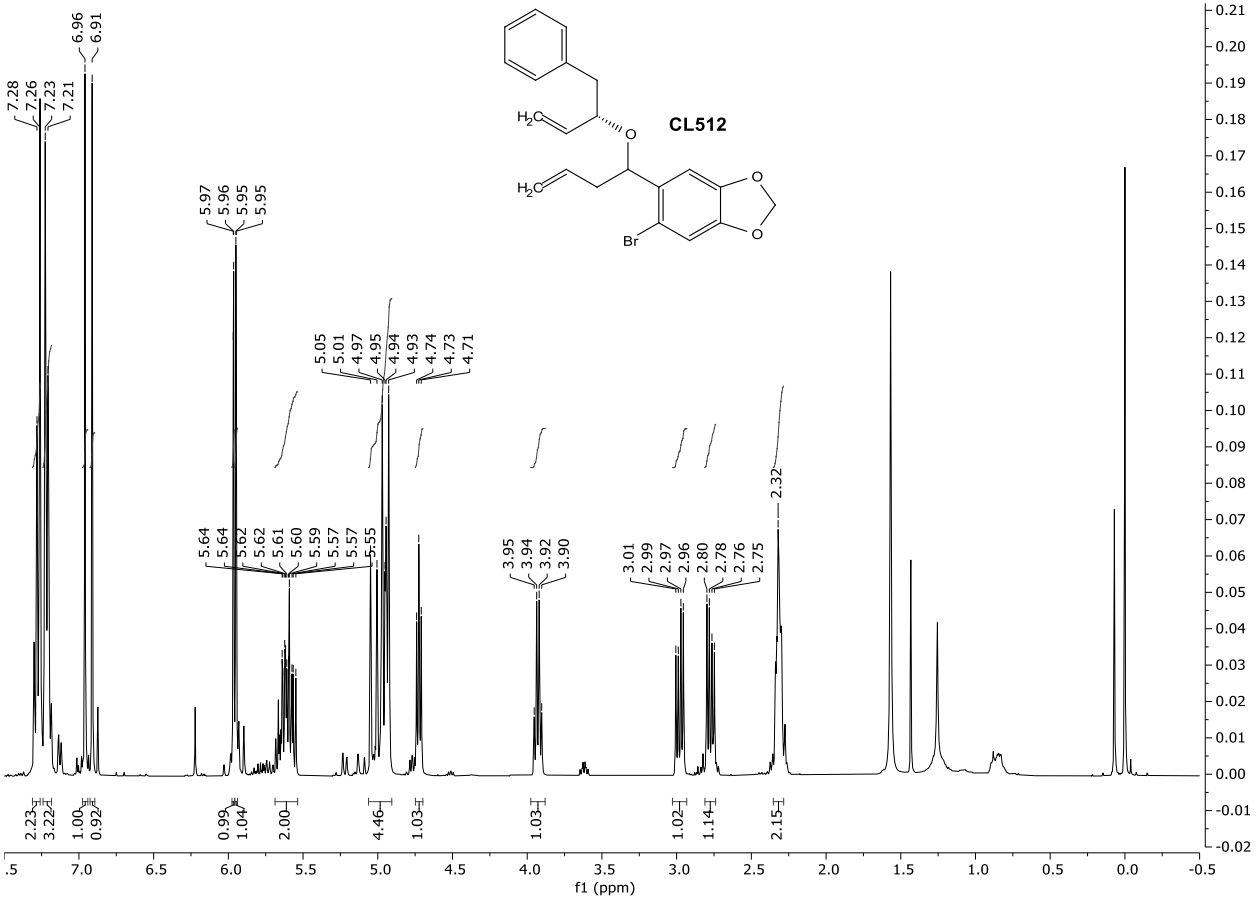
12c



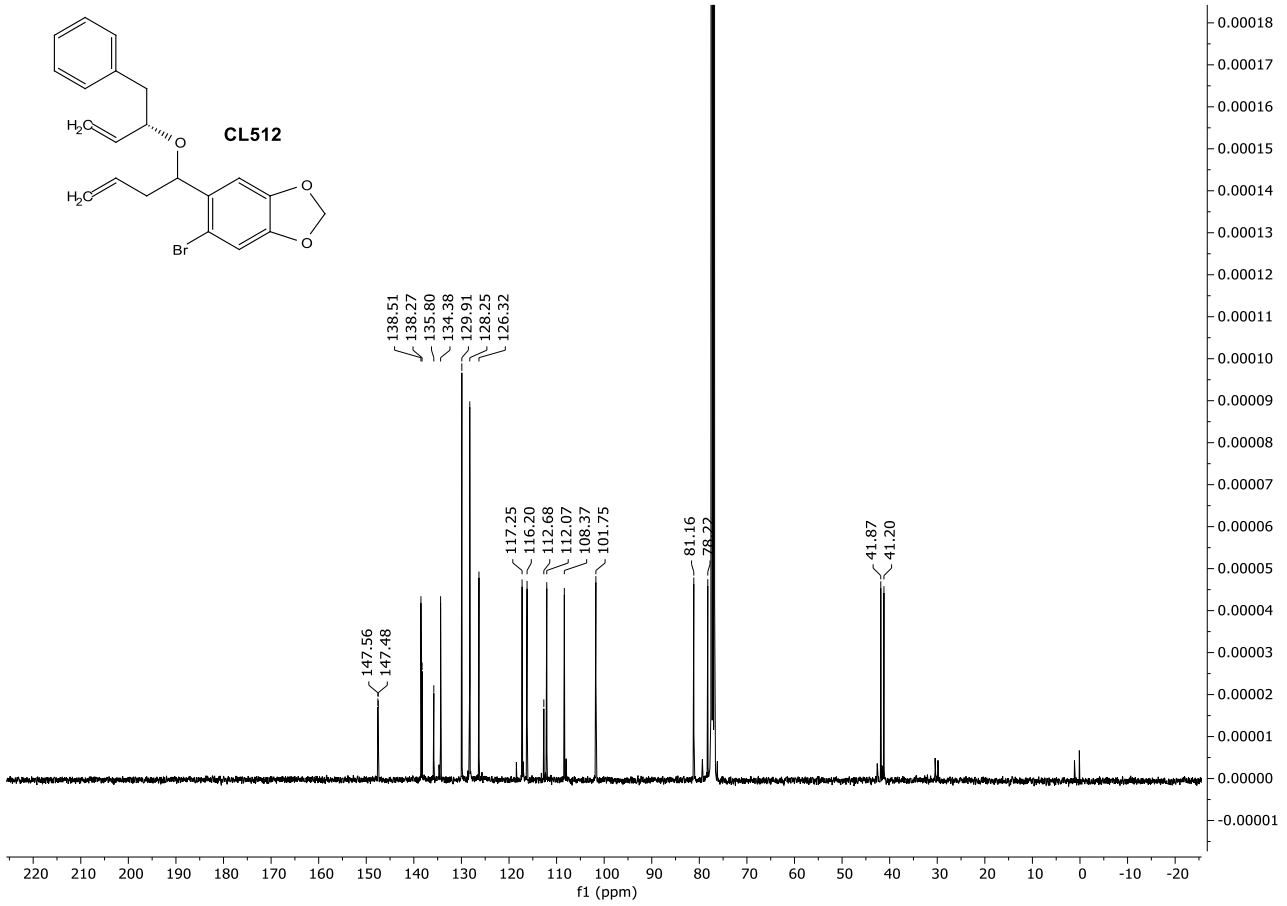
12c


LP018
Br
O
O
O
79.35
69.90
134.72
134.55
117.22
113.34
112.46
107.56
101.84
147.97
147.73
41.41
f1 (ppm)

