Stereoselective Synthesis of Benzannulated Spiroketals: Influence of the Aromatic Ring on Reactivity and Conformation

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I. MATERIALS AND METHODS

Reagents were obtained from Aldrich Chemical (www.sigma-aldrich.com), Strem (www.strem.com), or Acros Organics (www.fishersci.com) and used without further purification unless otherwise indicated. Solvents (Optima grade) were obtained from Fisher Scientific (www.fishersci.com), degassed with Ar, and purified on a solvent drying system as described[1] unless otherwise indicated. Reactions were performed in flame-dried glassware under positive Ar pressure with magnetic stirring. Cold baths were generated as follows: 0 °C, wet ice/water; –44 °C, dry ice/CH_3CN; –63 °C, dry ice/chloroform; –78 °C, dry ice/acetone.

TLC was performed on 0.25 mm E. Merck silica gel 60 F254 plates and visualized under UV light (254 nm) or by staining with potassium permanganate ($KMnO_4$), cerium ammonium molybdenate (CAM). Silica flash chromatography was performed on E. Merck 230–400 mesh silica gel 60. Parallel chromatography was performed on an ISCO CombiFlash OptiX 10 instrument with RediSep silica gel normal phase columns using a flow rate of 10.0 mL/min and a gradient of 5–10% MeOH in CH_2Cl_2 in hexanes over 20 min.

Optical rotations were recorded on a JASCO model PTC-103T digital polarimeter. IR spectra were recorded on a Bruker Optics Tensor 27 FTIR spectrometer with peaks reported in cm^{-1}. NMR spectra were recorded on Bruker UltraShield Plus 500 MHz instruments at 24 °C in $CDCl_3$ unless otherwise indicated. Chemical shifts are expressed in ppm relative to TMS (^1H, 0 ppm) or solvent signals: $CDCl_3$ (^1H, 7.26 ppm; ^{13}C, 77.0 ppm), C_6D_6 (^1H, 7.16 ppm; ^{13}C, 128.0 ppm), CD_2Cl_2 (^1H, 5.31 ppm; ^{13}C, 53.5 ppm), CD_3OD (^1H, 3.31 ppm; ^{13}C, 63.1 ppm) or acetone-d_6 (^1H, 2.05 ppm; ^{13}C, 206.2 ppm); coupling constants are expressed in Hz. Mass spectra were obtained at the MSKCC Analytical Core Facility on a Waters Acquity TM mass spectrometer by electrospray (ESI) ionization or atmospheric pressure chemical ionization (AP-CI).

N.B.: Atom numbering in IUPAC compound names herein does not correspond to conventional carbohydrate nomenclature and is used for naming purposes only. Atom numbering in the text and paper corresponds to conventional carbohydrate nomenclature. Compounds not cited in the paper are numbered herein **S1–S4**.

II. SYNTHESIS OF SIDECHAIN PRECURSORS (S1a–i, S2)

A. GENERAL PROCEDURE FOR ACETYLATION OF ALCOHOLS AND PHENOLS (S1a–d,f,h,i, S2)

The commercially available alcohol or phenol was dissolved in CH_2Cl_2 (0.1 M) and the solution was cooled to 0 °C. Triethylamine (2.0 equiv) and 4-dimethylaminopyridine (0.1 equiv) were added, followed by addition of acetyl chloride (1.5 equiv). After 30 min, the reaction mixture was warmed up to rt and stirred for 2 h. The mixture was quenched with satd aq $NaHCO_3$ and the aqueous layer was separated and extracted with Et_2O. The combined extracts were washed (H_2O, brine), dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography provided **S1a–d,f,h,i** and **S2**.

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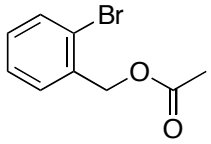
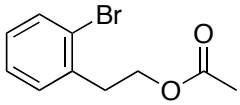
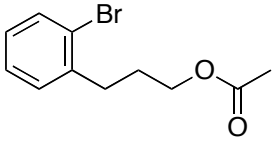
[1] Pangborn, A. B.; Giardello, M. A.; Grubbrs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996,** *15*, 1518–1520.



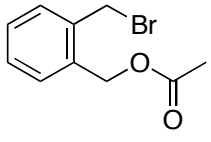
2-Bromobenzyl acetate (S1a).[2] Clear oil (1.50 g, 63%). **TLC**: R_f 0.29 (9:1 hexanes/EtOAc). **IR** (NaCl, film): 3021, 2959, 2898, 1744 (C=O st), 1593, 1570, 1472, 1440, 1379, 1229, 1029 (C–Br st), 753. **^{1}H-NMR** (500 MHz): δ 7.55 (dd, 1H, *J* = 8.0, 1.2), 7.40–7.38 (m, 1H), 7.30 (td, 1H, *J* = 7.6, 1.1), 7.18–7.14 (m, 1H), 5.18 (s, 2H), 2.12 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.5, 135.2, 132.8, 129.8, 129.7, 127.5, 123.4, 65.7, 20.8. **ESI-MS** *m/z* (rel int): (pos) 250.9 ([M+Na]$^+$, 100).



2-Bromophenethyl acetate (S1b).[3] Clear oil (1.15 g, 96%). **TLC**: R_f 0.55 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 3060, 2958, 2899, 1740 (C=O st), 1568, 1472, 1439, 1384, 1364, 1238, 1037 (C–Br st), 752. **^{1}H-NMR** (500 MHz): δ 7.54 (d, 1H, *J* = 7.8), 7.24 (dd, 2H, *J* = 5.0, 0.9), 7.09 (dt, 1H, *J* = 8.1, 4.5), 4.30 (t, 2H, *J* = 7.0), 3.08 (t, 2H, *J* = 7.0), 2.03 (s, 3H). **^{13}C-NMR** (125 MHz): δ 171.0, 137.2, 133.0, 131.1, 128.4, 127.5, 124.7, 63.4, 35.3, 21.0. **ESI-MS** *m/z* (rel int): (pos) 265.0 ([M+Na]$^+$, 100).



3-(2-Bromophenyl)propyl acetate (S1c).[4] Clear oil (2.4 g, 91%). **TLC**: R_f 0.28 (10:1 hexanes/EtOAc). **IR** (NaCl, film): 3013, 2897, 2868, 1739 (C=O st), 1541, 1470, 1440, 1387, 1367, 1240, 1039 (C–Br st), 1023, 752. **^{1}H-NMR** (500 MHz): δ 7.52 (d, 1H, *J* = 8.0), 7.22 (m, 2H), 7.07–7.04 (m, 1H), 4.11 (t, 2H, *J* = 6.4), 2.81 (t, 2H, *J* = 7.7), 2.06 (d, 3H, *J* = 0.7), 1.99–1.93 (m, 2H). **^{13}C-NMR** (125 MHz): δ 171.2, 140.6, 133.0, 130.4, 127.9, 127.6, 124.5, 63.8, 32.6, 28.7, 21.1. **ESI-MS** *m/z* (rel int): (pos) 278.9 ([M+Na]$^+$, 100); (neg) 254.9 ([M-H]$^-$, 100).



2-(Bromomethyl)benzyl acetate (S1d).[5] Clear oil (250 mg, 50%). **TLC**: R_f 0.14 (15:1 hexanes/EtOAc). **IR** (NaCl, film): 3068, 3029, 2971, 2902, 1740 (C=O st), 1494, 1453, 1380, 1362, 1229, 1027 (C–Br st), 894, 769, 731. **^{1}H-NMR** (500 MHz): δ 7.43–7.39 (m, 2H), 7.36–

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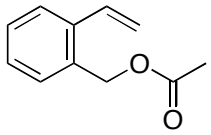
[2] Shirini, F.; Zolfigol, M. A.; Mohammadi, K. *Phosphorus, Sulfur and Silicon and the Related Elements* **2003**, *15*, 1617-1621.

[3] Sontag, D. *Ann. Chim.* **1934**, *1*, 359–438.

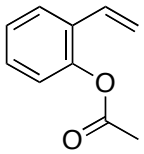
[4] Beak, P.; Selling, G. W. *J. Org. Chem.* **1989**, *54*, 5574–5580.

[5] Sato, H.; Isono, N.; Okamura, K.; Date, T.; Mori, M *Tetrahedron Lett.* **1994**, *35*, 2035–2038.

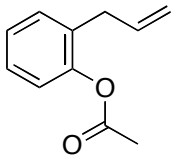
7.34 (m, 2H), 5.27 (s, 2H), 4.69 (s, 2H), 2.11 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.8, 136.2, 134.6, 130.5, 130.3, 129.15, 129.11, 63.6, 43.6, 21.1. **ESI-MS** *m/z* (rel int): (pos) 264.9 ([M+Na]$^+$, 100).



2-(Vinyl)phenyl acetate (S1f).[6] Clear oil (1.22 g, 76%). **TLC**: R_f 0.23 (15:1 hexanes/EtOAc). **IR** (NaCl, film): 3066, 3028, 2960, 2932, 2854, 1740 (C=O st), 1628 (Ar C=C st), 1485, 1454, 1420, 1380, 1362, 1228, 1024, 992, 773. **^{1}H-NMR** (500 MHz): δ 7.56–7.54 (m, 1H), 7.37–7.32 (m, 2H), 7.28 (td, 1H, *J* = 7.4, 1.4), 6.98 (dd, 1H, *J* = 17.4, 11.0), 5.70 (dd, 1H, *J* = 17.4, 1.3), 5.37 (dd, 1H, *J* = 11.0, 1.3), 5.19 (s, 2H), 2.10 (s, 3H). **^{13}C-NMR** (125 MHz): δ 170.9, 137.5, 133.7, 132.8, 129.9, 128.9, 127.9, 126.1, 116.9, 64.4, 21.1. **ESI-MS** *m/z* (rel int): (pos) 198.9 ([M+Na]$^+$, 100).



2-(Vinyl)benzyl acetate (S1h).[7] Clear oil (400 mg, 41%). **TLC**: R_f 0.56 (4:1 hexanes/EtOAc). **IR** (NaCl, film): 3068, 3024, 2936, 1763 (C=O st), 1630 (Ar C=C st), 1484, 1451, 1424, 1370, 1206, 1097, 1010, 914, 827, 765. **^{1}H-NMR** (500 MHz): δ 7.59 (dd, 1H, *J* = 7.7, 1.7), 7.30 (td, 1H, *J* = 7.7, 1.7), 7.23 (tdd, 1H, *J* = 7.5, 1.3, 0.5), 7.06 (dd, 1H, *J* = 8.0, 1.3), 6.77 (dd, 1H, *J* = 17.6, 11.1), 5.78 (dd, 1H, *J* = 17.6, 1.1), 5.35 (dd, 1H, *J* = 11.1, 1.1), 2.34 (s, 3H). **^{13}C-NMR** (125 MHz): δ 169.3, 148.1, 130.4, 130.3, 128.8, 126.6, 126.3, 122.7, 116.5, 21.0. **ESI-MS** *m/z* (rel int): (pos) 163.0 ([M+H]$^+$, 100); (neg) 160.9 ([M-H]$^-$, 100).



2-Allylphenyl acetate (S1i).[8] Clear oil (2.20 g, 84%). **TLC**: R_f 0.30 (15:1 hexanes/EtOAc). **IR** (NaCl, film): 3078, 3033, 3009, 2979, 2913, 2845, 1762 (C=O st), 1640 (Ar C=C st), 1489, 1452, 1433, 1370, 1207, 1171, 1009, 916, 752. **^{1}H-NMR** (500 MHz): δ 7.29–7.26 (m, 2H), 7.21 (td, 1H, *J* = 7.4, 1.7), 7.08–7.06 (m, 1H), 5.97–5.89 (m, 1H), 5.12–5.08 (m, 2H), 3.34 (d, 2H, *J* = 6.6), 2.33 (s, 3H). **^{13}C-NMR** (125 MHz): δ 169.4, 149.0, 136.0, 132.0, 130.5, 127.5, 126.2, 122.5, 116.3, 34.8, 21.0. **ESI-MS** *m/z* (rel int): (pos) 198.9 ([M+Na]$^+$, 100).

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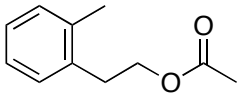
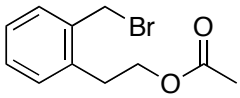
[6] Begasse, B.; Hercouet, A.; Le Corre, M. *Tetrahedron Lett*. **1979**, *23*, 2149–2150.
[7] Yamaguchi, M.; Hayashi, A.; Hirama, M. *J. Am. Chem. Soc*. **1995**, *117*, 1151–1152.
[8] Phukan, P. *Tetrahedron Lett*. **2004**, *45*, 4785–4787.

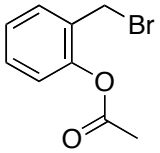


2-Methylphenethyl acetate (S2).[9] Clear oil (424 mg, 65%). **TLC**: R_f 0.24 (15:1 hexanes/EtOAc). **IR** (NaCl, film): 3064, 3023, 2957, 1742 (C=O st), 1492, 1461, 1382, 1366, 1236, 1034, 760, 726. **^{1}H-NMR** (500 MHz): δ 7.19 (m, 4H), 4.29 (t, 2H, *J* = 7.4), 2.98 (t, 2H, *J* = 7.4), 2.38 (s, 3H), 2.07 (s, 3H). **^{13}C-NMR** (125 MHz): δ 171.0, 136.5, 135.9, 130.4, 129.5, 126.8, 126.1, 64.1, 32.4, 21.0, 19.4. **ESI-MS** *m/z* (rel int): (pos) 200.8 ([M+Na]$^+$, 100); (neg) 212.9 ([M+Cl]$^-$, 100).

B. Synthesis of benzyl bromide sidechain precursors (S1e,g)



2-(Bromomethyl)phenethyl acetate (S1e).[10] To a solution of *o*-tolyl acetate (424 Mg, 2.4 mmol) in benzene (12 mL) was added *N*-bromosuccinimide (424 g, 2.4 mmol) and AIBN (195 mg, 1.2 mmol). The reaction mixture was heated to reflux for 6 h, then cooled to rt and diluted with CH_2Cl_2 (12 mL). The organic fraction was washed with satd aq Na_2CO_3 (12 mL), H_2O (12 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography provided **S1e** as a clear oil (200 mg, 33%). **TLC**: R_f 0.29 (1:1 hexanes/CH_2Cl_2). **IR** (NaCl, film): 3063, 3023, 2959, 2897, 1731 (C=O st), 1492, 1455, 1385, 1364, 1238, 1037 (C–Br st), 762. **^{1}H-NMR** (500 MHz): δ 7.36 (dd, 1H, *J* = 7.8, 1.5), 7.30–7.27 (m, 1H), 7.25–7.21 (m, 2H), 4.59 (s, 2H), 4.33 (t, 2H, *J* = 7.3), 3.09 (t, 2H, *J* = 7.3), 2.06 (s, 3H). **^{13}C-NMR** (125 MHz): δ 171.0, 136.8, 136.2, 130.8, 130.4, 129.2, 127.4, 64.3 (2C), 31.5, 21.1. **ESI-MS** *m/z* (rel int): (pos) 280.9 ([M+Na]$^+$, 100).



2-(Bromomethyl)phenyl acetate (S1g).[11] Prepared from *o*-tolyl acetate as described for **S1e** above. Clear oil (1.32 g, 87%). **TLC**: R_f 0.25 (20:1 hexanes/EtOAc). **IR** (NaCl, film): 3064, 3037, 2980, 2937, 1767 (C=O st), 1585, 1490, 1453, 1434, 1369, 1209, 1177, 1040 (C–Br st), 916, 789, 757. **^{1}H-NMR** (500 MHz): δ 7.42 (dd, 1H, *J* = 7.6, 1.7), 7.35 (td, 1H, *J* = 7.8, 1.7), 7.22 (td, 1H, *J* = 7.5, 1.2), 7.14 (dd, 1H, *J* = 8.1, 1.2), 4.43 (s, 2H), 2.37 (s, 3H). **^{13}C-NMR** (125 MHz): δ 168.9, 149.1, 130.9, 129.9, 129.6, 126.4, 123.2, 27.7, 21.0. **ESI-MS** *m/z* (rel int): (pos) 250.9 ([M+Na]$^+$, 100); (neg) 226.9 ([M–H]$^-$, 100).

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[9] Yus, M.; Gomis, J. *Tetrahedron* **2003**, *59*, 4967–4971.
[10] Payne, J. R; Toscano, M. D.; Bulloch, E. M.; Abell, A. D.; Abell, C. *Org. Biomol. Chem.* **2005**, *3*, 2271–2281.
[11] Hercouet, A.; Le Corre, M. *Tetrahedron* **1981**, *37*, 2867–2873.

III. ATTACHMENT OF *C*1 SIDECHAINS VIA CROSS COUPLING REACTIONS (2a–r)

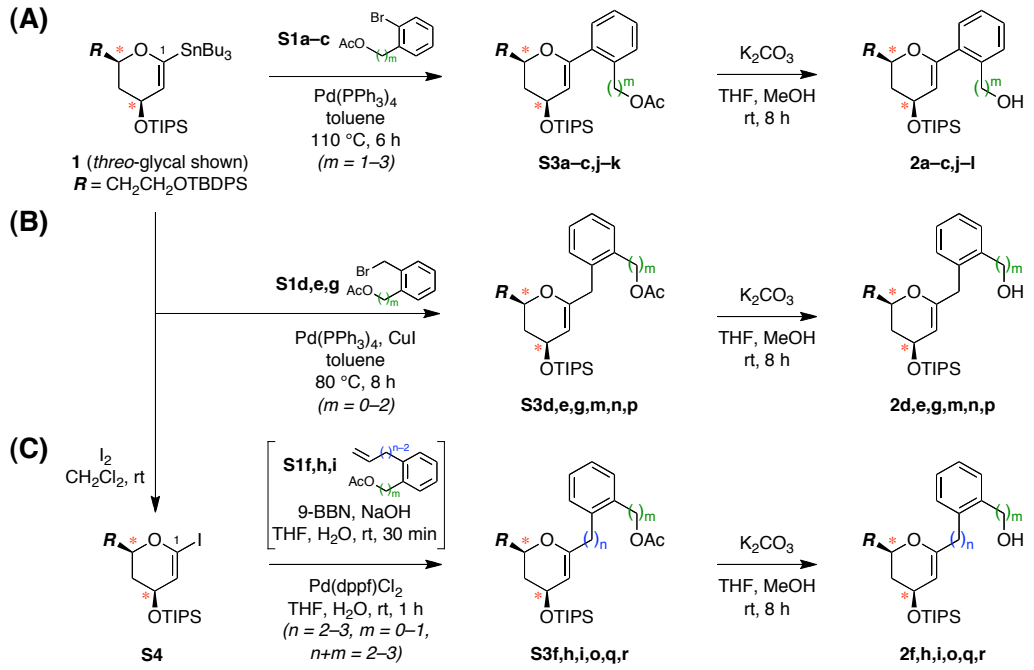

Figure S1. Synthesis of spirocyclization substrates **2a–r** from *threo* and *erythro*-glycal stannanes **1** by **(A)** Stille cross coupling of aryl bromides, (**B**) Stille cross coupling of benzyl bromides in the presence of CuI, or (**C**) iodination followed by *B*-alkyl Suzuki–Miyaura cross coupling of styrenes and allyl benzenes.

A. GENERAL PROCEDURE FOR STILLE COUPLING OF ARYL BROMIDES (n = 0) (2a–c,j–l)[12]

To a stirred solution of the glycal stannane **1** (1.0 equiv), prepared enantioselectively as previously described,[13] in anhyd toluene (0.1 M) under Ar was added the appropriate aryl bromide sidechain **S1a–c** (1.2 equiv) and $Pd(PPh_3)_4$ (0.2 equiv). The yellow solution was shielded from light with aluminum foil[14] and heated to reflux 6 h, then cooled to rt and concentrated to dryness. Purification by silica flash chromatography yielded the partially purified *O*-acetyl *C*1-aryl glycals **S3a–c,j–l**. These glycals were then dissolved in 1:1 THF/MeOH (0.1 M) and K_2CO_3 (2.0 equiv) was added.[13] After stirring for 12 h, the mixture was diluted with Et_2O, washed with satd aq $NaHCO_3$, dried (Na_2SO_4), and concentrated by rotary evaporation. Purification by silica flash chromatography (20:1–10:1 hexanes/EtOAc with 1% Et_3N) afforded the free alcohols **2a–c, j–l**.

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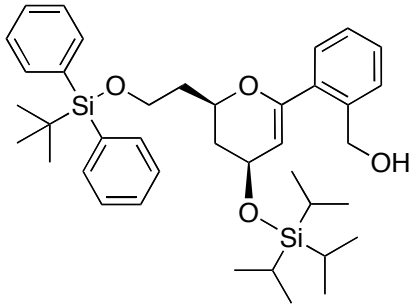
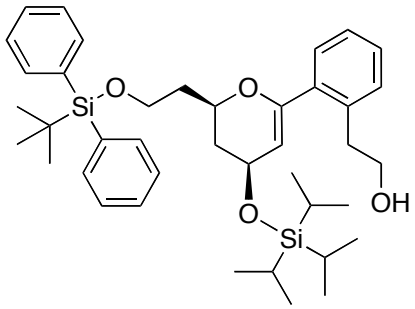
[12] Friesen, R. W.; Sturino, C. F. *J. Org. Chem.* **1990**, *55*, 2572–2574.

[13] (a) Potuzak, J. S.; Moilanen, S. B.; Tan, D. S. *J. Am. Chem. Soc.* **2005**, *127*, 13796–13797. (b) Moilanen, S. B.; Tan, D. S. *Org. Biomol. Chem.* **2005**, *3*, 798–803.

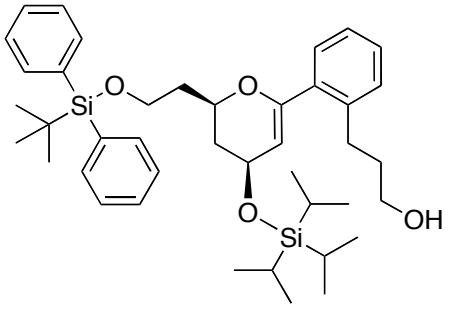
[14] Crawforth, C. M.; Burling, S.; Fairlamb, I. J. S.; Kapdi, A.; Taylor, R. J. K.; Whitwood, A. C. *Tetrahedron* **2005,** *61*, 9736–9751.



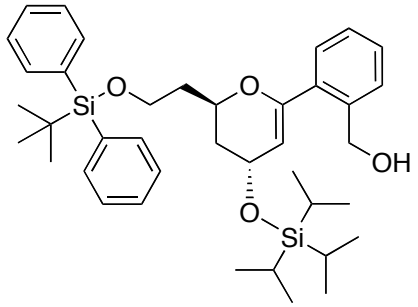
(–)-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)methanol (2a). Clear oil (50 mg, 65%). **TLC**: R_f 0.26 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –18.5° (*c* 2.3, $CHCl_3$). **IR** (NaCl, film): 3456 (O–H st), 3065, 2944, 2864, 1655, 1465, 1429, 1368, 1337, 1295, 1264, 1099 (C–O st), 884, 745, 700. **^{1}H-NMR** (500 MHz, C_6D_6): δ 7.86–7.84 (m, 4H), 7.55 (dd, 1H, *J* = 7.6, 1.3), 7.51 (dd, 1H, *J* = 7.6, 0.7), 7.33–7.29 (m, 6H), 7.22 (td, 1H, *J* = 7.5, 1.4), 7.13 (td, 1H, *J* = 7.5, 1.3), 5.28 (dd, 1H, *J* = 2.1, 1.5), 4.82–4.78 (m, 3H), 4.47 (dddd, 1H, *J* = 11.2, 7.6, 5.1, 2.2), 3.93 (ddd, 1H, *J* = 10.5, 7.7, 5.1), 3.84 (dt, 1H, *J* = 10.7, 5.5), 2.22 (ddt, 1H, *J* = 13.1, 6.6, 1.7), 2.05–1.96 (m, 3H), 1.87–1.81 (m, 1H), 1.26–1.22 (m, 30H). **^{13}C-NMR** (125 MHz, C_6D_6): δ 154.5, 140.4, 136.0, 134.1, 134.0, 130.0, 129.2, 129.1, 128.9, 128.4, 127.6, 106.5, 73.1, 64.8, 63.9, 60.6, 38.3, 38.2, 27.2, 19.5, 18.4, 12.7. **ESI-MS** *m/z* (rel int): (pos) 667.1 ($[M+Na]^+$, 100).



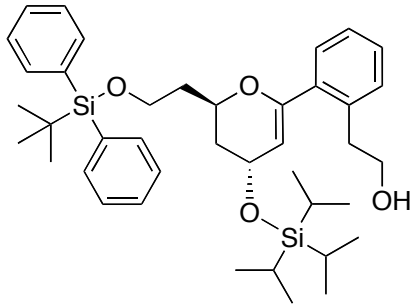
(–)-2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)ethanol (2b). Clear oil (51 mg, 78%). **TLC**: R_f 0.40 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –14.0° (*c* 2.6, $CHCl_3$). **IR** (NaCl, film): 3430 (O–H st), 3064, 3022, 2948, 2764, 1780, 1515, 1466, 1430, 1385, 1364, 1102, 1065 (C–O st), 885, 751, 700. **^{1}H-NMR** (500 MHz): δ 7.69–7.66 (m, 4H), 7.45–7.32 (m, 7H), 7.30 (dd, 1H, *J* = 7.5, 1.5), 7.24–7.20 (m, 2H), 4.91 (t, 1H, *J* = 1.8), 4.71 (ddd, 1H, *J* = 8.8, 6.6, 2.2), 4.40 (dddd, 1H, *J* = 11.1, 7.5, 5.2, 2.0), 3.88 (ddd, 1H, *J* = 10.5, 7.6, 5.2), 3.84–3.79 (m, 3H), 3.01 (dt, 1H, *J* = 13.4, 6.7), 2.89 (dt, 1H, *J* = 13.5, 6.7), 2.18 (ddt, 1H, *J* = 13.2, 6.6, 1.7), 2.05–1.99 (m, 1H), 1.90–1.80 (m, 2H), 1.72 (t, 1H, *J* = 5.7), 1.12–1.07 (m, 30H). **^{13}C-NMR** (125 MHz): δ 154.1, 136.8, 135.7, 133.9, 133.7, 130.2, 129.9, 129.8, 128.8, 127.8, 126.5, 106.5, 72.8, 64.4, 63.7, 60.3, 37.9, 37.8, 37.0, 27.0, 19.3, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 681.1 ($[M+Na]^+$, 100); (neg) 703.1 ($[M+HCOO]^-$, 100).



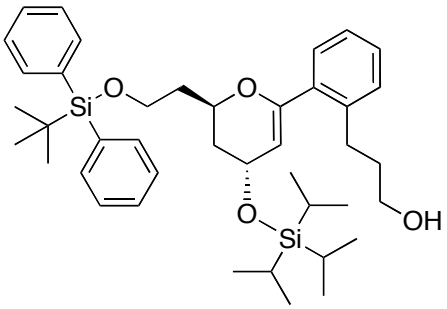
(–)-3-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)propan-1-ol (2c). Clear oil (24 mg, 82%). **TLC**: R_f 0.34 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –20.4° (*c* 1.2, $CHCl_3$). **IR** (NaCl, film): 3444 (O–H st), 3065, 3018, 2942, 2865, 1596, 1464, 1430, 1377, 1290, 1099, 1068 (C–O st), 884, 748, 700. **^{1}H-NMR** (500 MHz): δ 7.67–7.63 (m, 4H), 7.43–7.34 (m, 4H), 7.33–7.30 (m, 2H), 7.29–7.26 (m, 2H), 7.21–7.15 (m, 2H), 4.84 (t, 1H, *J* = 1.8), 4.70 (ddd, 1H, *J* = 8.8, 6.7, 2.2), 4.37 (dddd, 1H, *J* = 11.2, 7.5, 5.3, 2.0), 3.86 (ddd, 1H, *J* = 10.4, 7.6, 5.3), 3.79 (dt, 1H, *J* = 10.7, 5.5), 3.56 (t, 2H, *J* = 6.1), 2.79 (t, 2H, *J* = 7.6), 2.18 (ddt, 1H, *J* = 13.2, 6.7, 1.7), 2.02 (ddt, 1H, *J* = 13.8, 7.9, 5.7), 1.91–1.80 (m, 4H), 1.09–1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ 154.4, 140.7, 136.5, 135.7, 133.9, 133.8, 129.7, 129.6, 128.7, 127.8, 125.9, 105.9, 72.7, 64.6, 62.1, 60.4, 38.0, 37.9, 34.5, 29.4, 27.0, 19.4, 18.2, 12.4. **ESI-MS** *m*/*z* (rel int): (pos) 695.1 ([M+Na]$^+$, 100).



(+)-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)methanol (2j). Clear oil (120 mg, 55%). **TLC**: R_f 0.28 (10:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +79.8° (*c* 0.7, $CHCl_3$). **IR** (NaCl, film): 3445 (O–H st), 3064, 3024, 2936, 2863, 1650, 1463, 1428, 1383, 1357, 1339, 1296, 1099 (C–O st), 1006, 882, 739, 700. **^{1}H-NMR** (500 MHz): δ 7.67–7.64 (m, 4H), 7.44–7.33 (m, 7H), 7.32–7.28 (m, 3H), 5.16 (dd, 1H, *J* = 5.3, 1.4), 4.60 (d, 2H, *J* = 11.7), 4.58–4.53 (m, 1H), 4.42 (ddd, 1H, *J* = 5.3, 3.6, 1.8), 3.89 (ddd, 1H, *J* = 10.5, 8.2, 5.1), 3.81 (dt, 1H, *J* = 10.6, 5.3), 2.38 (t, 1H, *J* = 6.6), 1.97–1.84 (m, 3H), 1.73 (ddd, 1H, *J* = 13.7, 12.1, 3.7), 1.09–1.04 (m, 30H). **^{13}C-NMR** (125 MHz): δ 155.3, 139.5, 135.7, 133.9, 133.8, 129.8, 129.7, 129.2, 129.1, 127.8, 127.7, 104.2, 69.8, 64.1, 61.4, 60.2, 38.3, 38.0, 27.0, 18.33, 18.31, 12.6. **ESI-MS** *m*/*z* (rel int): (pos) 667.2 ([M+Na]$^+$, 100); (neg) 679.2 ([M+Cl]$^-$, 100).



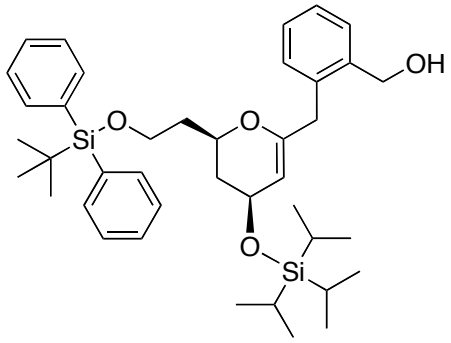
(+)-2-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)ethanol (2k). Clear oil (134 mg, 51%). **TLC**: R_f 0.42 (4:1 hexanes/EtOAc). $[\alpha]_D^{21}$: +82.38° (*c* 2.5, $CHCl_3$). **IR** (NaCl, film): 3427 (O–H st), 3064, 2945, 2865, 1560, 1428, 1382, 1342, 1294, 1096 (C–O st), 1006, 741, 700. **^{1}H-NMR** (500 MHz): δ 7.59–7.54 (m, 4H), 7.34–7.24 (m, 4H), 7.23–7.18 (m, 4H), 7.13–7.08 (m, 2H), 4.98 (dd, 1H, *J* = 5.3, 1.5), 4.44 (dddd, 1H, *J* = 12.1, 8.0, 4.3, 1.7), 4.31 (ddd, 1H, *J* = 5.4, 3.6, 1.9), 3.86–3.81 (m, 1H), 3.72 (dt, 3H, *J* = 16.3, 5.8), 2.87 (dt, 1H, *J* = 13.4, 6.6), 2.77 (dt, 1H, *J* = 13.5, 6.8), 1.84–1.78 (m, 2H), 1.76–1.72 (m, 1H), 1.62 (ddd, 2H, *J* = 13.7, 12.1, 3.7), 1.01–0.96 (m, 30H). **^{13}C-NMR** (125 MHz): δ 155.7, 137.4, 137.1, 135.7, 134.0, 133.8, 130.2, 129.8, 129.7, 128.8, 127.8, 126.4, 104.1, 69.3, 63.7, 61.4, 60.2, 38.2, 38.1, 37.0, 27.0, 19.3, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 681.2 ($[M+Na]^+$, 100).



