Stereocontrol in Radical Processes through the Exocyclic Effect: Dual Role of Triethylboron as Radical Initiator and In Situ Derivatization Agent

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SUPPORTING INFORMATION
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A. Experimental procedures and characterization data for compounds 1-3, 10-12, 13 and 14, boronates 2' and 3', and lactone 1'.

General Methods. All reactions requiring anhydrous conditions were conducted under a positive nitrogen atmosphere in oven-dried glassware using standard syringe techniques. The anhydrous solvents were purchased from Aldrich and used as received. *i*-Pr_2NH and Et_3N were freshly distilled from CaH_2 under N_2 atmosphere. *n*-Butyllithium (1.6 M solution in hexane) was purchased from Aldrich and titrated prior to use (diphenylacetic acid end-point in dry THF). Tributyltin hydride, triethylborane (1 M solution in hexane), *t*-butyl 2-bromoacetate, and 2,2-dimethoxypropane were also purchased from Aldrich and used as received. 1,1,2-trimethoxyethane and 1,1,3-trimethoxypropane were purchased from Aldrich and distilled prior to use. Flash chromatography was performed on Merck silica gel 60 (0.040-0.063 mm) using nitrogen pressure. Analytical thin-layer chromatography (TLC) was carried out on precoated (0.25 mm) Merck silica gel F-254 plates. Melting points were determined on an electrothermal melting point apparatus and are uncorrected.

The preparation and characterization data of **4-9** have been reported previously.[1]

Compound 1: To a 0.1 M solution of *tert*-butyl 2-phenylselenopropionate[2] in THF at 0 °C were successively added TBAF (5 equiv) and acetic acid (2 equiv). After being allowed to warm to room temperature, the reaction mixture was stirred until all of the substrate was consumed (2 h). The reaction mixture was diluted with EtOAc, quenched

(1) Guindon, Y.; Yoakim, C.; Gorys, V.; Ogilvie, W.W.; Delorme, D.; Renaud, J.; Robinson, G.; Lavallée, J.-F.; Slassi, A.; Jung, G.; Rancourt, J.; Durkin, K.; Liotta, D. *J. Org. Chem.* **1994**, *59*, 1166
(2) Guindon, Y.; Faucher, A.-M.; Bourque, É.; Caron, V.; Jung, G.; Landry, S. R. *J. Org. Chem.* **1997**, *62*, 9276.

with a phosphate buffer (pH 7.2) solution, and then extracted twice with EtOAc. The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$ and brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography to afford **1** as a white solid (81%): mp 70-71 °C, R_f 0.12 (hexanes-EtOAC, 6:4); IR (neat) υ_{max} 3550, 3500, 1720 cm^{-1}; MS (FAB) 360 (19, MH), 287 (49), 230 (28), 157 (19), 57 (100); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H), 1.46 (s, 9H), 1.68-1.77 (m, 1H), 2.09-2.13 (m, 1H), 2.50 (dd, *J* = 7.2, 3.6 Hz, 1H), 3.37 (d, *J* = 5.2 Hz, 1H), 3.81-3.88 (m, 2H), 4.03-4.08 (m, 1H), 7.32 (t, *J* = 7.2 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.8, 28.0, 33.3, 54.5, 61.9, 75.6, 82.4, 126.5, 128.8, 129.4, 138.1, 173.1; HRMS (FAB) calcd for $C_{16}H_{25}O_4{}^{80}Se$: 361.0918, found: 361.0933 (-4.2 ppm). Anal. calcd for $C_{16}H_{24}O_4Se$: C 53.48, H 6.73; found: C 53.29, H 6.81.

Compound 10: To a cold (0 °C) stirred solution of *i*Pr_2NH (1.3 equiv) in THF under a N_2 atmosphere was added a solution of *n*-butyllithium (1.2 equiv) in hexanes. The resultant mixture was stirred for 30 min and then cooled to -78 °C before *tert*-butyl 2-phenylselenopropionate[2] **(**9.4 g, 33 mmol) in THF was added. After the reaction mixture was stirred at -78 °C for 30 min, 3-(*N*-*tert*-butoxycarbonyl-*N*-ethylamino)-1-propanal[3] (6.0 g, 30 mmol) was added, and the resultant solution was stirred at -78 °C until all of the substrate was consumed (4 h). The cold bath was removed, and the reaction mixture was quenched with a saturated aq NH_4Cl. The mixture was then extracted successively with Et_2O (1X) and CH_2Cl_2 (2X), dried with anhydrous $MgSO_4$, filtered, and concentrated under

(3) Chaubet, F.; Nguyen Van Duong, M.; Courtieu, J.; Gaudemer, A. *Can. J. Chem.* **1991**, *69*, 1107.

reduced pressure. Purification of the crude material by flash column chromatography (CH_2Cl_2:EtOAc, 10:1) afforded two diastereomers (12.0 g, 82%). To a solution of the less polar *syn* isomer (R_f 0.33; CH_2Cl_2-EtOAc, 10:1) in CH_2Cl_2 was added a solution of 4M HCl in dioxane (4 equiv) at room temperature. The mixture was stirred until the starting material was no longer evident by TLC (1h). After concentration of the solvent, the residue was dissolved in water and extracted twice with ether. The cold (0 °C) aqueous solution was treated with a 1M aq solution of NaOH until a neutral pH was achieved and the resultant solution was extracted thrice with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with brine and dried with Na_2SO_4. Removal of the solvent gave the desired amino ester **10** (*syn*) as a yellow oil: R_f 0.19 (CH_2Cl_2-MeOH, 30:1; Al_2O_3); IR (neat) υ_{max} 1705 cm^{-1}; MS (FAB) 388 (100, MH), 386 (52), 332 (21), 230 (7), 174 (16); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, *J* = 7.3 Hz, 3H), 1.35 (s, 9H), 1.43 (s, 3H), 1.45-1.52 (m, 1H), 1.57-1.68 (m, 1H), 2.62 (dq, *J* = 11.4, 7.0 Hz, 1H), 2.71 (dq, *J* = 11.4, 7.0 Hz, 1H), 2.76 (ddd, *J* = 12.4, 10.8, 3.6 Hz, 1H), 2.97 (td, *J* = 12.1, 4.1 Hz, 1H), 4.15 (dd, *J* = 10.2, 1.9 Hz, 1H), 7.26-7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1, 17.3, 27.8, 28.2, 30.2, 43.7, 48.6, 56.3, 75.0, 81.0, 127.3, 128.5, 128.9, 138.1, 138.2, 171.9; HRMS (FAB) calcd for $C_{18}H_{30}O_3N^{80}Se$: 388.1391, found: 388.1375 (+4.1 ppm). Anal. calcd for $C_{18}H_{29}O_3NSe$: C 55.95, H 7.57, N 3.62; found: C 55.94, H 7.59, N 3.67.