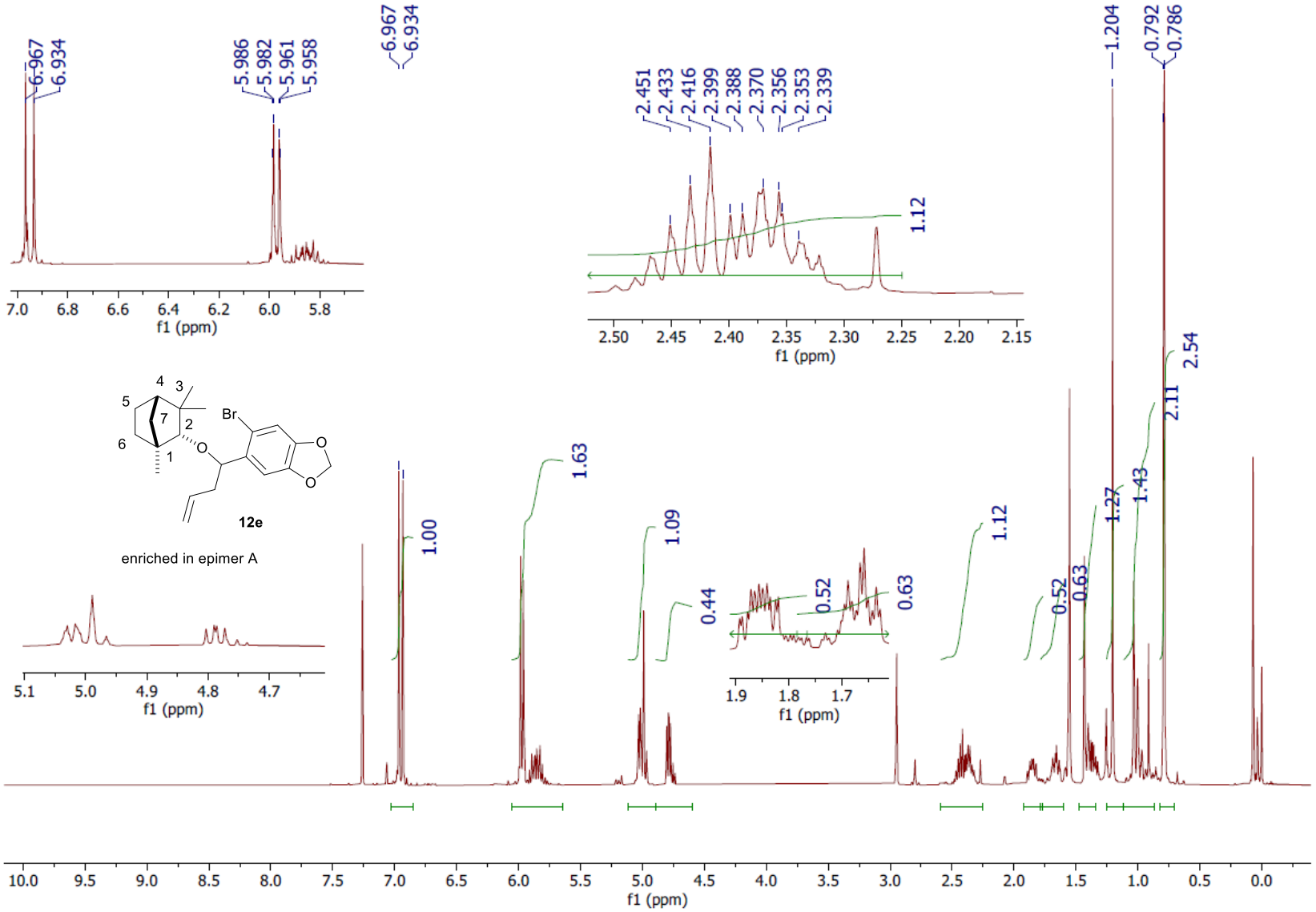
12d

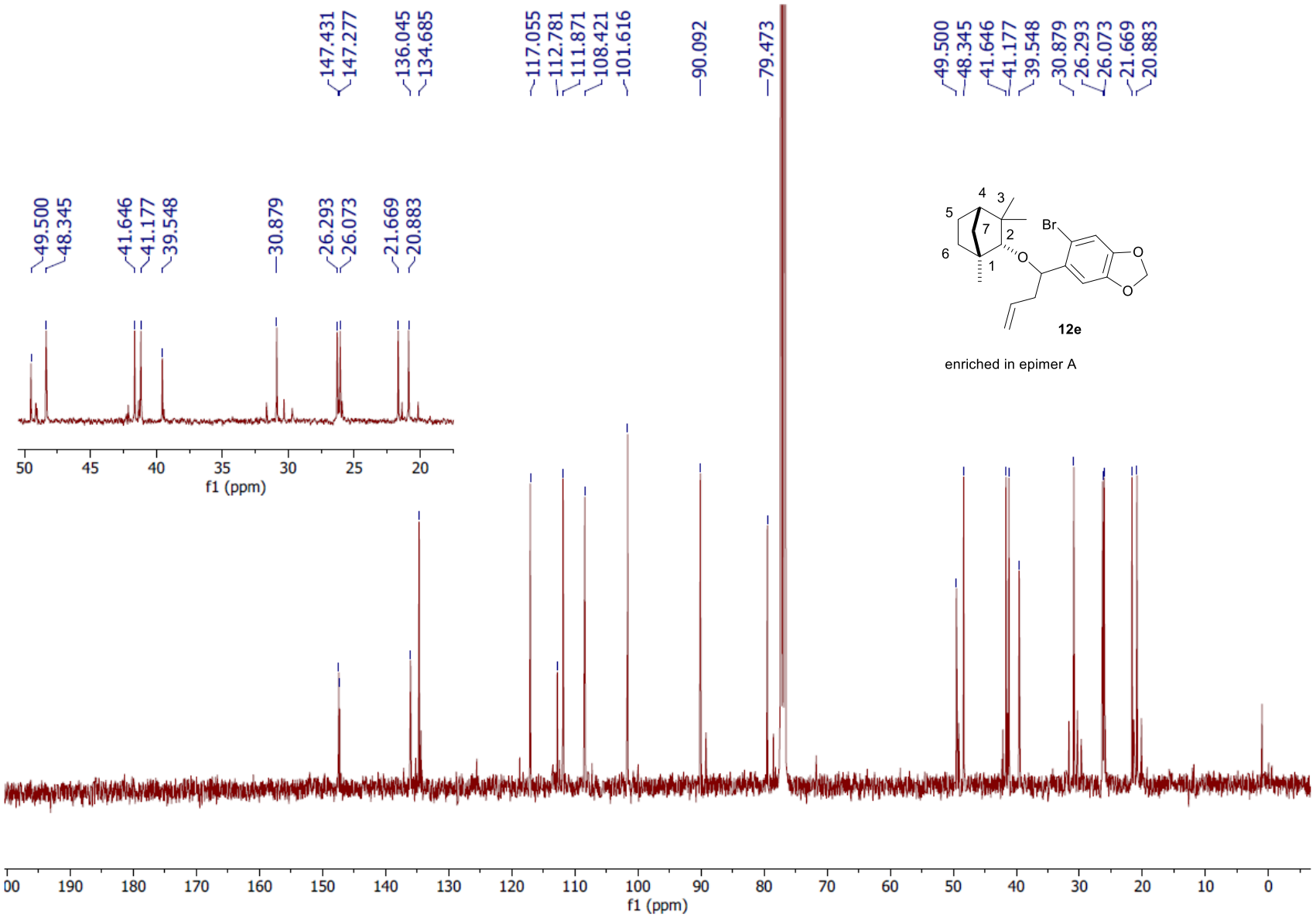

CL512
7.28
7.26
7.23
7.21
6.96
6.91
5.97
5.96
5.95
5.95
5.64
5.64
5.62
5.62
5.61
5.60
5.59
5.57
5.57
5.55
5.05
5.01
4.97
4.95
4.94
4.93
4.74
4.73
4.71
3.95
3.94
3.92
3.90
3.01
2.99
2.97
2.96
2.80
2.78
2.76
2.75
2.32
2.23
3.22
1.00
0.92
0.99
1.04
2.00
4.46
1.03
1.03
1.02
1.14
2.15
f1 (ppm)