(+)-3-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)propan-1-ol (2l). Clear oil (105 mg, 65%). **TLC**: R_f 0.29 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +90.4° (*c* 2.5, $CHCl_3$). **IR** (NaCl, film): 3353 (O–H st), 3064, 3022, 2945, 2864, 1596, 1464, 1428, 1382, 1294, 1099 (C–O st), 1005, 883, 740, 700. **^{1}H-NMR** (500 MHz): δ 7.69–7.66 (m, 4H), 7.44–7.35 (m, 4H), 7.33–7.29 (m, 3H), 7.27–7.25 (m, 1H), 7.21 (d, 1H, *J* = 7.4), 7.17 (td, 1H, *J* = 7.4, 1.2), 5.04 (dd, 1H, *J* = 5.3, 1.4), 4.56–4.51 (m, 1H), 4.42 (ddd, 1H, *J* = 5.3, 3.6, 1.8), 3.92 (ddd, 1H, *J* = 10.3, 8.1, 5.4), 3.83 (dt, 1H, *J* = 10.5, 5.4), 3.52 (app q, 2H, *J* = 5.6), 2.87 (dt, 1H, *J* = 13.8, 7.6), 2.73–2.67 (m, 1H), 1.98–1.92 (m, 2H), 1.91–1.84 (m, 2H), 1.81–1.72 (m, 2H), 1.59 (t, 1H, *J* = 5.6), 1.10–1.06 (m, 30H). **^{13}C-NMR** (125 MHz): δ 156.2, 140.9, 136.9, 135.7, 134.0, 133.9, 129.7, 129.6, 128.8, 127.7, 125.8, 103.6, 69.3, 61.8, 61.6, 60.3, 38.4, 38.1, 34.2, 29.3, 27.0, 19.3, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 695.2 ($[M+Na]^+$, 100); (neg) 671.2 ($[M-H]^-$, 100).

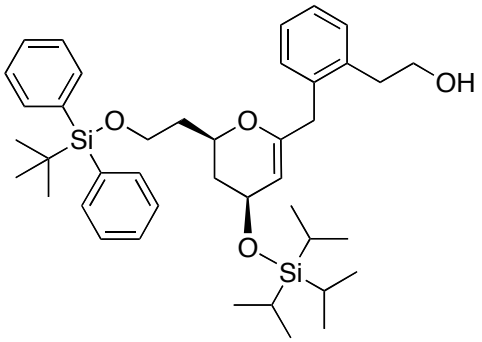
B. GENERAL PROCEDURE FOR STILLE COUPLING OF BENZYL BROMIDES (n = 1) (2d,e,g,m,n,p)[15]

To a stirred solution of the glycal stannane **1** (1.0 equiv), prepared as previously described,[13] in anhyd toluene (0.1 M) under Ar was added the appropriate benzyl bromide sidechain **S1d,e,g** (1.2 equiv), CuI (0.4 equiv) and $Pd(PPh_3)_4$ (0.2 equiv). The yellow solution shielded from light with aluminum foil was heated to 80 °C for 8 h, and then cooled to rt and concentrated to dryness. Purification by silica flash chromatography yielded the partially purified *O*-acetyl *C*1-benzyl glycals **S3d,e,g,m,n,p**. These glycals were then dissolved in 1:1 THF/MeOH (0.1 M) and K_2CO_3 (2.0 equiv) was added.[13] After stirring for 12 h, the mixture was diluted with Et_2O, washed with satd aq $NaHCO_3$, dried (Na_2SO_4), and concentrated by rotary evaporation. Purification by silica flash chromatography (20:1–10:1 hexanes/EtOAc with 1% Et_3N) afforded the free alcohols **2d,e,g,m,n,p**.

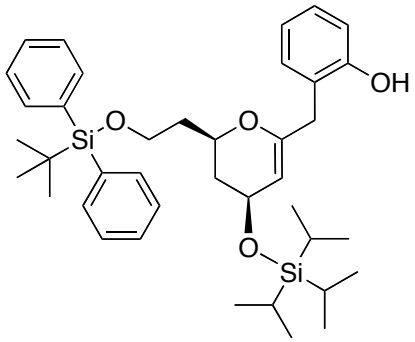


(–)-(2-(((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenyl)methanol (2d). Clear oil (53 mg, 77%). **TLC**: R_f 0.49 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –12.5° (*c* 2.7, $CHCl_3$). **IR** (NaCl, film): 3442 (O–H st), 3068, 3050, 2937, 2863, 1699, 1464, 1428, 1385, 1088 (C–O st), 1006, 883, 739, 703. **^{1}H-NMR** (500 MHz, C_6D_6): δ 7.88–7.85 (m, 4H), 7.40 (dd, 1H, *J* = 5.3, 3.7), 7.37–7.34 (m, 6H), 7.29–7.25 (m, 1H), 7.18–7.16 (m, 2H), 4.75 (dd, 1H, *J* = 2.2, 1.0), 4.68–4.62 (m, 2H), 4.60–4.56 (m, 1H), 4.31–4.26 (m, 1H), 3.90–3.80 (m, 2H), 3.50–3.42 (m, 2H), 2.11–2.00 (m, 2H), 1.86–1.76 (m, 3H), 1.26 (s, 9H), 1.20–1.09 (m, 21H). **^{13}C-NMR** (125 MHz, C_6D_6): δ 154.8, 140.2, 136.2, 136.0, 134.3, 130.6, 130.0, 129.1, 128.6, 128.4, 127.1, 103.0, 72.4, 64.3, 63.2, 60.7, 38.1, 37.9, 37.4, 27.2, 19.5, 18.4, 12.7**.** **ESI-MS** *m/z* (rel int): (pos) 681.1 ($[M+Na]^+$, 100); (neg) 703.1 ($[M+HCOO]^-$, 100); 693.1 ($[M+Cl]^-$, 20).

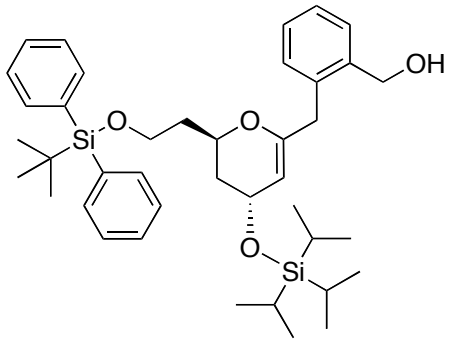
[15] (a) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 4992–4998. (b) Farina, V.; Kapadia, S.; Krishnan, B.; Wang, C.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 5905–5911.



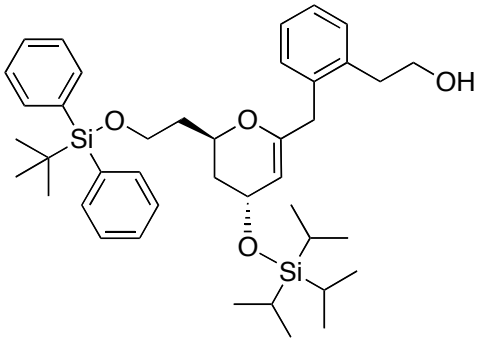
(–)-2-(2-(((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenyl)ethanol (2e). Clear oil (50 mg, 65%). **TLC**: R_f 0.38 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –19.1° (*c* 0.7, $CHCl_3$). **IR** (NaCl, film): 3419 (O–H st), 3061, 2942, 2862, 1667, 1462, 1429, 1380, 1243, 1097 (C–O st), 882, 744, 700. **^{1}H-NMR** (500 MHz): δ 7.66–7.64 (m, 4H), 7.44–7.41 (m, 2H), 7.39–7.36 (m, 4H), 7.17–7.14 (m, 3H), 7.13–7.11 (m, 1H), 4.51–4.48 (m, 1H), 4.45 (d, 1H, *J* = 1.0), 4.16 (dddd, 1H, *J* = 10.5, 8.2, 4.7, 2.3), 3.79–3.68 (m, 4H), 3.34 (m, 2H), 2.89 (t, 2H, *J* = 6.9), 2.08–2.03 (m, 1H), 1.92 (ddt, 1H, *J* = 13.9, 8.4, 5.5), 1.76 (dddd, 1H), *J* = 13.9, 7.8, 6.1, 4.8, 1.69–1.61 (m, 2H), 1.03 (m, 30H). **^{13}C-NMR** (125 MHz): δ 154.3, 137.1, 136.4, 135.7, 134.0, 130.7, 130.1, 129.7, 127.8, 126.8, 126.6, 102.9, 72.0, 64.1, 63.4, 60.3, 37.8 (2), 37.7, 36.3, 27.0, 19.4, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 695.2 ($[M+Na]^+$, 100); (neg) 707.1 ($[M+Cl]^-$, 100).



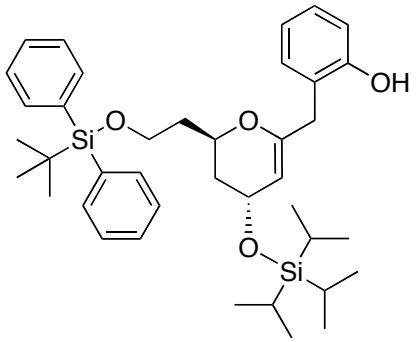
(–)-2-(((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenol (2g). Clear oil (95 mg, 71%). **TLC**: R_f 0.23 (10:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –12.4 ° (*c* 1.9, $CHCl_3$). **IR** (NaCl, film): 3415 (O–H st), 3066, 2949, 2864, 1673, 1589, 1463, 1428, 1381, 1237, 1099 (C–O st), 1005, 882, 745, 700. **^{1}H-NMR** (500 MHz): δ 7.69–7.66 (m, 4H), 7.46–7.38 (m, 6H), 7.17–7.13 (m, 1H), 7.09 (dd, 1H, *J* = 7.5, 1.5), 6.89–6.84 (m, 2H), 6.83 (s, 1H), 4.77 (s, 1H), 4.52–4.49 (m, 1H), 4.29 (dddd, 1H, *J* = 10.2, 7.6, 5.4, 2.3), 3.84–3.75 (m, 2H), 3.33 (m, 2H), 2.13–2.09 (m, 1H), 2.02 (m, 1H), 1.87–1.81 (m, 1H), 1.72 (ddd, 1H, *J* = 13.3, 10.6, 8.4), 1.08–1.07 (m, 30H). **^{13}C-NMR** (125 MHz): δ 155.1, 152.9, 135.7, 133.9, 130.9, 129.8, 128.5, 127.8, 124.9, 120.8, 117.1, 103.2, 73.4, 63.8, 60.2, 37.6, 37.3, 37.0, 27.0, 19.4, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 667.3 ($[M+Na]^+$, 100); (neg) 643.4 ($[M–H]^-$, 100).



(+)-(2-(((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenyl)methanol (2m). Clear oil (263 mg, 88%). **TLC**: R_f 0.21 (10:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +80.2° (*c* 1.6, $CHCl_3$). **IR** (NaCl, film): 3422 (O–H st), 3066, 2943, 2864, 1663, 1463, 1428, 1385, 1324, 1098 (C–O st), 1005, 882, 739, 700. **^{1}H-NMR** (500 MHz): δ 7.67–7.64 (m, 4H), 7.44–7.34 (m, 7H), 7.24–7.19 (m, 3H), 4.70 (d, 1H, *J* = 4.8), 4.68–4.60 (m, 2H), 4.28 (tdd, 1H, *J* = 9.7, 4.6, 2.3), 4.22–4.20 (m, 1H), 3.81–3.72 (m, 2H), 3.41 (s, 2H), 2.16 (t, 1H, *J* = 6.1), 1.87–1.74 (m, 3H), 1.54 (ddd, 1H, *J* = 13.7, 12.0, 3.7), 1.03 (m, 30H). **^{13}C-NMR** (125 MHz): δ 155.7, 139.3, 136.4, 135.7, 134.1, 130.6, 129.7, 129.1, 128.1, 127.7, 127.1, 100.9, 69.4, 63.5, 61.3, 60.2, 38.1, 37.9, 37.4, 36.0, 27.0, 19.3, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 681.1 ($[M+Na]^+$, 100).



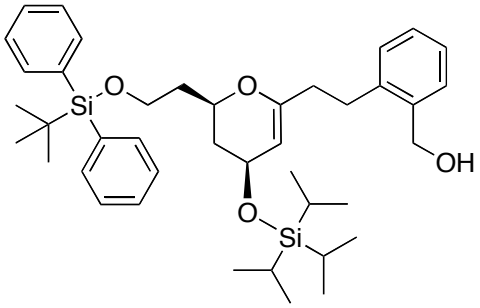
(+)-2-(2-(((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenyl)ethanol (2n). Clear oil (160 mg, 62%). **TLC**: R_f 0.17 (10:1 hexanes/EtOAc). $[\alpha]_D^{18}$: +77.9° (*c* 1.8, $CHCl_3$). **IR** (NaCl, film): 3378 (O–H st), 3065, 3022, 2945, 2864, 1626, 1464, 1427, 1384, 1326, 1245, 1097 (C–O st), 1006, 882, 740, 701. **^{1}H-NMR** (500 MHz): δ 7.69–7.67 (m, 4H), 7.45–7.42 (m, 2H), 7.40–7.37 (m, 4H), 7.20–7.11 (m, 4H), 4.60 (d, 1H, *J* = 4.7), 4.30 (dddd, 1H, *J* = 12.0, 7.8, 4.4, 1.9), 4.23–4.21 (m, 1H), 3.86–3.75 (m, 4H), 3.36 (t, 2H, *J* = 3.7), 2.89 (t, 2H, *J* = 7.0), 1.86–1.79 (m, 3H), 1.57 (ddd, 2H, *J* = 13.6, 12.0, 3.7), 1.06–1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ 155.7, 137.0, 136.5, 135.7, 134.1, 130.6, 130.0, 129.7, 127.7, 126.8, 126.6, 100.9, 68.9, 63.4, 61.4, 60.3, 38.3, 38.0, 37.6, 36.2, 27.0, 19.3, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 695.4 ($[M+Na]^+$, 100); (neg) 671.2 ($[M–H]^-$, 40).



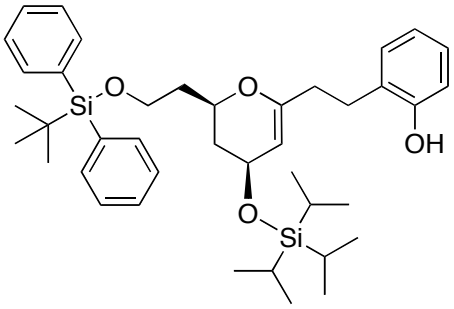
(+)-2-(((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenol (2p). Clear oil (175 mg, 66%). **TLC**: R_f 0.52 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +80.9° (*c* 1.7, $CHCl_3$). **IR** (NaCl, film): 3417 (O–H st), 3064, 3044, 2949, 2864, 1668, 1559, 1463, 1427, 1384, 1360, 1240, 1100 (C–O st), 1004, 883, 743, 700. **^{1}H-NMR** (500 MHz): δ 7.70–7.67 (m, 4H), 7.45–7.38 (m, 6H), 7.14 (td, 1H, *J* = 7.7, 1.3), 7.08 (dd, 1H, *J* = 7.5, 1.4), 6.88–6.83 (m, 2H), 6.79 (s, 1H), 4.92 (d, 1H, *J* = 5.0), 4.43 (tdd, 1H, *J* = 9.6, 4.6, 2.3), 4.25–4.23 (m, 1H), 3.89–3.80 (m, 2H), 3.34 (m, 2H), 1.93 (ddt, 1H, *J* = 13.8, 8.0, 5.5), 1.88–1.81 (m, 2H), 1.59 (ddd, 1H, *J* = 13.7, 12.1, 3.6), 1.06 (m, 30H). **^{13}C-NMR** (125 MHz): δ 155.1, 154.5, 135.7, 134.0, 133.9, 129.7, 128.4, 127.8, 124.9, 120.7, 117.1, 100.9, 70.2, 61.1, 60.0, 38.1, 37.7, 37.2, 26.7, 19.3, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 667.2 ($[M+Na]^+$, 100); (neg) 643.2 ($[M-H]^-$, 100).

C. General procedure for *B*-alkyl Suzuki–Miyaura coupling of styrenes and allyl benzenes (n = 2,3) (2f,h,i,o,q,r)

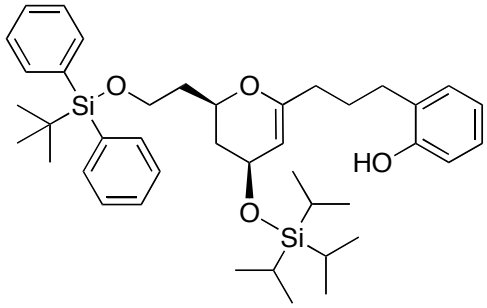
In a flame-dried 10 mL round bottom flask equipped with a magnetic stir bar, septum and argon inlet needle, the appropriate styrene or allyl benzene sidechain **S1f,h,i** (1.5 equiv) was dissolved in anhyd THF (0.1 M). A freshly prepared solution of 9-BBN (0.5 M in THF, 3.0 equiv) was added dropwise at rt. After 3 h, 1 N aq NaOH (3.0 equiv) was added, and the reaction was stirred for an additional 30 min at rt. In a separate flask, the *C*1-iodoglycal **S4** (1.0 equiv), prepared as previously described,[13] was dissolved in 3:1 THF/water (0.1 M), and solid $Pd(dppf)Cl_2$ (0.2 equiv) was added. The boron 'ate' complex was added to the solution of *C*1-iodoglycal via syringe. The reaction was stirred for 1 h at rt, diluted with pentane, filtered through celite/silica (1:1), washed with 1 N aq NaOH, H_2O, and brine, then dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography yielded the *O*-acetyl *C*1-alkyl glycals **S3f,h,i,o,q,r**. These glycals were then dissolved in 1:1 THF/MeOH (0.1 M) and K_2CO_3 (2.0 equiv) was added. After stirring for 12 h, the mixture was diluted with Et_2O, washed with satd aq $NaHCO_3$, dried (Na_2SO_4), and concentrated by rotary evaporation. Purification by silica flash chromatography (20:1–10:1 hexanes/EtOAc with 1% Et_3N) afforded the free alcohols **2f,h,i,o,q,r**.



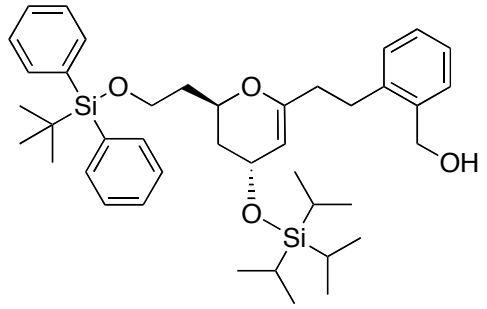
(–)-(2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)ethyl)phenyl)methanol (2f). Clear oil (90 mg, 74%). **TLC**: R_f 0.45 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –6.9° (*c* 1.7, $CHCl_3$). **IR** (NaCl, film): 3321 (O–H st), 3068, 3022, 2939, 2864, 1669, 1464, 1428, 1385, 1362, 1104 (C–O st), 1087, 1005, 884, 741, 702. **^{1}H-NMR** (500 MHz): δ 7.71–7.69 (m, 4H), 7.45–7.37 (m, 7H), 7.24–7.20 (m, 2H), 7.17 (td, 1H, *J* = 6.3, 1.7), 4.67 (app qd, 2H, *J* = 10.9, 5.5), 4.53–4.50 (m, 2H), 4.18 (dddd, 1H, *J* = 10.5, 7.8, 5.0, 2.4), 3.87 (ddd, 1H, *J* = 10.2, 7.6, 5.6), 3.80 (dt, 1H, *J* = 10.6, 5.4), 2.82 (m, 2H), 2.29–2.26 (m, 2H), 2.08 (dd, 1H, *J* = 13.1, 6.2), 2.02–1.95 (m, 1H), 1.83 (m, 2H), 1.72–1.65 (m, 1H), 1.11–1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ 154.3, 139.7, 138.8, 135.7, 134.0, 129.7, 129.6, 128.2, 127.9, 127.8, 126.4, 101.8, 71.7, 64.2, 62.9, 60.4, 38.0, 37.9, 35.9, 29.9, 27.0, 19.4, 18.2, 12.4. **ESI-MS** *m/z* (rel int): (pos) 695.1 ($[M+Na]^+$, 100); (neg) 707.3 ($[M+Cl]^-$, 100).



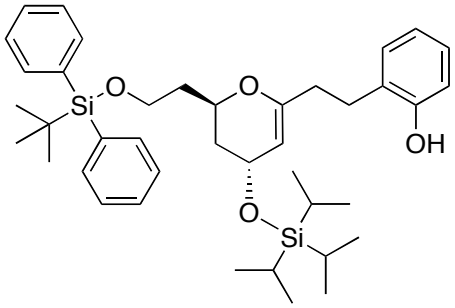
(–)-2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)ethyl)phenol (2h). Clear oil (180 mg, 55%). **TLC**: R_f 0.27 (10:1 hexanes/EtOAc). $[\alpha]_D^{18}$: –10.3° (*c* 6.0, $CHCl_3$). **IR** (NaCl, film): 3417 (O–H st), 3065, 3044, 2949, 2863, 1669, 1461, 1431, 1382, 1355, 1336, 1240, 1100 (C–O st), 1004, 885, 746, 700. **^{1}H-NMR** (500 MHz): δ 7.73–7.70 (m, 4H), 7.44–7.38 (m, 6H), 7.10–7.06 (m, 2H), 6.84 (t, 1H, *J* = 7.4), 6.77 (d, 1H, *J* = 8.5), 4.56 (s, 1H), 4.51–4.48 (m, 1H), 4.26 (dddd, 1H, *J* = 10.3, 7.7, 5.0, 2.5), 3.89 (ddd, 1H, *J* = 10.3, 7.6, 5.4), 3.82 (dt, 1H, *J* = 10.6, 5.4), 2.77 (t, 2H, *J* = 7.4), 2.32 (ddd, 2H, *J* = 6.7, 7.8, 6.4), 2.12–2.01 (m, 2H), 1.86 (ddt, 1H, *J* = 13.5, 7.8, 5.6), 1.71 (ddd, 1H, *J* = 13.1, 10.4, 8.3), 1.10–1.06 (m, 30H). **^{13}C-NMR**(125 MHz): δ 154.2, 153.7, 135.7, 134.0, 130.4, 129.7, 127.8, 127.7, 127.5, 120.5, 115.8, 102.5, 72.1, 63.9, 60.4, 46.0, 37.7, 34.7, 27.5, 27.0, 19.4, 18.2, 12.4, 11.0. **ESI-MS** *m/z* (rel int): (pos) 681.5 ($[M+Na]^+$, 100); (neg) 657.5 ($[M+Cl]^-$, 100).



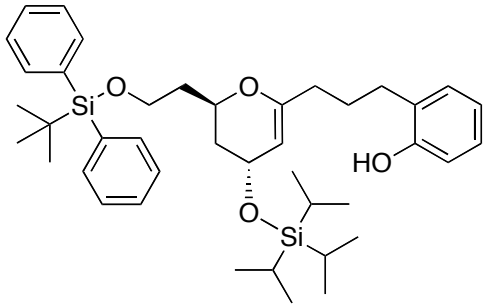
(–)-2-(3-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)propyl)phenol (2i). Clear oil (47 mg, 77%). **TLC**: R_f 0.20 (15:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –6.7° (*c* 1.8, $CHCl_3$). **IR** (NaCl, film): 3429 (O–H st), 3064, 2940, 2863, 1668, 1460, 1380, 1340, 1243, 1095 (C–O st), 1006, 884, 747, 699. **^{1}H-NMR** (500 MHz, CD_3CN): δ 7.56–7.54 (m, 4H), 7.33–7.30 (m, 2H), 7.28–7.25 (m, 4H), 6.94–6.89 (m, 2H), 6.66–6.62 (m, 3H), 4.45 (d, 1H, *J* = 1.0), 4.43–4.40 (m, 1H), 4.06 (dddd, 1H, *J* = 10.3, 8.0, 4.7, 2.4), 3.72 (ddd, 1H, *J* = 10.2, 7.8, 5.4), 3.66 (dt, 1H, *J* = 10.3, 5.7), 2.43 (dd, 2H, *J* = 8.4, 6.9), 1.97 (dddd, 1H, *J* = 13.1, 6.4, 2.3, 1.4), 1.87 (t, 2H, *J* = 7.6), 1.85–1.79 (m, 1H), 1.71 (dddd, 1H, *J* = 14.0, 7.8, 6.1, 4.8), 1.60–1.53 (m, 2H), 1.46 (ddd, 1H, *J* = 13.2, 10.3, 8.0), 0.96–0.90 (m, 30H). **^{13}C-NMR** (125 MHz, CD_3CN): δ 155.6, 136.3, 134.7, 131.2, 130.7, 129.4, 129.3, 128.7, 127.9, 120.7, 115.9, 102.2, 72.4, 64.9, 61.2, 38.6, 38.3, 34.3, 30.1, 27.8, 27.2, 19.8, 18.5, 13.1. **ESI-MS** *m/z* (rel int): (pos) 695.2 ($[M+Na]^+$, 40) 711.2 ($[M+K]^+$, 100); (neg) 717.3 ($[M+HCOO]^-$, 100).



(+)-(2-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)ethyl)phenyl)methanol (2o). Clear oil (92 mg, 57%). **TLC**: R_f 0.26 (10:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +70.7° (*c* 3.1, $CHCl_3$). **IR** (NaCl, film): 3412 (O–H st), 3063, 3025, 2947, 2865, 1664, 1463, 1428, 1386, 1355, 1100 (C–O st), 1003, 819, 742, 699. **^{1}H-NMR** (500 MHz): δ 7.73–7.71 (m, 4H), 7.45–7.36 (m, 7H), 7.20 (m, 3H), 4.66 (m, 3H), 4.29 (dddd, 1H, *J* = 12.0, 7.8, 4.4, 1.8), 4.21 (s, 1H), 3.91 (ddd, 1H, *J* = 10.2, 7.9, 5.8), 3.84 (dt, 1H, *J* = 10.5, 5.4), 2.89–2.78 (m, 2H), 2.36–2.26 (m, 2H), 1.92–1.77 (m, 4H), 1.58–1.52 (m, 1H), 1.08 (m, 30H). **^{13}C-NMR** (125 MHz): δ 155.6, 139.7, 138.7, 135.7, 134.1, 134.0, 129.7, 128.4, 127.9, 127.8, 126.4, 99.8, 68.6, 63.0, 61.4, 60.3, 38.4, 38.1, 36.1, 29.9, 27.0, 19.3, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 695.3 ($[M+Na]^+$, 100).



(+)-2-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)ethyl)phenol (2q). Clear oil (98 mg, 62%). **TLC**: R_f 0.24 (10:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +78.3° (*c* 1.3, $CHCl_3$). **IR** (NaCl, film): 3420 (O–H st), 3065, 3044, 2948, 2864, 1666, 1462, 1429, 1385, 1337, 1099 (C–O st), 1002, 856, 744, 700. **^{1}H-NMR** (500 MHz): δ 7.71–7.69 (m, 4H), 7.44–7.36 (m, 6H), 7.08–7.05 (m, 2H), 6.83 (t, 1H, *J* = 7.4), 6.77 (d, 1H, *J* = 8.2), 5.57–5.56 (brs, 1H), 4.69 (d, 1H, *J* = 5.2), 4.37–4.32 (m, 1H), 4.16 (s, 1H), 3.93 (ddd, 1H, *J* = 10.2, 8.2, 5.5), 3.84 (dt, 1H, *J* = 10.5, 5.3), 2.81 (dt, 1H, *J* = 14.5, 7.4), 2.71 (dt, 1H, *J* = 13.9, 6.8), 2.43 (dt, 1H, *J* = 13.8, 6.8), 2.26 (dt, 1H, *J* = 14.5, 7.5), 1.96–1.85 (m, 2H), 1.81 (dd, 1H, *J* = 13.7, 1.5), 1.61–1.55 (m, 1H), 1.07–1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ 154.7, 154.3, 135.7, 134.0, 130.5, 129.7, 127.8, 127.6, 127.4, 120.7, 115.9, 101.2, 69.1, 61.2, 60.2, 38.3, 38.0, 35.0, 27.1, 27.0, 19.4, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 681.4 ($[M+Na]^+$, 100); (neg) 657.3 ($[M–H]^-$, 100).



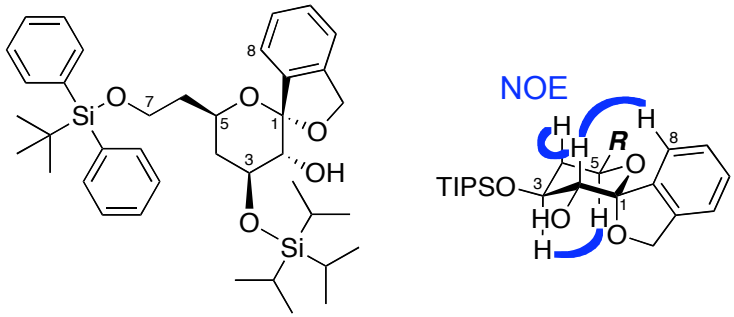
(+)-2-(3-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)propyl)phenol (2r). Clear oil (82 mg, 82%). **TLC**: R_f 0.55 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +65.2° (*c* 2.7, $CHCl_3$). **IR** (NaCl, film): 3412 (O–H st), 3065, 3043, 2945, 2863, 1662, 1461, 1429, 1385, 1352, 1246, 1100 (C–O st), 1001, 882, 744, 700. **^{1}H-NMR** (500 MHz): δ 7.72–7.70 (m, 4H), 7.45–7.36 (m, 6H), 7.11–7.07 (m, 2H), 6.86 (td, 1H, *J* = 7.4, 1.1), 6.75 (dd, 1H, *J* = 7.9, 0.8), 5.13–5.11 (br s, 1H), 4.78 (d, 1H, *J* = 5.1), 4.34 (dddd, 1H, *J* = 11.9, 7.8, 4.3, 1.6), 4.27–4.26 (m, 1H), 3.93 (ddd, 1H, *J* = 10.3, 8.1, 5.5), 3.85 (dt, 1H, *J* = 10.5, 5.4), 2.61 (td, *J* = 7.6, 2.6, 2H), 2.10 (d, *J* = 14.1, 2H), 1.96–1.77 (m, 5H), 1.59 (ddd, 1H, *J* = 13.6, 12.0, 3.7), 1.10–1.07 (m, 30H). **^{13}C-NMR** (125 MHz): δ 156.3, 153.9, 135.7, 134.1, 130.4, 129.7, 128.2, 127.7, 127.3, 120.7, 115.7, 100.1, 68.9, 61.4, 60.3, 38.3, 38.2, 33.4, 29.2, 27.3, 27.0, 19.3, 18.3, 12.6. **ESI-MS** *m/z* (rel int): (pos) 695.3 ($[M+Na]^+$, 100); (neg) 671.3 ($[M–H]^-$, 100).

IV. SPIROCYCLIZATION WITH RETENTION OF CONFIGURATION (Ti[O*i*-Pr]$_4$) (4a–r)

GENERAL PROCEDURE FOR EPOXIDATION AND Ti(O*i*-Pr)$_4$-MEDIATED SPIROCYCLIZATION[16]

The glycal alcohol **2a–r** (1.0 equiv) was dissolved in CH_2Cl_2 (final ratio 1:1 acetone/CH_2Cl_2) and cooled to –78 °C. DMDO (0.09 M in acetone, 1.2 equiv) was added via syringe, and the mixture was stirred at –78 °C. After 10 min, Ti(O*i*-Pr)$_4$ (2.0 equiv) was added via syringe. The reaction mixture was then warmed immediately to 0 °C and stirred for 1 h. The cold reaction mixture was quenched with satd aq $NaHCO_3$. The aq layer was separated and extracted with Et_2O, and the combined extracts were washed with H_2O and brine, dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. Silica flash chromatography provided the 'retention' spiroketals **4a–r**.

^{1}H-NMR resonances were assigned based on COSY analysis of purified products. The 'retention' spiroketals **4** and 'inversion' spiroketals **5** could be readily distinguished by examination of diagnostic ^{1}H-NMR peaks: C5-H (*threo*: δ 3.46–4.22; δ **4** > δ **5**) or (*erythro*: δ 3.88–4.73; δ **5** > δ **4**). Conformational assignments were based on analyses of NOESY spectra and/or coupling constants.[17] *J* values were determined by ^{1}H-NMR, except for compound **4j**, where a *J*-resolve experiment was used. The $^4C_1$ and $^1C_4$ chair conformers could be distinguished based on *J* values: $^4C_1$ chair conformation (*threo*: J_{23} >7.0 and J_{54ax} > 7.0; *erythro*: J_{23} < 7.0 and J_{54ax} > 7.0) or $^1C_4$ chair conformation (*erythro*: J_{23} > 7.0 and J_{54ax} < 7.0).