General procedure for reduction with *in situ* derivatization or Lewis acid: To a solution of **1** in CH_2Cl_2 (0.1 M) at room temperature was added either Et_3B (1.3 equiv)/air, DIEA (1.8 equiv)/Bu_2BOTf (1.3 equiv), or DIEA (2.2 equiv)/Me_2SiCl_2 (1.8 equiv). The

resultant mixture was stirred for 1-2 h, cooled to 0 ^{o}C, and subjected to reduction as described below.

General procedure for radical reduction in the absence of Lewis acid: To a cooled (0 ^{o}C) stirred solution of **1** in CH_2Cl_2 (0.1 M) were added Bu_3SnH (2 equiv) and either Et_3B (0.2 equiv) or AIBN (0.2 equiv; initiation by sunlamp irradiation). The resultant solution was stirred for 1-2 h, after which 0.2 equiv of Et_3B was added every 30 min until all of the substrate was consumed. 1,3-Dinitrobenzene (0.2 equiv) was then added, and the resultant mixture was stirred at 0 ^{o}C for 15 min before being allowed to warm to room temperature. After concentration under reduced pressure, the crude residue was analyzed by ^{1}H NMR to determine the *anti:syn* ratio. The crude mixture of *anti* and *syn* products was derivatized as boronates, for which ratios were determined by ^{1}H NMR and GC. The boronate mixture was then treated with silica gel and MeOH (25 mL) to regenerate the diol products, which were separated by flash column chromatography.

Compound 2: colorless oil; R_f 0.12 (hexanes-EtOAc, 1:1); IR (neat) υ_{max} 3400, 1715 cm^{-1}; MS (FAB) 205 (10, MH), 149 (76), 131 (52), 89(9); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.18 (d, J = 6.8 Hz, 3H), 1.47 (s, 9H), 1.69-1.76 (m, 2H), 2.44 (quint, J = 7.2 Hz, 1H), 2.63 (dd, J = 6.0, 4.8 Hz, 1H), 3.42 (d, J = 5.6 Hz, 1H), 3.84-3.91 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 28.1, 36.0, 46.1, 61.5, 73.7, 81.4, 175.4 ; HRMS (FAB) calcd for $C_{10}H_{21}O_4$: 205.1440, found: 205.1446. (-3.0 ppm).

Compound 3: white solid; mp 48-49 °C, R_f 0.12 (hexanes-EtOAc, 1:1); IR ($CDCl_3$) υ_{max} 3400, 1715 cm^{-1}; MS (FAB) *m/z* 205 (21, MH^{+}), 149 (100), 131 (66), 113 (19), 77 (16); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.17 (d, J = 7.2 Hz, 3H), 1.46 (s, 9H), 1.53-1.60 (m,

1H), 1.72-1.81 (m, 1H), 2.43 (qd, *J* = 7.2, 4.0 Hz, 1H), 2.55 (t, *J* = 5.2 Hz, 1H), 3.29 (d, *J* = 3.6 Hz, 1H), 3.85 (q, *J* = 4.8 Hz, 2H), 4.07-4.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.4, 28.0, 35.3, 45.4, 61.5, 71.8, 81.2, 175.4**;** HRMS (FAB) calcd for $C_{10}H_{21}O_4$: 205.1440, found: 205.1448 (-4.0 ppm).

Compounds 11 (*anti*) and **12** (*syn*) were obtained from the radical reduction of phenylselenoester **10**. After the *anti*:*syn* ratio of the crude reduced products was determined by ^{1}H NMR, the mixture was treated with di-*tert*-butyl dicarbonate (2.1 equiv) in THF (0.02M) for 12 h at room temperature. After concentration, the residue was purified by flash chromatography to afford a mixture of *N*-Boc derivatives as a colorless oil: R_f 0.21 (hexanes-EtOAc, 8:2); MS (FAB) 332 (51, MH), 298 (8), 232 (62), 176 (100); ^{1}H NMR (400 MHz, $CDCl_3$, 3:1 mixture of diastereomers) δ 1.10 (t, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 7.2 Hz, 3H), 1.44 (s, 9H), 1.45 (s, 9H), 1.58-1.68 (m, 2H), 2.33-2.42 (m, 1H), 2.98-3.17 (m, 2H), 3.21-3.30 (m, 1H), 3.63-3.73 (m, 1H), 4.08-4.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 3:1 mixture of diastereomers) δ 12.7, 13.7, 28.1, 28.5, 29.1, 33.2, 42.2, 43.3, 46.0, 69.0, 79.7, 80.5, 156.4, 175.1; HRMS (FAB) calcd for $C_{17}H_{34}O_5N$: 332.2437, found: 332.2427 (3.1 ppm).

Compound 13 was isolated as a yellow oil: R_f 0.53 (hexanes-EtOAc, 1:1); IR (neat) υ_{max} 1725 cm^{-1}; MS (FAB) 398 (45, MH), 343 (90), 297 (37), 241 (91), 133 (100); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.62 (q, *J* = 7.6 Hz, 2H), 0.81 (t, *J* = 7.6 Hz, 3H), 1.36 (s, 3H), 1.39 (s, 9H), 1.82 (qd, *J* = 12.4, 5.2 Hz, 1H), 2.34 (dd, *J* = 13.6, 2.0 Hz, 1H), 3.97 (td, *J* = 12.4, 2.8 Hz, 1H), 4.06-4.10 (m, 1H), 4.43 (dd, *J* = 11.6, 2.8 Hz, 1H), 7.30 (t, *J* = 7.2, 2H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.6, 16.6,

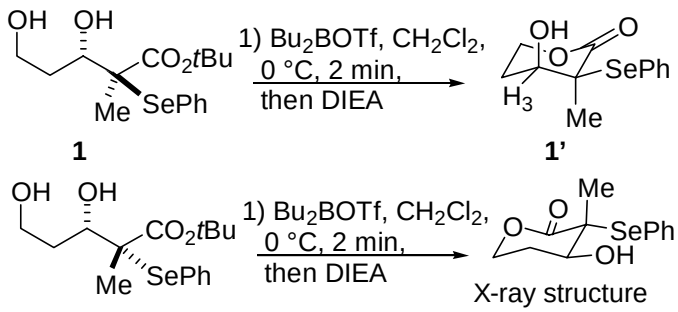
27.6, 27.8, 53.0, 61.8, 74.4, 81.2, 126.5, 128.8, 129.3, 138.0, 171.6; ^{11}B NMR (400 MHz, $CDCl_3$) δ 31 ppm; HRMS (EI) calcd for $C_{18}H_{27}O_4{}^{11}B^{80}Se$: 398.1168, found: 398.1157 (2.7 ppm). Anal. calcd for $C_{18}H_{27}O_4BSe$: C 54.48, H 6.85; found: C 54.58, H 7.20.