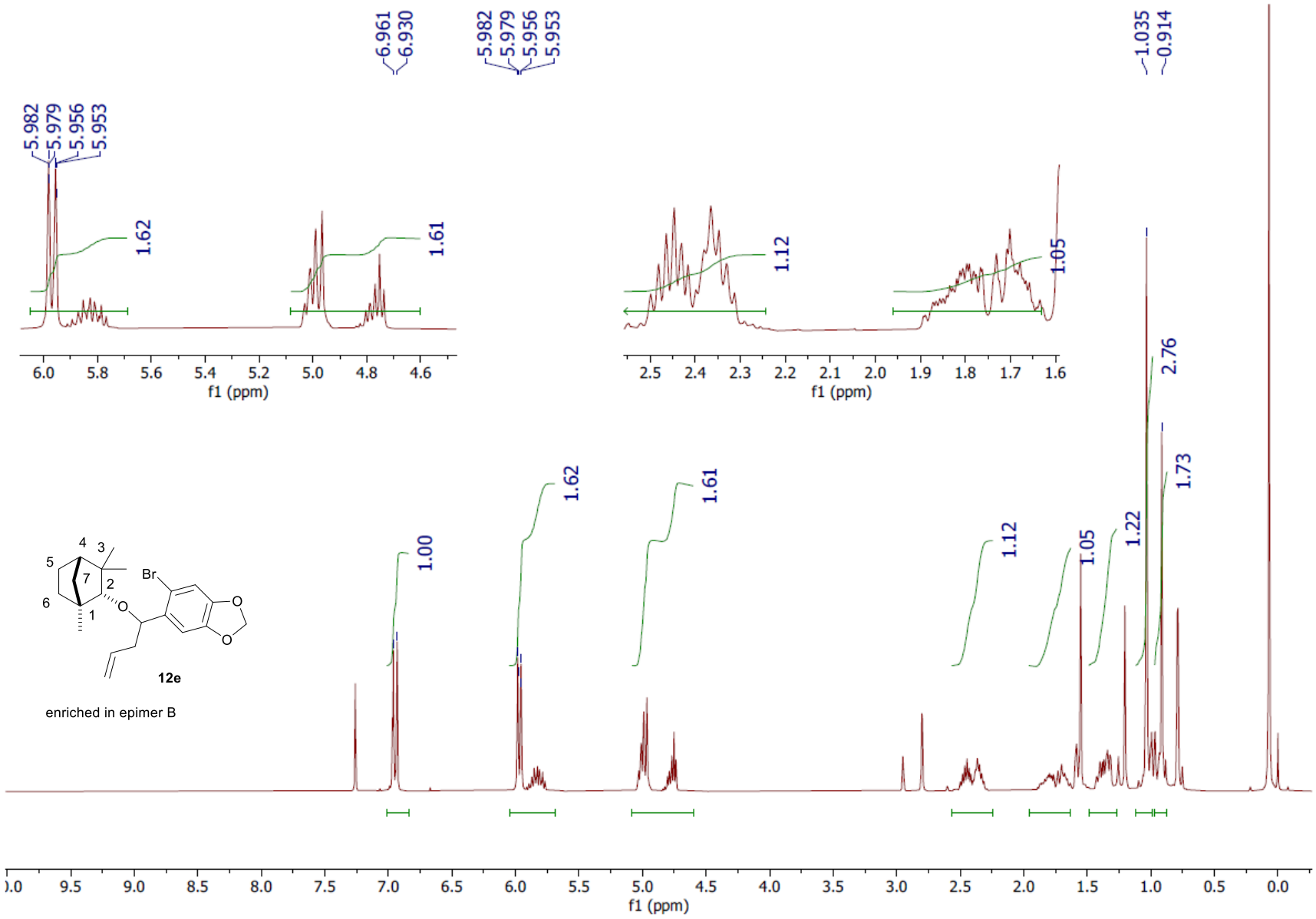
12d

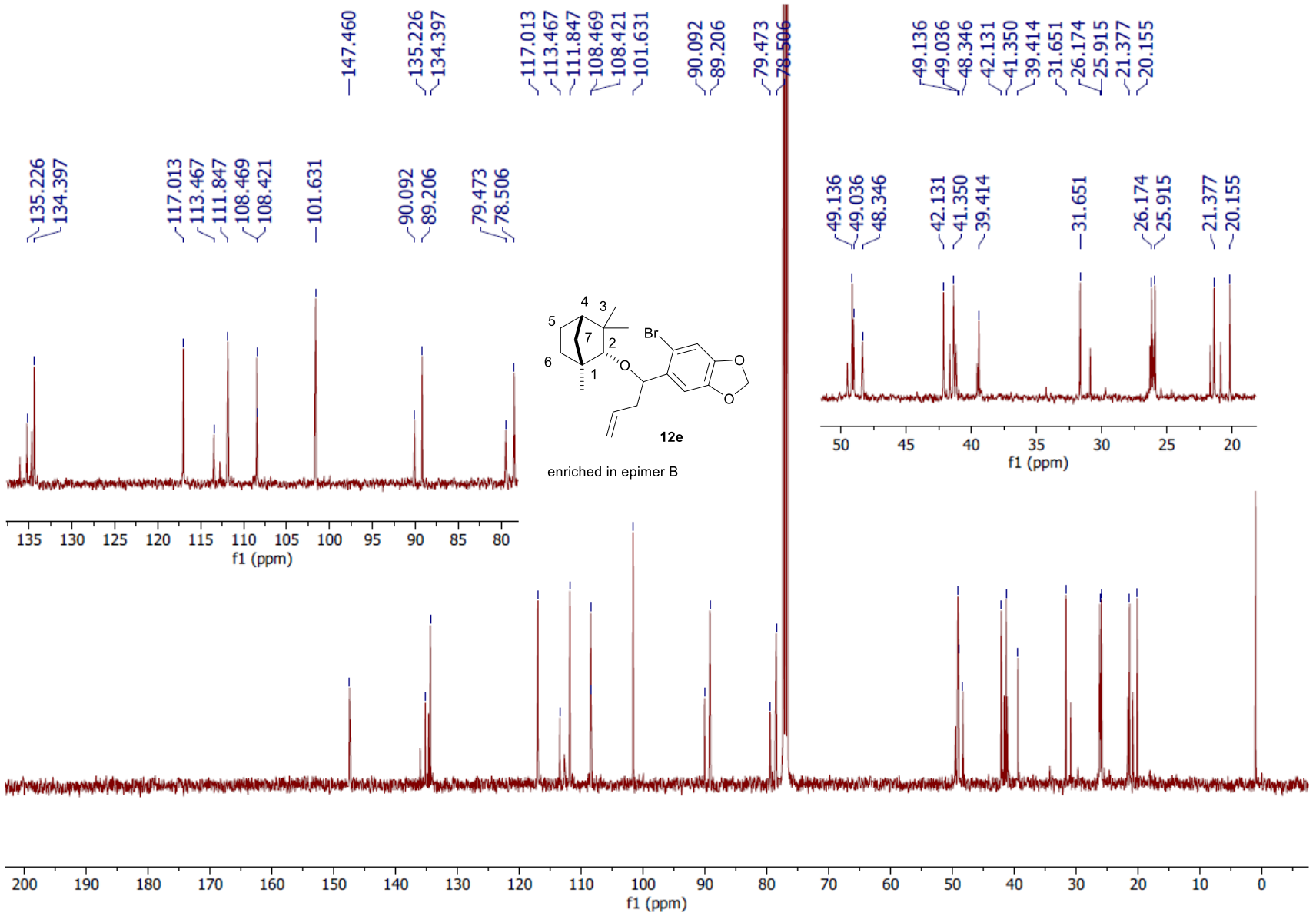

CL512
H2C
O
H2C
Br
O
O
138.51
138.27
135.80
134.38
129.91
128.25
126.32
117.25
116.20
112.68
112.07
108.37
101.75
81.16
78.22
41.87
41.20
147.56
147.48
0.00018
0.00017
0.00016
0.00015
0.00014
0.00013
0.00012
0.00011
0.00010
0.00009
0.00008
0.00007
0.00006
0.00005
0.00004
0.00003
0.00002
0.00001
0.00000
-0.00001
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

12e

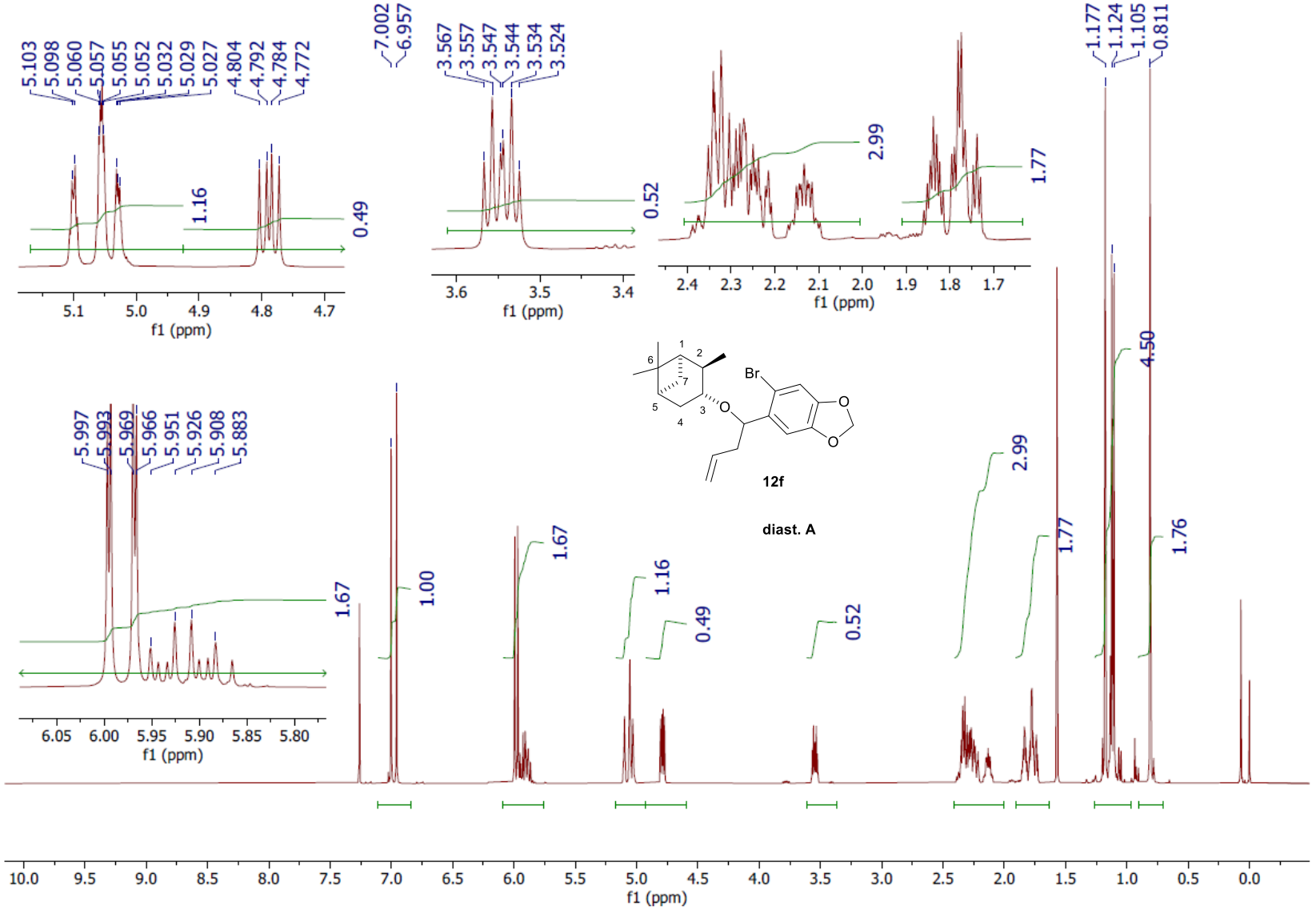

6.967
6.934
5.986
5.982
5.961
5.958
2.451
2.433
2.416
2.399
2.388
2.370
2.356
2.353
2.339
1.204
0.792
0.786
2.54
2.11
1.43
1.27
1.63
1.12
1.09
1.00
0.44
0.52
0.63
0.52
0.63
1.12
Br
O
12e
enriched in epimer A
f1 (ppm)