(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (4a). Clear oil (34 mg, 81%). **TLC**: R_f 0.58 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +23.4° (*c* 1.7, $CHCl_3$). **IR** (NaCl, film): 3574 (O–H st), 3061, 3044, 2937, 2864, 1464, 1430, 1386, 1251, 1103 (C–O st), 1008, 881, 821, 746, 698. **^{1}H-NMR** (500 MHz): δ 7.65–7.61 (m, 4H), 7.41–7.33 (m, 7H), 7.29–7.26 (m, 3H), 5.15 (d, 1H, *J* = 12.6), 5.10 (d, 1H, *J* = 12.6), 4.32 (dddd, 1H, *J* = 12.1, 7.2, 5.0, 2.1), 4.22 (ddd, 1H, *J* = 11.1, 8.9, 5.0), 3.83 (dd, 1H, *J* = 8.9, 6.4), 3.74 (ddd, 1H, *J* = 10.2, 7.8, 5.2), 3.67 (dt, 1H, *J* = 10.5, 5.4), 2.10 (ddd, 1H, *J* = 12.8, 5.0, 2.0), 1.94 (d, 1H, *J* = 6.4), 1.81–1.70 (m, 2H), 1.65 (dd, *J* = 24.0, 11.9, 1H), 1.11–1.04 (m, 30H). **^{13}C-NMR** (125 MHz): δ 140.3, 139.1, 135.7, 134.1, 129.7, 129.2, 128.0, 127.7, 122.1, 121.1, 110.6, 76.8, 72.6, 71.7, 67.4, 60.3, 41.0, 38.4, 26.9, 19.3, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (pos) 683.4 ([M+Na]$^+$, 100); (neg) 659.5 ([M–H]$^-$, 100).

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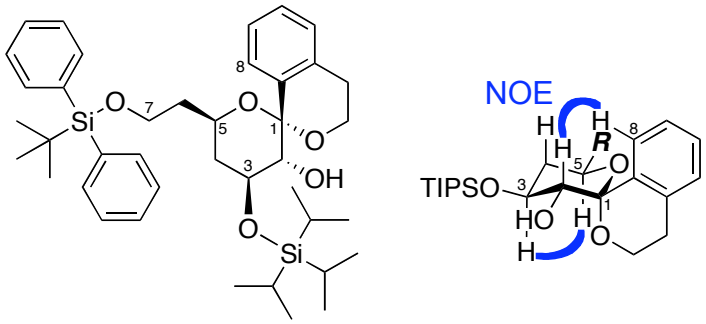
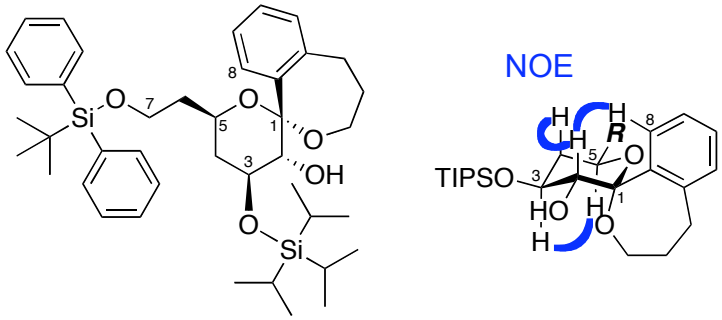
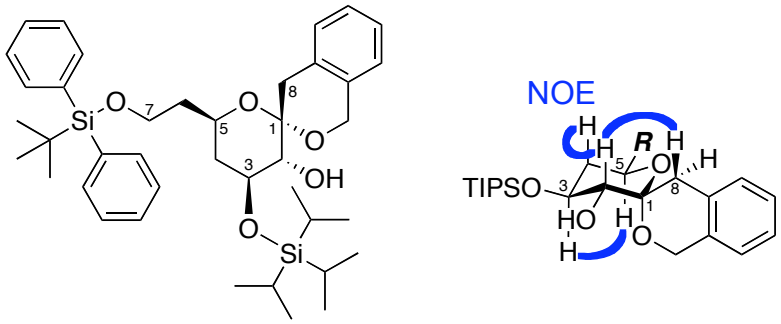
[16] Moilanen, S. B.; Potuzak, J. S.; Tan, D. S. *J. Am. Chem. Soc.* **2006**, *128*, 1792–1793.
[17] Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11–15.



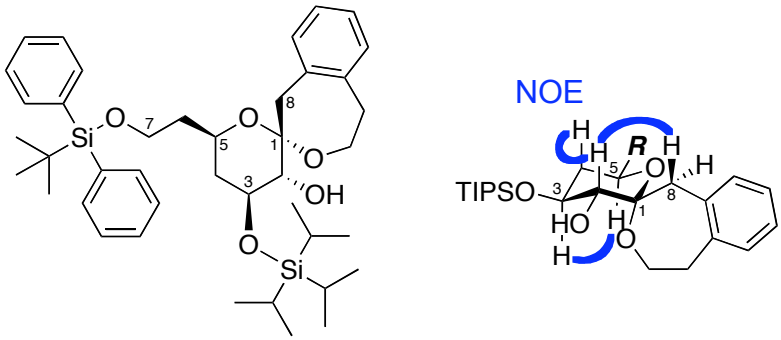
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (4b). Clear oil (40 mg, 91%). **TLC**: R_f 0.49 (5:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +7.1° (*c* 2.0, $CHCl_3$). **IR** (NaCl, film): 3573 (O–H st), 3064, 3040, 2938, 2864, 1463, 1429, 1385, 1251, 1105 (C–O st), 1083, 1033, 1002, 884, 744, 698. **^{1}H-NMR** (500 MHz): δ 7.65 (dt, 4H, *J* = 8.0, 1.3), 7.43–7.39 (m, 3H), 7.37–7.32 (m, 4H), 7.28–7.22 (m, 2H), 7.11 (d, 1H, *J* = 6.7), 4.22–4.17 (m, 2H), 4.00 (ddd, 1H, *J* = 12.5, 11.0, 2.8), 3.94 (dt, 1H, *J* = 5.9, 5.1), 3.83–3.71 (m, 3H), 3.12 (ddd, 1H, *J* = 16.9, 12.0, 5.5), 2.54 (dd, 1H, *J* = 16.4, 2.2), 2.08 (ddd, 1H, *J* = 12.8, 5.0, 2.1), 1.97 (d, 1H, *J* = 7.3), 1.84–1.78 (m, 1H), 1.71 (ddt, 1H, *J* = 13.5, 7.9, 5.5), 1.62 (q, 1H, *J* = 12.0), 1.14–1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ 135.7, 135.5, 135.1, 134.1, 129.7, 128.6, 128.1, 127.7, 126.9, 126.5, 99.0, 78.4, 71.4, 65.8, 60.6, 58.6, 41.0, 38.4, 28.7, 27.0, 19.4, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (pos) 697.3 ($[M+Na]^+$, 100); (neg) 673.5.0 ($[M–H]^-$, 100).



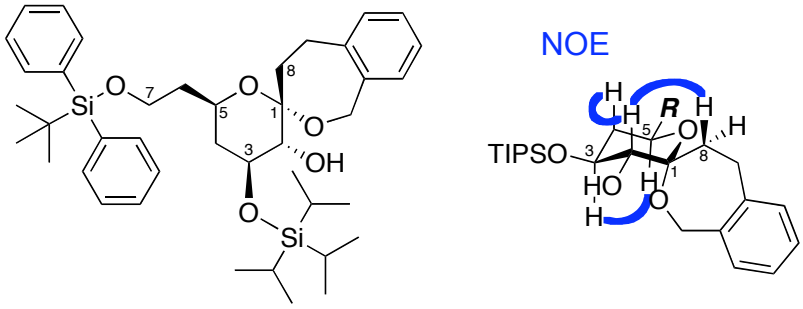
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (4c). Clear oil (19 mg, 90%). **TLC**: R_f 0.24 (10:1 hexanes/EtOAc). $[\alpha]_D^{18}$: +37.1° (*c* 2.8, $CHCl_3$). **IR** (NaCl, film): 3589 (O–H st), 3063, 3020, 2946, 2864, 1462, 1437, 1386, 1297, 1102 (C–O st), 1020, 882, 754, 698. **^{1}H-NMR** (500 MHz): δ 7.68–7.66 (m, 4H), 7.48 (dd, 1H, *J* = 7.6, 1.6), 7.45–7.34 (m, 6H), 7.27–7.21 (m, 2H), 7.09 (dd, 1H, *J* = 7.2, 1.5), 4.22 (ddd, 1H, *J* = 11.0, 8.8, 5.0), 4.14 (tdd, 1H, *J* = 9.6, 4.5, 2.3), 3.86–3.77 (m, 3H), 3.69 (dd, 1H, *J* = 12.6, 8.3), 3.62 (dt, 1H, *J* = 13.2, 6.6), 3.42 (dd, 1H, *J* = 8.8, 5.7), 2.49–2.46 (m, 1H), 2.26 (dddd, 1H, *J* = 11.4, 6.6, 4.7, 1.7), 2.13 (d, 1H, *J* = 5.7), 2.08 (ddd, 1H, *J* = 12.7, 5.0, 2.1), 1.92–1.86 (m, 1H), 1.81–1.67 (m, 2H), 1.60 (q, 1H, *J* = 11.9), 1.15–1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ 139.9, 138.9, 135.7, 134.1, 129.7, 129.6, 128.7, 128.4, 127.7, 126.9, 105.6, 82.2, 71.2, 65.3, 60.8, 58.9, 41.0, 38.6, 30.4, 29.0, 27.0, 19.3, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (pos) 711.4 ($[M+Na]^+$, 100); (neg) 687.3 ($[M–H]^-$, 100).



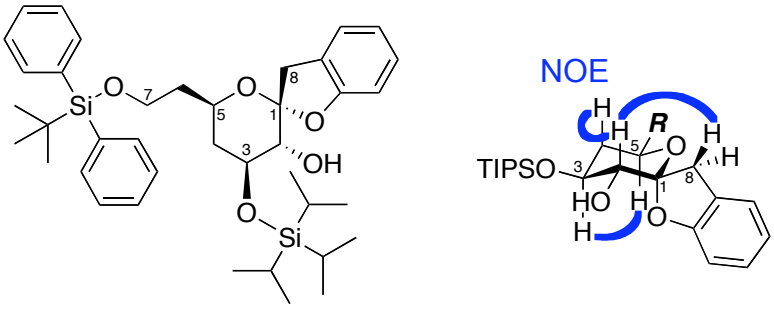
(+)-(2′*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-3,2′-pyran]-3′-ol (4d). Clear oil (24 mg, 86%). **TLC**: R_f 0.63 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +44.8° (*c* 1.1, $CHCl_3$). **IR** (NaCl, film): 3573 (O–H st), 3064, 3024, 2940, 2864, 1463, 1429, 1384, 1251, 1103 (C–O st), 881, 821, 778, 700. **^{1}H-NMR** (500 MHz): δ 7.59 (dd, 4H, *J* = 22.3, 6.8), 7.43–7.38 (m, 2H), 7.33 (dt, 4H, *J* = 16.1, 7.8), 7.19–7.13 (m, 2H), 7.10 (d, 1H, *J* = 7.3), 6.91 (d, 1H, *J* = 7.3), 4.92 (d, 1H, *J* = 14.6), 4.67 (d, 1H, *J* = 14.6), 4.19 (ddd, 1H, *J* = 11.0, 8.8, 4.9), 4.13–4.08 (m, 1H), 3.72–3.67 (m, 1H), 3.55 (td, 2H, *J* = 11.0, 5.5), 3.35 (dd, 1H, *J* = 8.5, 7.0), 2.62 (d, 1H, *J* = 16.8), 2.23 (d, 1H, *J* = 6.8), 2.01 (ddd, 1H, *J* = 12.6, 4.8, 1.4), 1.64 (app q, 2H, *J* = 6.0), 1.51 (q, 1H, *J* = 12.0), 1.15–1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ 135.6, 134.0, 133.1, 131.5, 129.7, 129.1, 127.8, 126.6, 125.7, 123.8, 98.2, 78.3, 71.1, 65.0, 61.8, 60.1, 40.9, 38.3, 34.3, 27.0, 19.3, 18.3, 12.8. **ESI-MS** *m/z* (rel int): (pos) 697.1 ($[M+Na]^+$, 100); (neg) 719.3 ($[M+HCOO]^-$, 100) 673.3.2 ($[M–H]^-$, 30) 709.2 ($[M+Cl]^-$, 25).



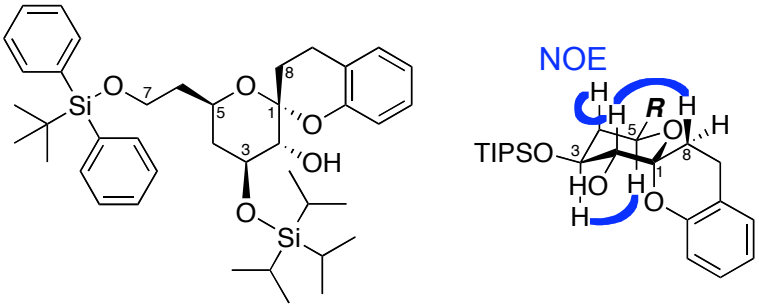
(+)-(2*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*d*]oxepine-2,2′-pyran]-3′-ol (4e). Clear oil (27 mg, 99%). **TLC**: R_f 0.58 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +31.8° (*c* 1.8, $CHCl_3$). **IR** (NaCl, film): 3573 (O–H st), 3064, 3023, 2939, 2864, 1463, 1430, 1384, 1253, 1102 (C–O st), 1075, 883, 746, 696. **^{1}H-NMR** (500 MHz): δ 7.57 (dd, 2H, *J* = 8.0, 1.3), 7.51 (dd, 2H, *J* = 7.9, 1.3), 7.44–7.40 (m, 2H), 7.38–7.34 (m, 4H), 7.12–7.05 (m, 3H), 7.00 (d, 1H, *J* = 6.7), 4.05 (ddd, 1H, *J* = 11.0, 8.7, 5.0), 3.89–3.81 (m, 3H), 3.76 (d, 1H, *J* = 14.8), 3.40 (dd, 2H, *J* = 8.3, 5.1), 3.32 (dd, 1H, *J* = 8.6, 6.5), 3.30–3.26 (m, 1H), 2.82 (d, 1H, *J* = 14.8), 2.65 (dd, 1H, *J* = 15.3, 4.1), 2.33 (d, 1H, *J* = 6.5), 1.94–1.90 (m, 1H), 1.56–1.49 (m, 2H), 1.43 (q, 1H, *J* = 12.2), 1.13–1.08 (m, 21H), 0.99 (s, 9H). **^{13}C-NMR** (125 MHz): δ 140.5, 136.9, 135.6, 134.1, 130.9, 129.7, 128.2, 127.7, 126.3, 126.2, 98.0, 81.3, 71.1, 64.3, 61.4, 60.1, 45.7, 40.9, 38.3, 38.1, 27.0, 19.3, 18.3, 12.8. **ESI-MS** *m/z* (rel int): (pos) 711.5 ($[M+Na]^+$, 100); (neg) 687.3 ($[M–H]^-$, 100).



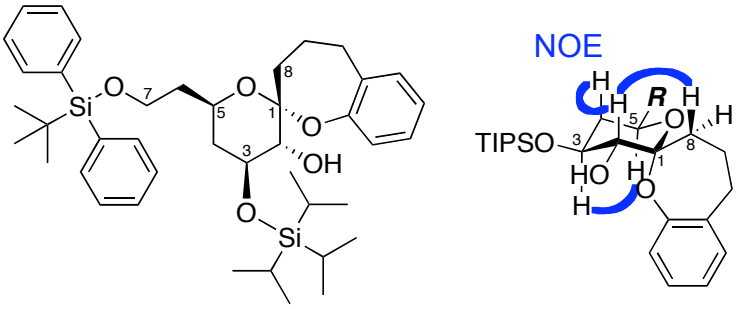
(+)-(2′*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*c*]oxepine-3,2′-pyran]-3′-ol (4f). Clear oil (25 mg, 90%). **TLC**: R_f 0.55 (4:1 hexanes/EtOAc). $[\alpha]_D^{18}$: +18.9° (*c* 1.5, $CHCl_3$). **IR** (NaCl, film): 3650 (O–H st), 3061, 3026, 2938, 2863, 1672, 1461, 1435, 1384, 1264, 1103 (C–O st), 1076, 1015, 884, 749, 697. **^{1}H-NMR** (500 MHz): δ 7.64–7.59 (m, 4H), 7.41–7.38 (m, 1H), 7.35–7.32 (m, 3H), 7.25–7.22 (m, 2H), 7.20–7.17 (m, 1H), 7.15–7.12 (m, 3H), 5.07 (d, 1H, *J* = 13.4), 4.14 (d, 1H, *J* = 13.4), 4.04–3.98 (m, 2H), 3.93 (ddd, 1H, *J* = 10.2, 7.7, 5.7), 3.79 (dt, 1H, *J* = 10.3, 5.2), 3.25 (t, 1H, *J* = 13.6), 3.09 (t, 1H, *J* = 8.1), 2.57–2.53 (m, 1H), 2.25–2.20 (m, 1H), 2.02 (d, 1H, *J* = 7.6), 1.98 (ddd, 1H, *J* = 12.7, 5.0, 2.0), 1.84–1.76 (m, 3H), 1.45 (q, 1H, *J* = 12.0), 1.09–1.03 (m, 30H). **^{13}C-NMR** (125 MHz): δ 143.1, 139.1, 135.7, 135.6, 133.8, 129.8, 128.6, 128.1, 127.8, 126.0, 101.1, 79.9, 71.1, 64.4, 63.6, 60.4, 40.9, 38.6, 35.6, 28.6, 27.0, 19.3, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (pos) 711.1 ([M+Na]$^+$, 100); (neg) 687.4 ([M–H]$^-$, 100).



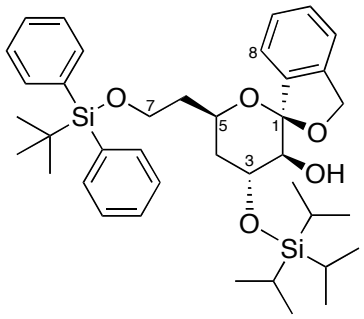
(+)-(2*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[benzofuran-2,2′-pyran]-3′-ol (4g). Clear oil (20 mg, 98%). **TLC**: R_f 0.23 (10:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +47.05° (*c* 0.7, $CHCl_3$). **IR** (NaCl, film): 3582 (O–H st), 3063, 3046, 2938, 2863, 1598, 1471, 1428, 1387, 1237, 1103 (C–O st), 1003, 875, 745, 701. **^{1}H-NMR** (500 MHz): δ 7.62 (dd, 2H, *J* = 8.0, 1.4), 7.53–7.51 (m, 2H), 7.43–7.39 (m, 1H), 7.36–7.33 (m, 3H), 7.23–7.19 (m, 3H), 7.12–7.09 (m, 1H), 6.91 (d, 1H, *J* = 7.4), 6.80 (d, 1H, *J* = 8.0), 4.37 (dtd, 1H, *J* = 12.1, 6.1, 1.9), 4.22 (ddd, 1H, *J* = 11.1, 8.9, 4.9), 3.69 (dt, 1H, *J* = 10.2, 6.5), 3.64–3.59 (m, 2H), 3.52 (dd, 1H, *J* = 8.9, 6.8), 3.02 (d, 1H, *J* = 16.3), 2.09 (ddd, 1H, *J* = 12.9, 4.9, 2.1), 2.02 (d, 1H, *J* = 6.8), 1.71 (app q, 2H, *J* = 6.1), 1.58 (q, 1H, *J* = 12.1), 1.11 (m, 21H), 0.99 (s, 9H). **^{13}C-NMR** (125 MHz): δ 158.6, 135.6, 134.0, 133.7, 129.6, 127.9, 126.1, 124.9, 121.1, 111.3, 110.1, 76.9, 71.4, 66.8, 59.9, 40.7, 39.3, 38.2, 26.9, 19.3, 18.3, 12.8. **ESI-MS** *m/z* (rel int): (pos) 683.4 ([M+Na]$^+$, 100); (neg) 659.4 ([M–H]$^-$, 100).

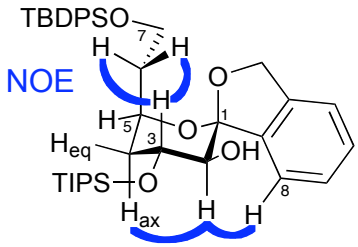


(+)-(2*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[chroman-2,2′-pyran]-3′-ol (4h). Clear oil (40 mg, 88%). **TLC**: R_f 0.33 (10:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +51.3° (*c* 1.03 $CHCl_3$). **IR** (NaCl, film): 3580 (O–H st), 3064, 2943, 2865, 1586, 1463, 1386, 1301, 1223, 1102 (C–O st), 990, 882, 820, 746, 698. **^{1}H-NMR** (500 MHz): δ 7.55 (d, 2H, *J* = 7.7), 7.47 (d, 2H, *J* = 7.6), 7.40 (m, 2H), 7.33 (m, 4H), 7.05 (t, 2H, *J* = 7.7), 6.85 (dd, 2H, *J* = 17.3, 7.9), 4.33–4.28 (m, 1H), 4.06–4.01 (m, 1H), 3.55–3.47 (m, 2H), 3.35–3.33 (m, 1H), 2.94 (td, 1H, *J* = 14.8, 5.8), 2.61 (dd, 1H, *J* = 16.0, 5.7), 2.32 (ddd, 1H, *J* = 16.2, 10.9, 5.5), 2.11 (d, 1H, *J* = 6.9), 2.07–2.04 (m, 1H), 1.85 (dd, 1H, *J* = 13.4, 5.9), 1.71–1.58 (m, 2H), 1.52 (q, 1H, *J* = 12.1), 1.16–1.13 (m, 21H), 0.92 (s, 9H). **^{13}C-NMR** (125 MHz): δ 151.9, 135.6, 134.0, 129.6, 129.1, 127.7, 127.2, 122.8, 121.1, 117.3, 98.8, 78.5, 70.9, 66.0, 60.3, 40.8, 38.3, 27.9, 26.9, 20.8, 19.2, 18.3, 12.8. **ESI-MS** *m*/*z* (rel int): (pos) 697.1 ($[M+Na]^+$, 100); (neg) 673.3 ($[M–H]^-$, 100).



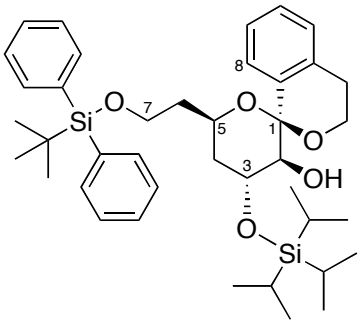
(+)-(2*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*b*]oxepine-2,2′-pyran]-3′-ol (4i). Clear oil (53 mg, 96%). **TLC**: R_f 0.41 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +45.1° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3578 (O–H st), 3069, 3023, 2934, 2863, 1676, 1462, 1431, 1387, 1231, 1107 (C–O st), 1077, 883, 761, 702. **^{1}H-NMR** (500 MHz): δ 7.57 (m, 4H), 7.42 (t, 2H, *J* = 7.3), 7.36 (m, 4H), 6.93 (t, 2H, *J* = 6.9), 6.87 (d, 1H, *J* = 7.8), 6.80 (t, 1H, *J* = 7.3), 4.28 (ddd, 1H, *J* = 11.1, 8.8, 4.7), 3.99–3.94 (m, 1H), 3.42 (dd, 1H, *J* = 16.7, 8.0), 3.28 (dd, 1H, *J* = 8.7, 6.6), 3.16 (dd, 1H, *J* = 15.2, 9.1), 2.75–2.65 (m, 2H), 2.35 (d, 1H, *J* = 6.5), 2.29 (ddd, 1H, *J* = 14.3, 9.3, 5.4), 1.99 (ddd, 1H, *J* = 12.6, 4.6, 1.6), 1.82 (dt, 1H, *J* = 14.2, 4.6), 1.74 (dt, 2H, *J* = 11.1, 5.6), 1.65 (td, 1H, *J* = 14.1, 8.1), 1.53–1.43 (m, 2H), 1.14 (m, 21H), 1.01 (s, 9H). **^{13}C-NMR** (125 MHz): δ 152.9, 135.6, 134.7, 134.1, 129.9, 129.6, 127.7, 126.8, 123.5, 122.7, 102.1, 80.2, 71.2, 67.0, 60.8, 40.3, 38.3, 37.4, 33.5, 27.0, 20.1, 19.3, 18.4, 12.8. **ESI-MS** *m*/*z* (rel int): (pos) 711.3 ($[M+Na]^+$, 100); (neg) 687.3 ($[M–H]^-$, 100).

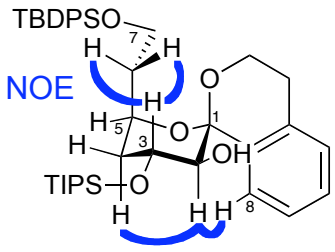




CD$_2$Cl$_2$: $J_{2,3}$ = 7.9
$J_{5,4ax}$ = 4.7

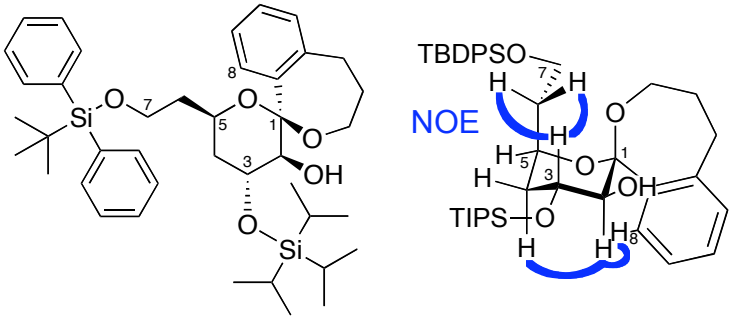
(+)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (4j). Clear oil (17 mg, 85%). **TLC**: R_f 0.23 (10:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +4.0° (*c* 0.5, $CHCl_3$). **IR** (NaCl, film): 3567 (O–H st), 3054, 2940, 2864, 1464, 1427, 1382, 1250, 1103 (C–O st), 1007, 882, 745, 698. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.62 (dd, 2H, Ar-H, *J* = 8.0, 1.4), 7.56 (dd, 2H, Ar-H, *J* = 8.0, 1.4), 7.43 (dd, 1H, C8-H, *J* = 6.6, 1.4), 7.39–7.30 (m, 6H, Ar-H), 7.23–7.21 (m, 1H, Ar-H), 7.18–7.15 (m, 2H, Ar-H), 4.94–4.88 (m, 2H, C12-H), 4.38 (app dq, 1H, C5-H, *J* = 9.3, 4.7), 4.27 (td, 1H, C3-H, *J* = 8.2, 5.8), 3.79 (dd, 1H, C2-H, *J* = 7.9, 7.0), 3.76 (dt, 1H, C7-H, *J* = 8.4, 3.3), 3.68 (dt, 1H, C7-H, *J* = 10.3, 5.3), 2.25 (ddt, 1H, C6-H, *J* = 17.7, 8.6, 4.2), 2.05–2.02 (m, 2H, C4-H), 2.01 (d, 1H, C2-OH, *J* = 7.0), 1.75 (ddt, 1H, C6-H, *J* = 13.6, 8.0, 5.5), 1.11–1.07 (m, 21H, TIPS), 0.97 (s, 9H, *t*-Bu). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.65–7.63 (m, 2H), 7.58–7.56 (m, 2H), 7.52 (dd, 1H, *J* = 6.0, 2.1), 7.41–7.37 (m, 1H), 7.36–7.31 (m, 5H), 7.22–7.20 (m, 1H), 7.20–7.16 (m, 2H), 4.97 (d, 2H, *J* = 13.2), 4.44 (app dq, 1H, *J* = 9.2, 4.6), 4.33 (td, 1H, *J* = 8.3, 4.8), 3.87 (dd, 1H, *J* = 7.8, 5.9), 3.77 (ddd, 1H, *J* = 10.2, 8.0, 5.1), 3.68 (dt, 1H, *J* = 10.4, 5.3), 2.26 (ddt, 1H, *J* = 13.7, 9.4, 4.8), 2.18 (d, 1H, *J* = 5.9), 2.11–2.02 (m, 2H), 1.80 (ddt, 1H, *J* = 13.6, 8.0, 5.7), 1.16–1.04 (m, 21H), 1.01–0.97 (s, 9H). **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 140.1, 139.5, 135.7, 134.0, 133.8, 129.6, 129.2, 127.9, 122.5, 121.0, 111.6, 76.3, 72.5, 70.1, 68.8, 60.9, 38.6, 37.6, 26.9, 19.3, 18.3, 12.6. **ESI-MS** *m/z* (rel int): (pos) 683.3.0 ($[M+Na]^+$, 100); (neg) 659.1.0 ($[M–H]^-$, 100).



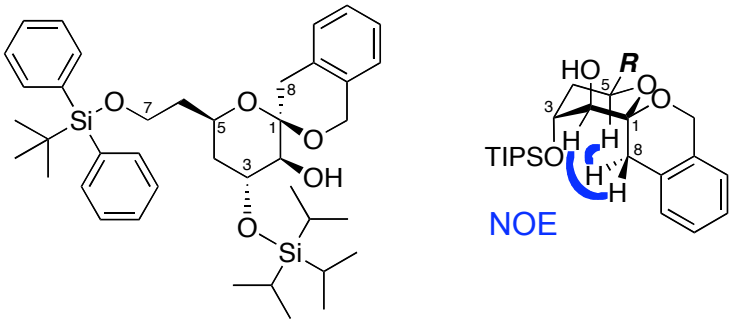


(–)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (4k). Clear oil (19 mg, 96%). **TLC**: R_f 0.35 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –20.1° (*c* 0.3, $CHCl_3$). **IR** (NaCl, film): 3571 (O–H st), 3068, 3048, 2934, 2862, 1463, 1427, 1384, 1251, 1108 (C–O st), 1077, 1032, 883, 745, 704. **^{1}H-NMR** (500 MHz, C_6D_6): δ 7.80 (m, 4H), 7.40–7.38 (m, 1H), 7.23–7.20 (m, 4H), 7.09–7.05 (m, 4H), 6.84–6.82 (m, 1H), 4.60 (dtd, 1H, *J* = 8.7, 5.8, 3.1), 4.42 (td, 1H, *J* = 8.8, 4.9), 3.96 (ddd, 1H, *J* = 10.2, 8.0, 5.0), 3.91 (t, 1H, *J* = 8.5), 3.83 (dt, 1H, *J* = 10.4, 5.3), 3.64 (ddd, 1H, *J* = 12.7, 10.6, 2.3), 3.39 (dd, 1H, *J* = 10.8, 4.5), 2.61 (ddd, 1H, *J* = 16.4, 12.1, 4.9), 2.33 (ddt, 1H, *J*

= 13.8, 8.7, 5.2), 2.16–2.06 (m, 2H), 1.97–1.90 (m, 2H), 1.87 (d, 1H, *J* = 8.7), 1.21–1.17 (m, 30H). **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 136.2, 135.7, 135.4, 133.9, 133.7, 129.7, 128.4, 128.0, 127.7, 127.0, 100.5, 79.6, 70.9, 68.2, 61.4, 59.4, 38.4, 37.8, 28.9, 27.0, 19.3, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (pos) 697.3 ($[M+Na]^+$, 100); (neg) 673.3 ($[M–H]^-$, 100).

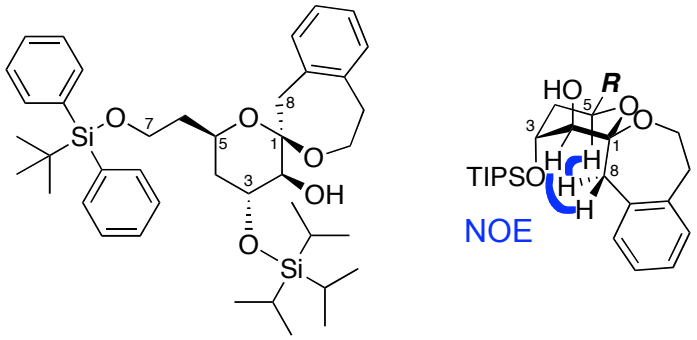


(–)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (4l). Clear oil (40 mg, 91%). **TLC**: R_f 0.67 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –15.2° (*c* 1.4 $CHCl_3$). **IR** (NaCl, film): 3586 (O–H st), 3063, 3021, 2944, 2864, 1464, 1384, 1253, 1102 (C–O st), 1018, 889, 751, 698. **^{1}H-NMR** (500 MHz): δ 7.65 (m, 4H), 7.53 (d, 1H, *J* = 7.7), 7.41–7.33 (m, 4H), 7.28–7.24 (m, 3H), 7.21 (t, 1H, *J* = 7.3), 7.05 (d, 1H, *J* = 7.4), 4.49 (app qd, 1H, *J* = 6.7, 2.5), 4.30 (td, 1H, *J* = 9.0, 4.6), 3.82 (dt, 1H, *J* = 10.3, 6.2), 3.68 (tt, 2H, *J* = 11.2, 5.7), 3.55 (td, 1H, *J* = 13.1, 6.8), 3.49 (d, 1H, *J* = 8.5), 3.46 (t, 1H, *J* = 8.8), 2.43 (dd, 1H, *J* = 13.3, 5.3), 2.25 (d, 1H, *J* = 5.6), 2.22–2.14 (m, 2H), 2.10 (dt, 1H, *J* = 13.3, 3.8), 2.00 (ddd, 1H, *J* = 13.3, 9.9, 6.1), 1.89 (app dq, 1H, *J* = 13.4, 6.7), 1.63 (tt, 1H, *J* = 12.9, 6.3), 1.08 (m, 30H). **^{13}C-NMR** (125 MHz): δ 140.6, 138.7, 135.7, 134.0, 133.8, 129.7, 128.9, 128.5, 127.7, 127.0, 106.8, 82.7, 69.9, 68.2, 61.2, 59.9, 38.6, 37.8, 30.5, 28.9, 27.0, 19.4, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (pos) 711.4 ($[M+Na]^+$, 100); (neg) 687.3 ($[M+Cl]^-$, 100).