Compound 14 was isolated as a yellow oil: R_f 0.74 (hexanes-EtOAc, 1:1); IR (neat) υ_{max} 1730 cm^{-1}; MS (FAB) 426 (MH, 11), 371 (22), 241 (29), 167 (19), 57 (100); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.63 (t, *J* = 6.4 Hz, 2H), 0.82 (t, *J* = 7.2 Hz, 3H), 0.88-1.34 (m, 1H), 1.35 (s, 3H), 1.38 (s, 9H), 1.76-1.87 (m, 1H), 2.34 (dd, *J* = 14.0, 1.6 Hz, 1H), 3.96 (td, *J* = 12.4, 2.8 Hz, 1H), 4.06-4.10 (m, 1H), 4.43 (dd, *J* = 11.6, 2.4 Hz, 1H), 7.30 (t, *J* = 6.8, 2H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 16.7, 25.3, 26.2, 27.7, 27.8, 53.1, 61.8, 74.4, 81.2, 126.5, 128.8, 129.3, 138.0, 171.6; ^{11}B NMR (400 MHz, $CDCl_3$) δ 31 ppm; HRMS (FAB) calcd for $C_{20}H_{31}O_4{}^{11}B^{80}Se$: 426.1481, found: 426.1462 (+4.4 ppm). Anal. calcd for $C_{20}H_{31}O_4BSe$: C 56.49, H 7.35; found: C 56.77, H 7.65.

Ethylboronate 2' (*anti*) was prepared from reduced product **2** (*anti*) and isolated as a colorless oil. Capillary GC analyses were performed on a Hewlett Packard 6890 instrument using a 0.25 mm × 30 m SE-30 column. GC t_R 7.77 min ($t_{inj.}$ 280 °C, t_{FID} 280 °C, split method, 83:1, 0.5 mL/min, program 150 °C/8min, 20 °C/min, 280/ 5min). R_f 0.58 (hexanes-EtOAc, 40:60); IR (neat) υ_{max} 1735 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.65 (q, *J* = 7.8 Hz, 2H), 0.85 (t, *J* = 7.8 Hz, 3H), 1.08 (d, *J* = 7.1 Hz, 3H), 1.46 (s, 9H), 1.63-1.75 (m, 1H), 1.90 (qd, *J* = 11.0, 2.9 Hz, 1H), 2.45 (quint, *J* = 7.1 Hz, 1H), 3.92 (td, *J* = 11.1, 3.1 Hz, 1H), 3.99-4.04 (m, 1H), 4.07-4.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.7, 12.5, 28.1, 29.3, 47.0, 61.0, 72.7, 173.9.

Ethylboronate 3' (*syn*) was prepared from reduced product **3** (*syn*) and isolated as a colorless oil. GC t_R 7.40 min ($t_{inj.}$ 280 °C, t_{FID} 280 °C, split method, 83:1, 0.5 mL/min, program 150 °C/8min, 20 °C/min, 280/ 5min). R_f 0.58 (hexanes-EtOAc, 40:60); IR (neat) υ_{max} 1730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.66 (q, *J* = 7.9 Hz, 2H), 0.86 (t, *J* = 7.9 Hz, 3H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.45 (s, 9H), 1.74-1.82 (m, 1H), 1.90 (qd, *J* = 10.8, 3.2 Hz, 1H), 2.40 (quint, *J* = 7.1 Hz, 1H), 3.93 (td, *J* = 11.0, 3.3 Hz, 1H), 3.99-4.07 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.7, 12.9, 28.1, 30.4, 46.8, 61.1, 72.2, 80.6, 173.6.

Scheme 1. Lactone derivatization.



B. Determination of relative configuration for compounds 1-3, 11, and 12.

A rigorous stereochemical assignment was performed for compound **1** and its *syn* counterpart **19** (not presented in the present work), which were then transformed into lactones. For lactone **19'**, X-ray structure was elucidated. The ^1H NMR spectra of lactones derivatized from reduced products **2** and **3** were identical to those reported previously.[2]

Compound 19, yellow oil (83%). R_f 0.12 (hexanes-EtOAc, 6:4); IR (neat) υ_{max} 3450, 1710 cm^{-1}; MS (FAB) 360 (19, MH), 287 (49), 230 (28), 157 (19), 57 (100); ^1H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.38 (s, 9H), 1.61-1.64 (m, 1H), 1.86-1.92 (m, 1H), 2.66 (t, *J* = 5.2 Hz, 1H), 3.57 (s, 1H), 3.78-3.88 (m, 2H), 4.07 (d, *J* = 10.2 Hz, 1H), 7.32 (t, *J* = 8 Hz, 2H), 7.40 (t, *J* = 8 Hz, 1H), 7.63 (d, *J* = 8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.4, 27.8, 33.4, 57.1, 61.7, 73.3, 81.9, 126.4, 128.9, 129.4, 138.2, 172.4; HRMS