147.431
147.277
136.045
134.685
117.055
112.781
111.871
108.421
101.616
90.092
79.473
49.500
48.345
41.646
41.177
39.548
30.879
26.293
26.073
21.669
20.883
f1 (ppm)
Br
O
O
O
12e
enriched in epimer A

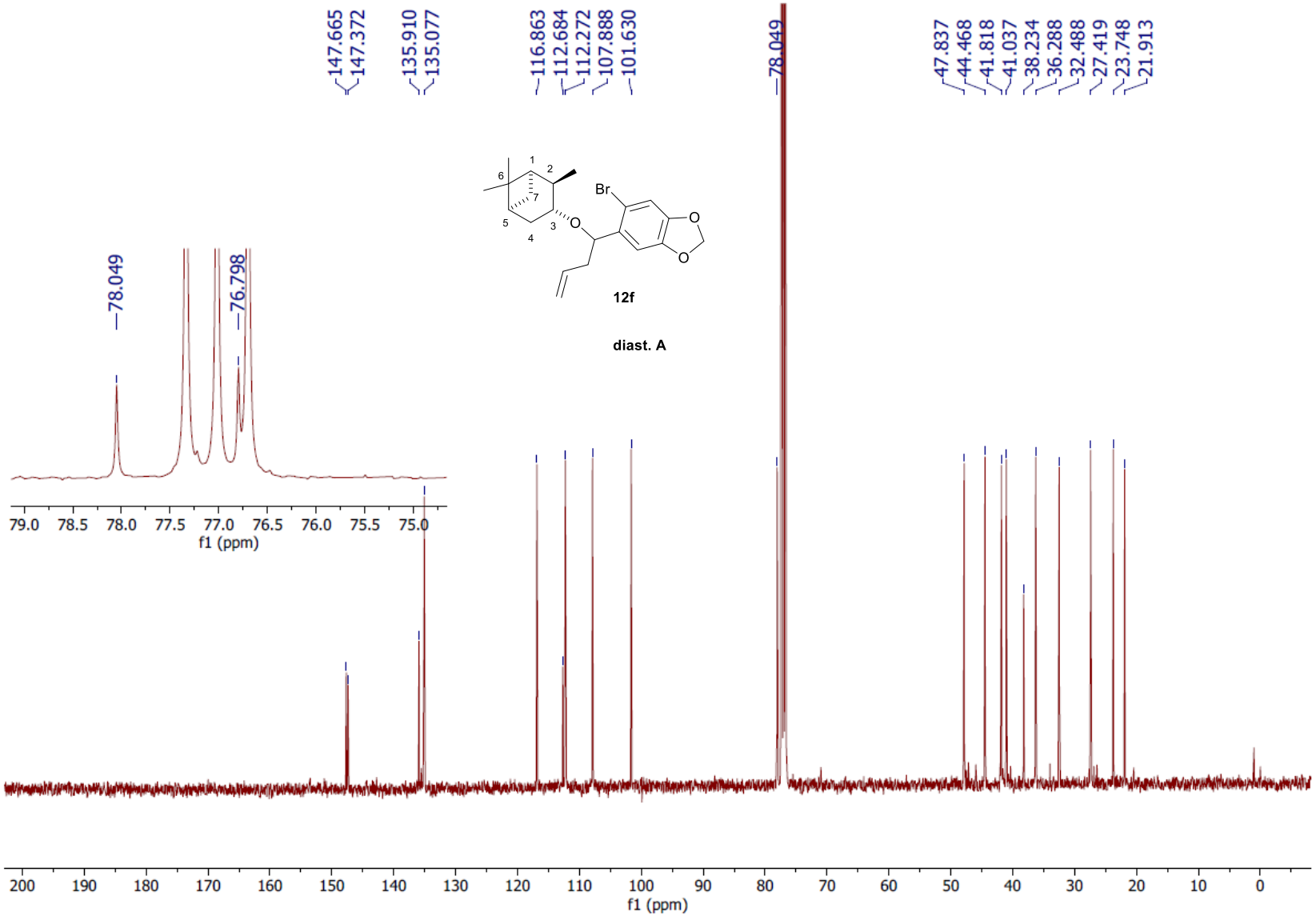

6.961
6.930
5.982
5.979
5.956
5.953
1.035
0.914
1.62
1.61
1.12
1.05
2.76
1.73
1.00
1.22
f1 (ppm)
Br
O
12e
enriched in epimer B


147.460
135.226
134.397
117.013
113.467
111.847
108.469
108.421
101.631
90.092
89.206
79.473
78.506
49.136
49.036
48.346
42.131
41.350
39.414
31.651
26.174
25.915
21.377
20.155
Br
O
O
O
12e
enriched in epimer B
f1 (ppm)