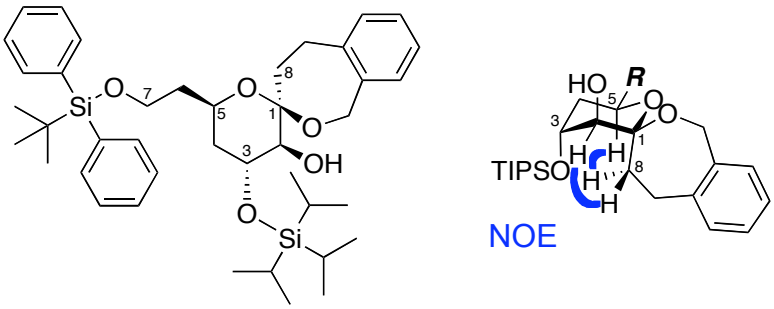


(–)-(2′*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-3,2′-pyran]-3′-ol (4m). Clear oil (40 mg, 84%). **TLC**: R_f 0.40 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –1.5° (*c* 1.2, $CHCl_3$). **IR** (NaCl, film): 3562 (O–H st), 3073, 3013, 2959, 2862, 1465, 1427, 1387, 1258, 1108 (C–O st), 1062, 884, 740, 700. **^{1}H-NMR** (500 MHz): δ 7.57–7.55 (m, 2H), 7.45–7.42 (m, 2H), 7.42–7.32 (m, 4H), 7.29–7.26 (m, 2H), 7.18–7.15 (m, 1H), 7.11 (td, 1H, *J* = 7.3, 0.9), 7.01 (dd, 2H, *J* = 16.1, 7.4), 4.99 (d, 1H, *J* = 14.3), 4.73 (d, 1H, *J* = 14.4), 4.32 (q, 1H, *J* = 3.3), 4.26–4.21 (m, 1H), 3.57 (dd, 1H, *J* = 3.7, 2.0), 3.55-3.46 (m, 3H), 3.06 (d, 1H, *J* = 16.8), 3.02 (d, 1H, *J* = 1.6), 1.93 (ddd, 1H, *J* = 13.9, 11.1, 2.9), 1.73–1.62 (m, 2H), 1.58 (dt, 1H, *J* = 13.9, 2.7), 1.21–1.08 (m, 21H), 0.95 (s, 9H).

^{13}C-NMR (125 MHz): δ 135.6, 134.1, 131.4, 129.6, 129.5, 129.1, 127.7, 126.9, 126.0, 123.7, 97.1, 72.5, 69.5, 65.0, 63.0, 60.0, 38.8, 34.6, 33.6, 26.9, 19.2, 18.3, 12.4. **ESI-MS** *m/z* (rel int): (pos) 697.5 ([M+Na]$^+$, 100); (neg) 673.4 ([M–H]$^-$, 100).

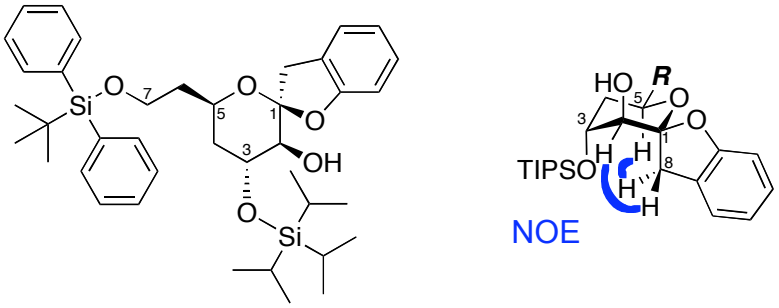


(–)-(2*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*d*]oxepine-2,2′-pyran]-3′-ol (4n). Clear oil (15 mg, 98%). **TLC**: R_f 0.23 (10:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –25.6° (*c* 0.5, $CHCl_3$). **IR** (NaCl, film): 3541 (O–H st), 3065, 3018, 2944, 2866, 1462, 1428, 1390, 1240, 1200, 1095 (C–O st), 1053, 885, 749, 699. **^{1}H-NMR** (500 MHz): δ 7.56–7.53 (m, 4H), 7.42–7.33 (m, 6H), 6.98 (t, 1H, *J* = 4.3), 6.87 (m, 1H), 6.83 (m, 2H), 4.26 (q, 1H, *J* = 2.8), 4.04 (t, 1H, *J* = 11.0), 3.93 (d, 1H, *J* = 15.4), 3.89–3.85 (m, 1H), 3.82 (ddd, 1H, *J* = 12.0, 5.0, 2.7), 3.49 (d, 1H, *J* = 2.8), 3.20–3.14 (m, 3H), 3.06–3.01 (m, 2H), 2.62 (dd, 1H, *J* = 15.2, 4.5), 1.80 (ddd, 1H, *J* = 14.1, 11.5, 2.9), 1.62 (dtd, 1H, *J* = 14.0, 8.6, 5.5), 1.54–1.47 (m, 2H), 1.07 (m, 30H). **^{13}C-NMR** (125 MHz): δ 140.8, 136.1, 135.7, 134.1, 130.5, 129.5, 128.6, 127.6, 126.7, 126.4, 96.5, 70.9, 69.7, 64.9, 61.9, 60.7, 41.5, 39.0, 38.2, 34.2, 27.0, 19.2, 18.3, 12.3. **ESI-MS** *m/z* (rel int): (pos) 711.3 ([M+Na]$^+$, 100); (neg) 687.4 ([M–H]$^-$, 100).

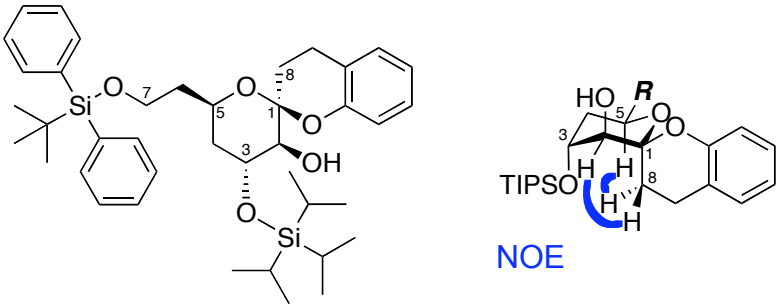


(–)-(2′*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*c*]oxepine-3,2′-pyran]-3′-ol (4o). Clear oil (39 mg, 86%). **TLC**: R_f 0.43 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –32.2° (*c* 1.3, $CHCl_3$). **IR** (NaCl, film): 3547 (O–H st), 3065, 3020, 2937, 2764, 1463, 1429, 1390, 1251, 1108 (C–O st), 1075, 1040, 1004, 886, 740, 699. **^{1}H-NMR** (500 MHz): δ 7.64–7.63 (m, 4H), 7.39–7.29 (m, 4H), 7.26–7.23 (m, 3H), 7.19 (td, 1H, *J* = 7.1, 1.8), 7.17–7.12 (m, 3H), 5.39 (d, 1H, *J* = 14.2), 4.31 (d, 1H, *J* = 14.2), 4.27–4.23 (m, 2H), 4.00–3.95 (m, 1H), 3.79 (dt, 1H, *J* = 10.1, 5.0), 3.48 (d, 1H, *J* = 3.1), 3.18 (dd, 1H, *J* = 15.1, 11.1), 3.07 (d, 1H, *J* = 0.6), 2.75–2.70 (m, 1H), 2.62 (dd, 1H, *J* = 15.2, 8.7), 2.01–1.96 (m, 1H), 1.91 (ddd, 1H, *J* = 14.0, 11.3, 2.9), 1.84–1.71 (m, 2H), 1.56–1.53 (m, 1H), 1.12–1.06 (m, 30H). **^{13}C-NMR** (125 MHz): δ 142.6, 138.8, 135.7, 133.9, 129.7, 129.1, 127.9,

127.8, 127.7, 126.0, 100.0, 71.5, 69.5, 64.7, 64.5, 60.1, 39.1, 34.7, 32.5, 28.8, 27.0, 19.3, 18.3, 12.3. **ESI-MS** *m/z* (rel int): (pos) 711.3 ([M+Na]$^+$, 100); (neg) 687.1 ([M–H]$^-$, 100) 723.1 ([M+Cl]$^-$, 40).

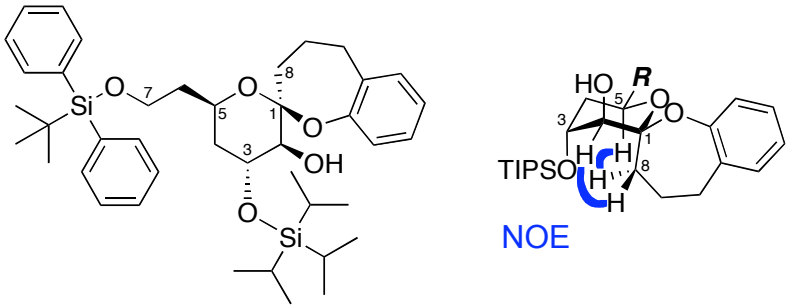


(–)-(2*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[benzofuran-2,2′-pyran]-3′-ol (4p). Clear oil (12 mg, 67%). **TLC**: R_f 0.31 (1:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –9.2° (*c* 0.5, $CHCl_3$). **IR** (NaCl, film): 3581 (O–H st), 3060, 2934, 2862, 1662, 1471, 1427, 1388, 1240, 1097 (C–O st), 1013, 878, 745, 696. **^{1}H-NMR** (500 MHz): δ 7.62 (dd, 2H, *J* = 8.0, 1.4), 7.53 (dd, 2H, *J* = 7.9, 1.2), 7.42–7.38 (m, 1H), 7.33 (td, 3H, *J* = 7.4, 1.6), 7.20–7.16 (m, 3H), 7.12 (d, 1H, *J* = 7.3), 6.92 (td, 1H, *J* = 7.4, 0.7), 6.87 (d, 1H, *J* = 7.9), 4.55–4.51 (m, 1H), 4.37 (q, 1H, *J* = 3.9), 3.82–3.77 (dd, 1H, *J* = 4.7, 3.4), 3.78–3.75 (m, 1H), 3.62–3.58 (m, 1H), 3.42 (m, 2H), 2.65 (d, 1H, *J* = 3.0), 2.03 (ddd, 1H, *J* = 13.5, 9.8, 3.4), 1.92–1.87 (m, 1H), 1.81–1.77 (m, 1H), 1.73–1.69 (ddd, 1H, *J* = 13.6, 4.5, 3.1), 1.18–1.09 (m, 21H), 1.03–1.00 (s, 9H). **^{13}C-NMR** (125 MHz): δ 157.2, 135.6, 133.8, 129.6, 128.0, 127.7, 126.5, 125.3, 121.6, 111.2, 109.9, 73.2, 69.4, 66.0, 59.6, 38.3, 38.1, 34.8, 26.9, 19.3, 18.3, 12.5. **ESI-MS** *m/z* (rel int): (pos) 683.2 ([M+Na]$^+$, 100); (neg) 659.2 ([M–H]$^-$, 100).



(–)-(2*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[chroman-2,2′-pyran]-3′-ol (4q). Clear oil (60 mg, 90%). **TLC**: R_f 0.48 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: –0.5° (*c* 1.7, $CHCl_3$). **IR** (NaCl, film): 3582 (O–H st), 3069, 2952, 2861, 1539, 1462, 1425, 1385, 1225, 1109 (C–O st), 1068, 1000, 880, 747, 697. **^{1}H-NMR** (500 MHz): δ 7.60 (m, 4H), 7.43–7.38 (m, 2H), 7.37–7.32 (m, 4H), 7.08 (t, 1H, *J* = 7.7), 7.01(d, 1H, *J* = 7.1), 6.88 (t, 1H, *J* = 7.4), 6.82 (d, 1H, *J* = 7.6), 4.41–4.36 (m, 2H), 3.67 (td, 1H, *J* = 10.0, 3.7), 3.61 (dd, 1H, *J* = 4.6, 3.1), 3.51(dt, 1H, *J* = 10.0, 4.8), 3.06–2.99 (m, 1H), 2.86 (d, 1H, *J* = 3.0), 2.75 (ddd, 1H, *J* = 14.0, 5.5, 2.0), 2.55 (dt, 1H, *J* = 16.2, 2.6), 2.00 (ddd, 1H, *J* = 13.3, 9.3, 3.7), 1.86 (td, 1H, *J* = 13.9, 5.5), 1.82–1.77 (m, 1H), 1.73–1.64 (m, 2H), 1.18–1.06 (m, 21H), 1.01 (s, 9H). **^{13}C-NMR** (125 MHz): δ 151.8, 135.6, 134.0, 129.6, 129.2, 127.7,

127.3, 122.9, 121.1, 116.9, 98.8, 73.9, 69.2, 65.8, 59.9, 38.6, 35.4, 27.0, 26.6, 20.7, 19.3, 18.3, 12.4. **ESI-MS** *m/z* (rel int): (pos) 697.4 ([M+Na]$^+$, 100); (neg) 6735 ([M–H]$^-$, 100).



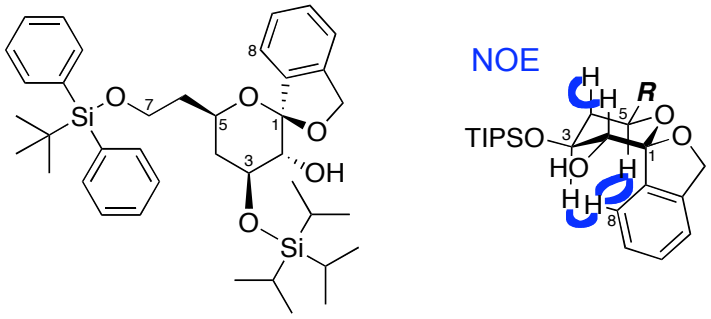
(+)-(2*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*b*]oxepine-2,2′-pyran]-3′-ol (4r). Clear oil (5 mg, 90%). **TLC**: R_f 0.62 (4:1 hexanes/EtOAc). $[\alpha]_D^{21}$: +3.3° (*c* 0.8, $CHCl_3$). **IR** (NaCl, film): 3619 (O–H st), 3064, 3044, 2935, 2863, 1460, 1431, 1389, 1235, 1105 (C–O st), 1071, 1004, 880, 736, 697. **^{1}H-NMR** (500 MHz): δ 7.60–7.57 (m, 4H), 7.44–7.32 (m, 6H), 7.09–7.04 (m, 2H), 6.97 (td, 1H, *J* = 7.3, 1.2), 6.90 (dd, 1H, *J* = 7.8, 1.1), 4.32 (q, 1H, *J* = 3.1), 4.20–4.16 (m, 1H), 3.64–3.60 (m, 1H), 3.59 (d, 1H, *J* = 2.9), 3.51 (dt, 1H, *J* = 9.8, 4.9), 3.33 (d, 1H, *J* = 0.9), 2.78–2.71 (m, 3H), 1.90 (ddd, 1H, *J* = 14.0, 11.4, 2.9), 1.83–1.78 (m, 1H), 1.78–1.71 (m, 1H), 1.65–1.56 (m, 3H), 1.48 (dt, 1H, *J* = 13.7, 2.2), 1.13–0.99 (m, 30H). **^{13}C-NMR** (125 MHz): δ 153.0, 135.6, 134.8, 134.2, 129.6, 129.2, 127.7, 127.0, 124.1, 122.6, 101.4, 71.5, 69.6, 64.9, 59.7, 38.9, 34.3, 32.3, 32.0, 27.0, 20.2, 19.3, 18.3, 12.3. **ESI-MS** *m/z* (rel int): (pos) 711.3 ([M+Na]$^+$, 100); (neg) 687.3 ([M+Cl]$^-$, 100).

V. SPIROCYCLIZATION WITH INVERSION OF CONFIGURATION (MeOH or AcOH) (5a–r)

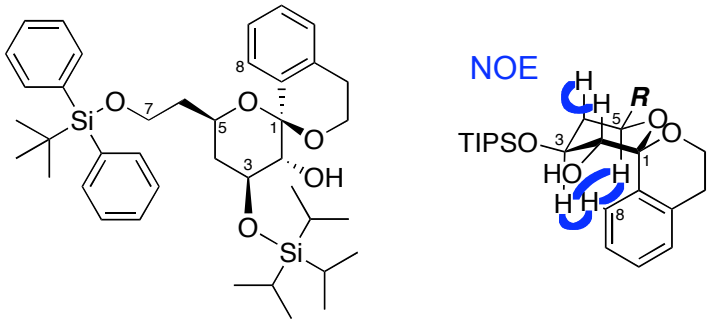
A. GENERAL PROCEDURE FOR EPOXIDATION AND MeOH-INDUCED SPIROCYCLIZATION (5a,b,d,j,m)

The glycal alcohol **2a,b,d,j,m** (1.0 equiv) was dissolved in 5:1 MeOH/CH_2Cl_2 (final ratio 5:1:1 MeOH/CH_2Cl_2/acetone) and cooled to –63 °C. DMDO (0.09 M in acetone, 1.2 equiv) was added via syringe, and the reaction mixture was stirred at –63 °C. After 3 h, the mixture was warmed to rt and concentrated to dryness. Silica flash chromatography provided the 'inversion' spiroketals **5a,b,d,j,m**.

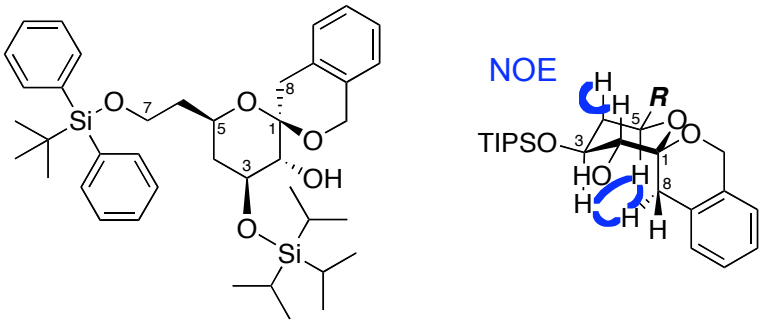
^{1}H-NMR resonances were assigned based on COSY analysis of purified products. The 'retention' spiroketals **4** and 'inversion' spiroketals **5** could be readily distinguished by examination of diagnostic ^{1}H-NMR peaks: C5-H (*threo*: δ 3.46–4.22; δ **4** > δ **5**) or (*erythro*: δ 3.88–4.73; δ **5** > δ **4**). Conformational assignments were based on analyses of NOESY spectra and/or coupling constants.[17] *J* values were determined by ^{1}H-NMR, except for compound **5j**, where a *J*-resolve experiment was used. The $^4C_1$ and $^1C_4$ chair conformers could be distinguished based on *J* values: $^4C_1$ chair conformation (*threo*: J_{23} >7.0 and J_{54ax} > 7.0; *erythro*: J_{23} < 7.0 and J_{54ax} > 7.0) or $^1C_4$ chair conformation (*erythro*: J_{23} > 7.0 and J_{54ax} < 7.0).



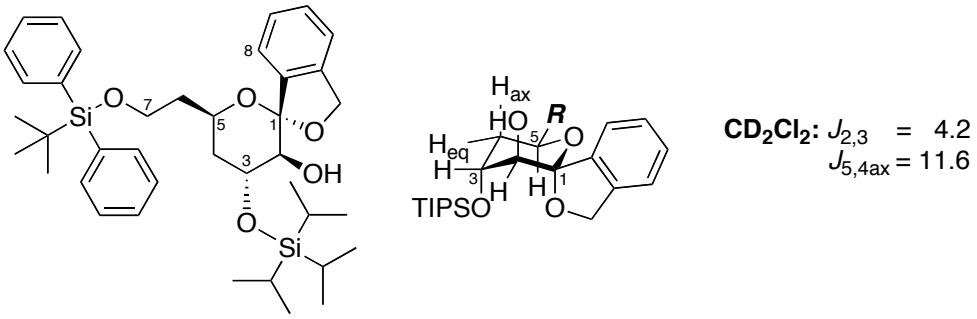
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (5a). Clear oil (37 mg, 88%). **TLC**: R_f 0.35 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +34.1° (*c* 1.2, $CHCl_3$). **IR** (NaCl, film): 3491 (O–H st), 3065, 2941, 2866, 1465, 1428, 1367, 1256, 1106 (C–O st), 1029, 880, 742, 700. **^{1}H-NMR** (500 MHz): δ 7.52 (dd, 2H, *J* = 8.0, 1.4), 7.45–7.41 (m, 3H), 7.39–7.36 (m, 2H), 7.35–7.31 (m, 4H), 7.28–7.25 (m, 3H), 5.29 (d, 1H, *J* = 12.5), 5.10 (d, 1H, *J* = 12.6), 4.55 (ddd, 1H, *J* = 11.2, 9.4, 5.1), 4.15–4.10 (m, 1H), 3.83 (dd, 1H, *J* = 9.4, 2.9), 3.65 (ddd, 1H, *J* = 10.2, 8.2, 4.3), 3.58–3.54 (m, 1H), 2.22 (d, 1H, *J* = 2.9), 2.17 (ddd, 1H, *J* = 12.9, 5.1, 1.9), 1.76–1.62 (m, 3H), 1.13–1.10 (m, 21H), 0.90 (s, 9H). **^{13}C-NMR** (125 MHz): δ 141.8, 137.2, 135.6, 133.8, 129.6, 129.1, 127.7, 127.2, 123.3, 121.9, 111.5, 78.5, 72.1, 71.0, 65.9, 59.7, 40.6, 38.6, 26.9, 19.2, 18.3, 12.7. ESI-MS *m/z* (rel int): (pos) 683.4 ($[M+Na]^+$, 100); (neg) 659.5 ($[M–H]^-$, 100).



(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (5b). Clear oil (29 mg, 68%). **TLC**: R_f 0.55 (5:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +16.8° (*c* 1.2, $CHCl_3$). **IR** (NaCl, film): 3491 (O–H st), 3064, 2935, 2864, 1464, 1429, 1382, 1249, 1101 (C–O st), 1014, 881, 822, 741, 698. **^{1}H-NMR** (500 MHz): δ 7.53–7.47 (m, 5H), 7.42–7.38 (m, 2H), 7.36–7.30 (m, 4H), 7.27–7.24 (m, 1H), 7.21 (td, 2H, *J* = 8.0, 2.3), 4.60 (ddd, 1H, *J* = 10.9, 8.9, 5.6), 4.30 (ddd, 1H, *J* = 10.4, 7.1, 5.8), 3.89–3.85 (m, 1H), 3.83–3.78 (m, 1H), 3.75 (dd, 1H, *J* = 8.9, 3.4), 3.67–3.58 (m, 2H), 2.91 (dd, 2H, *J* = 9.5, 4.0), 2.21 (d, 1H, *J* = 3.4), 2.10 (ddd, 1H, *J* = 12.9, 5.6, 2.2), 1.77 (ddt, 1H, *J* = 13.7, 8.4, 5.2), 1.72–1.63 (m, 2H), 1.16–1.12 (m, 21H), 0.91 (s, 9H). **^{13}C-NMR** (125 MHz): δ 136.6, 135.6, 134.1, 133.9, 129.6, 129.2, 128.2, 127.7, 127.3, 125.4, 99.9, 81.1, 71.8, 66.6, 60.9, 60.1, 40.2, 39.0, 29.9, 26.9, 19.2, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (pos) 697.4 ($[M+Na]^+$, 100); (neg) 673.5 ($[M–H]^-$, 100).

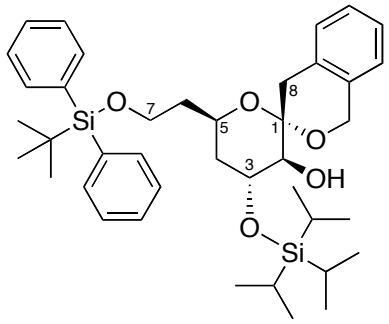


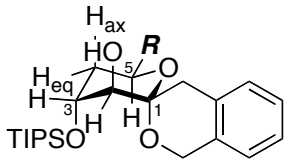
(–)-(2′*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-3,2′-pyran]-3′-ol (5d). Clear oil (40 mg, 87%). **TLC**: R_f 0.57 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –0.7° (*c* 1.1 $CHCl_3$). **IR** (NaCl, film): 3484 (O–H st), 3061, 3039, 2939, 2864, 1462, 1432, 1376, 1240, 1224, 1102 (C–O st), 1054, 881, 827, 741, 698. **^{1}H-NMR** (500 MHz): δ 7.56–7.54 (m, 2H), 7.47–7.45 (m, 2H), 7.43–7.33 (m, 4H), 7.31–7.28 (m, 2H), 7.16–7.10 (m, 2H), 7.07 (d, 1H, *J* = 7.1), 7.00 (dd, 1H, *J* = 7.2, 0.9), 4.99 (d, 1H, *J* = 14.3), 4.75 (d, 1H, *J* = 14.4), 3.98 (ddd, 1H, *J* = 11.1, 9.3, 4.9), 3.77–3.73 (m, 1H), 3.49 (dd, 3H, *J* = 7.0, 5.5), 3.31 (d, 1H, *J* = 16.6), 2.82 (d, 1H, *J* = 16.7), 2.42 (d, 1H, *J* = 1.3), 1.98 (ddd, 1H, *J* = 12.8, 4.9, 2.1), 1.74–1.63 (m, 2H), 1.55 (q, 1H, *J* = 12.1), 1.14–1.10 (m, 21H), 0.96 (s, 9H). **^{13}C-NMR** (125 MHz): δ 135.6, 134.3, 133.9, 131.2, 129.6, 129.0, 127.7, 126.8, 125.9, 123.8, 99.3, 79.4, 71.2, 66.6, 63.3, 60.2, 40.7, 38.6, 27.5, 27.0, 19.3, 18.3, 12.7. **ESI-MS** *m*/*z* (rel int): (pos) 697.3 ($[M+Na]^+$, 100); (neg) 673.3 ($[M–H]^-$, 100).



(+)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (5j). Clear oil (31 mg, 84%). **TLC**: R_f 0.44 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +12.4° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3469 (O–H st), 3063, 3012, 2944, 2863, 1465, 1428, 1381, 1252, 1111 (C–O st), 1072, 1016, 975, 887, 741, 699. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.64–7.61 (m, 4H, Ar-H), 7.52 (d, 1H, Ar-H, *J* = 7.6), 7.38–7.31 (m, 5H, Ar-H), 7.29–7.22 (m, 4H, Ar-H), 5.04 (d, 1H, C12-H, *J* = 12.8), 4.97 (d, 1H, C12-H, *J* = 12.8), 4.73 (dtd, 1H, C5-H, *J* = 11.6, 6.4, 2.4), 4.23 (q, 1H, C3-H, *J* = 3.8), 3.77–3.73 (m, 1H, C2-H), 3.72 (dd, 1H, C7-H, *J* = 6.8, 4.2), 3.65 (dt, 1H, C7-H, *J* = 10.3, 5.2), 2.04 (d, 1H, C2-OH, *J* = 7.0), 1.96 (ddd, 1H, C4-H, *J* = 13.9, 11.6, 3.8), 1.73–1.67 (m, 3H, C4-H, C6-H), 1.13–1.06 (m, 21H, TIPS), 1.01 (s, 9H, *t*-Bu). **^{1}H-NMR** (500 MHz, C_6D_6): δ 7.77–7.75 (m, 4H), 7.73 (dt, 1H, *J* = 4.4, 2.2), 7.22–7.18 (m, 4H), 7.12 (d, 2H, *J* = 7.6), 7.10–7.09 (m, 2H), 6.87–6.85 (m, 1H), 5.09–5.03 (m, 2H), 4.86 (d, 1H, *J* = 12.8), 4.22 (q, 1H, *J* = 3.2), 3.95 (ddd, 1H, *J* = 10.0, 8.3, 5.5), 3.71 (dt, 1H, *J* = 9.9, 5.0), 3.63 (dd, 1H, *J* = 6.8, 3.2), 2.03 (ddd, 1H, *J* = 13.8, 11.6, 3.1), 1.77 (td, 2H, *J* = 8.2, 5.2), 1.68 (dt, 1H, *J* = 13.7, 2.3), 1.45 (d, 1H, *J* = 6.8), 1.22–1.10 (m, 30H). **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 140.8, 140.4, 135.7, 134.2, 129.5, 129.1, 127.7,

127.4, 124.6, 121.2, 109.8, 72.2, 71.7, 69.9, 64.2, 60.2, 38.9, 35.4, 26.9, 19.3, 18.2, 12.5. **ESI-MS** *m/z* (rel int): (pos) 683.3 ([M+Na]$^+$, 100); (neg) 659.3 ([M–H]$^-$, 100).





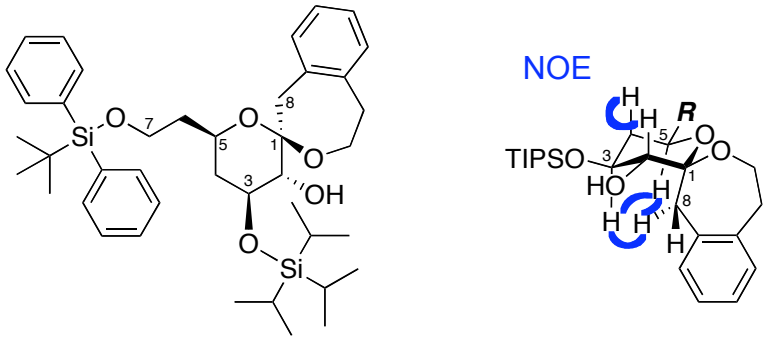
CDCl$_3$: $J_{2,3}$ = 3.1

(+)-(2´*S*,3´*S*,4´*R*,6´*R*)-6´-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4´-(triisopropylsilyloxy)-3´,4´,5´,6´-tetrahydrospiro[isochroman-3,2´-pyran]-3´-ol (5m). Clear oil (40 mg, 84%). **TLC**: R_f 0.26 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +1.0° (*c* 2.5, $CHCl_3$). **IR** (NaCl, film): 3482 (O–H st), 3068, 3019, 2952, 2861, 1465, 1425, 1382, 1348, 1247, 1114 (C–O st), 1073, 885, 741, 696. **^{1}H-NMR** (500 MHz): δ 7.59 (m, 4H), 7.41–7.38 (m, 2H), 7.34–7.30 (m, 4H), 7.17–7.12 (m, 2H), 7.09 (m, 1H), 6.89 (t, 1H, *J* = 4.3), 4.98 (d, 1H, *J* = 14.9), 4.61–4.56 (m, 2H), 4.18 (q, 1H, *J* = 3.1), 3.73 (td, 1H, *J* = 9.8, 4.1), 3.59 (dd, 1H, *J* = 7.6, 2.7), 3.53 (dt, 1H, *J* = 10.0, 4.9), 3.02 (d, 1H, *J* = 16.7), 2.86 (d, 1H, *J* = 16.7), 1.78 (m, 2H), 1.68–1.54 (m, 3H), 1.16–0.96 (m, 30H). **^{13}C-NMR** (125 MHz): δ 135.6, 134.1, 134.0, 131.3, 129.6, 129.2, 127.7, 126.4, 125.7, 123.8, 98.2, 72.1, 70.0, 61.6, 61.4, 59.8, 38.7, 35.7, 35.0, 27.0, 19.3, 18.2, 12.5. **ESI-MS** *m/z* (rel int): (pos) 697.5 ([M+Na]$^+$, 100).

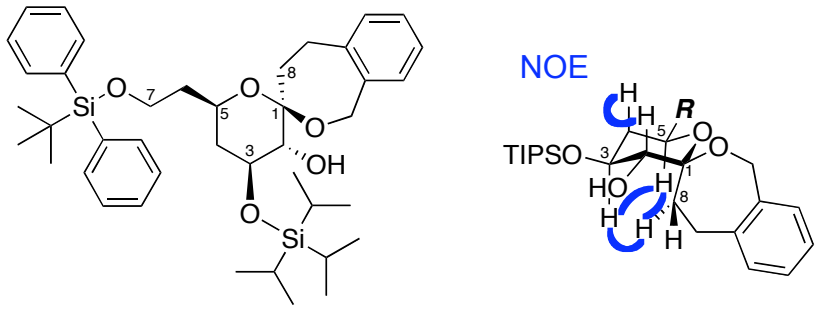
B. General procedure for epoxidation and AcOH-induced spirocyclization (5e–i,k,n–r)

The glycal alcohol **2e–i,k,n–r** (1.0 equiv) was dissolved in CH_2Cl_2 (0.002 M) and cooled to –63 °C. A solution of AcOH (1 M in CH_2Cl_2, 10 equiv) was cooled to –78 °C, then added to the alcohol. Next, DMDO (0.09 M in acetone, 1.2 equiv) was added via syringe and the reaction mixture was stirred at –63 °C. After 1 h, the mixture was warmed to–44 °C and stirred for 3 h. The reaction mixture was then warmed to rt and quenched with satd aq $NaHCO_3$. The aqueous layer was separated and extracted with Et_2O, then the combined extracts were washed with H_2O and brine, dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. Silica flash chromatography provided the ´inversion´ spiroketals **5e–i,k,n–r**.