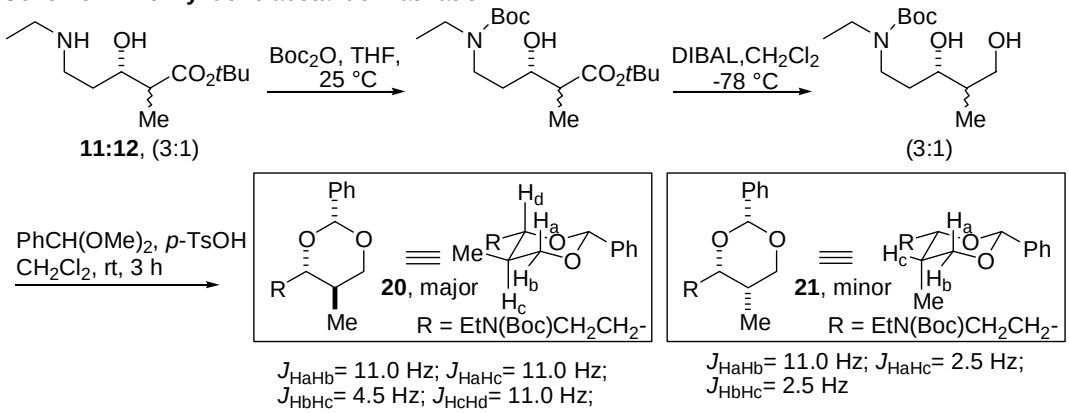
(FAB) calcd for $C_{16}H_{25}O_4{}^{80}Se$: 361.0918, found: 361.0929 (-3.1 ppm); Anal. Calcd for $C_{16}H_{24}O_4Se$: C, 53.48; H, 6.73. Found: C, 53.31; H, 6.65.

Lactone 19'. To a solution of the *syn* phenylseleno ester **19** (120 mg, 0.33 mmol) in CH_2Cl_2 (3.4 mL) at 0 °C was added Bu_2BOTf (440 μL, 0.44 mmol). The reaction mixture was stirred 1 min at the same temperature, and *N*,*N*-diisopropylethylamine (200 μL, 1.15 mmol)) was added. After an additional 2 min, the solvent was removed, and the crude residue was purified by flash chromatography to give the desired product **19'** as a white solid (42 mg, 43%). Mp = 105-106 °C, R_f 0.28 (hexanes-EtOAc, 1:1); IR ($CDCl_3$) υ_{max} 3620, 1715 cm^{-1}; MS (FAB) *m/z* 287 (100, MH^+), 157 (62), 136 (63), 107 (31), 89 (36), 77 (47); ^1H NMR (400 MHz, $CDCl_3$) δ 1.52 (s,3H), 1.95 (qd, *J* = 14.6, 4.8 Hz, 1H), 2.33 (s, 1H), 2.47-2.56 (m, 1H), 4.22-4.30 (m, 1H), 4.35-4.40 (m, 1H), 4.63 (td, *J* = 10.8, 4.4 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 27.9, 49.9, 65.5, 71.5, 126.3, 129.2, 130.0, 138.0, 172.3; HRMS (FAB) calcd for $C_{12}H_{14}O_3{}^{80}Se$: 287.0186, found: 287.0179 (2.6 ppm); Anal. Calcd for $C_{12}H_{14}O_3Se$: C, 50.54; H, 4.95. Found: C, 50.88; H, 4.90.

Lactone 1', prepared from **1** (*anti*), was obtained as a yellow oil: R_f 0.19 (hexanes-EtOAc, 1:1); MS (FAB) *m/z* 287 (44, MH^+), 154 (100), 136 (88), 107 (32), 89 (35), 77 (40); ^1H NMR (400 MHz, $CDCl_3$) δ 1.59 (s,3H), 2.12-2.18 (m, 2H), 2.83 (d, *J* = 6.8, 1H), 3.79 (q, *J* = 6.4 Hz, 1H), 4.23-4.29 (m, 1H), 4.50-4.59 (m, 1H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 6.8 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.3, 29.1, 56.8, 65.4, 71.1, 125.0, 129.2, 130.0, 138.3, 171.9.

The relative stereochemistry of the reduced products **11** and **12** was elucidated from NMR studies of their corresponding benzylidene acetals **20** and **21**. Acetal **20**, which is derivatized from *anti* product **11**, is characterized by two large coupling constants (11Hz) between Ha-Hc and Hc-Hd. The small coupling constants (2.5 Hz) between Ha-Hc and Hb-Hc confirmed the *syn* relative stereochemistry between Me at C-2 and the hydroxyl group at C-3 for acetal **21** and product **12**.

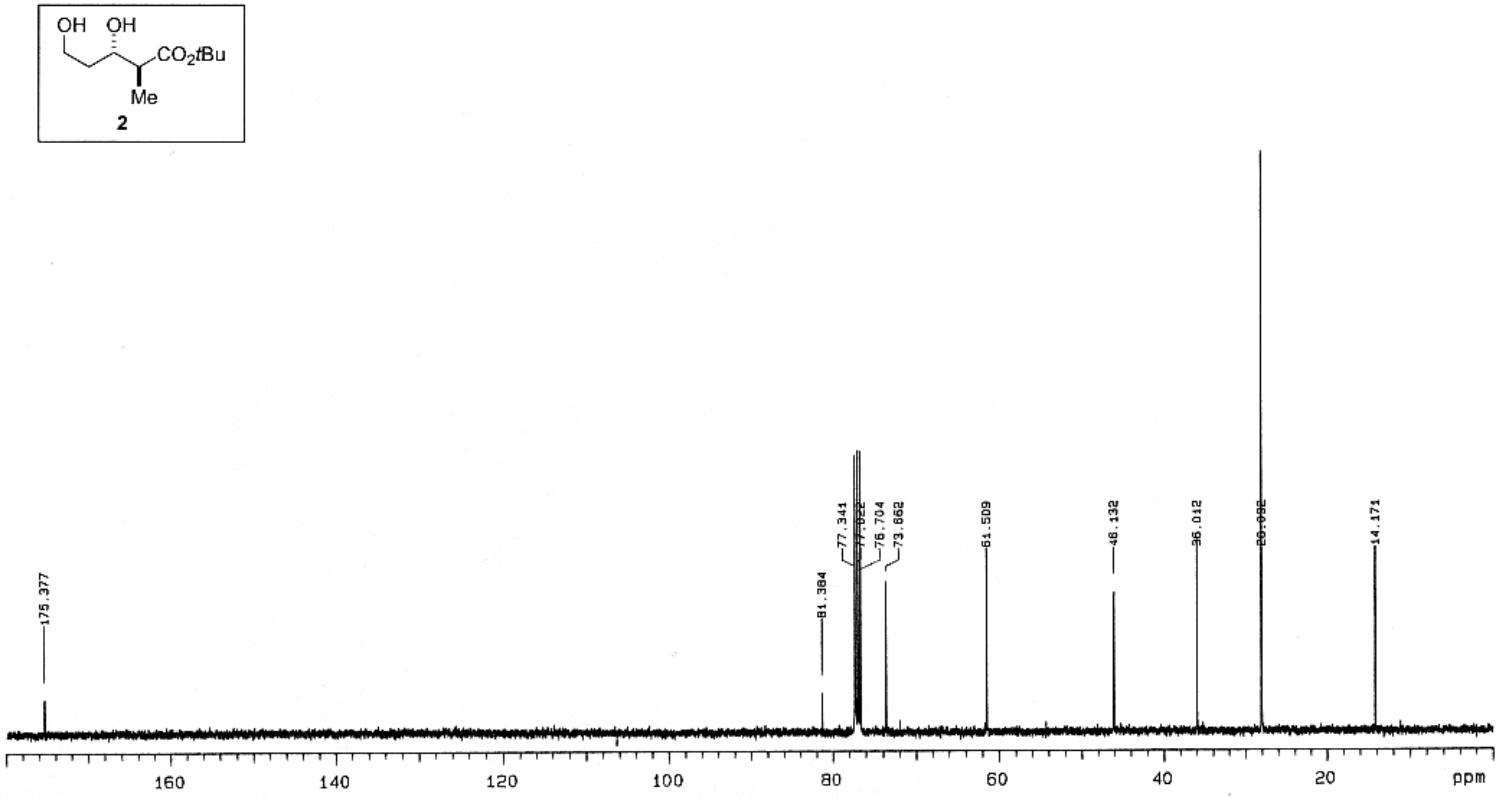
Scheme 2. Benzylidene acetal derivatization.