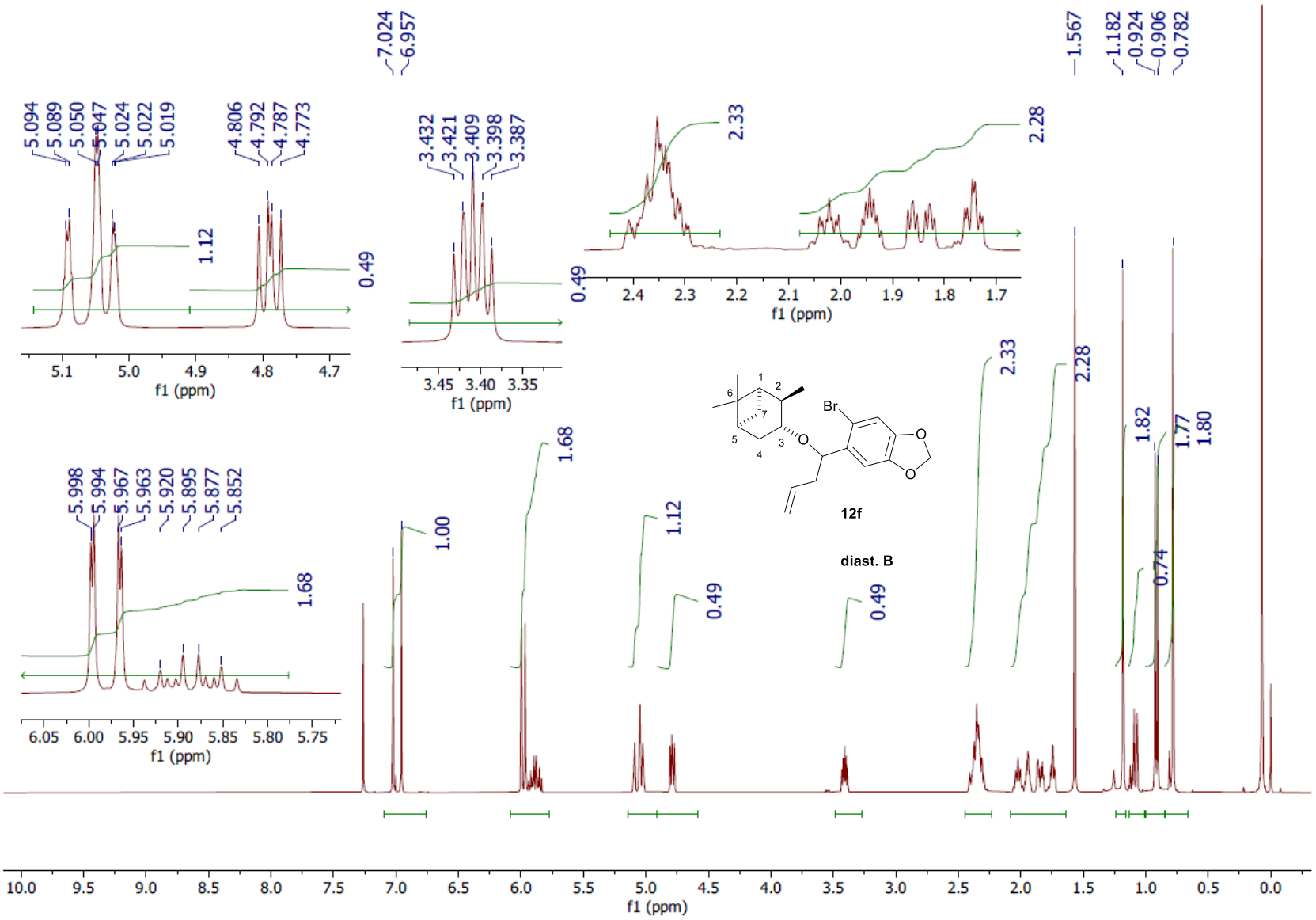
12f



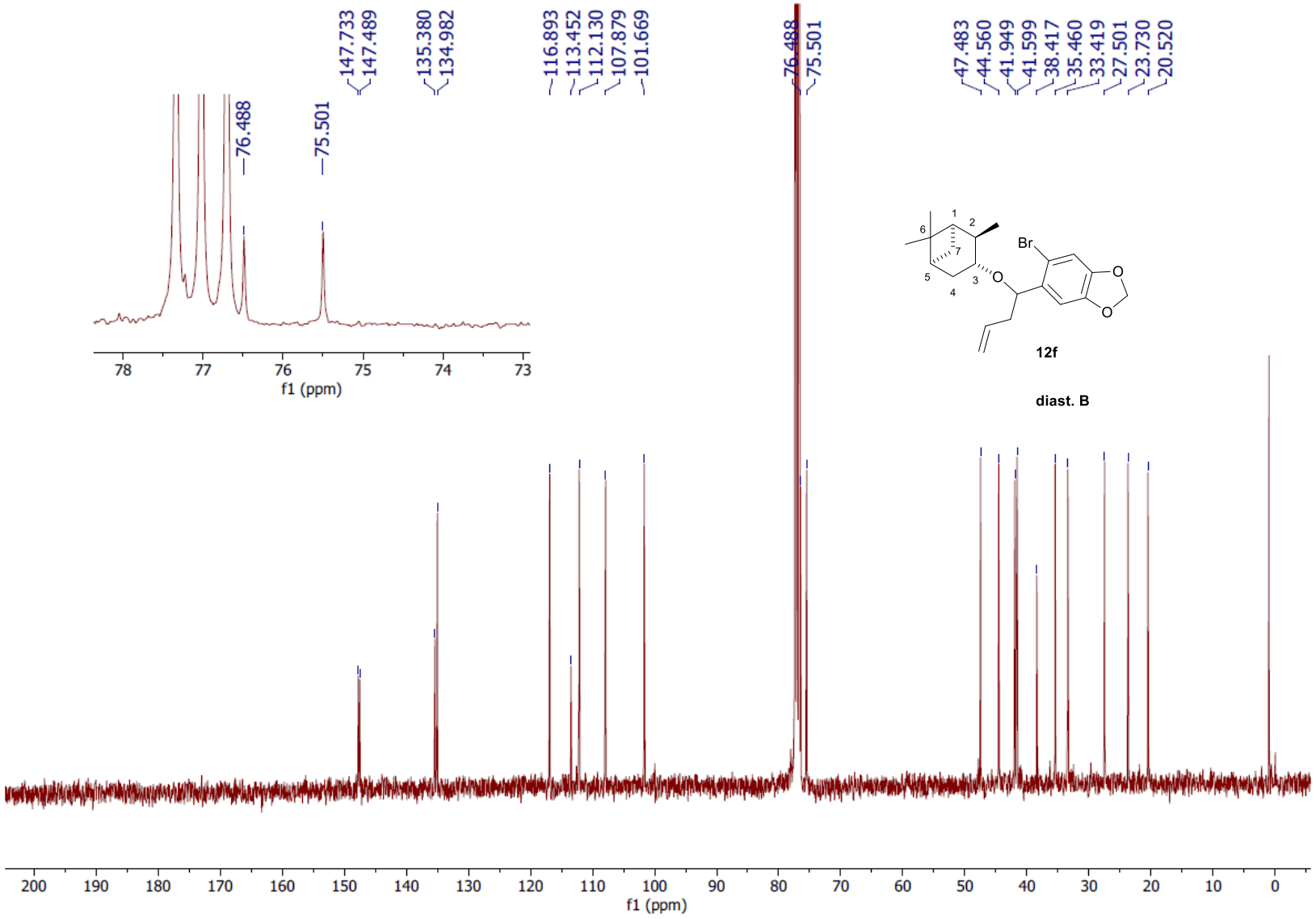
12f


147.665
147.372
135.910
135.077
116.863
112.684
112.272
107.888
101.630
78.049
47.837
44.468
41.818
41.037
38.234
36.288
32.488
27.419
23.748
21.913
78.049
76.798
79.0 78.5 78.0 77.5 77.0 76.5 76.0 75.5 75.0
f1 (ppm)
Br
O
O
O
12f
diast. A
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

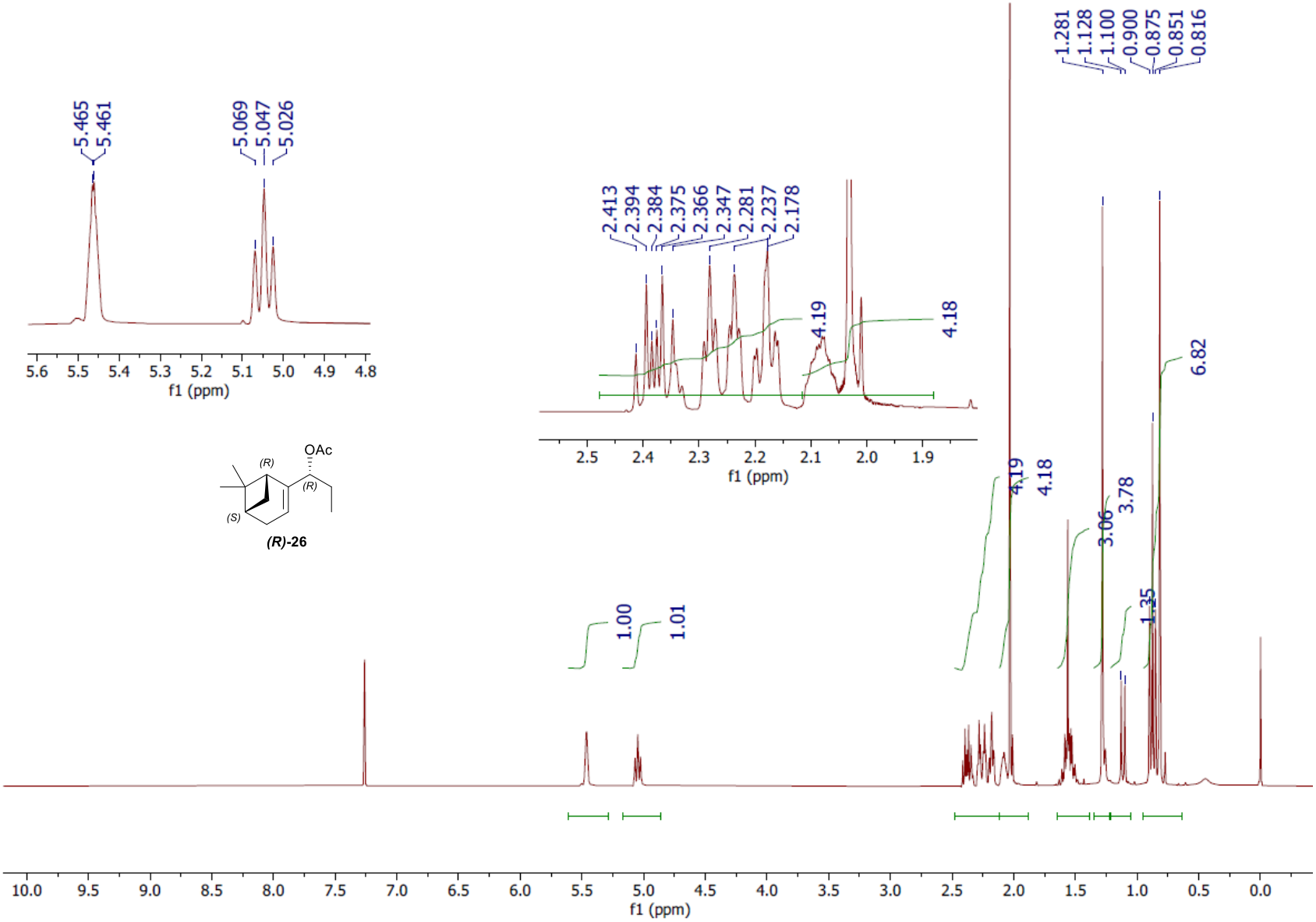
12f


7.024
6.957
1.567
1.182
0.924
0.906
0.782
5.094
5.089
5.050
5.047
5.024
5.022
5.019
4.806
4.792
4.787
4.773
3.432
3.421
3.409
3.398
3.387
2.33
2.28
1.12
0.49
f1 (ppm)
5.998
5.994
5.967
5.963
5.920
5.895
5.877
5.852
1.68
1.00
1.12
0.49
2.33
2.28
1.82
1.77
1.80
0.74
Br
O
12f
diast. B
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