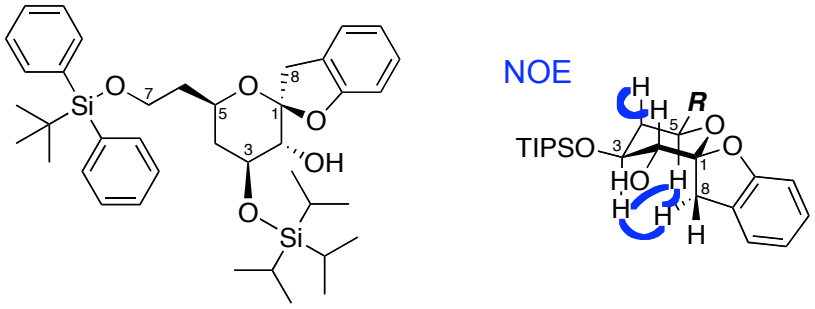
^{1}H-NMR resonances were assigned based on COSY analysis of purified products. The 'retention' spiroketals **4** and 'inversion' spiroketals **5** could be readily distinguished by examination of diagnostic ^{1}H-NMR peaks: C5-H (*threo*: δ 3.46–4.22; δ **4** > δ **5**) or (*erythro*: δ 3.88–4.73; δ **5** > δ **4**). Conformational assignments were based on analyses of NOESY spectra and/or coupling constants.[17] *J* values were determined by ^{1}H-NMR. The $^4C_1$ and $^1C_4$ chair conformers could be distinguished based on *J* values: $^4C_1$ chair conformation (*threo*: J_{23} >7.0 and J_{54ax} > 7.0; *erythro*: J_{23} < 7.0 and J_{54ax} > 7.0) or $^1C_4$ chair conformation (*erythro*: J_{23} > 7.0 and J_{54ax} < 7.0).



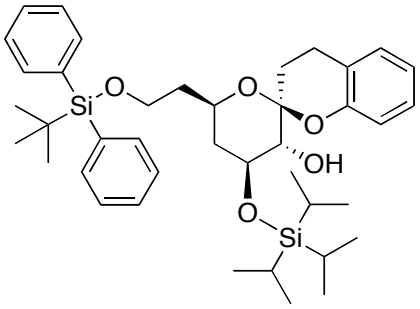
(+)-(2*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*d*]oxepine-2,2′-pyran]-3′-ol (5e). Clear oil (31 mg, 57%). **TLC**: R_f 0.51 (5:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +18.4° (*c* 1.5, $CHCl_3$). **IR** (NaCl, film): 3477 (O–H st), 3064, 3018, 2938, 2864, 1463, 1383, 1306, 1250, 1107 (C–O st), 1006, 883, 747, 698. **^{1}H-NMR** (500 MHz): δ 7.55 (m, 4H), 7.45–7.35 (m, 6H), 6.96 (t, 1H, *J* = 4.2), 6.84 (m, 3H), 4.02–3.97 (m, 2H), 3.85 (ddd, 1H, *J* = 12.0, 5.5, 2.3), 3.50 (d, 1H, *J* = 15.8), 3.48–3.43 (m, 1H), 3.36 (dd, 1H, *J* = 9.0, 2.1), 3.22–3.14 (m, 2H), 2.99 (ddd, 1H, *J* = 10.3, 9.2, 5.5), 2.91 (d, 1H, *J* = 15.9), 2.62 (dd, 1H, *J* = 15.3, 5.1), 2.43 (d, 1H, *J* = 2.2), 1.93 (ddd, 1H, *J* = 12.7, 5.1, 1.7), 1.69–1.61 (m, 1H), 1.53–1.43 (m, 2H), 1.11 (m, 21H), 0.99 (s, 9H). **^{13}C-NMR** (125 MHz): δ 140.9, 135.7, 135.1, 134.2, 130.5, 129.6, 128.7, 127.7, 126.7, 126.1, 99.0, 81.0, 72.1, 66.9, 62.0, 60.7, 40.3, 38.7, 38.6, 38.1, 27.0, 19.2, 18.3, 12.8. **ESI-MS** *m/z* (rel int): (pos) 711.5 ($[M+Na]^+$, 100); (neg) 687.4 ($[M–H]^-$, 100).



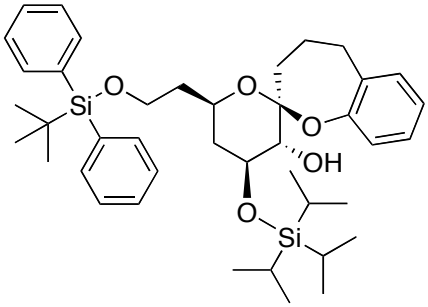
(+)-(2′*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*c*]oxepine-3,2′-pyran]-3′-ol (5f). Clear oil (35 mg, 54%). **TLC**: R_f 0.55 (4:1 hexanes/EtOAc). $[\alpha]_D^{18}$: +7.5° (*c* 1.3, $CHCl_3$). **IR** (NaCl, film): 3493 (O–H st), 3070, 2942, 2891, 2864, 1463, 1427, 1388, 1361, 1244, 1111 (C–O st), 1063, 1022, 941, 882, 853, 759, 701. **^{1}H-NMR** (500 MHz, C_6D_6): δ 7.85 (m, 4H), 7.31–7.29 (m, 3H), 7.26–7.23 (m, 3H), 7.18 (td, 1H, *J* = 7.3, 1.7), 7.12–7.09 (m, 2H), 7.07–7.05 (m, 1H), 5.55 (d, 1H, *J* = 13.9), 4.30 (d, 1H, *J* = 13.9), 4.08–3.99 (m, 2H), 3.94 (dt, 1H, *J* = 10.4, 5.3), 3.85–3.80 (m, 1H), 3.64 (dd, 1H, *J* = 9.1, 1.0), 3.32 (t, 1H, *J* = 13.4), 2.55 (dd, 1H, *J* = 14.6, 6.8), 2.24–2.19 (m, 1H), 2.10–2.07 (m, 1H), 2.06–2.02 (m, 1H), 1.93–1.86 (m, 2H), 1.83–1.78 (m, 1H), 1.68 (q, 1H, *J* = 12.0), 1.29–1.26 (m, 30H). **^{13}C-NMR** (125 MHz, C_6D_6): δ 143.2, 140.1, 136.0, 134.1, 131.1, 130.0, 128.8, 128.6, 128.5, 126.3, 102.2, 81.2, 70.8, 66.2, 64.9, 60.9, 41.4, 39.4, 28.3, 28.0, 27.2, 19.5, 18.5, 13.0. **ESI-MS** *m/z* (rel int): (pos) 711.1 ($[M+Na]^+$, 100); (neg) 687.4 ($[M–H]^-$, 100).



(+)-(2*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[benzofuran-2,2′-pyran]-3′-ol (5g). Clear oil (25 mg, 43%). **TLC**: R_f 0.23 (10:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +8.2° (*c* 1.3, $CHCl_3$). **IR** (NaCl, film): 3519 (O–H st), 3061, 3047, 2932, 2862, 1471, 1430, 1319, 1250, 1108 (C–O st), 1017, 954, 884, 824, 779, 700. **^{1}H-NMR** (500 MHz): δ 7.61 (dd, 2H, *J* = 8.0, 1.4), 7.51 (dd, 2H, *J* = 8.0, 1.3), 7.42–7.38 (m, 1H), 7.35–7.31 (m, 3H), 7.18 (m, 3H), 7.11 (d, 1H, *J* = 7.3), 6.93–6.90 (m, 2H), 4.04–3.99 (m, 1H), 3.87 (ddd, 1H, *J* = 11.0, 9.4, 4.7), 3.79–3.73 (m, 2H), 3.61 (dt, 1H, *J* = 10.1, 5.0), 3.48 (d, 1H, *J* = 16.0), 3.07 (d, 1H, *J* = 16.0), 2.44 (d, 1H, *J* = 2.4), 2.01 (ddd, 1H, *J* = 12.8, 4.7, 2.0), 1.84–1.74 (m, 2H), 1.60 (q, 1H, *J* = 12.1), 1.13–1.10 (m, 21H), 1.02 (s, 9H). **^{13}C-NMR** (125 MHz): δ 158.1, 135.6, 133.7, 129.7, 128.0, 127.7, 125.7, 125.2, 121.4, 112.4, 109.7, 76.7, 71.7, 66.4, 59.7, 40.2, 38.0, 32.4, 26.9, 19.3, 18.3, 12.7. **ESI-MS** *m/z* (rel int): (pos) 683.3 ($[M+Na]^+$, 100); (neg) 659.4 ($[M–H]^-$, 65) 695.4 ($[M+Cl]^-$, 100).

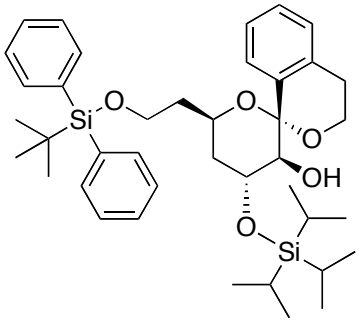


(2*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[chroman-2,2′-pyran]-3′-ol (5h). Inseparable mixture of **5h** and **4h**. Clear oil (50 mg, 98%). **TLC**: R_f 0.76 (4:1 hexanes/EtOAc). **ESI-MS** *m/z* (rel int): (pos) 697.2 ($[M+Na]^+$, 100); (neg) 673.4 ($[M–H]^-$, 100).

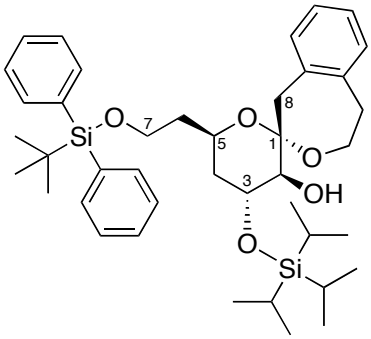


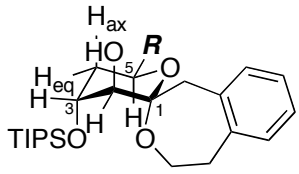
(2*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-hexahydro-3*H*-spiro[benzo[*b*]oxepine-2,2′-pyran]-3′-ol (5i). Inseparable mixture of **5i** and **4i**.

Clear oil (37 mg, 76%). **TLC**: R_f 0.66 (4:1 hexanes/EtOAc). **ESI-MS** *m/z* (rel int): (pos) 711.4 ([M+Na]$^+$, 100); (neg) 687.3 ([M–H]$^-$, 100).



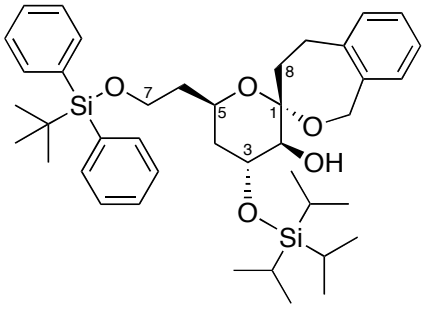
(1*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (5k). Inseparable mixture of **5k** and **4k**. Clear oil (60 mg, 97%). **TLC**: R_f 0.60 (4:1 hexanes/EtOAc). **ESI-MS** *m/z* (rel int): (pos) 697.3 ([M+Na]$^+$, 100); (neg) 673.4 ([M–H]$^-$, 100).

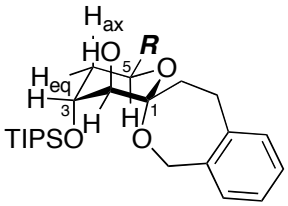




CDCl$_3$: $J_{2,3}$ = 4.0

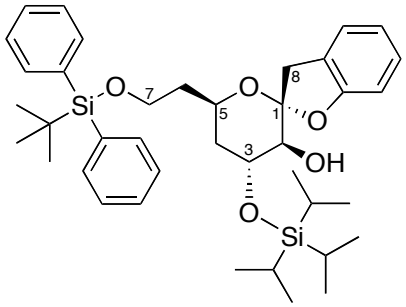
(+)-(2*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*d*]oxepine-2,2′-pyran]-3′-ol (5n). Clear oil (26 mg, 56%). **TLC**: R_f 0.16 (10:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +34.9° (*c* 0.9, $CHCl_3$). **IR** (NaCl, film): 3450 (O–H st), 3062, 3025, 2941, 2863, 1462, 1429, 1386, 1244, 1081 (C–O st), 1031, 944, 885, 788, 697. **^{1}H-NMR** (500 MHz): δ 7.59–7.56 (m, 4H), 7.43–7.32 (m, 6H), 7.11–7.06 (m, 3H), 7.01 (d, 1H, *J* = 7.0), 4.31 (tdd, 1H, *J* = 7.9, 7.4, 3.9), 4.07 (q, 1H, *J* = 4.0), 3.93 (ddd, 1H, *J* = 11.9, 9.8, 1.9), 3.73 (ddd, 1H, *J* = 12.2, 5.4, 3.3), 3.51 (td, 2H, *J* = 9.6, 4.8), 3.45 (dt, 1H, *J* = 10.0, 5.1), 3.22–3.13 (m, 3H), 2.73 (ddd, 1H, *J* = 15.2, 5.4, 1.8), 1.84 (d, 1H, *J* = 7.5), 1.74 (ddd, 1H, *J* = 14.1, 10.9, 3.6), 1.55–1.49 (m, 3H), 1.05 (m, 30H). **^{13}C-NMR** (125 MHz): δ 140.8, 136.8, 135.6, 134.2, 130.9, 129.6, 128.4, 127.7, 126.3, 126.1, 99.1, 71.8, 70.1, 61.4, 60.9, 59.9, 43.1, 38.9, 38.1, 35.5, 27.0, 19.3, 18.2, 12.5. **ESI-MS** *m/z* (rel int): (pos) 711.3 ([M+Na]$^+$, 100); (neg) 687.5 ([M–H]$^-$, 100).

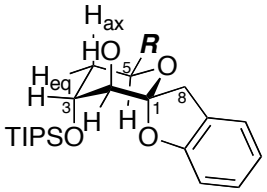




CDCl$_3$: $J_{2,3}$ = 3.6

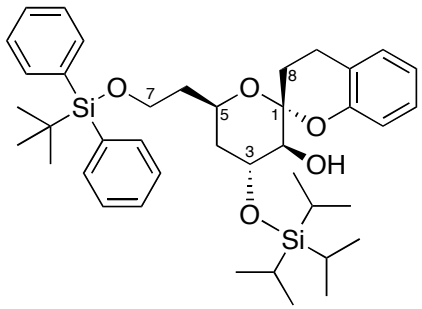
(+)-(2′*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*c*]oxepine-3,2′-pyran]-3′-ol (5o). Clear oil (39 mg, 43%). **TLC**: R_f 0.36 (4:1 hexanes/EtOAc). $[\alpha]_D^{19}$: +23.2° (*c* 1.3, $CHCl_3$). **IR** (NaCl, film): 3375 (O–H st), 3066, 3019, 2939, 2863, 1463, 1429, 1384, 1361, 1242, 1111 (C–O st), 1075, 1003, 886, 750, 699. **^{1}H-NMR** (500 MHz): δ 7.65–7.61 (m, 4H), 7.40–7.37 (m, 1H), 7.34–7.32 (m, 3H), 7.24 (t, 2H, *J* = 7.4), 7.18–7.10 (m, 3H), 7.05 (d, 1H, *J* = 7.1), 5.12 (d, 1H, *J* = 13.9), 4.44 (dt, 1H, *J* = 5.0, 3.1), 4.17 (d, 1H, *J* = 14.0), 4.07 (q, 1H, *J* = 3.6), 3.96 (ddd, 1H, *J* = 10.1, 8.0, 5.8), 3.78 (dt, 1H, *J* = 10.2, 5.1), 3.47 (dd, 1H, *J* = 7.2, 3.7), 3.19–3.14 (m, 1H), 2.66 (dd, 1H, *J* = 15.0, 7.8), 2.13–2.09 (m, 1H), 1.84–1.68 (m, 4H), 1.66 (d, 1H, *J* = 7.4), 1.61 (dt, 1H, *J* = 13.8, 3.0), 1.12–0.92 (m, 30H). **^{13}C-NMR** (125 MHz): δ 142.4, 140.2, 135.7, 134.0, 129.7, 128.8, 127.9, 127.5, 126.0, 120.2, 101.5, 72.0, 70.0, 63.4, 61.3, 60.2, 39.1, 35.5, 34.7, 28.7, 27.0, 19.3, 18.2, 12.4. **ESI-MS** *m*/*z* (rel int): (pos) 711.2 ([M+Na]$^+$, 100); (neg) 687.5 ([M–H]$^-$, 100).

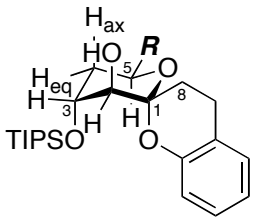




CDCl$_3$: $J_{2,3}$ = 3.0

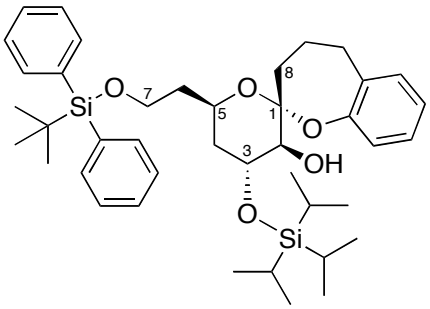
(+)-(2*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[benzofuran-2,2′-pyran]-3′-ol (5p). Clear oil (34 mg, 68%). **TLC**: R_f 0.31 (1:1 hexanes/EtOAc). $[\alpha]_D^{80}$: +51.8° (*c* 1.5, $CHCl_3$). **IR** (NaCl, film): 3416 (O–H st), 3060, 3045, 2944, 2864, 1599, 1471, 1428, 1384, 1358, 1240, 1106 (C–O st), 1059, 970, 878, 743, 698. **^{1}H-NMR** (500 MHz): δ 7.66 (dd, 2H, *J* = 8.0, 1.4), 7.53 (dd, 2H, *J* = 8.0, 1.3), 7.44–7.33 (m, 4H), 7.24 (dd, 1H, *J* = 7.3, 0.6), 7.18 (t, 2H, *J* = 7.6), 7.15–7.12 (m, 1H), 6.92 (td, 1H, *J* = 7.4, 0.8), 6.75 (d, 1H, *J* = 7.9), 4.91–4.86 (m, 1H), 4.27 (q, 1H, *J* = 3.0), 3.78–3.73 (m, 1H), 3.73 (dd, 1H, *J* = 9.1, 3.3), 3.62 (dt, 1H, *J* = 10.0, 5.0), 3.50 (d, 1H, *J* = 16.8), 3.09 (d, 1H, *J* = 16.7), 1.91–1.85 (m, 2H), 1.76–1.69 (m, 3H), 1.20–1.10 (m, 21H), 1.04–0.99 (s, 9H). **^{13}C-NMR** (125 MHz): δ 159.1, 135.7, 134.1, 129.5, 128.0, 127.7, 125.4, 124.8, 120.6, 110.8, 110.2, 71.0, 69.5, 63.4, 59.6, 41.1, 38.7, 34.5, 26.9, 19.3, 18.3, 12.5. **ESI-MS** *m*/*z* (rel int): (pos) 683.4 ([M+Na]$^+$, 100); (neg) 659.3 ([M–H]$^-$, 50).

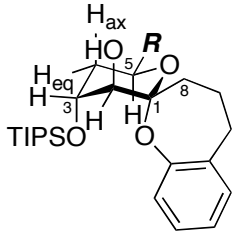




CDCl$_3$: $J_{2,3}$ = 3.4

(+)-(2*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[chroman-2,2′-pyran]-3′-ol (5q). Clear oil (12 mg, 16%). **TLC**: R_f 0.34 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +34.8° (*c* 0.9, $CHCl_3$). **IR** (NaCl, film): 3452 (O–H st), 3065, 2940, 2864, 2767, 1586, 1463, 1428, 1383, 1234, 1107 (C–O st), 1062, 1002, 886, 745, 699. **^{1}H-NMR** (500 MHz): δ 7.58–7.52 (m, 2H), 7.44–7.41 (m, 2H), 7.41–7.26 (m, 6H), 7.03–6.97 (m, 2H), 6.84–6.79 (m, 2H), 4.49–4.43 (m, 1H), 4.16 (q, 1H, *J* = 3.4), 3.66 (dt, 1H, *J* = 7.4, 3.6), 3.50-3.42 (m, 2H), 2.93–2.85 (m, 1H), 2.63–2.58 (m, 1H), 2.22–2.16 (m, 1H), 1.84–1.76 (m, 2H), 1.73 (d, 1H, *J* = 7.5), 1.70–1.57 (m, 3H), 1.22–1.05 (m, 21H), 0.96-0.85 (s, 9H). **^{13}C-NMR** (125 MHz): δ 152.2, 135.6, 134.2, 129.5, 128.9, 127.6, 127.2, 122.7, 120.7, 117.4, 98.4, 71.6, 70.1, 62.7, 60.2, 38.9, 35.3, 28.0, 26.9, 20.8, 19.2, 18.3, 12.4. **ESI-MS** *m*/*z* (rel int): (pos) 697.5 ([M+Na]$^+$, 100); (neg) 673.4 ([M–H]$^-$, 100).





CDCl$_3$: $J_{2,3}$ = 4.0

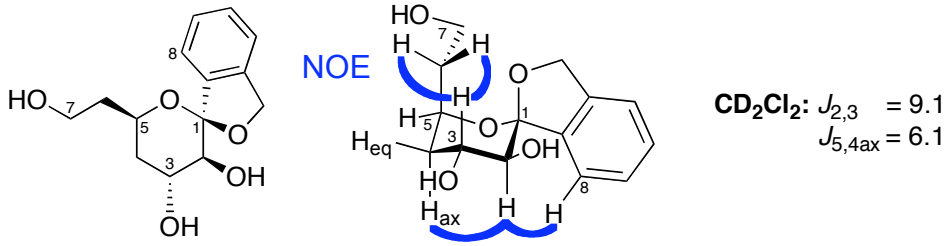
(+)-(2*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*b*]oxepine-2,2′-pyran]-3′-ol (5r). Clear oil (19 mg, 49%). **TLC**: R_f 0.19 (4:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +49.6° (*c* 0.9, $CHCl_3$). **IR** (NaCl, film): 3418 (O–H st), 3063, 2941, 2863, 1660, 1460, 1434, 1386, 1230, 1106 (C–O st), 1064, 1000, 935, 886, 763, 697. **^{1}H-NMR** (500 MHz): δ 7.63–7.60 (m, 4H), 7.44–7.35 (m, 6H), 7.02 (dd, 1H, *J* = 7.8, 1.0), 6.94–6.88 (m, 2H), 6.80 (td, 1H, *J* = 7.4, 1.2), 4.50 (ddt, 1H, *J* = 11.6, 8.6, 3.2), 4.12 (q, 1H, *J* = 4.0), 3.84 (m, 1H), 3.41 (ddd, 1H, *J* = 10.4, 7.7, 5.5), 3.34–3.29 (m, 1H), 2.85 (ddd, 1H, *J* = 14.3, 10.8, 4.0), 2.60–2.53 (m, 1H), 1.89–1.76 (m, 5H), 1.70–1.59 (m, 3H), 1.53 (ddd, 1H, *J* = 13.9, 6.7, 4.0), 1.10 (m, 30H). **^{13}C-NMR** (125 MHz): δ 169.6, 154.6, 149.1, 135.7, 134.1, 130.5, 129.7, 127.8, 127.1, 126.2, 122.3, 101.4, 76.8, 71.6, 64.2, 60.4, 38.0, 37.9, 33.9, 29.8, 27.0, 21.1, 19.4, 18.3, 12.5. **ESI-MS** *m*/*z* (rel int): (pos) 711.3 ([M+Na]$^+$, 65); (neg) 687.3 ([M–H]$^-$, 100).

VI. DESILYLATION OF SPIROKETALS (7, 8)

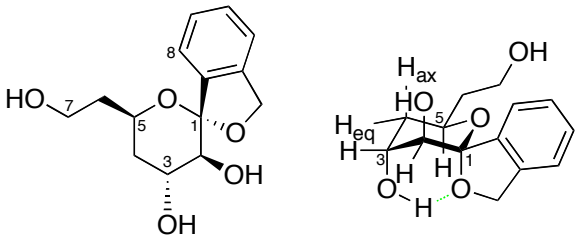
GENERAL PROCEDURE FOR DESILYLATION OF SPIROKETALS

Spiroketals **4j**, **5j** (1.0 equiv) were dissolved in 1:1 CH_3CN/THF (0.1 M), followed by addition of tris(dimethylamino)sulfonium difluorotrimethylsilicate (TAS-F, 10 equiv). The reaction was stirred for 12 h at rt, then concentrated by rotary evaporation. Purification by silica flash chromatography (10:1 CH_2Cl_2/MeOH) provided the desilylated spiroketals **7**, **8**, respectively.

^{1}H-NMR resonances were assigned based on COSY analysis of purified products. The 'retention' spiroketal **7** and 'inversion' spiroketal **8** could be readily distinguished by examination of diagnostic ^{1}H-NMR peaks: C5-H (δ **8** > δ **7** (4.55 > 4.34)). Conformational assignments were based on analyses of NOESY spectra and/or coupling constants.[17] *J* values were determined by *J*-resolve experiments. The $^4C_1$ and $^1C_4$ chair conformers could be distinguished based on *J* values: $^4C_1$ chair conformation (*threo*: J_{23} >7.0 and J_{54ax} > 7.0; *erythro*: J_{23} < 7.0 and J_{54ax} > 7.0) or $^1C_4$ chair conformation (*erythro*: J_{23} > 7.0 and J_{54ax} < 7.0).



(–)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-hydroxyethyl)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′,4′-diol (7). White solid (8 mg, 89%). **TLC**: R_f 0.29 (20:1 EtOAc/MeOH). $[\alpha]_D^{19}$: –5.1° (*c* 0.4, $CHCl_3$). **IR** (NaCl, film): 3371 (O–H st), 3046, 2928, 2868, 1455, 1420, 1373, 1253, 1199, 1067 (C–O st), 1004, 960, 746, 725. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.39–7.37 (m, 3H, Ar-H), 7.27 (m, 1H, C8-H), 5.23 (d, 1H, C12-H, *J* = 12.7), 5.08 (d, 1H, C12-H, *J* = 12.7), 4.36–4.31 (m, 1H, C5-H), 4.20 (td, 1H, C3-H, *J* = 9.5, 6.1), 3.81 (t, 1H, C2-H, *J* = 9.1), 3.76 (td, 2H, C7-H, *J* = 4.4, 0.5), 2.60 (s, 1H, C-OH), 2.44 (ddt, 1H, C6-H, *J* = 14.1, 10.7, 5.4), 2.01 (ddd, 1H, C4-H, *J* = 13.4, 5.3, 2.1), 1.97 (ddd, 1H, C4-H, *J* = 13.4, 10.4, 6.1), 1.88 (brs, 1H, C-OH), 1.75 (dtd, 1H, C6-H, *J* = 14.0, 6.8, 4.7), 1.66–1.65 (brs, 1H, C-OH). **^{1}H-NMR** (500 MHz, CD_3OD): δ 7.39–7.32 (m, 3H), 7.30–7.29 (m, 1H), 5.15 (d, 1H, *J* = 14.9), 5.10 (d, 1H, *J* = 14.9), 4.22 (dtd, 1H, *J* = 9.8, 5.8, 2.1), 4.15 (ddd, 1H, *J* = 10.5, 9.3, 4.9), 3.76 (d, 1H, *J* = 9.1), 3.64 (ddd, 2H, *J* = 7.2, 5.6, 1.8), 2.36 (ddt, 1H, *J* = 13.7, 9.9, 5.7), 2.11 (ddd, 1H, *J* = 13.3, 5.0, 2.3), 2.01 (ddd, 1H, *J* = 13.3, 10.6, 6.2), 1.74 (dtd, 1H, *J* = 13.8, 7.0, 5.4). **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 139.9, 138.7, 129.7, 128.3, 122.1, 121.2, 111.9, 76.6, 72.9, 72.4, 67.0, 60.9, 38.0, 36.3. **ESI-MS** *m/z* (rel int): (pos) 289.1 ($[M+Na]^+$, 100); (neg) 265.1 ($[M–H]^-$, 100).



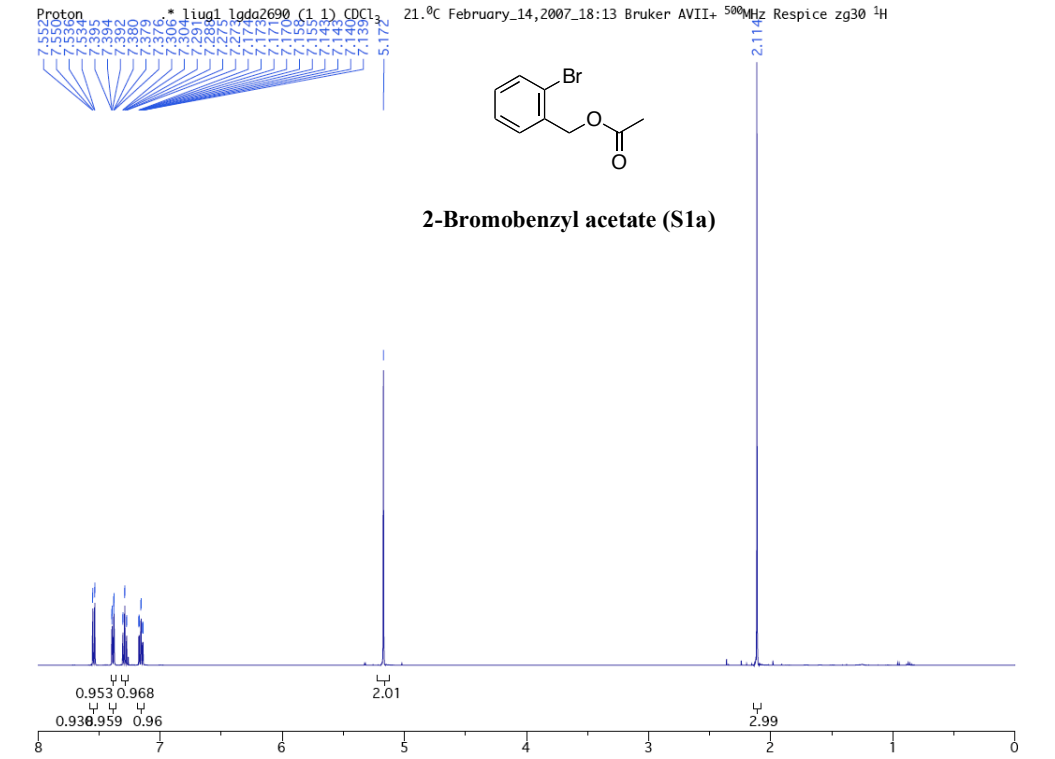
CD$_2$Cl$_2$: $J_{2,3}$ = 3.2
$J_{5,4ax}$ = 12.2

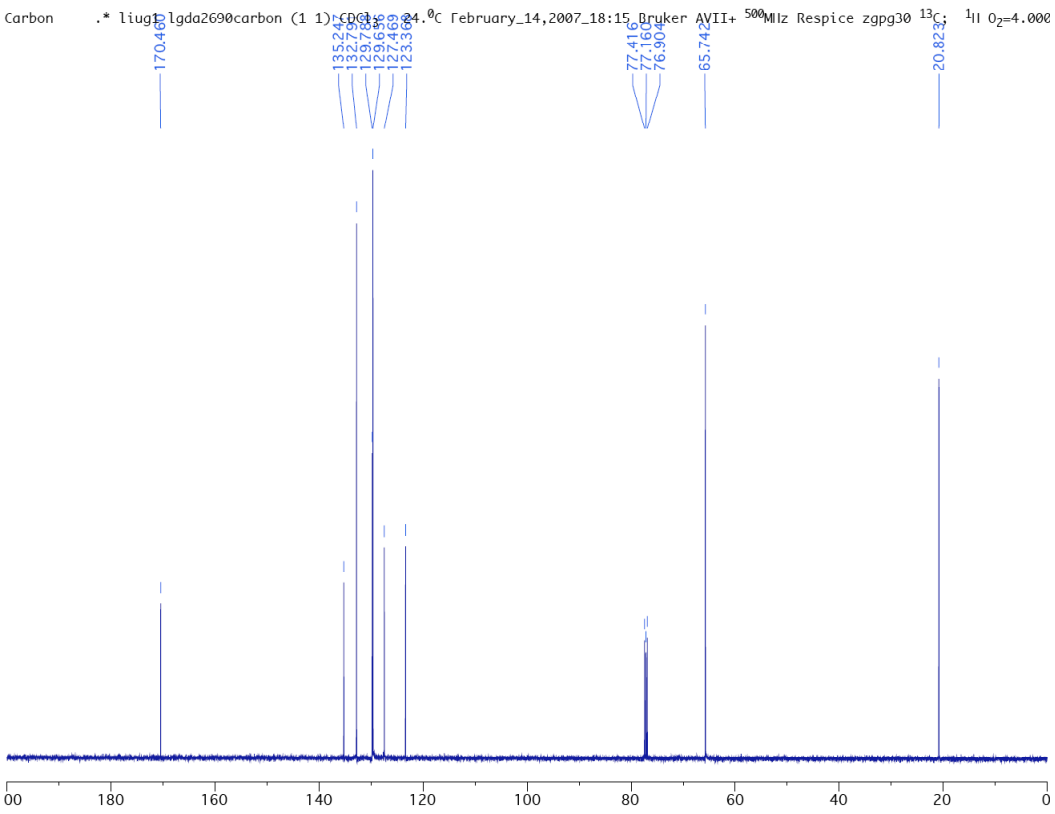
(+)-(1*S*,3′*S*,4′*R*,6′*R*)-6′-(2-hydroxyethyl)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′,4′-diol (8). Clear oil (11 mg, 86%). **TLC**: R_f 0.43 (20:1 EtOAc/MeOH). $[\alpha]_D^{20}$: +59.1° (*c* 0.5, $CHCl_3$). **IR** (NaCl, film): 3394 (O–H st), 3079, 3044, 2928, 2878, 1455, 1408, 1363, 1296, 1259, 1063 (C–O st), 1009, 964, 913, 758, 729. **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ 7.59 (dd, 1H, Ar-H, *J* = 7.6, 0.2), 7.38 (td, 1H, Ar-H, *J* = 7.5, 1.1), 7.32–7.27 (m, 2H, Ar-H), 5.20 (d, C12-H, *J* = 12.5, 1H), 5.12 (d, 1H, C12-H, *J* = 12.5), 4.55 (dddd, 1H, C5-H, *J* = 12.2, 8.4, 3.9, 2.6), 3.97 (ddd, 1H, C3-H, *J* = 10.2, 6.1, 3.2), 3.88 (d, 1H, C3-OH, *J* = 10.4), 3.72–3.70 (m, 1H, C2-H), 3.66 (app q, 2H, C7-H, *J* = 5.1), 2.18 (d, 1H, C2-OH, *J* = 7.4), 2.01 (ddd, 1H, C4-H, *J* = 14.3, 12.2, 3.2), 1.93 (brs, 1H, C7-OH), 1.82–1.74 (m, 1H, C6-H), 1.74–1.68 (m, 2H, C4-H, C6-H). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.62 (d, 1H, *J* = 7.6), 7.39 (t, 1H, *J* = 7.5), 7.32 (t, 1H, *J* = 7.5), 7.27 (m, 1H), 5.24 (d, 1H, *J* = 12.4), 5.14 (d, 1H, *J* = 12.5), 4.56 (ddt, 1H, *J* = 11.9, 8.7, 3.1), 4.07–4.02 (m, 2H), 3.75 (m, 3H), 2.28 (d, 1H, *J* = 7.6), 2.21 (t, 1H, *J* = 5.5), 2.08 (td, 1H, *J* = 13.3, 2.6), 1.90–1.83 (m, 1H), 1.80–1.74 (m, 2H). **^{1}H-NMR** (500 MHz, CH_3OD): δ 7.68–7.66 (m, 1H), 7.38–7.35 (m, 1H), 7.30–7.27 (m, 2H), 5.15 (d, 1H, *J* = 17.5), 5.10 (d, 1H, *J* = 17.5), 4.51–4.46 (m, 1H), 3.99 (q, 1H, *J* = 3.1), 3.65 (d, 1H, *J* = 2.9), 3.60 (t, 2H, *J* = 6.5), 2.07 (ddd, 1H, *J* = 14.1, 12.1, 3.4), 1.79 (ddt, 1H, *J* = 14.0, 8.1, 6.0), 1.71–1.64 (m, 2H). **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 138.9, 138.8, 129.8, 128.0, 124.5, 121.1, 109.8, 72.7, 69.5, 69.3, 67.5, 61.1, 37.7, 33.1. **ESI-MS** *m*/*z* (rel int): (pos) 289.0 ($[M+Na]^+$, 100); (neg) 265.0 ($[M–H]^-$, 100).