Benzylidene acetal (20 and 21). To an inseparable (3:1) mixture of reduced products **11** and **12** (33.9 mg, 0.088 mmol) in THF (5 mL) was added di-*tert*-butyl dicarbonate (Boc_2O, 42 mg, 0.19 mmol). The reaction mixture was stirred at room temperature until judged complete by TLC (12 h). After concentration, the two diastereoisomers were separated by flash chromatography to afford *N*-Boc derivatives. ***Major***: White solid, mp 48 ° C; R_f 0.21 (CH_2Cl_2-EtOAc, 10:1); IR (CCl_4) υ_{max} 3430, 2975, 1720, 1695, 1480 cm^{-1}; MS (FAB) *m/z* 488 (12, MH^+), 388 (16), 332(23), 258 (100); ^1H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, *J* = 7.0 Hz, 3H), 1.35 (s,3H), 1.41 (s, 9H), 1.46 (s, 9H), 2.17-2.24 (m, 2H), 3.22-

3.37 (m, 4H), 3.90 (bs, 1H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 6.8 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 18.0, 27.9, 28.5, 30.2, 42.3, 43.5, 54.6, 71.7, 79.3, 81.4, 128.7, 129.1, 138.0, 156.2, 172.9; HRMS (FAB) calcd for $C_{23}H_{38}NO_5{}^{80}Se$: 488.1915, found: 488.1889; Anal. Calcd for $C_{23}H_{37}NO_5Se$: C, 56.78; H, 7.67; N, 2.88. Found: C, 56.62; H, 7.60; N, 2.89. ***Minor***: light yellow oil; R_f 0.33 (CH_2Cl_2-EtOAc, 10:1); IR (CCl_4) υ_{max} 3420, 2970, 1720, 1690, 1475 cm^{-1}; MS (FAB) *m/z* 488 (20, MH^+), 388 (38), 332(76), 176 (100); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, *J* = 7.3 Hz, 3H), 1.37 (s,12H), 1.46 (s, 9H), 1.58-1.63 (m, 2H), 3.46-3.54 (m, 4H), 4.00 (bs, 1H), 7.30 (t, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 6.8 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 17.3, 27.7, 28.4, 30.5, 42.0, 43.6, 56.6, 70.2, 79.3 81.2, 128.7, 129.1, 138.1, 156.2, 171.9; HRMS (FAB) calcd for $C_{23}H_{38}NO_5{}^{80}Se$: 488.1915, found: 488.1898; Anal. Calcd for $C_{23}H_{37}NO_5Se$: C, 56.78; H, 7.67; N, 2.88. Found: C, 56.62; H, 7.60; N, 2.89. To the diastereoisomeric mixture (3:1) of *N*-Boc aminoesters (56.3mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was added DIBAL (0.56 mL of 1M solution, 0.56 equiv) at –78 °C. The reaction mixture was stirred 2 h at this temperature, quenched with MeOH (0.5 mL) and NH_4Cl (2 mL) and then filtered through celite. The two phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (5 x 5 mL). The combined organic layers were washed with brine (10 mL) and dried with Na_2SO_4, filtered, and concentrated under reduced pressure to give 97% (43.2mg) of the diols, which were used for the next step without further purification. To the CH_2Cl_2 solution (2 mL) of crude diols (43.2 mg, 0.165 mmol) were added benzaldehyde dimethyl acetal (28 μL, 0.19 mmol) and a catalytic amount of *p*-toluensulfonic acid. The resulting mixture was stirred 3 h at room temperature before being