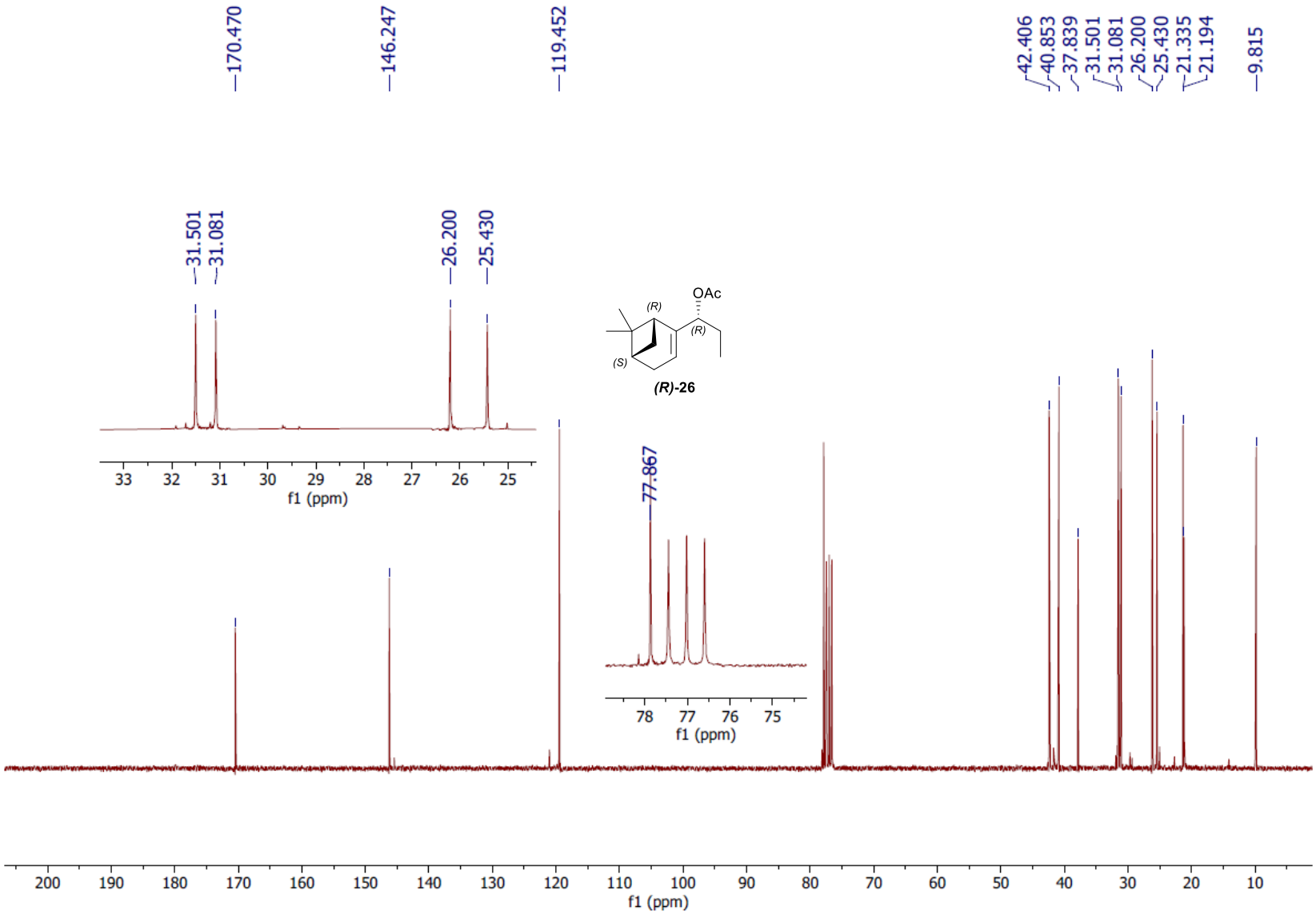
12f


147.733
147.489
135.380
134.982
116.893
113.452
112.130
107.879
101.669
76.488
75.501
47.483
44.560
41.949
41.599
38.417
35.460
33.419
27.501
23.730
20.520
76.488
75.501
78
77
76
75
74
73
f1 (ppm)
Br
O
O
O
12f
diast. B
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

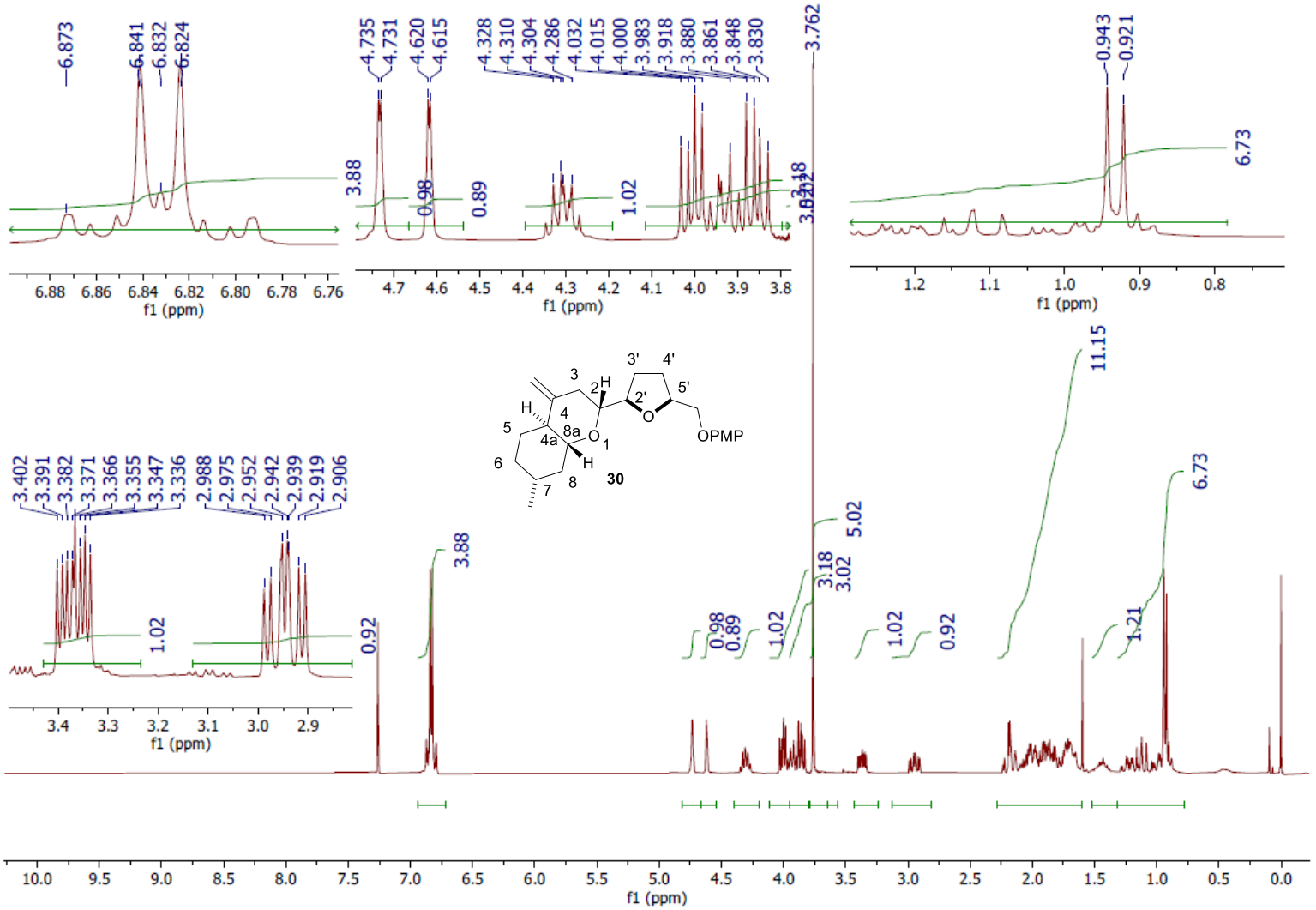
26


5.465
5.461
5.069
5.047
5.026
5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8
f1 (ppm)
2.413
2.394
2.384
2.375
2.366
2.347
2.281
2.237
2.178
4.19
4.18
2.5 2.4 2.3 2.2 2.1 2.0 1.9
f1 (ppm)
1.281
1.128
1.100
0.900
0.875
0.851
0.816
6.82
4.19
4.18
3.78
3.06
1.35
1.00
1.01
OAc
(R)
(R)
(S)
(R)-26
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

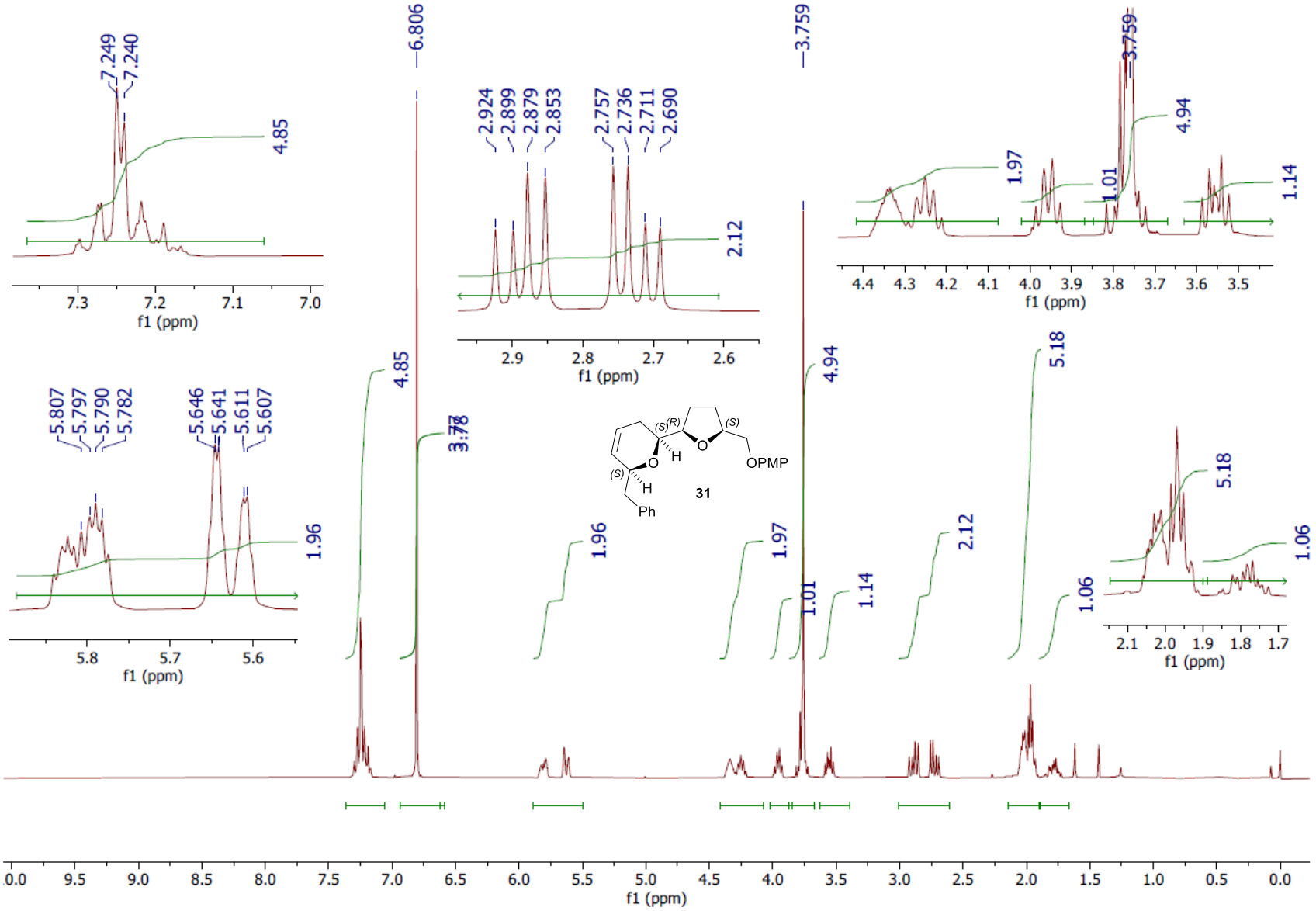
26


170.470
146.247
119.452
42.406
40.853
37.839
31.501
31.081
26.200
25.430
21.335
21.194
9.815
31.501
31.081
26.200
25.430
33 32 31 30 29 28 27 26 25
f1 (ppm)
OAc
(R)
(R)
(S)
(R)-26
77.867
78 77 76 75
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