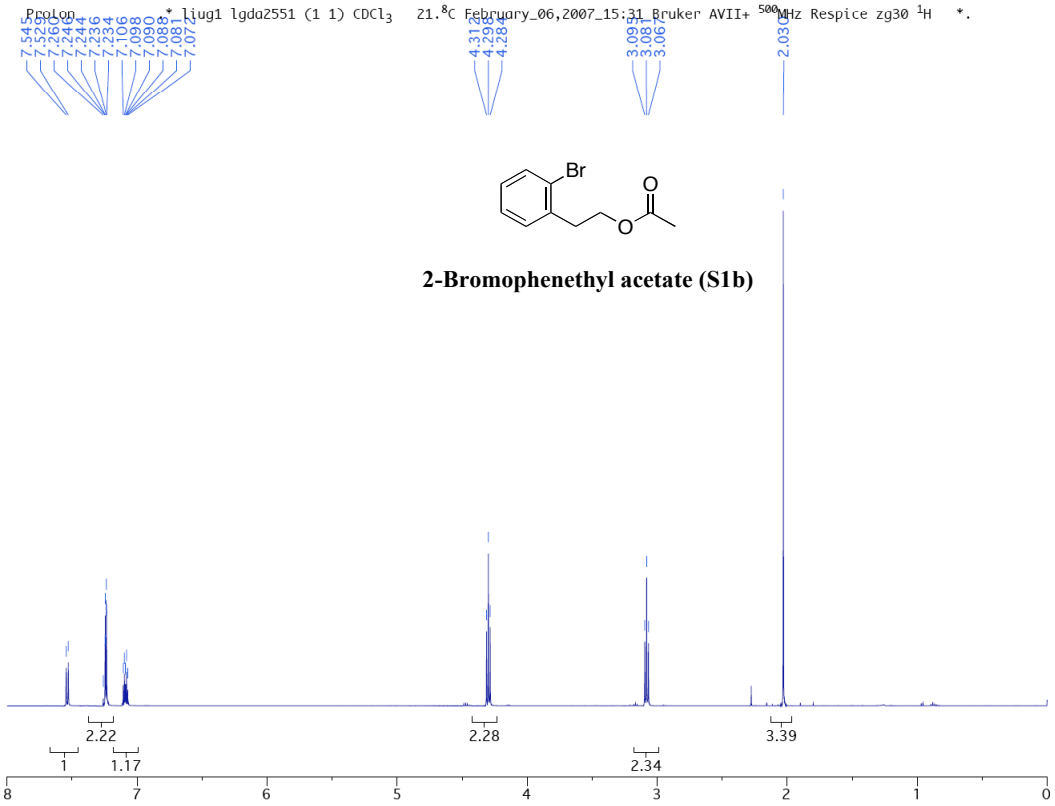
VII. ^{1}H-NMR and ^{13}C-NMR spectra (S1, S2, 2, 4, 5, 7, 8)

A. Synthesis of sidechain precursors (**S1a–i**, **S2**) S38
B. Attachment of *C*1 sidechains via cross coupling reactions (**2a–r**) S48
C. Spirocyclization with retention of configuration (Ti[Oi-Pr]$_4$) (**4a–r**) S66
D. Spirocyclization with inversion of configuration (MeOH or AcOH) (**5a–r**) S84
E. Desilylation of spiroketals (**7, 8**) S97

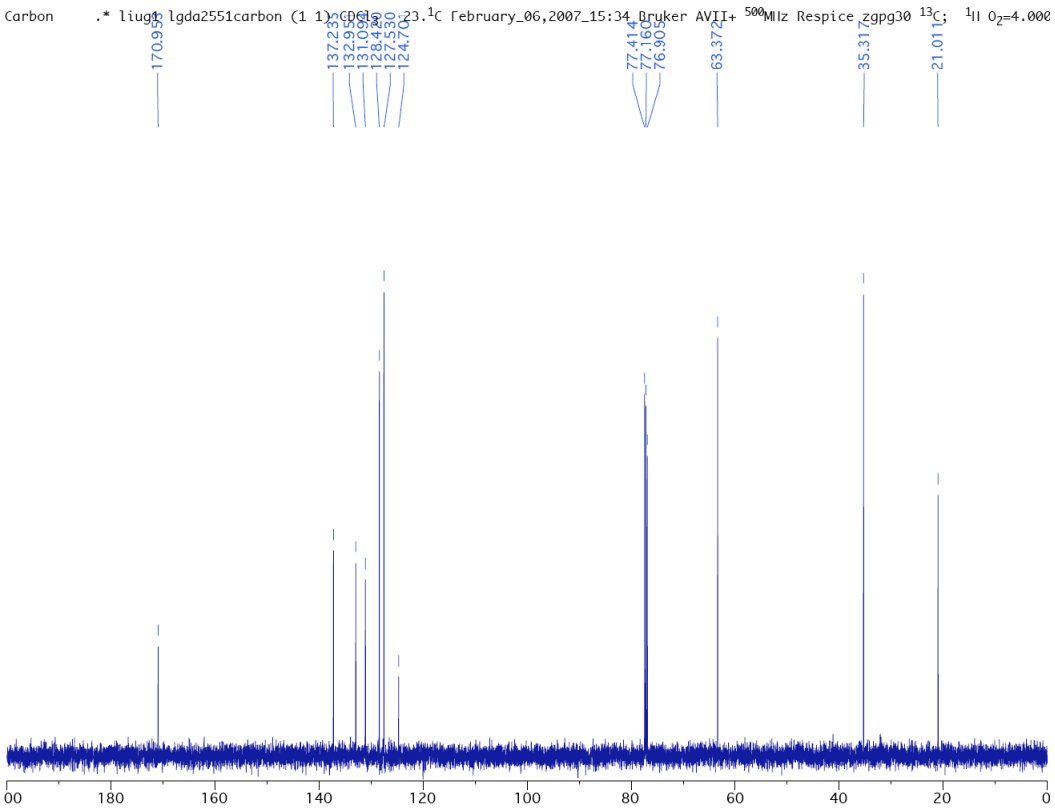
A. SYNTHESIS OF SIDECHAIN PRECURSORS (S1a–i, S2)

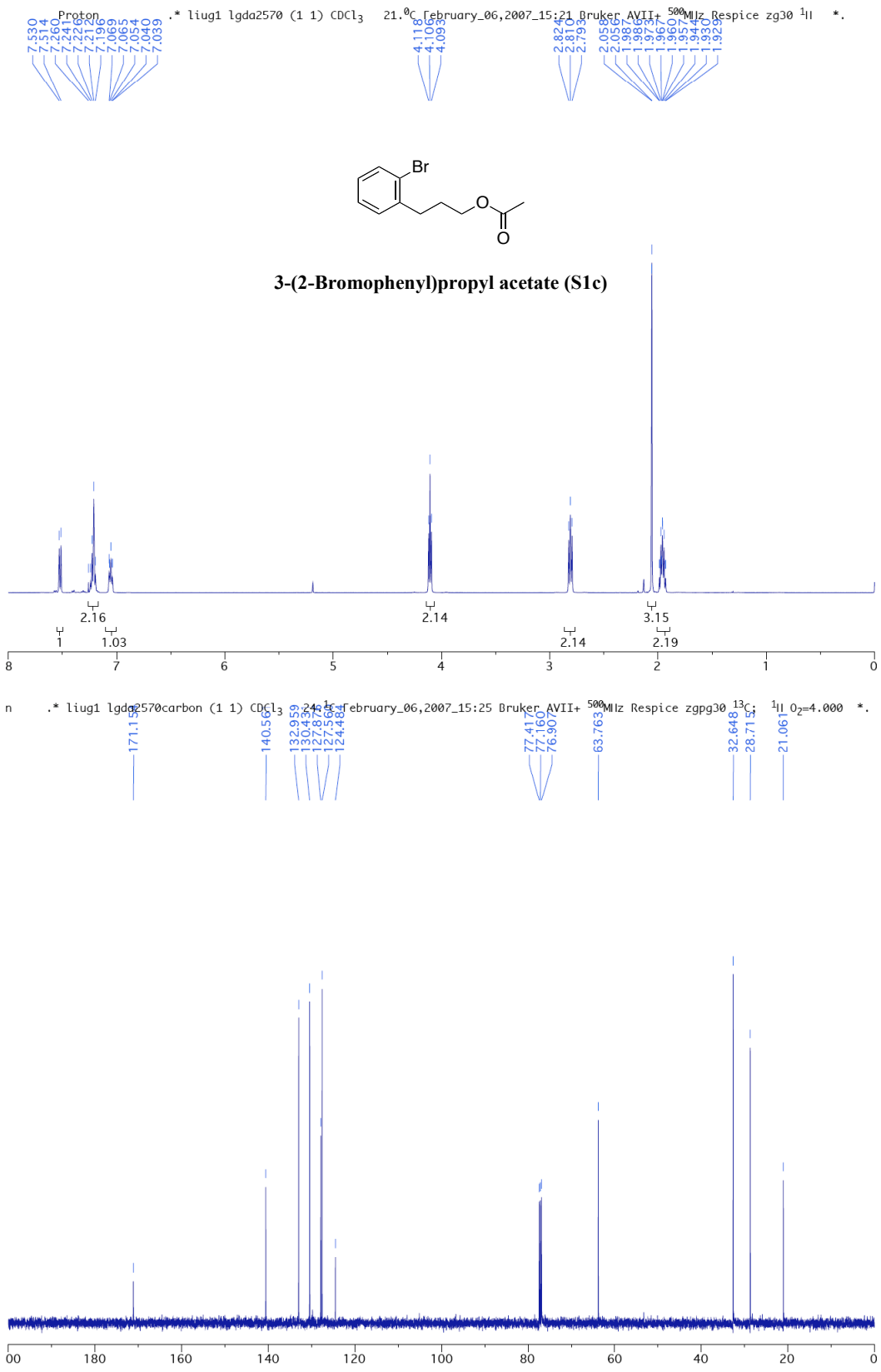


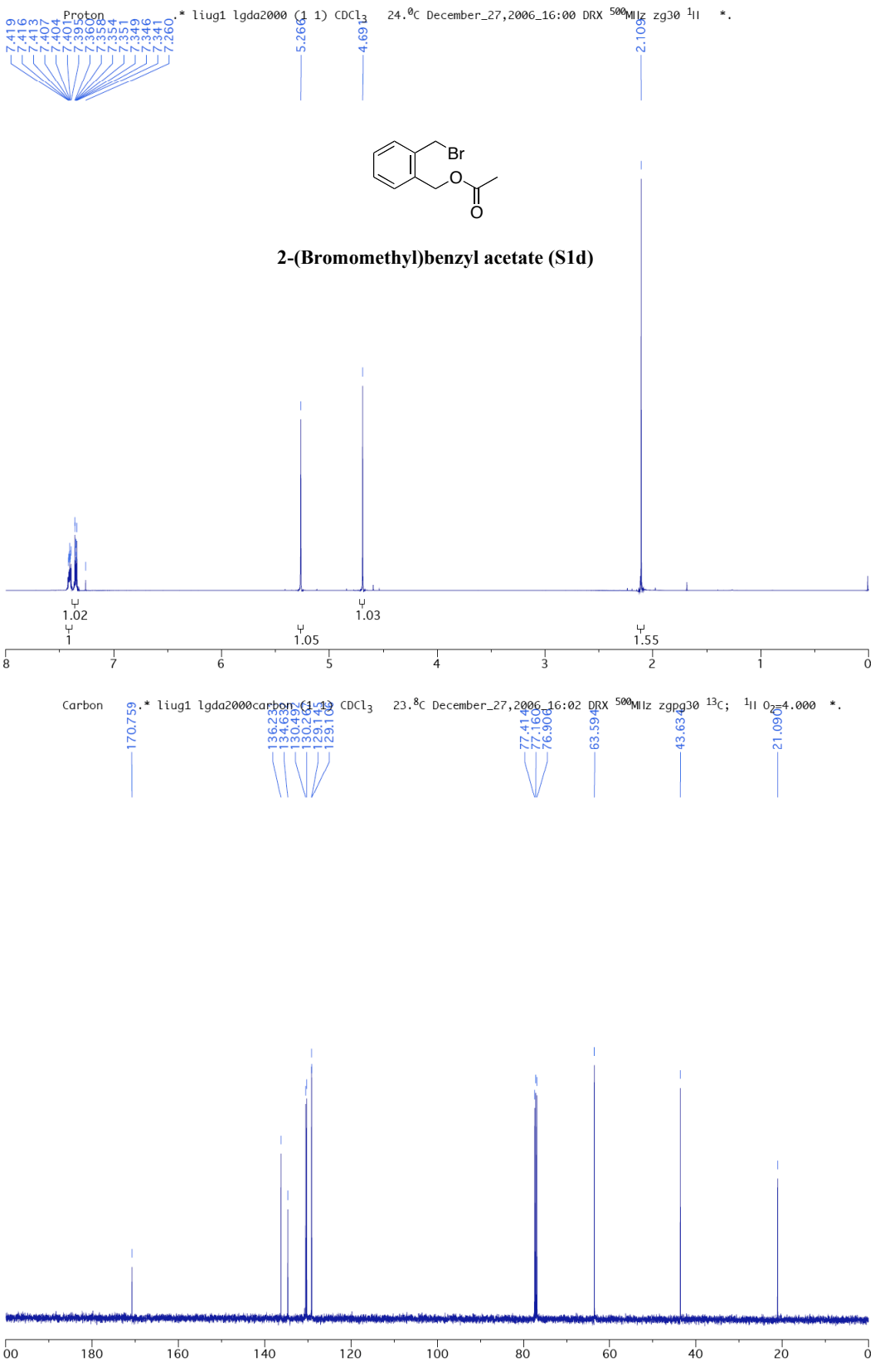




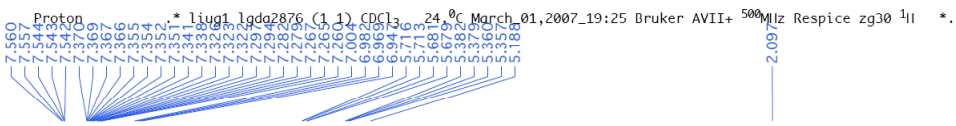
2-Bromophenethyl acetate (S1b)

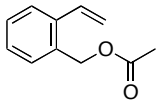



Br
O
O
3-(2-Bromophenyl)propyl acetate (S1c)
2.16
1.03
2.14
2.14
3.15
2.19

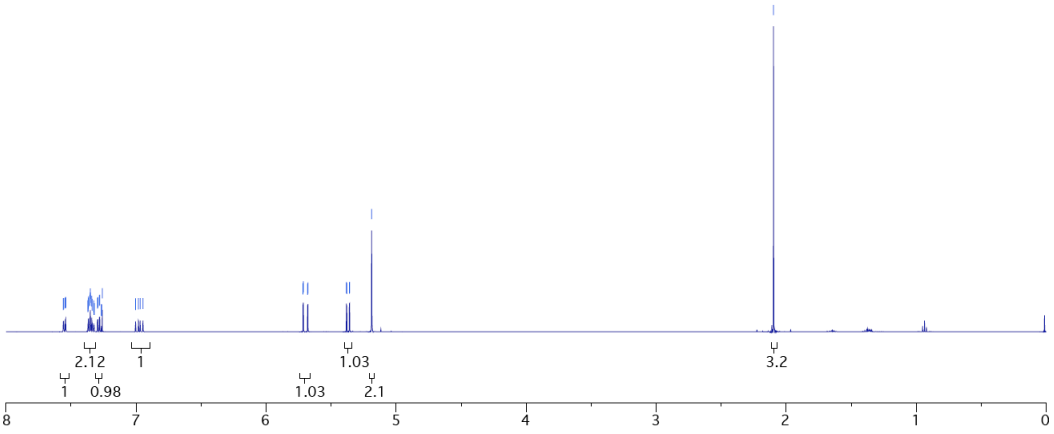


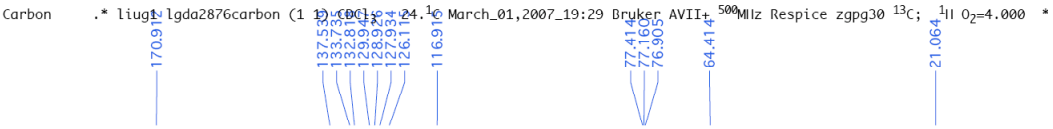
2-(Bromomethyl)benzyl acetate (S1d)

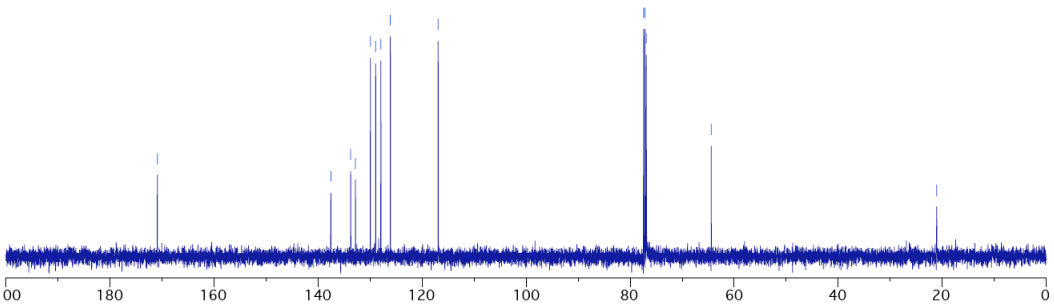


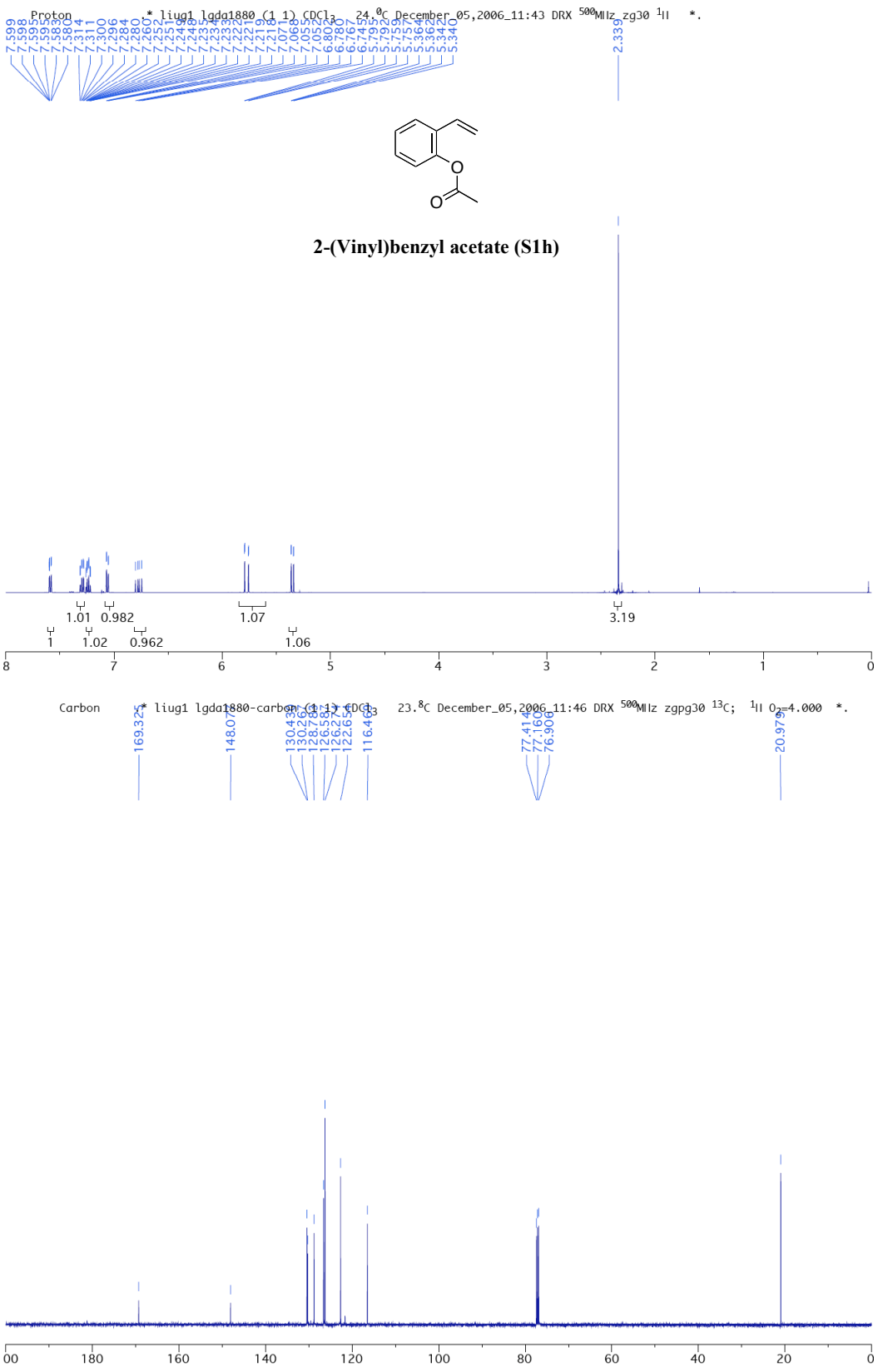


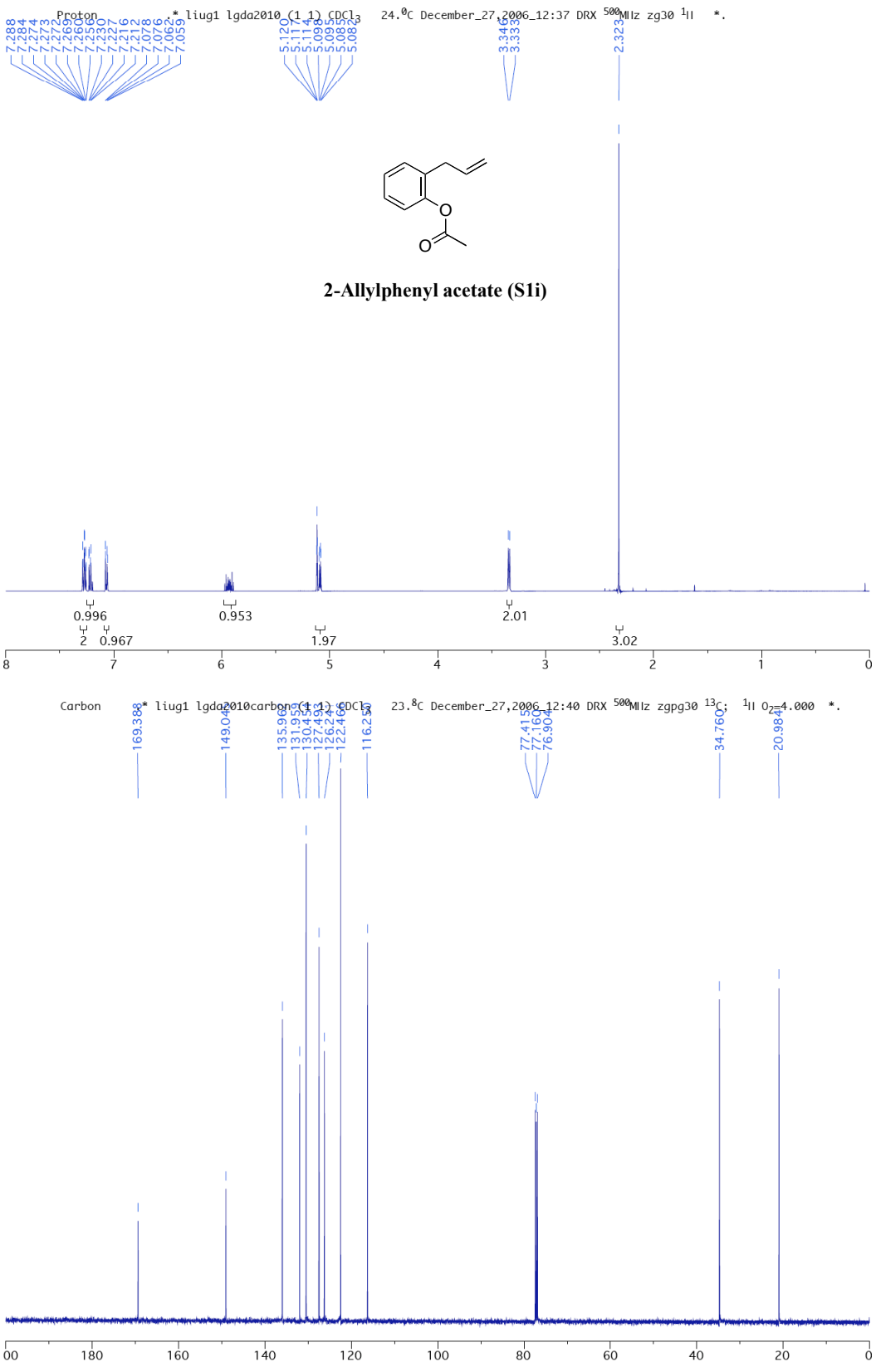
2-(Vinyl)phenyl acetate (S1f)