diluted with CH_2Cl_2 (20 mL), washed with saturated aq $NaHCO_3$ (5 mL) and brine (5 mL), and dried with Na_2SO_4. After filtration and evaporation of the solvent, the residue was purified by flash chromatography (CH_2Cl_2:AcOEt, 20:1) to give 73% of desired benzylidene acetals **20** and **21**. The two diastereoisomers were separated by a second flash chromatography (hexanes:EtOAc, 5:1). ***Major compound*** **20**: oil; R_f 0.38 (Hexanes:EtOAc, 4:1); MS (FAB) *m/z* 350 (18, MH^+), 292 (35), 250(59), 188 (71), 57 (100); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (d, *J* = 6.7 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H), 1.47 (s, 9H), 1.67-1.72 (m, 1H), 1.88-1.93 (m, 1H), 2.09-2.15 (m, 1H) 3.26-3.34 (m, 5H), 3.36 (t, *J* = 11.1 Hz, 1H), 4.12 (dd, *J* = 11.1 and 4.5 Hz, 1H), 5.18 (s, 1H), 7.37-7.42 (m, 3H), 7.46-7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 13.6, 28.5, 31.8, 33.8, 42.3, 43.3, 73.0, 79.0, 81.1, 100.9, 126.0, 128.2, 128.6, 138.6, 155.5; HRMS (FAB) calcd for $C_{20}H_{32}NO_4$: 350.2331, found: 350.2322; Anal. Calcd for $C_{20}H_{31}NO_4$: C, 68.74; H, 8.94; N, 4.01. Found: C, 68.54; H, 8.90; N, 4.05. ***Minor compound*** **21**: oil; R_f 0.25 (Hexanes:EtOAc, 4:1); MS (FAB) *m/z* 350 (17, MH^+), 291 (27), 248(11), 188 (90), 57 (100); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (d, *J* = 7.0 Hz, 3H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.46 (s, 9H), 1.57-1.62 (m, 1H), 1.67-1.72 (m, 1H), 1.88-1.93 (m, 1H) 3.26-3.34 (m, 4H), 3.88-3.93 (m, 1H), 4.03 (dd, *J* = 11.1 and 1.0 Hz, 1H), 4.10 (dd, *J* = 11.1 and 2.5 Hz, 1H), 5.49 (s, 1H), 7.37-7.42 (m, 3H), 7.46-7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.3, 12.4, 28.5, 32.0, 43.3, 73.8, 79.2, 101.7, 