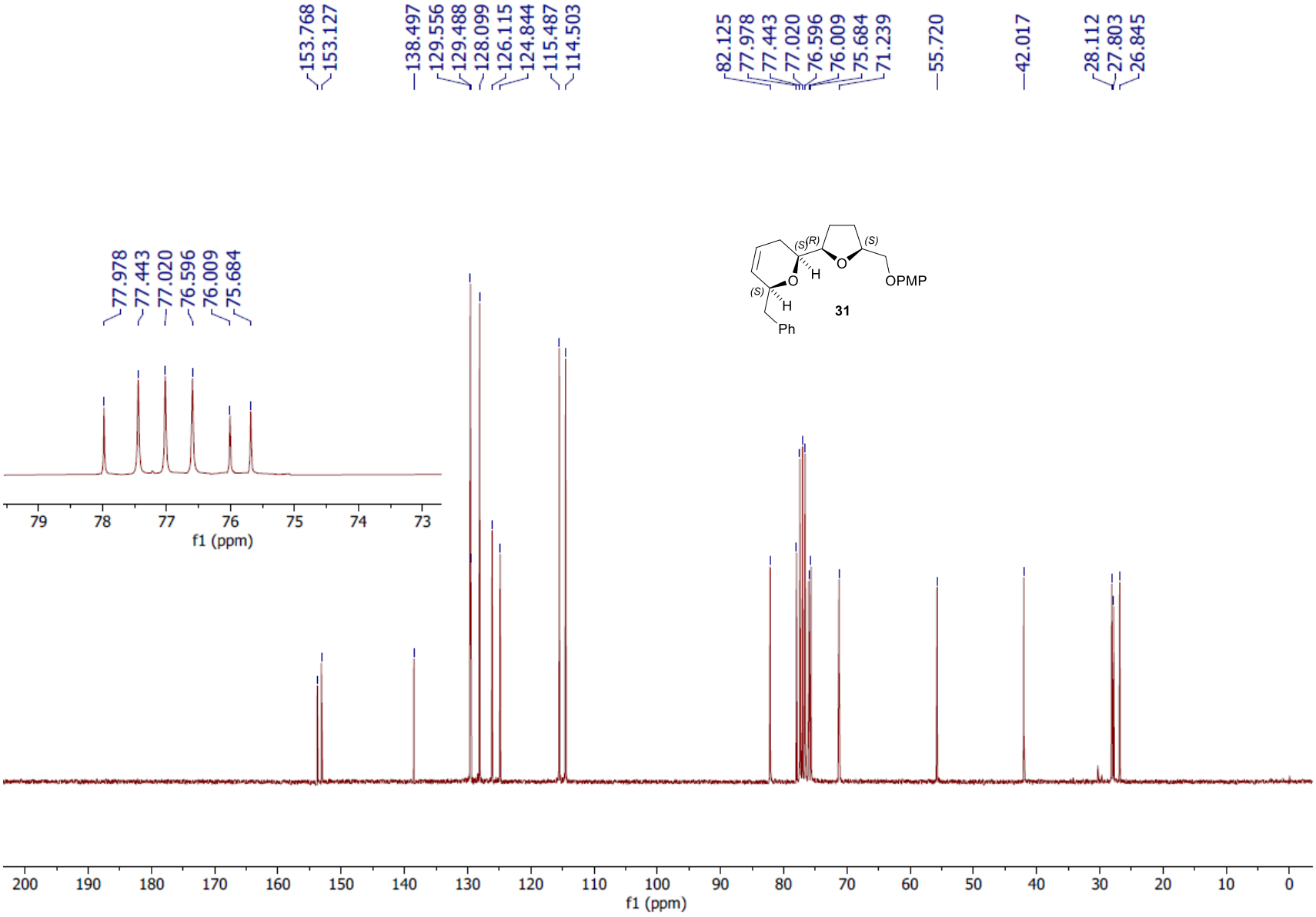
30


6.873
6.841
6.832
6.824
4.735
4.731
4.620
4.615
4.328
4.310
4.304
4.286
4.032
4.015
4.000
3.983
3.918
3.880
3.861
3.848
3.830
3.762
0.943
0.921
6.73
3.88
0.98
0.89
1.02
3.18
3.02
5.02
11.15
3.402
3.391
3.382
3.371
3.366
3.355
3.347
3.336
2.988
2.975
2.952
2.942
2.939
2.919
2.906
0.92
1.21
OPMP
30
f1 (ppm)

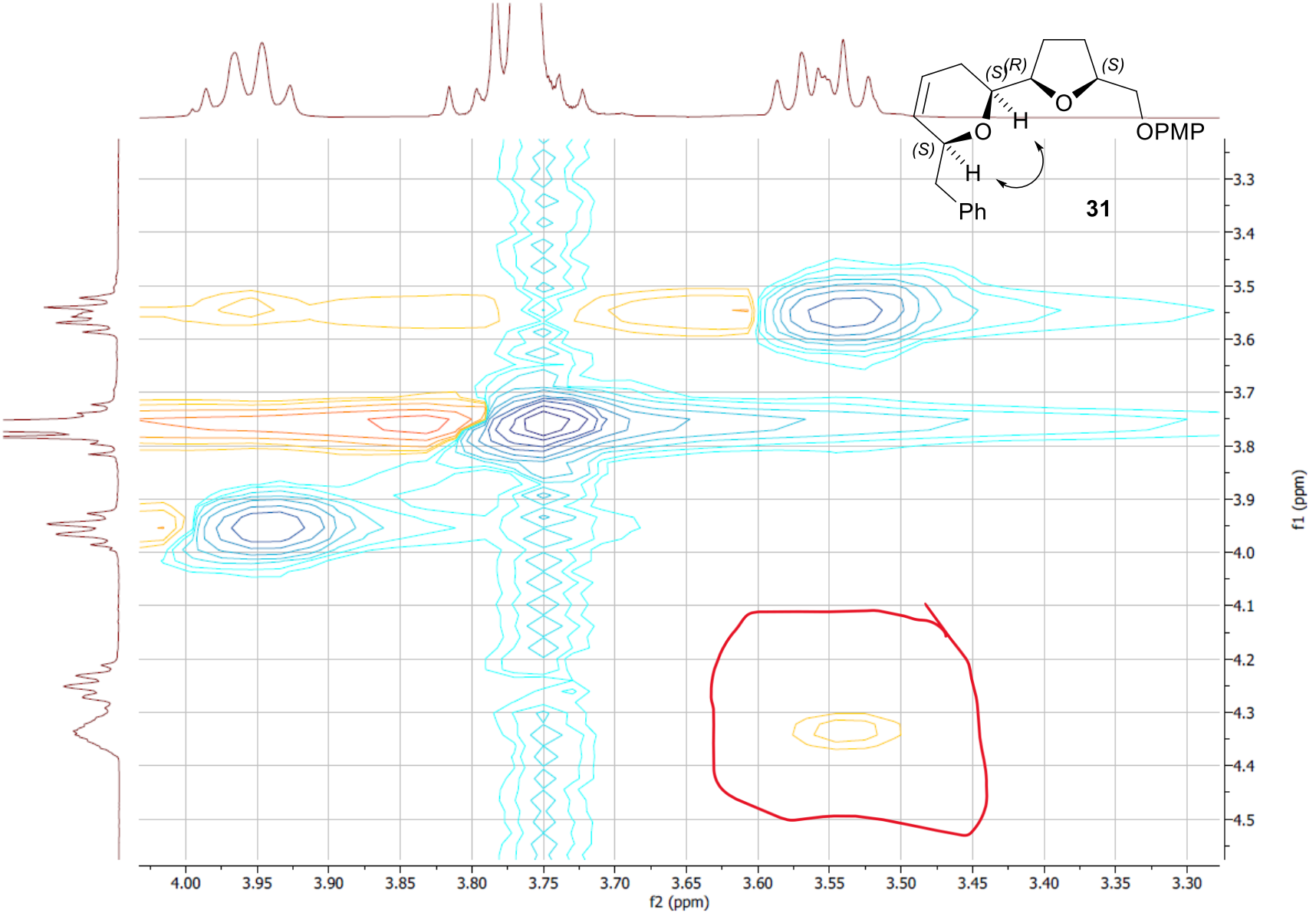
31


7.249
7.240
4.85
6.806
3.778
2.924
2.899
2.879
2.853
2.757
2.736
2.711
2.690
2.12
3.759
1.97
1.01
4.94
1.14
5.807
5.797
5.790
5.782
5.646
5.641
5.611
5.607
1.96
OPMP
31
Ph
1.97
1.14
2.12
5.18
1.06
f1 (ppm)