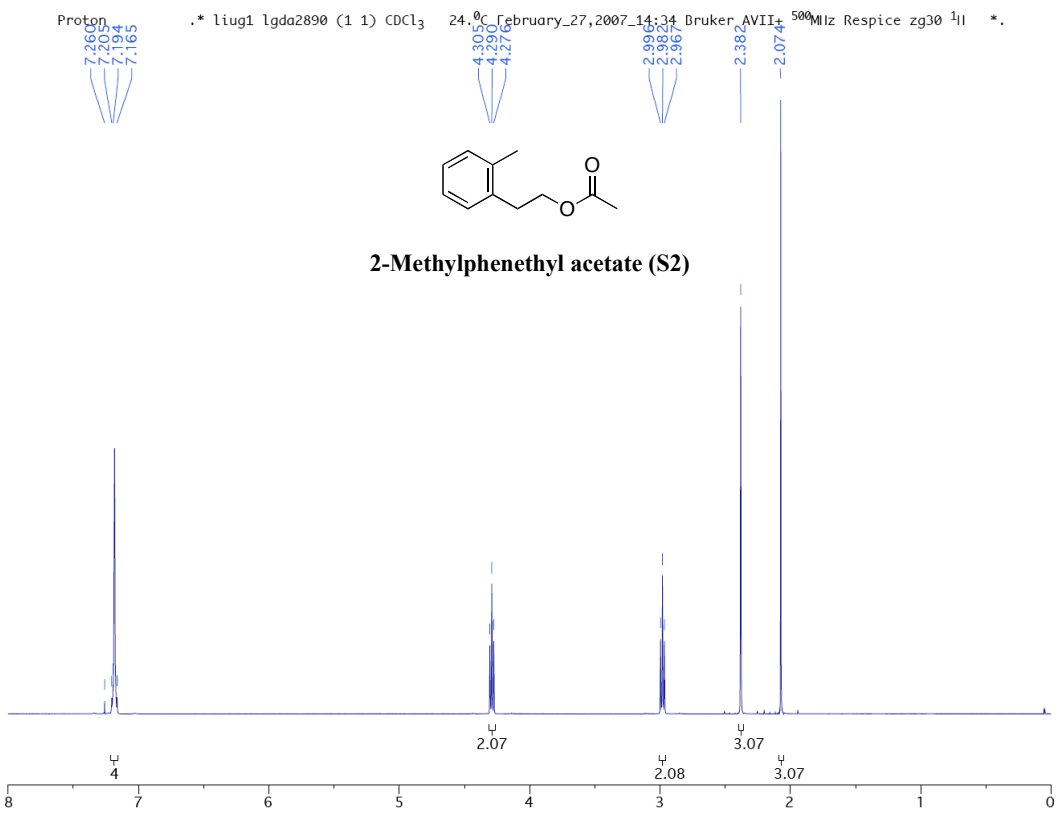




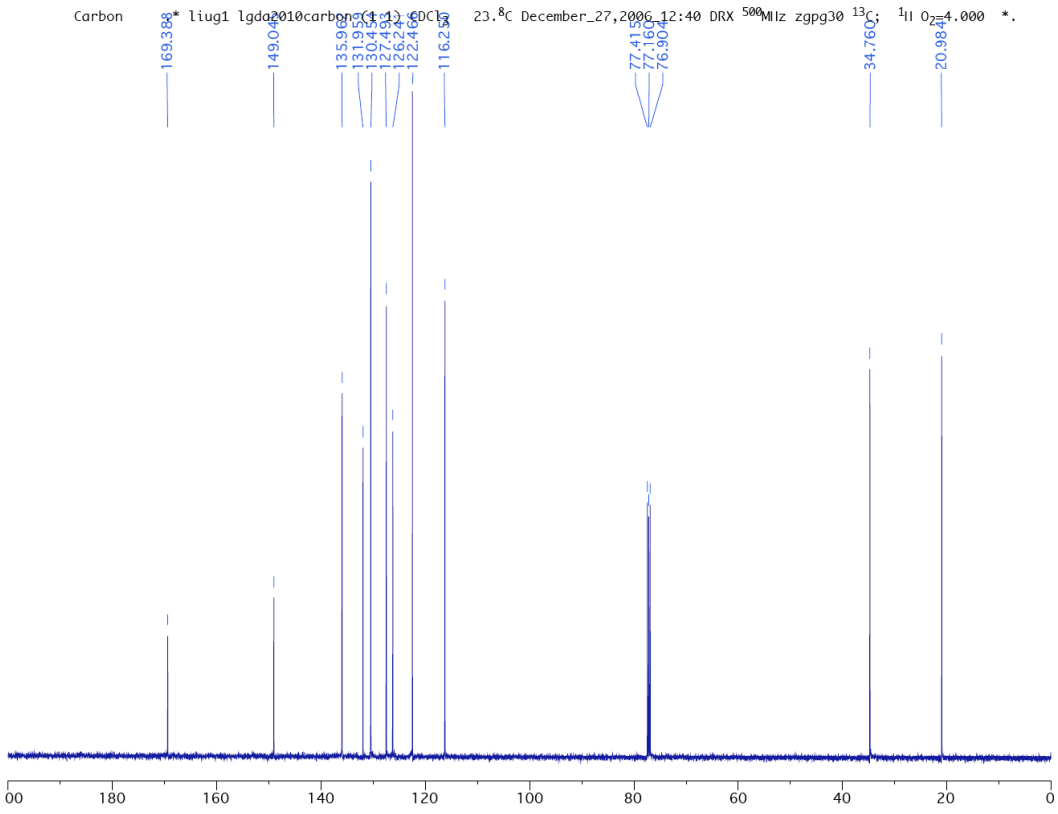


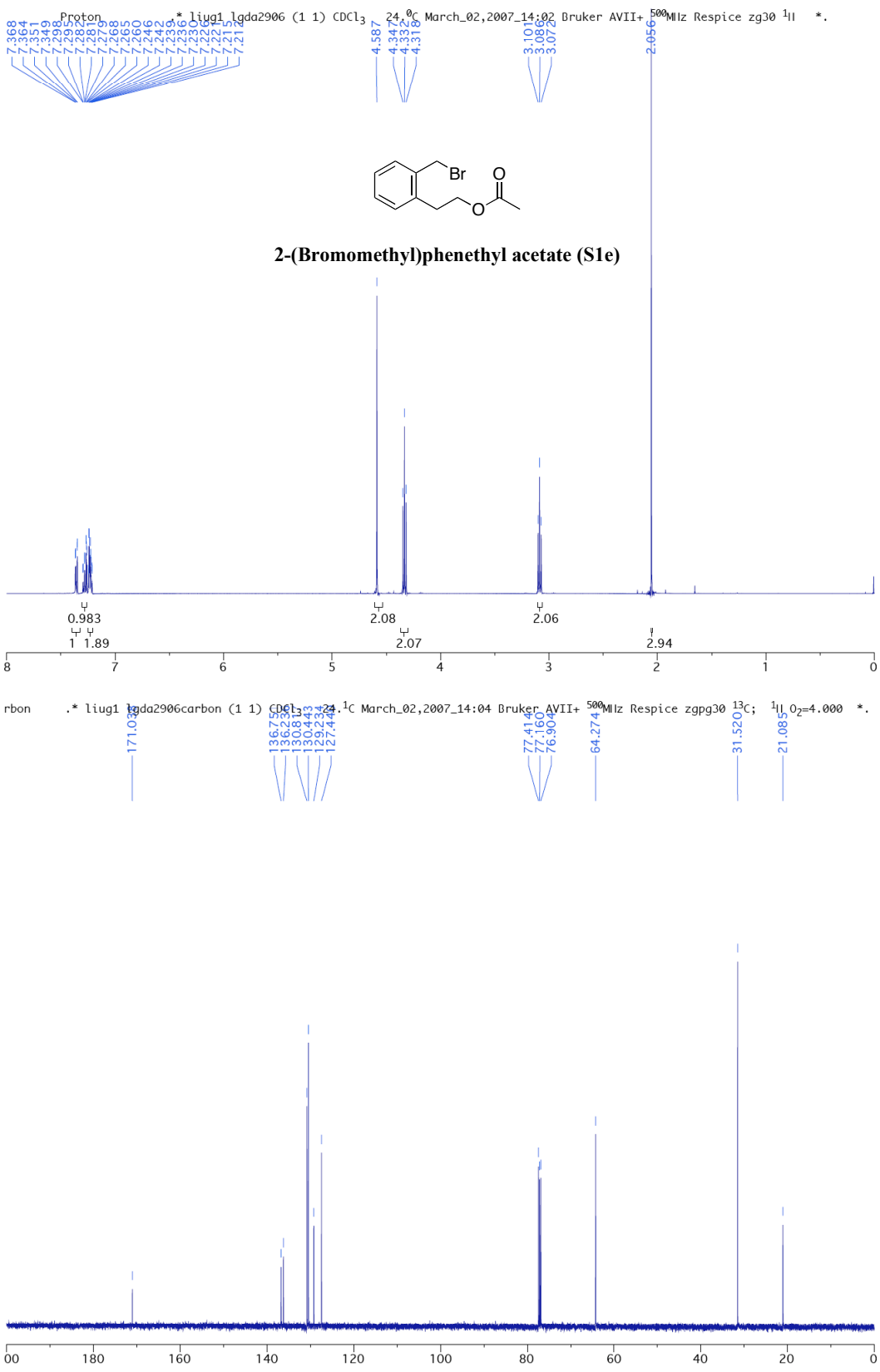

Proton * liug1 lgda1880 (1 1) CDCl3 24.0°C December_05,2006_11:43 DRX 500MHz zg30 1H *.
7.599
7.598
7.595
7.595
7.583
7.580
7.314
7.311
7.300
7.296
7.284
7.280
7.260
7.252
7.251
7.249
7.248
7.235
7.234
7.233
7.222
7.221
7.219
7.218
7.071
7.069
7.057
7.052
6.802
6.780
6.767
6.745
5.795
5.792
5.759
5.757
5.364
5.362
5.342
5.340
2.339
O
O
2-(Vinyl)benzyl acetate (S1h)
1.01
0.982
1.07
3.19
1
1.02
0.962
1.06
8
7
6
5
4
3
2
1
0
Carbon * liug1 lgda1880-carbon (1 1) CDCl3 23.8°C December_05,2006_11:46 DRX 500MHz zgpg30 13C; 1H O1=4.000 *.
169.325
148.076
130.463
130.262
128.788
126.588
126.252
122.657
116.463
77.414
77.160
76.906
20.975
00
180
160
140
120
100
80
60
40
20
0


Proton * liug1 lgda2010 (1 1) CDCl3 24.0C December_27,2006_12:37 DRX 500MHz zg30 1H *.
7.288
7.284
7.274
7.273
7.272
7.269
7.260
7.256
7.230
7.227
7.216
7.212
7.078
7.076
7.062
7.059
5.120
5.117
5.114
5.098
5.095
5.085
5.082
3.346
3.333
2.323
O
O
2-Allylphenyl acetate (S1i)
0.996
0.953
2.01
2
0.967
1.97
3.02
8
7
6
5
4
3
2
1
0
Carbon * liug1 lgda2010carbon (1 1) CDCl3 23.8C December_27,2006_12:40 DRX 500MHz zgpg30 13C; 1H O2=4.000 *.
169.388
149.044
135.960
131.955
130.453
127.494
126.244
122.466
116.250
77.415
77.163
76.904
34.760
20.984
00
180
160
140
120
100
80
60
40
20
0

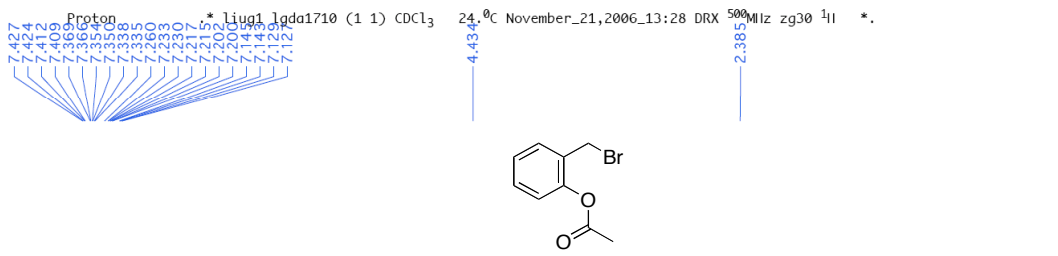


2-Methylphenethyl acetate (S2)

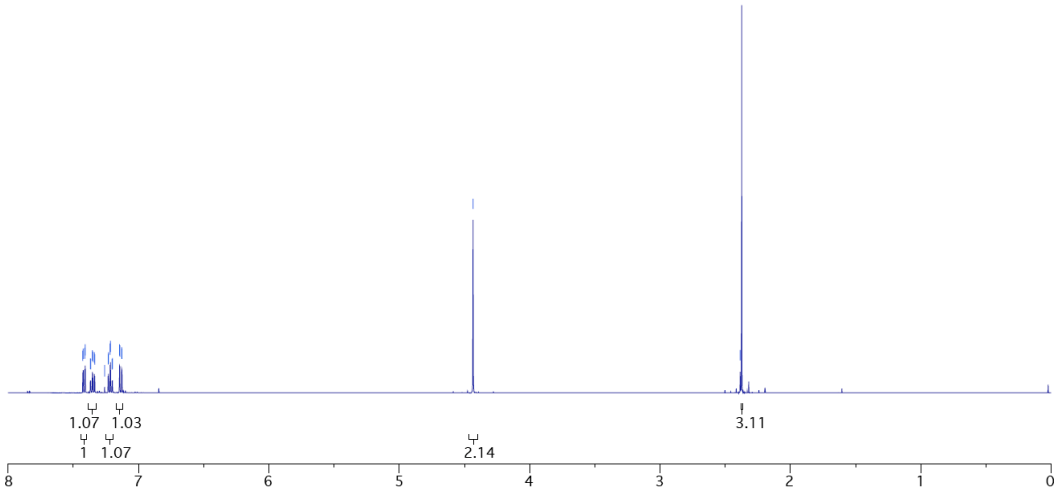


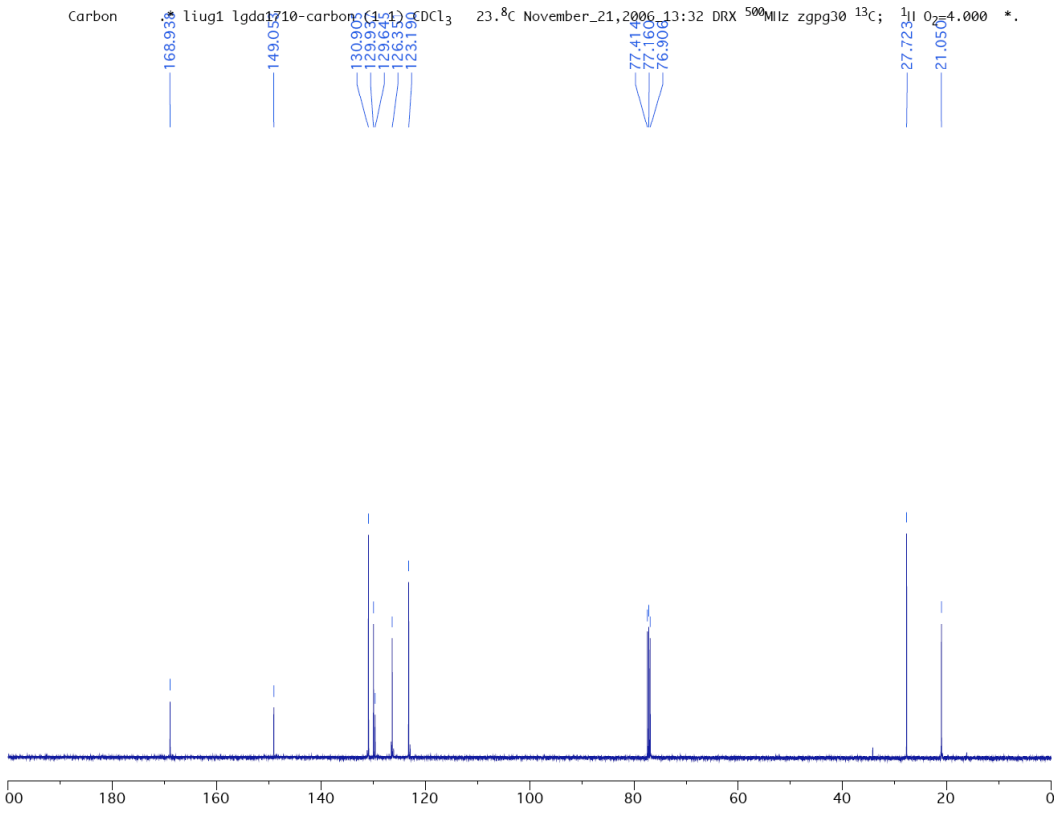


2-(Bromomethyl)phenethyl acetate (S1e)

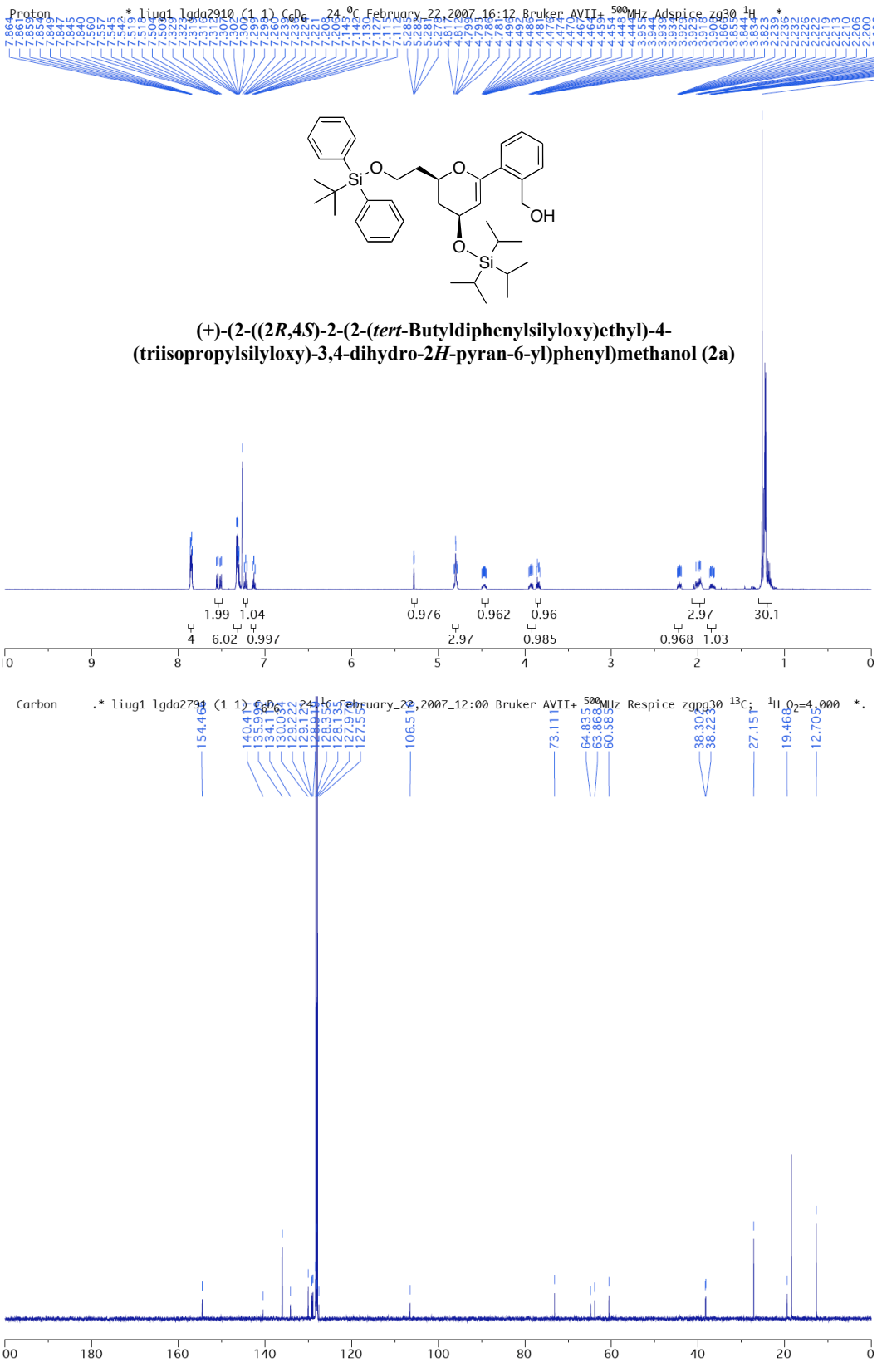


2-(Bromomethyl)phenyl acetate (S1g)

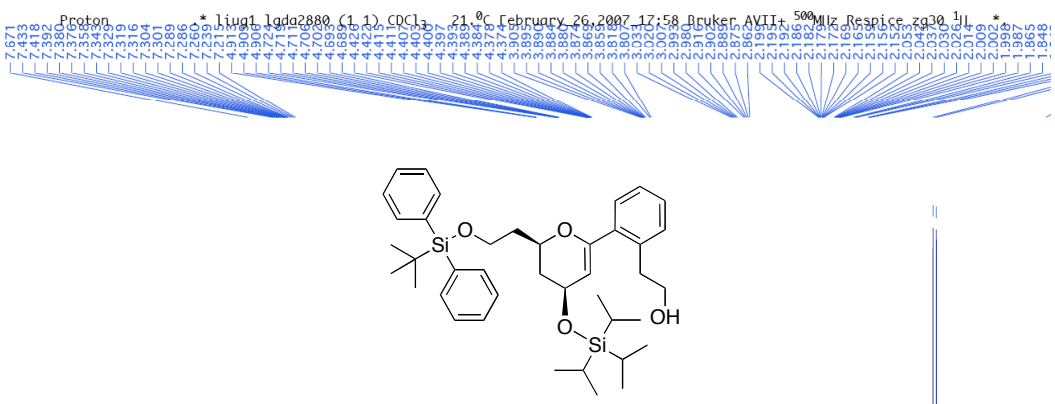




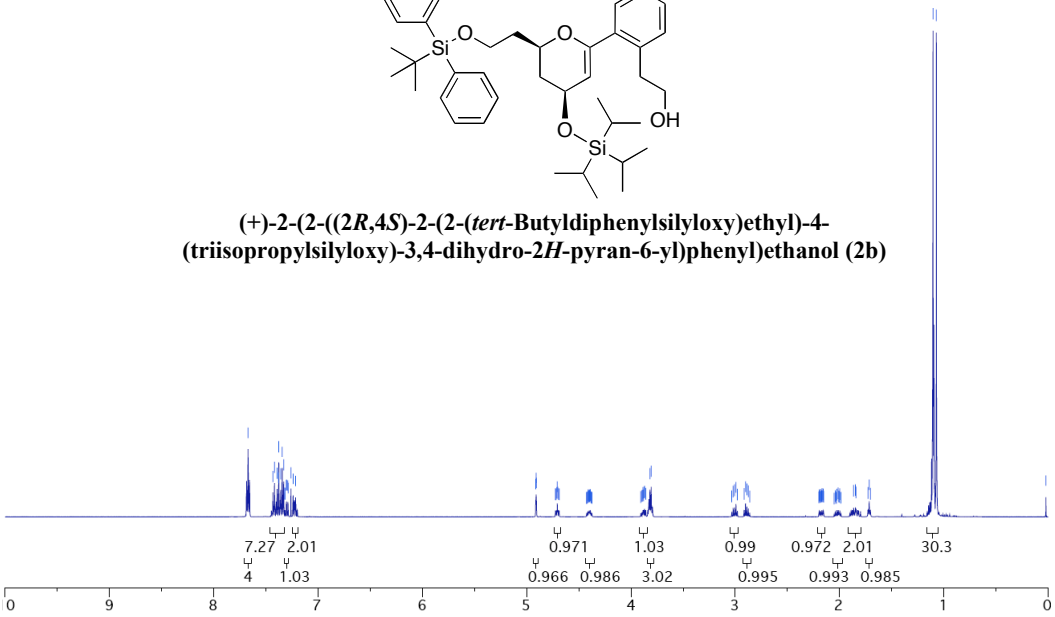
B. ATTACHMENT OF *C*1 SIDECHAINS VIA CROSS COUPLING REACTIONS (2a–r)

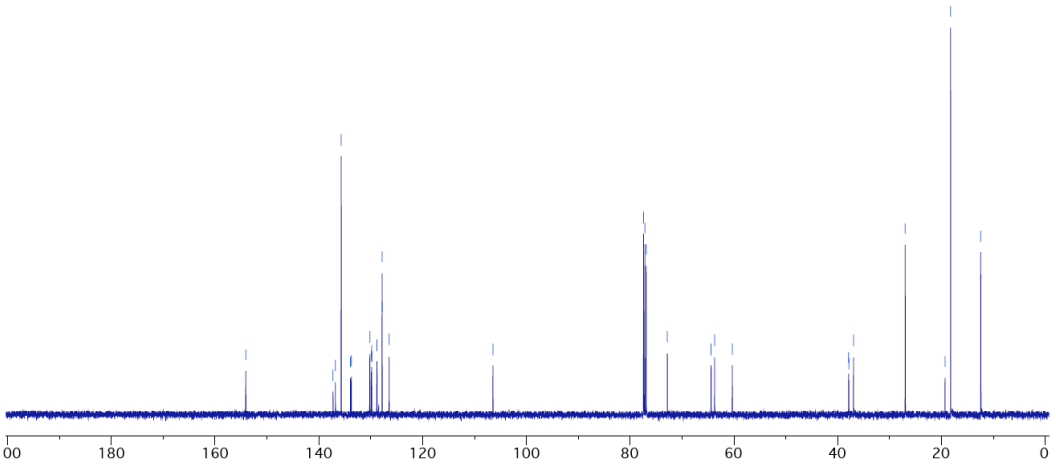


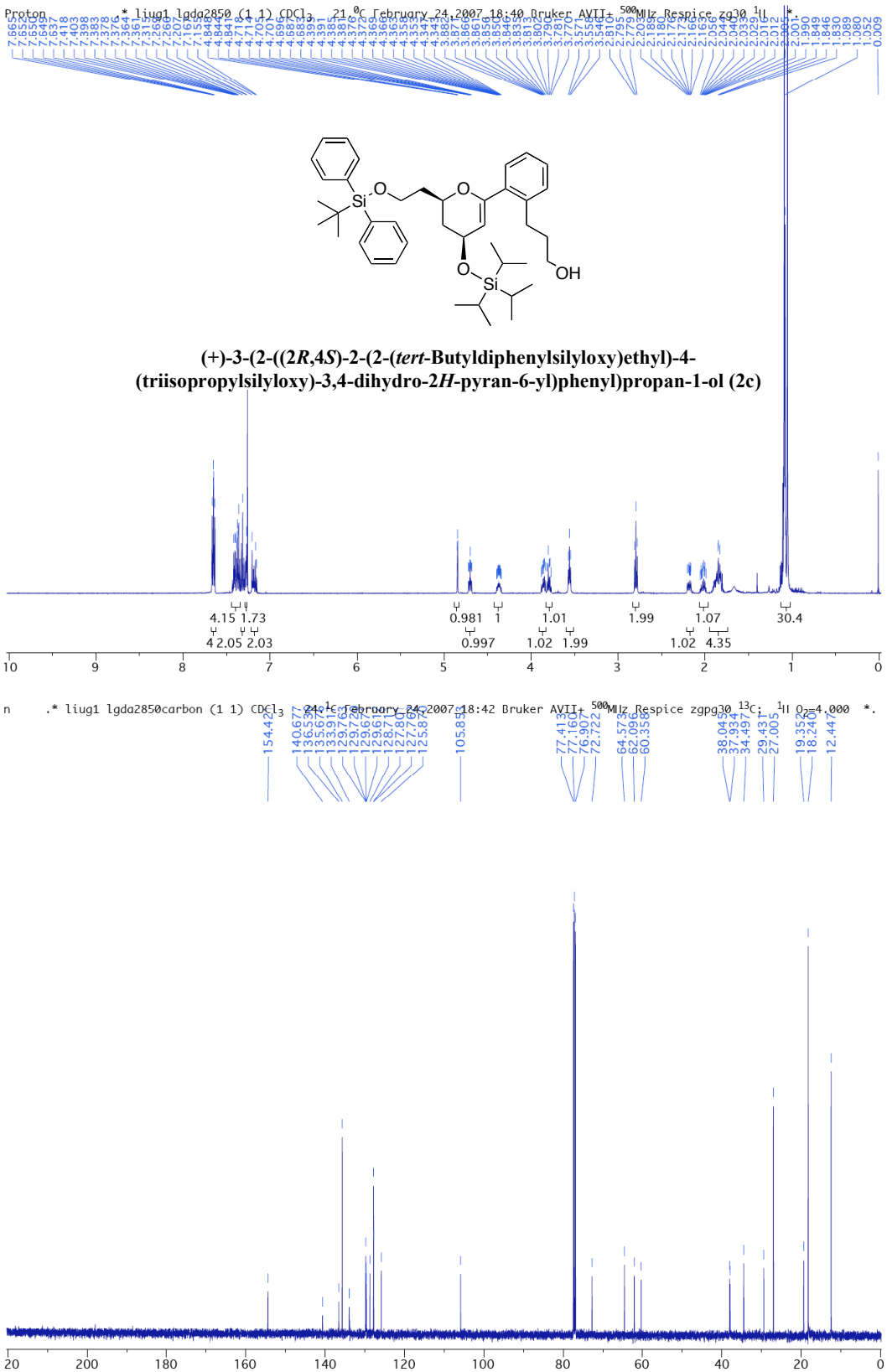
(+)-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)methanol (2a)



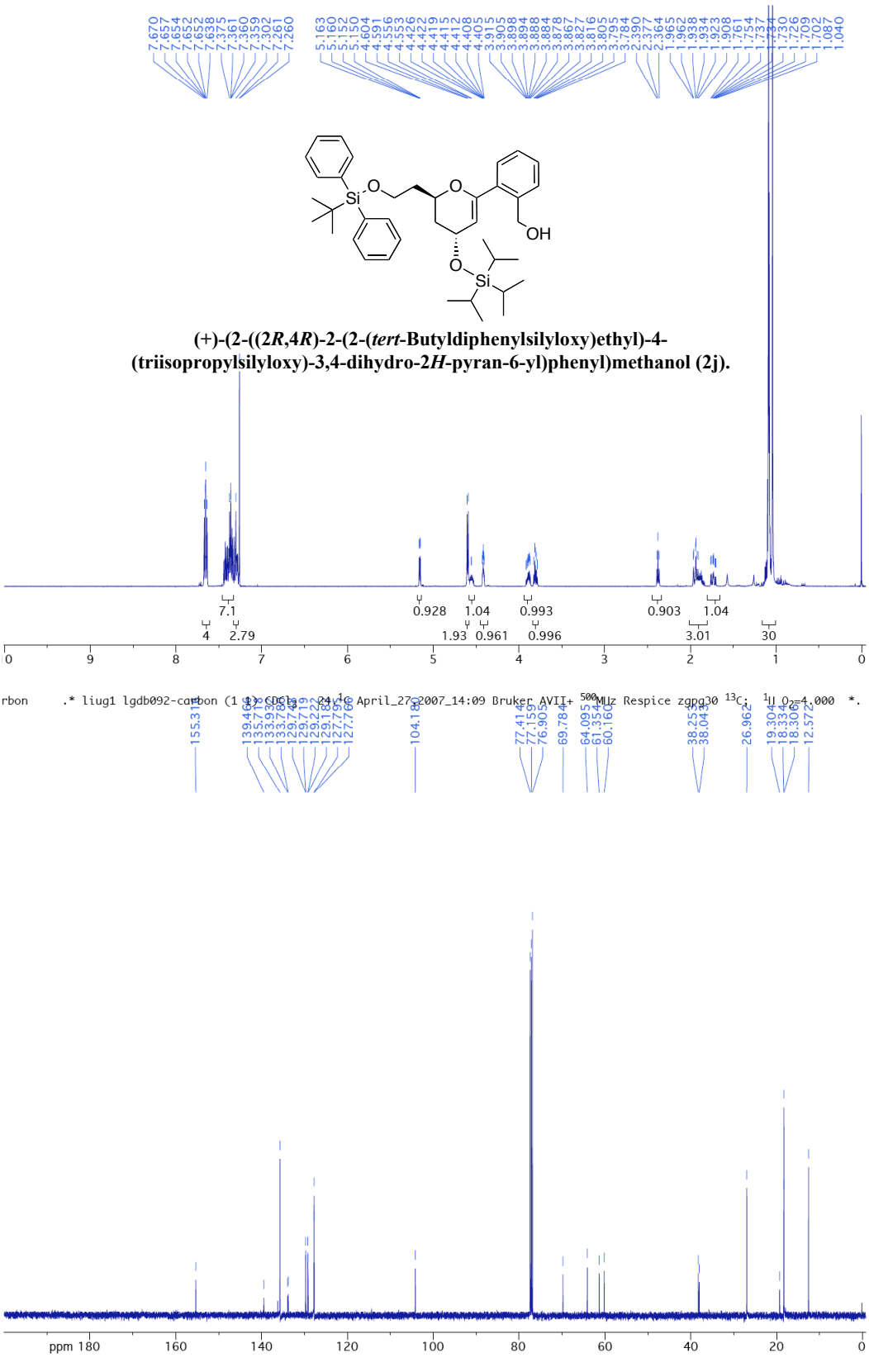
(+)-2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)ethanol (2b)