126.0, 128.2, 128.7, 153.9; HRMS (FAB) calcd for $C_{20}H_{32}NO_4$: 350.2331, found: 350.2326; Anal. Calcd for $C_{20}H_{31}NO_4$: C, 68.74; H, 8.94; N, 4.01. Found: C, 68.54; H, 8.90; N, 4.05.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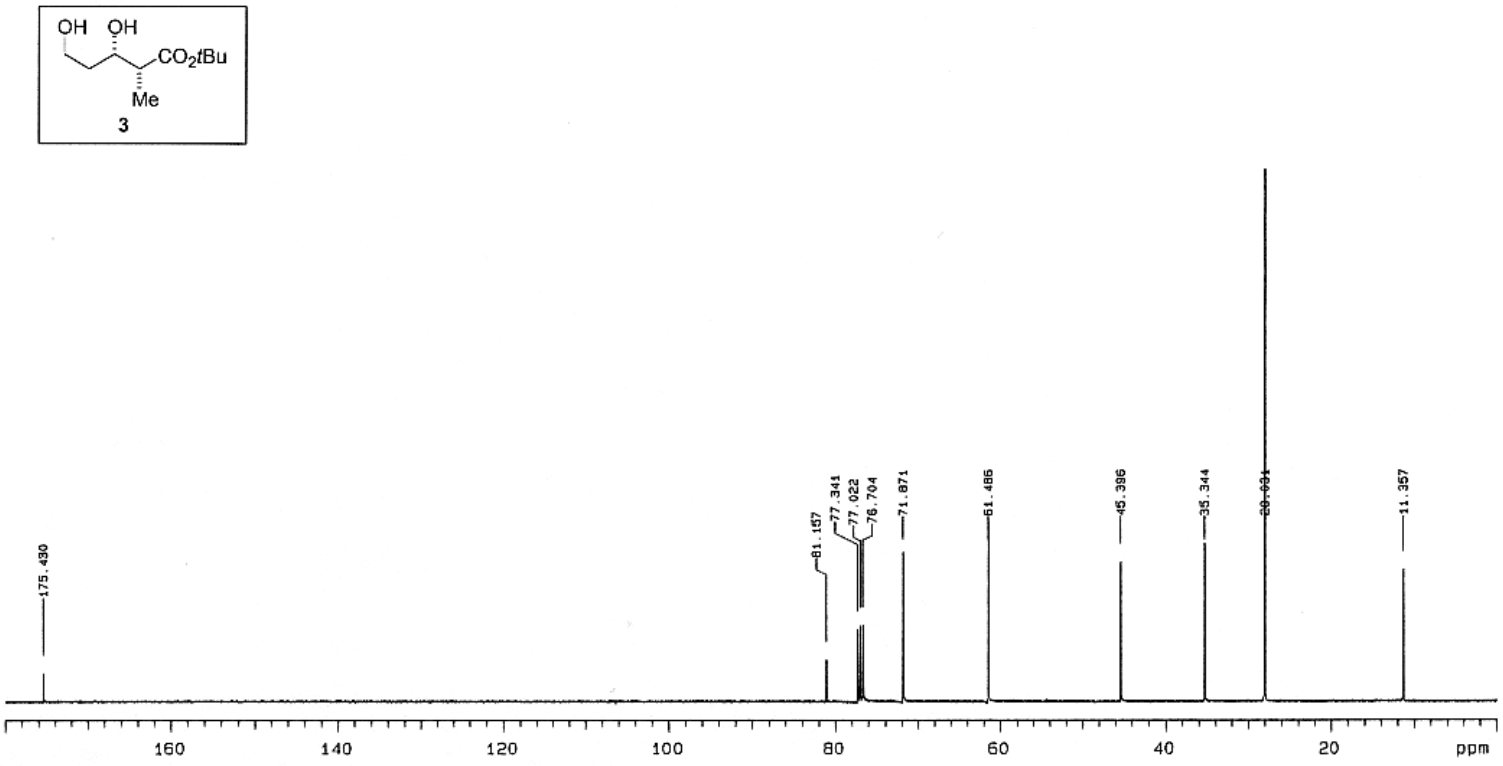
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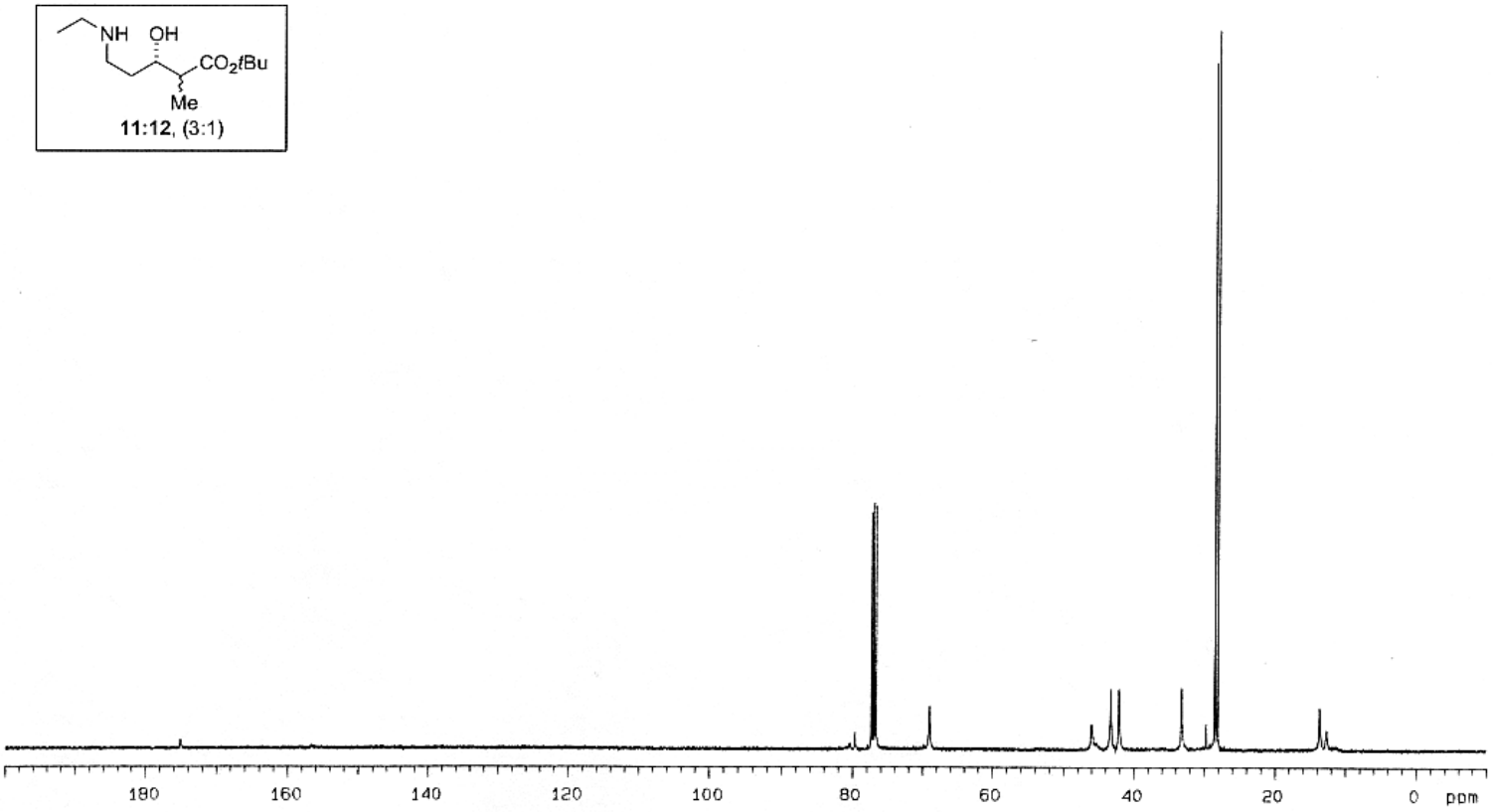
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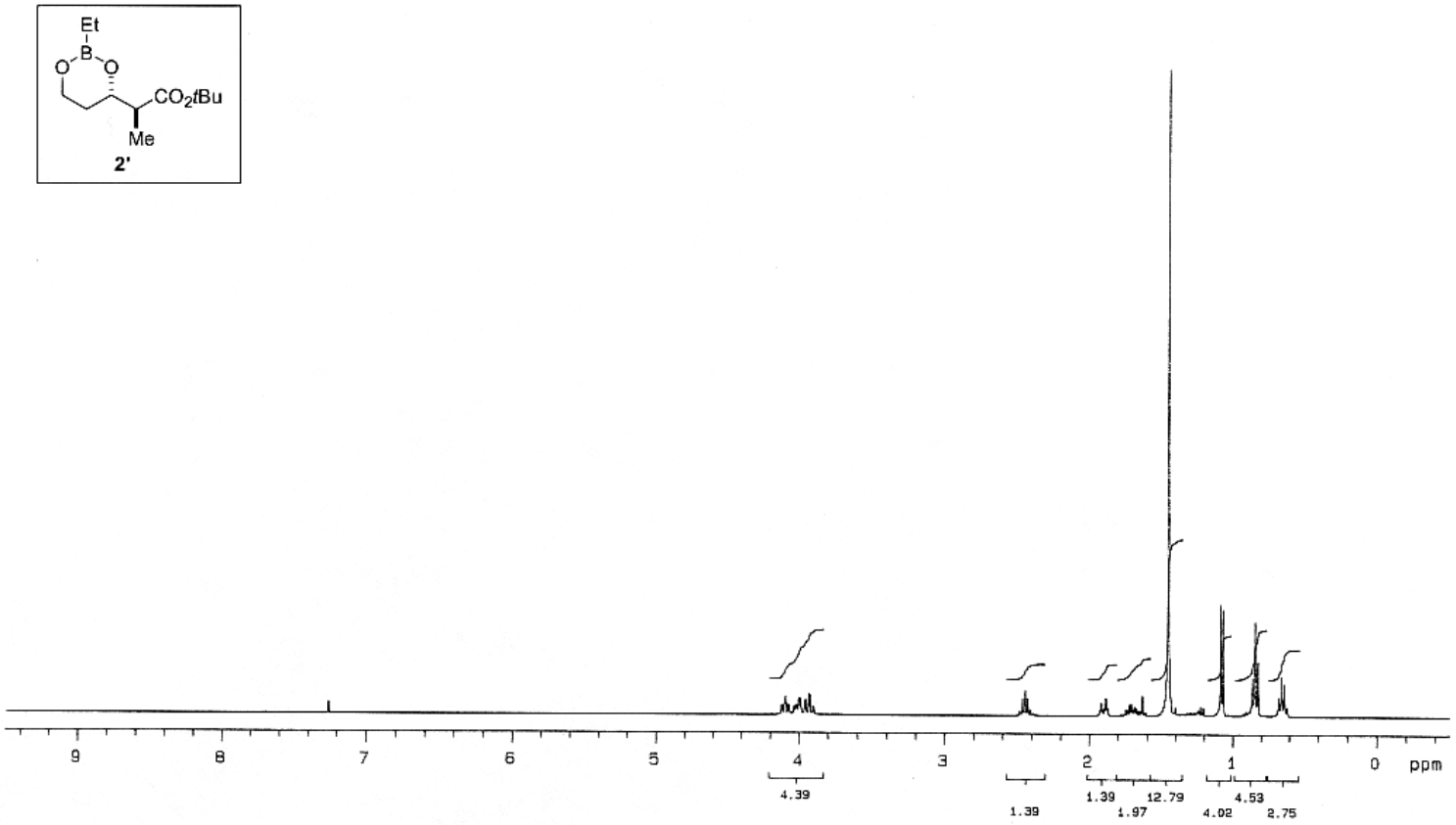
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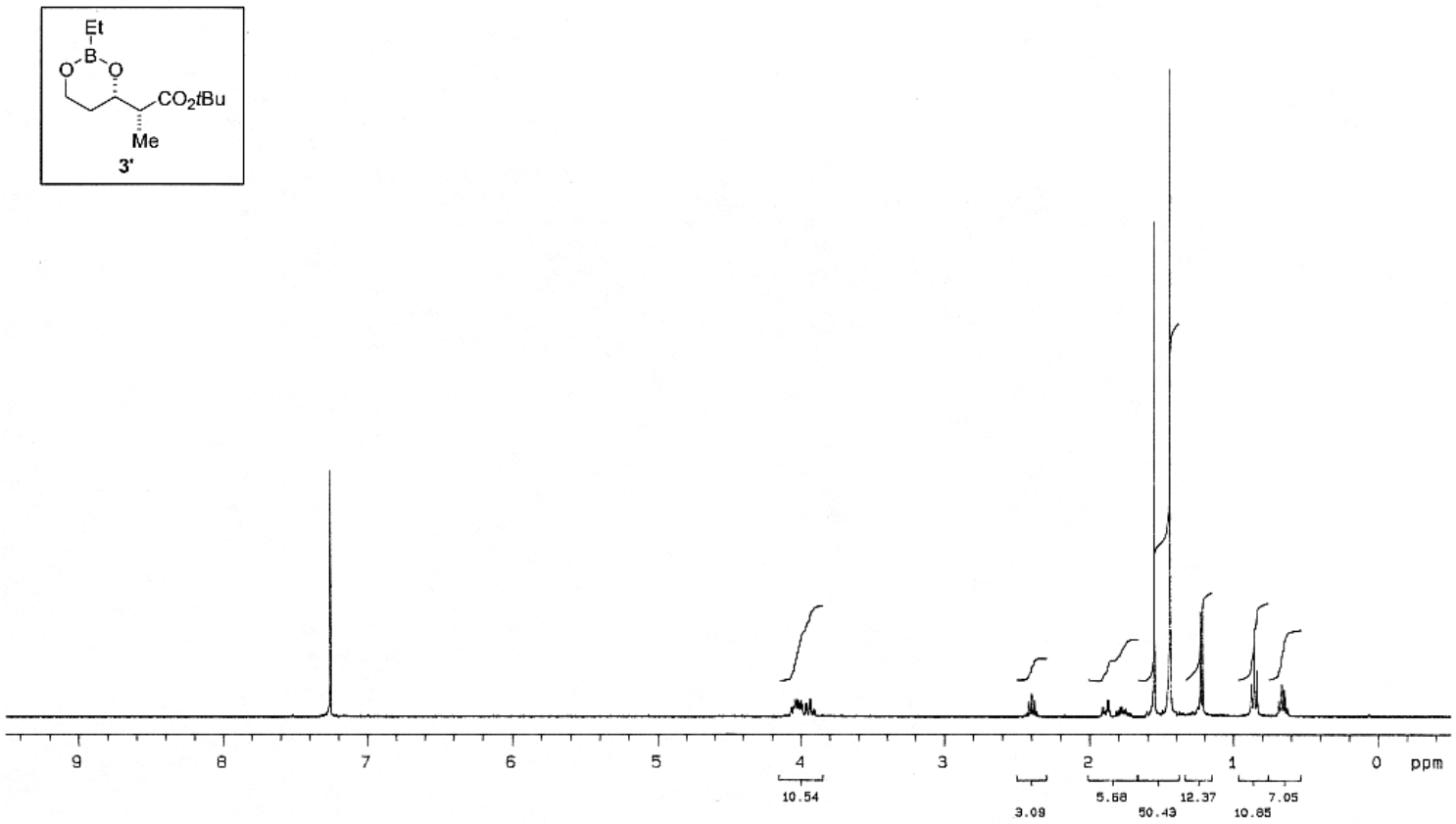
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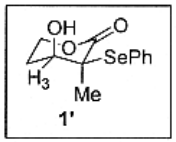
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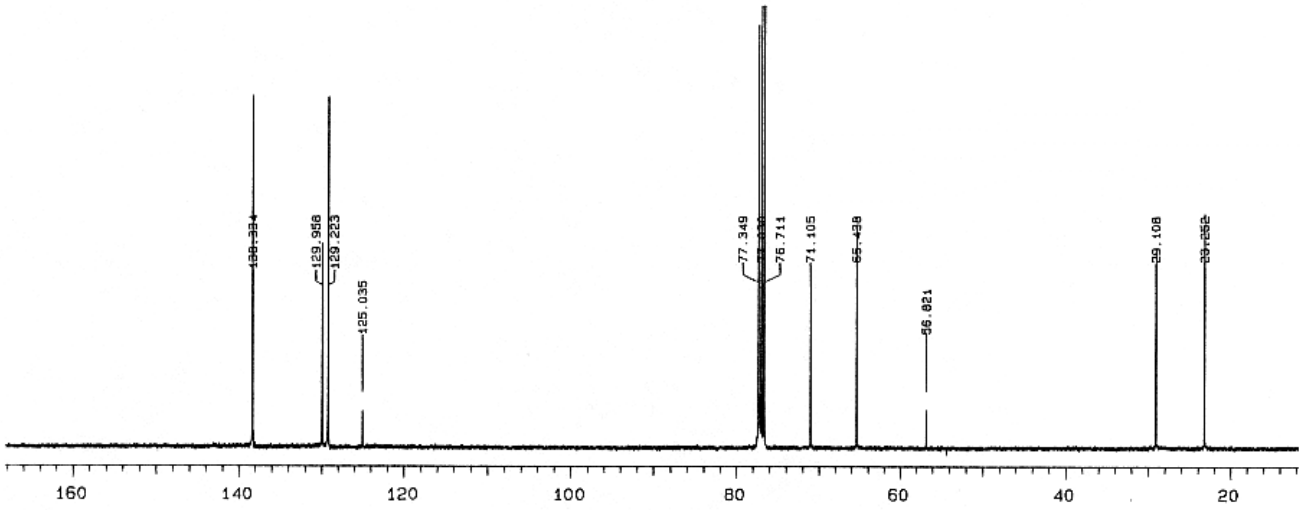
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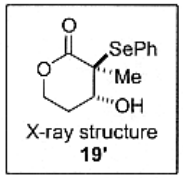

X-ray structure
19'