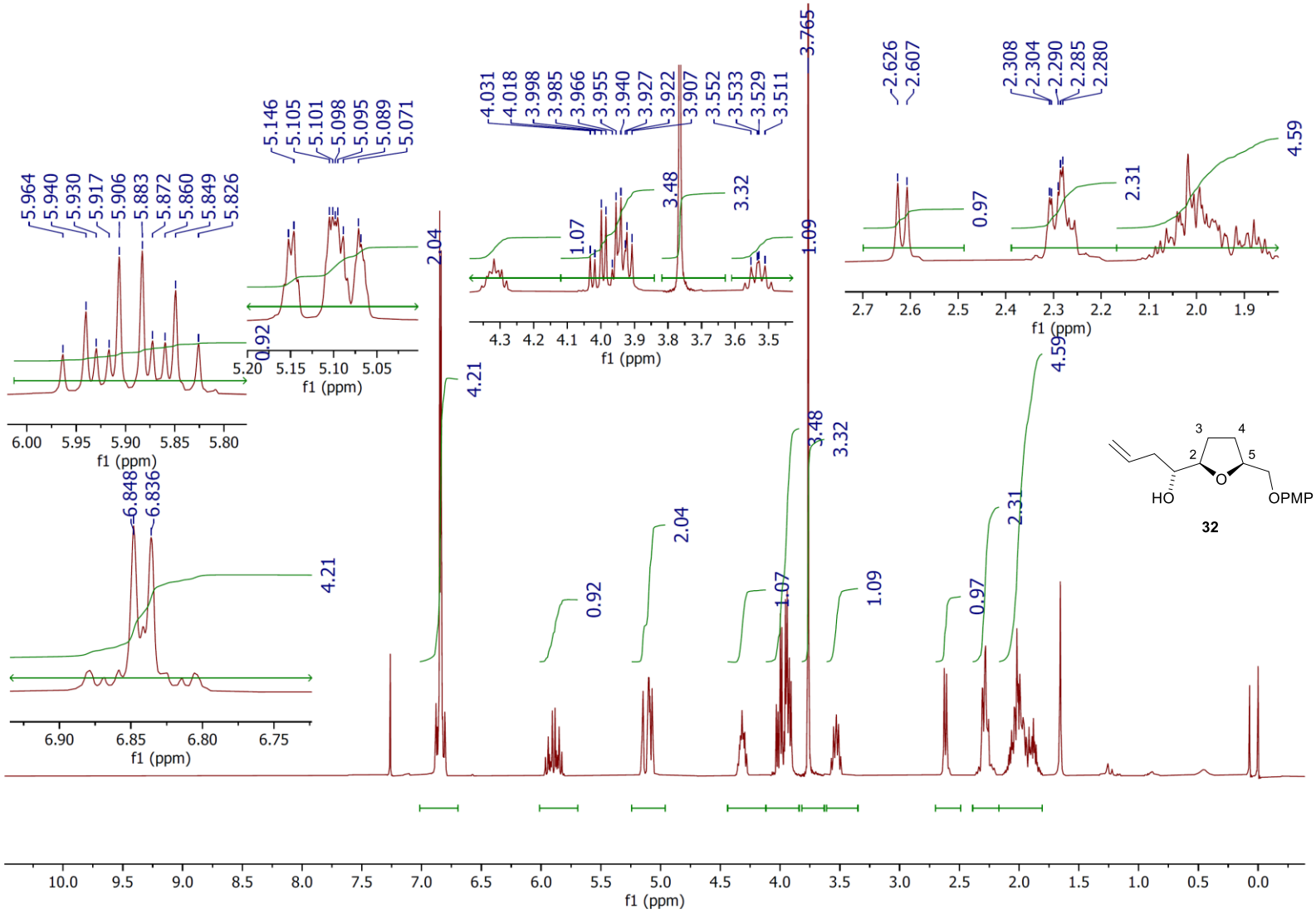
31

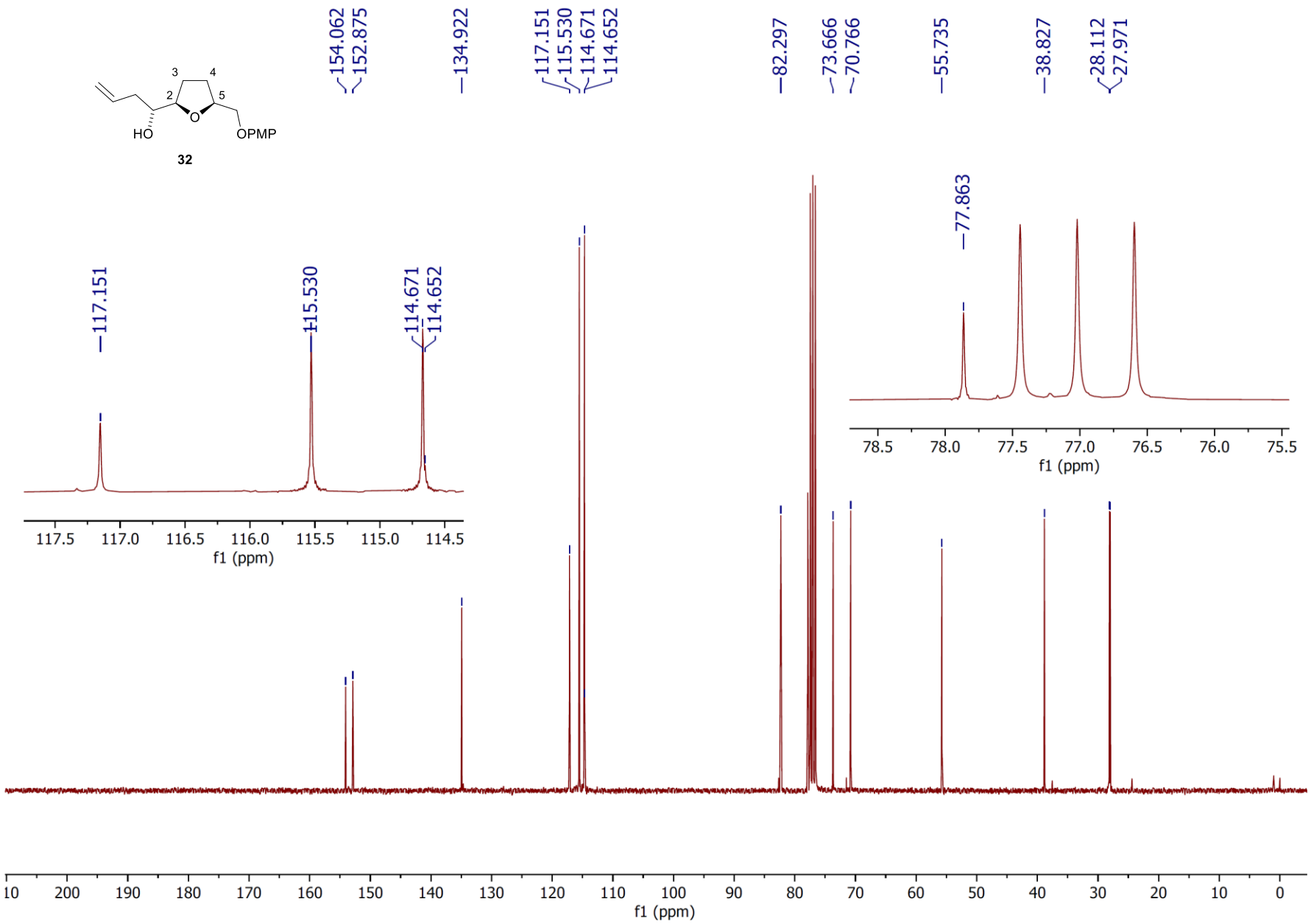

153.768
153.127
138.497
129.556
129.488
128.099
126.115
124.844
115.487
114.503
82.125
77.978
77.443
77.020
76.596
76.009
75.684
71.239
55.720
42.017
28.112
27.803
26.845
(S)
(R)
(S)
O
H
O
(S)
H
Ph
OPMP
31
f1 (ppm)
f1 (ppm)

NOESY of 31 showing the cross peak between *H*-2 of THP (3.57) and *H*-6 of THP (4.33)



32


5.964
5.940
5.930
5.917
5.906
5.883
5.872
5.860
5.849
5.826
5.146
5.105
5.101
5.098
5.095
5.089
5.071
4.031
4.018
3.998
3.985
3.966
3.955
3.940
3.927
3.922
3.907
3.552
3.533
3.529
3.511
3.765
2.626
2.607
2.308
2.304
2.290
2.285
2.280
6.848
6.836
4.21
2.04
0.92
1.07
3.48
3.32
1.09
0.97
2.31
4.59
f1 (ppm)
HO
OPMP
32


154.062
152.875
134.922
117.151
115.530
114.671
114.652
82.297
73.666
70.766
55.735
38.827
28.112
27.971
HO
OPMP
32
77.863
f1 (ppm)

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