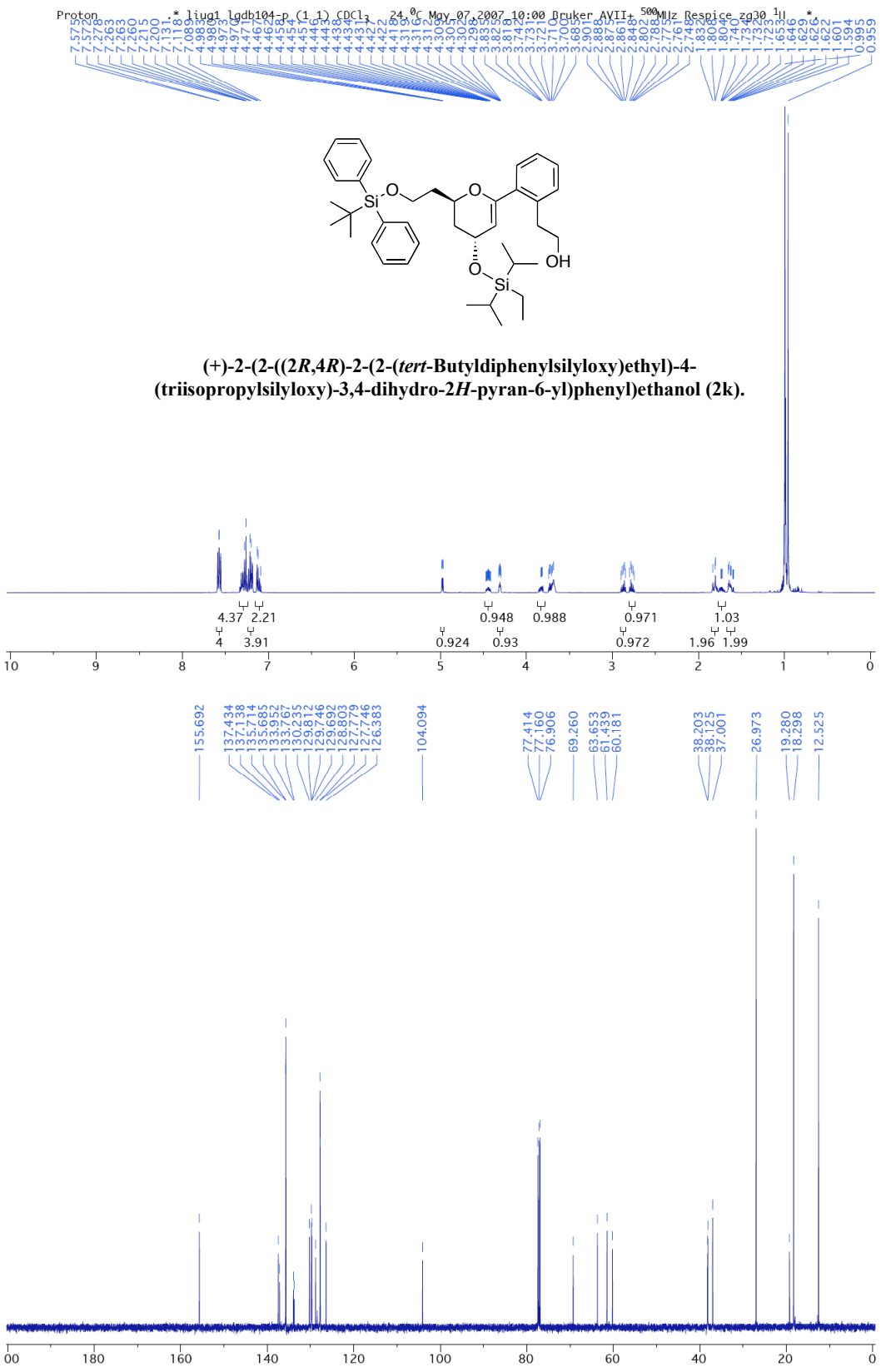




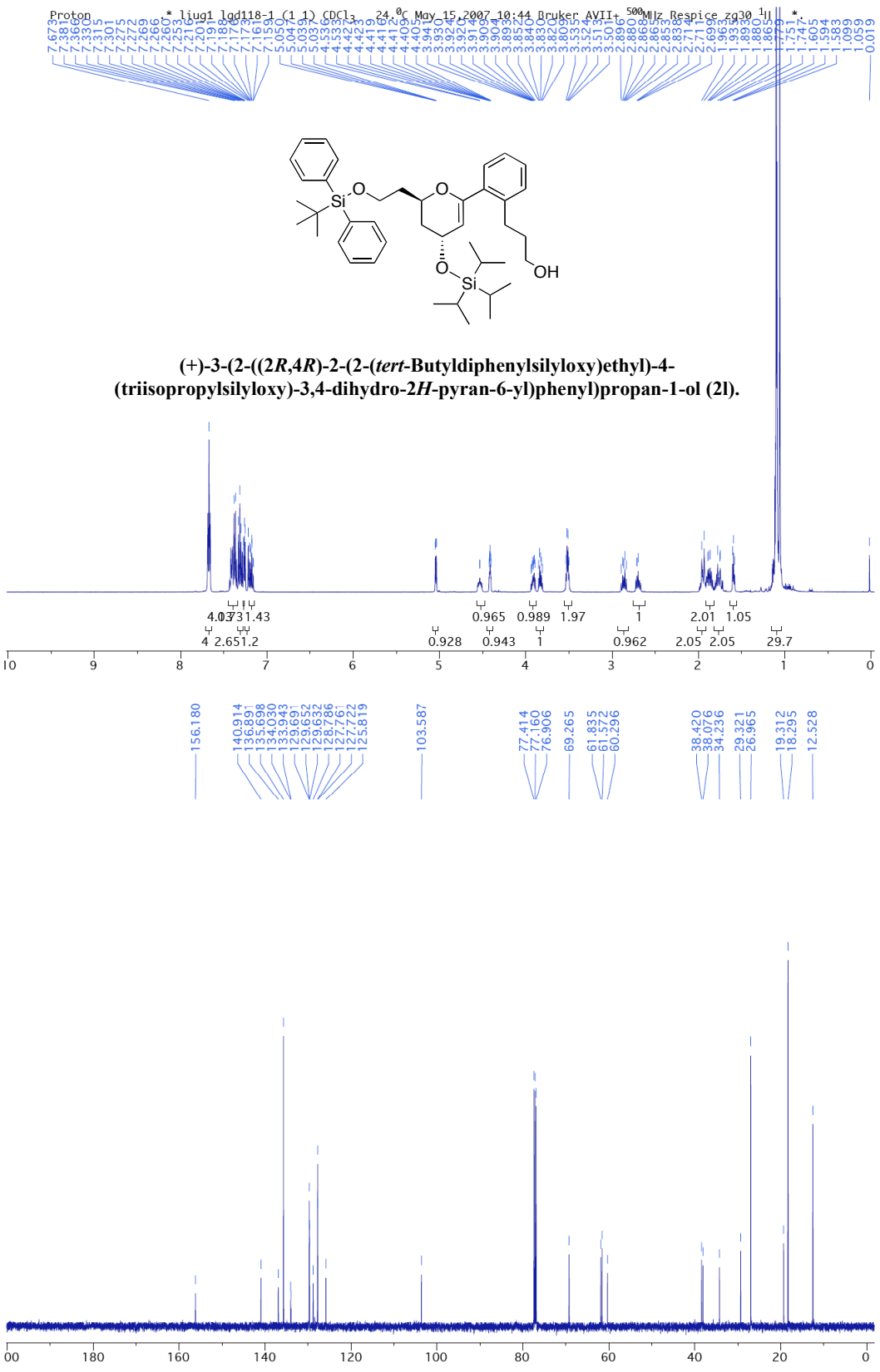
(+)-3-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)propan-1-ol (2c)



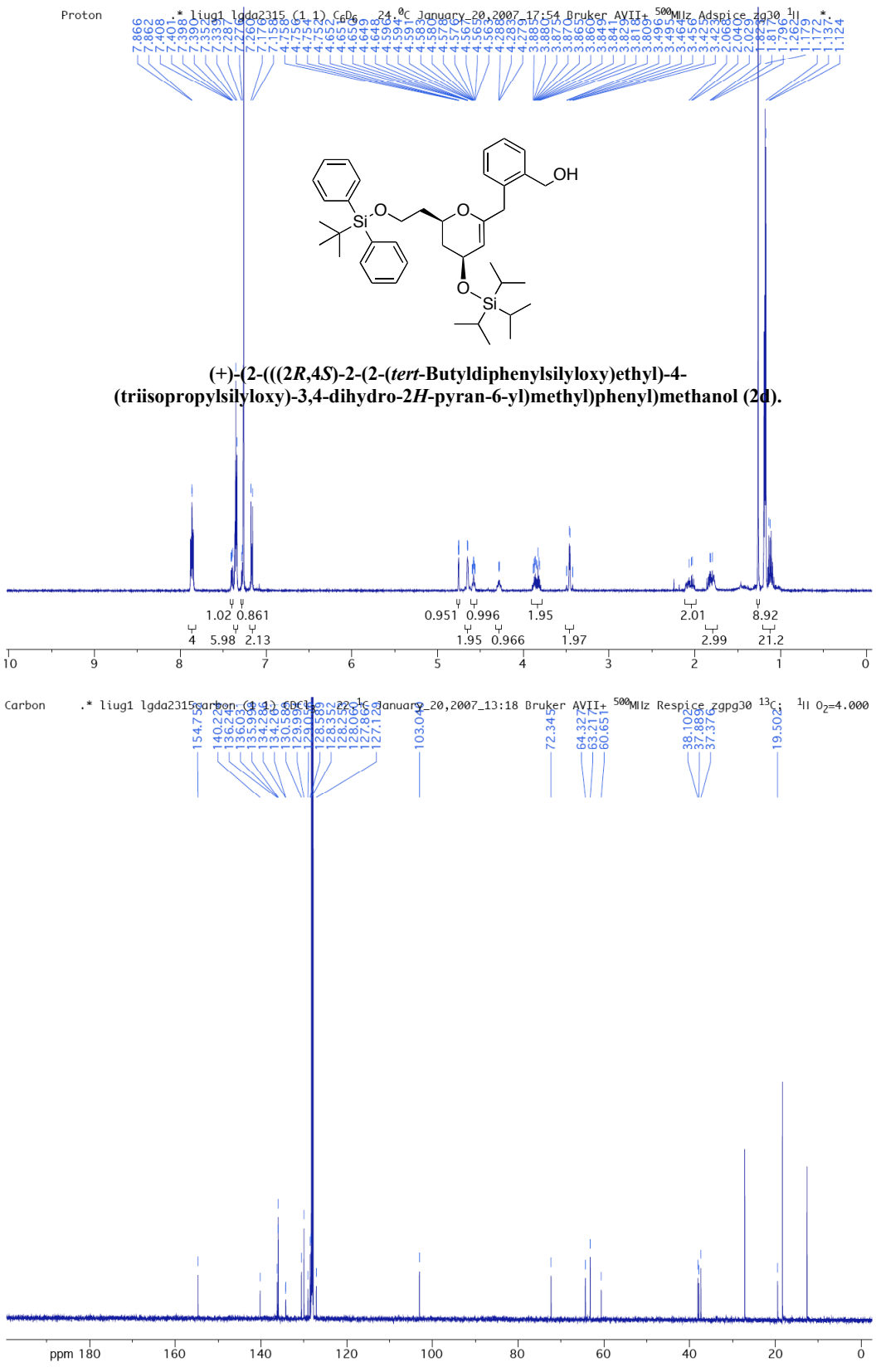
(+)-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)methanol (2j).



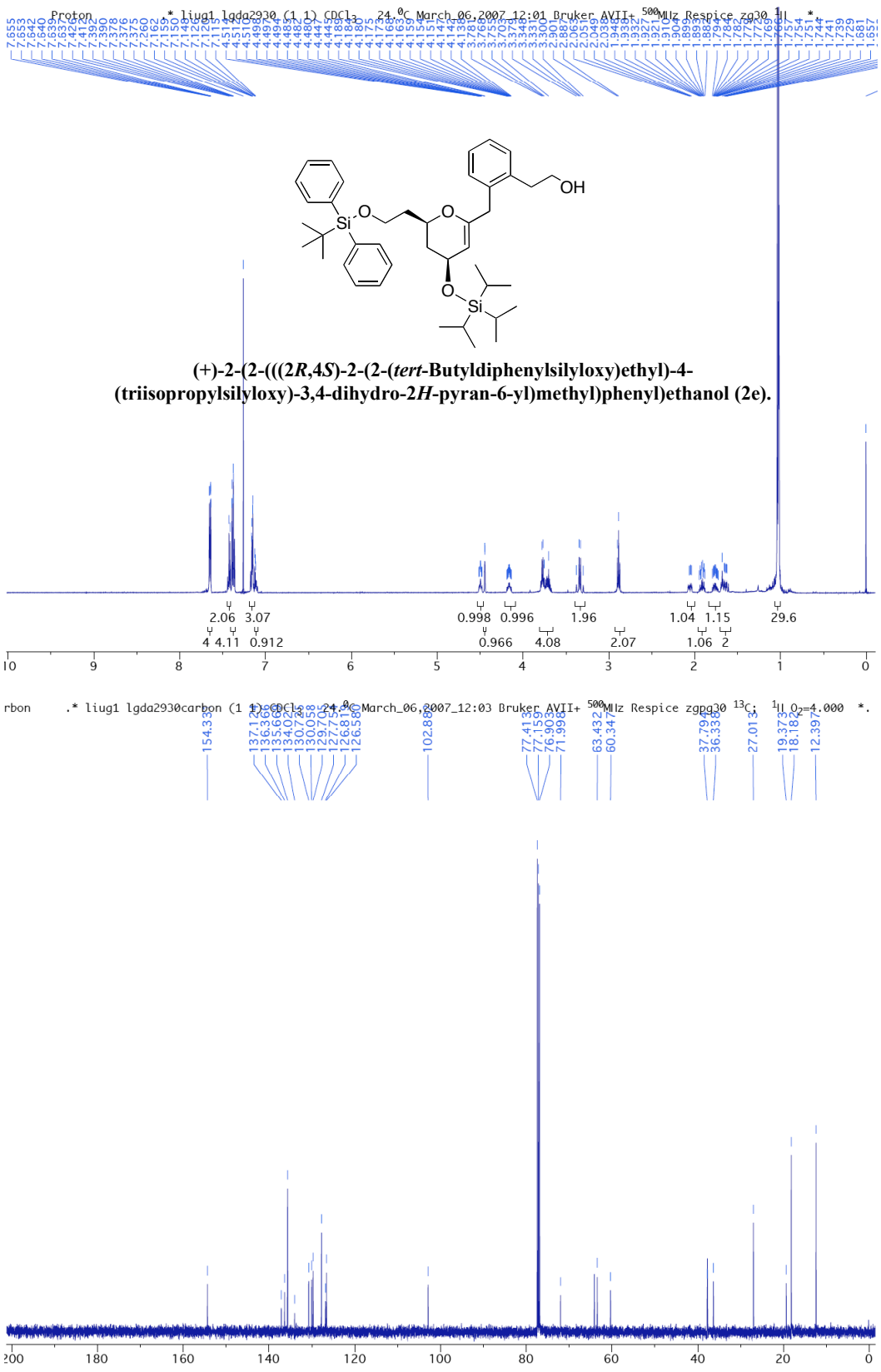
(+)-2-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)ethanol (2k).



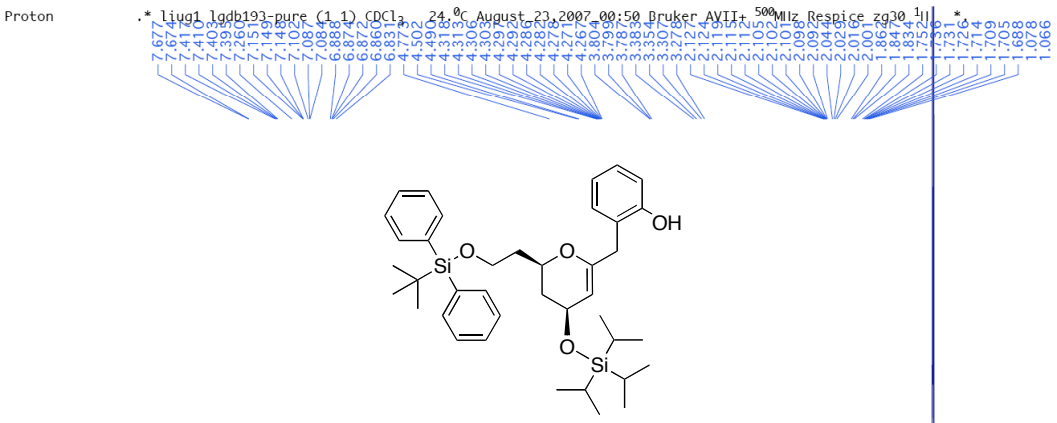
(+)-3-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)phenyl)propan-1-ol (2l).



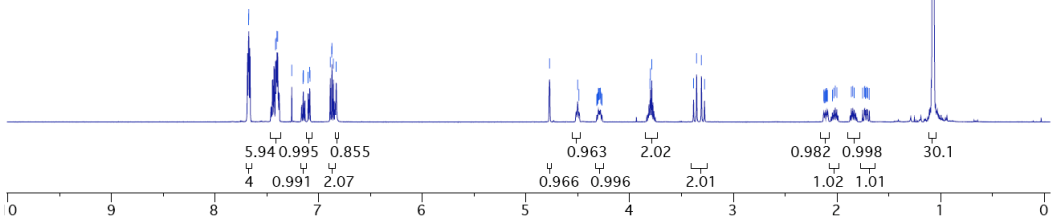
(+)-(2-(((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenyl)methanol (2d).

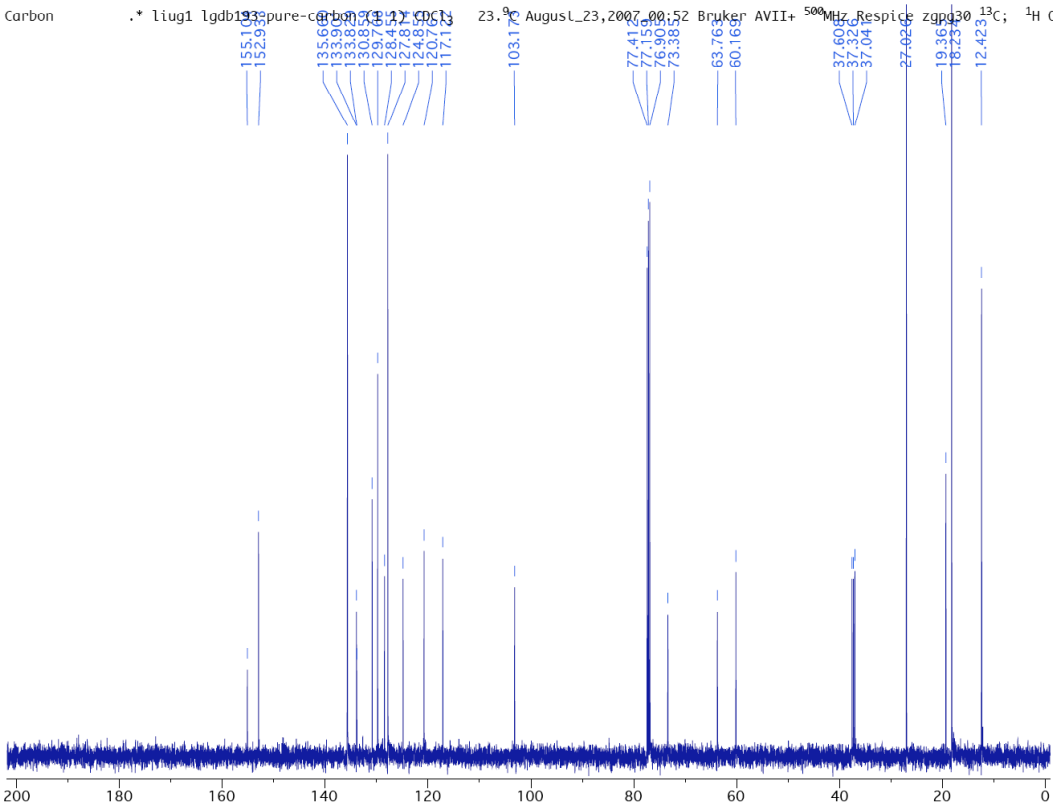


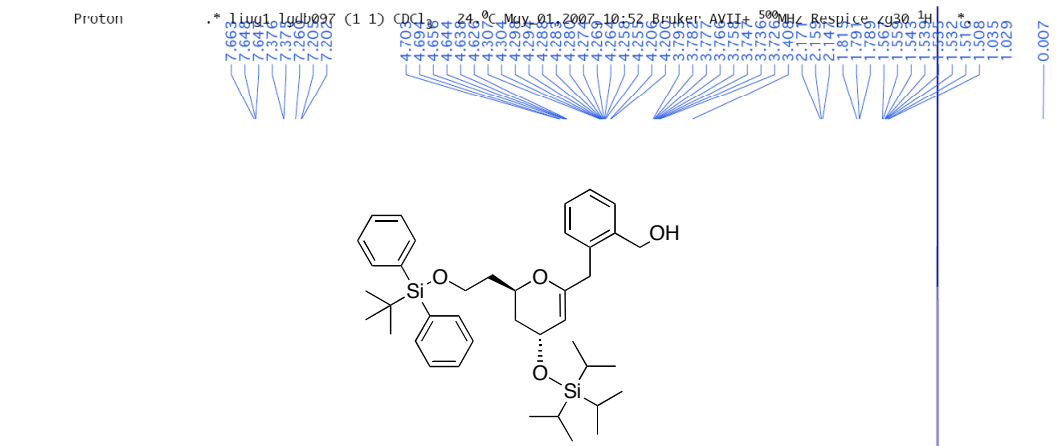
(+)-2-(2-(((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenyl)ethanol (2e).



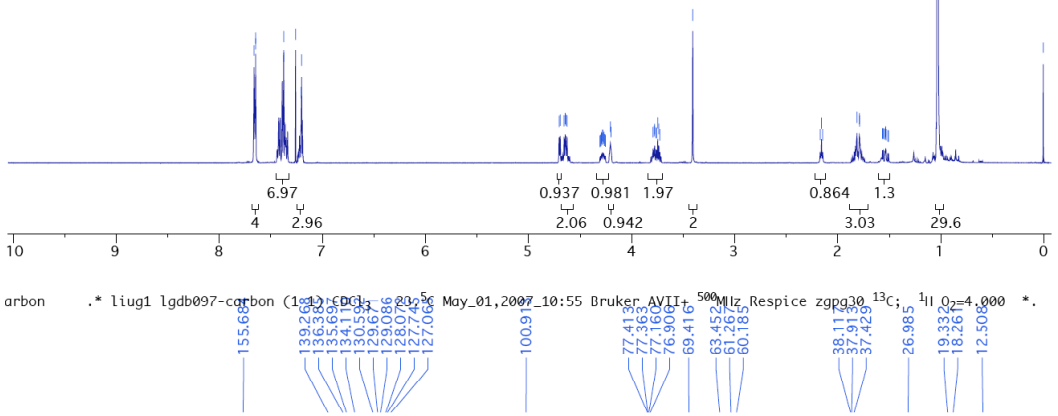
(+)-2-(((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenol (2g).

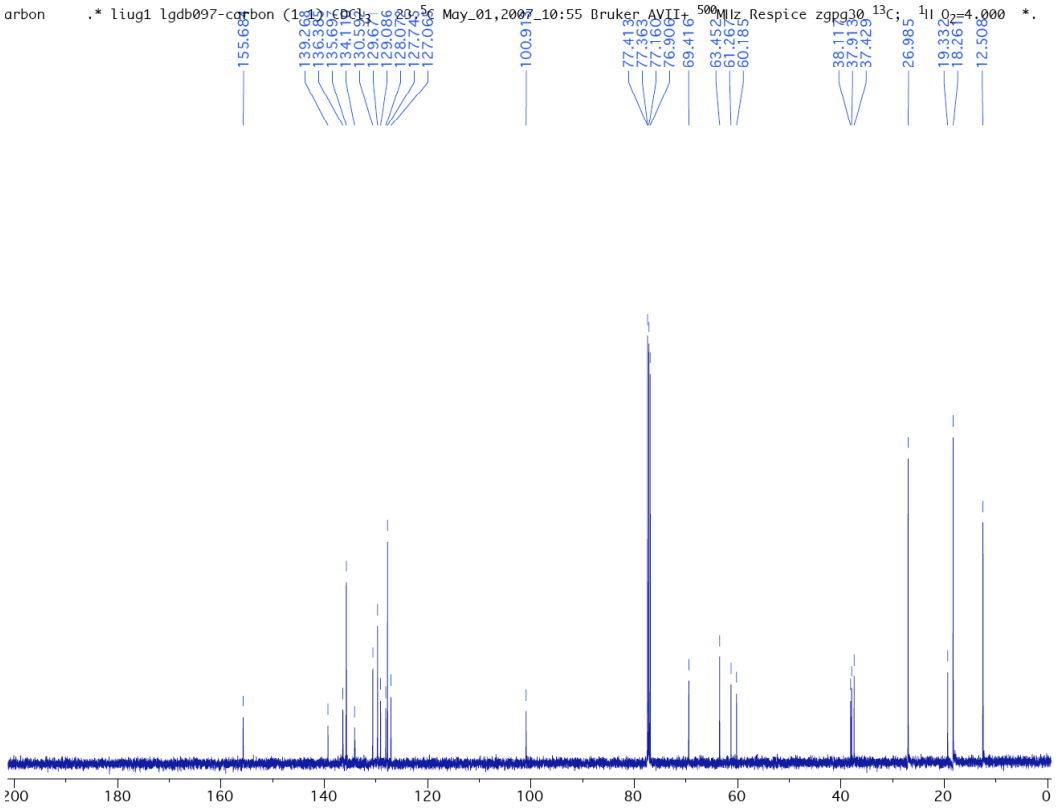


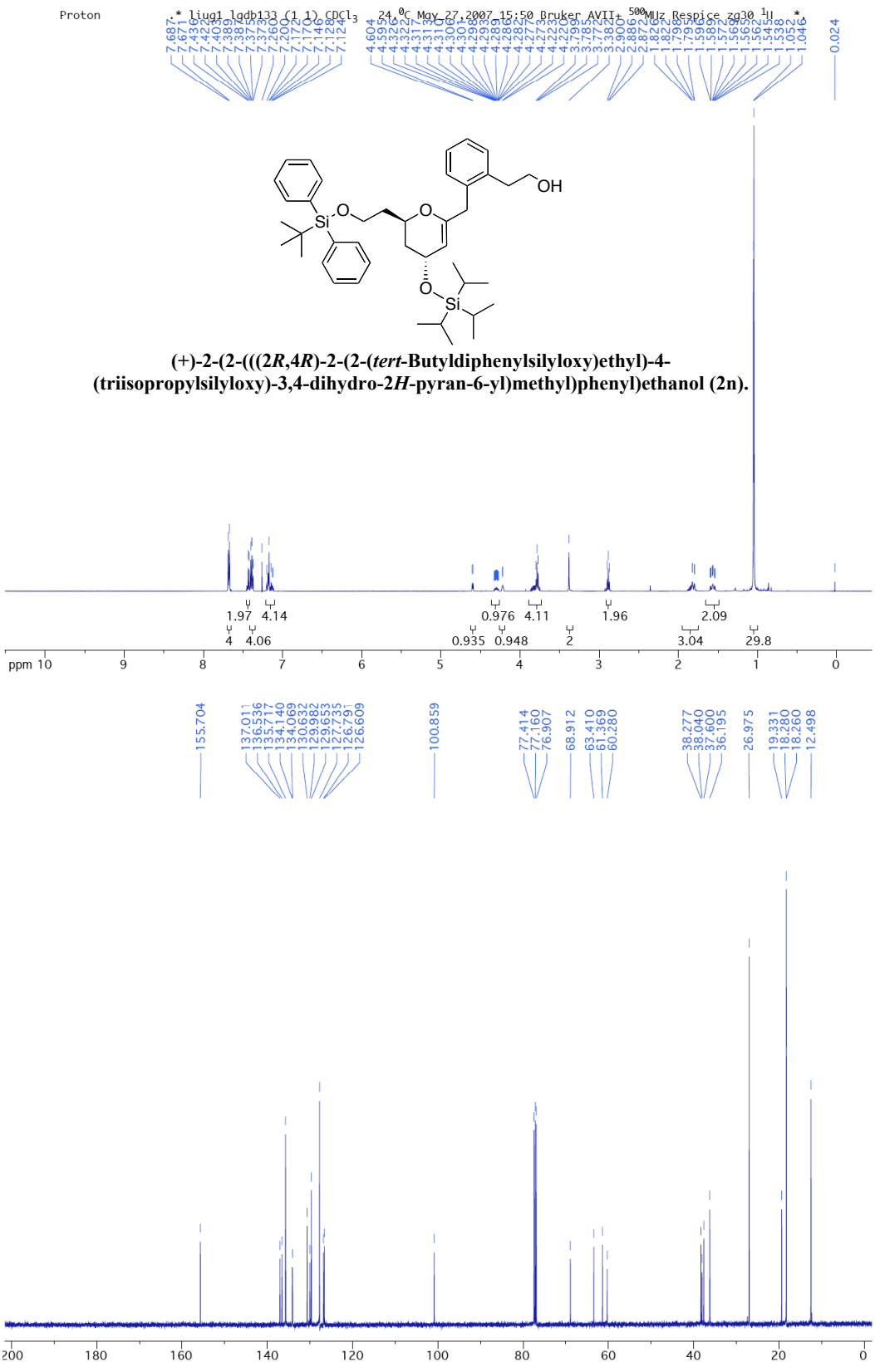




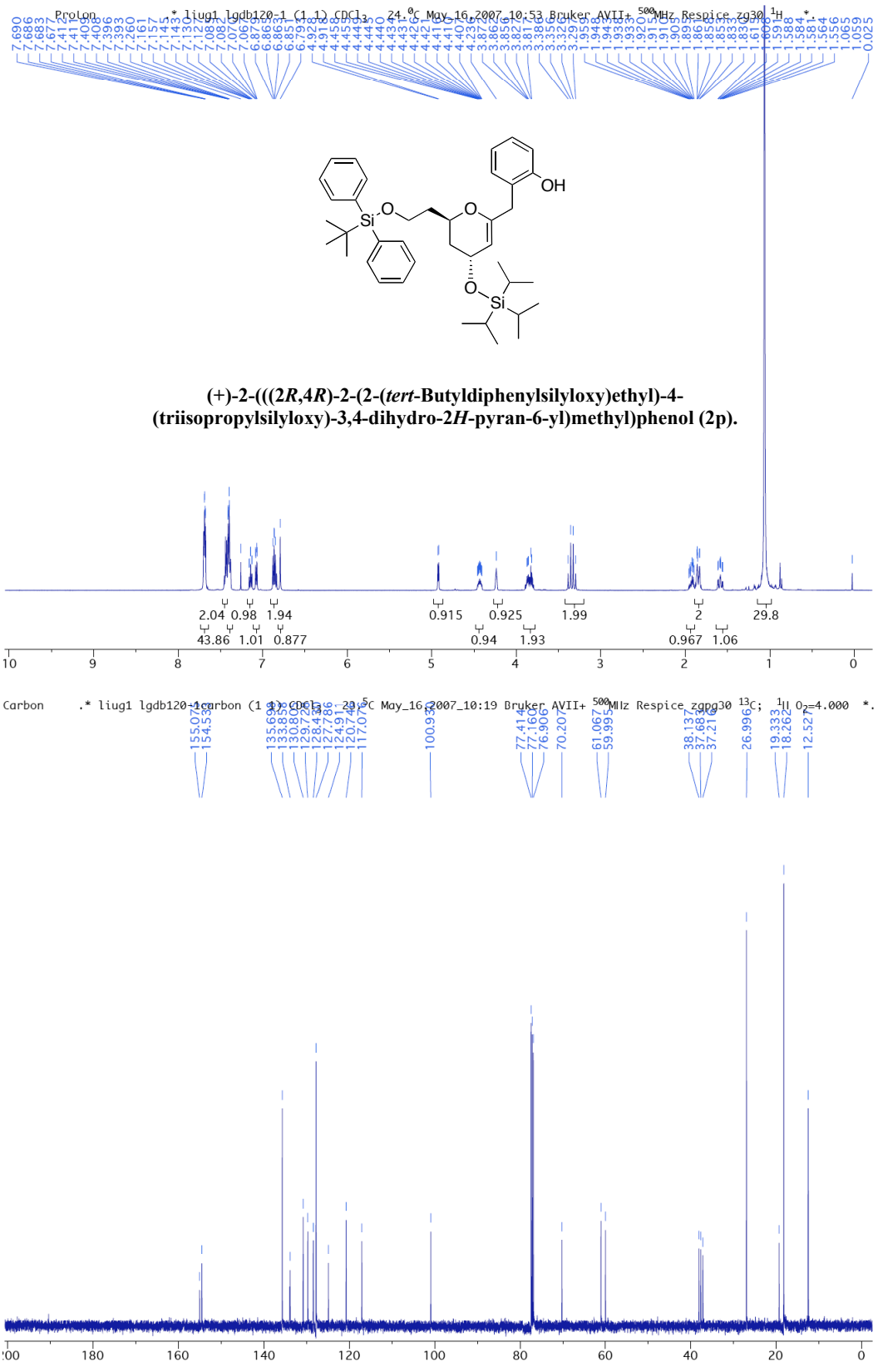
(+)-(2-(((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenyl)methanol (2m).



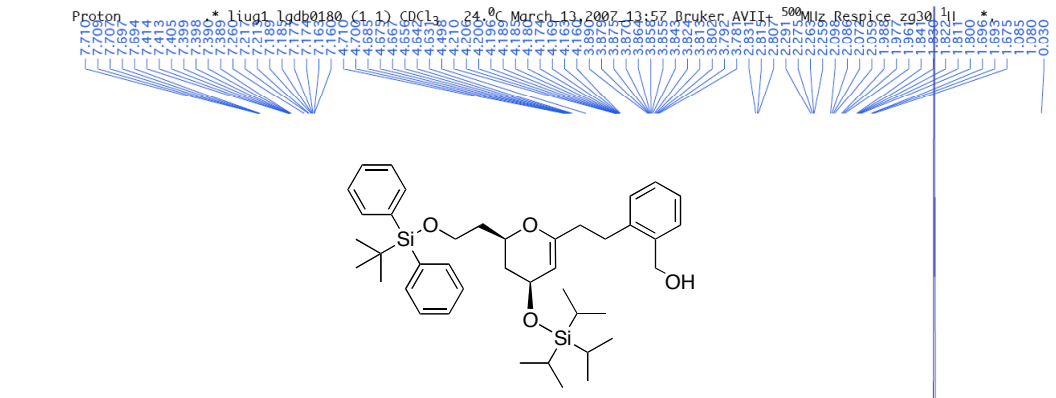




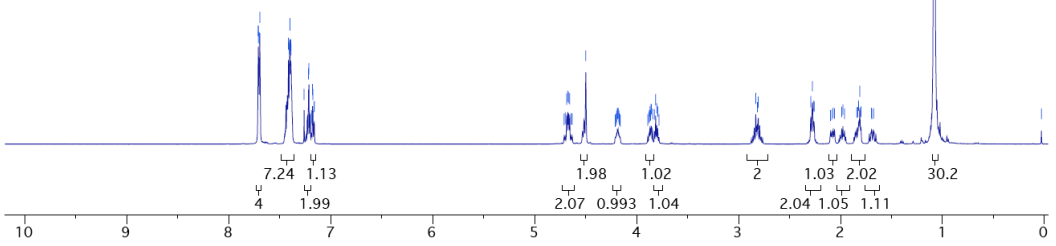
(+)-2-(2-(((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenyl)ethanol (2n).

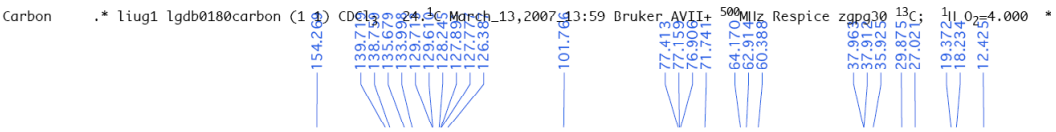


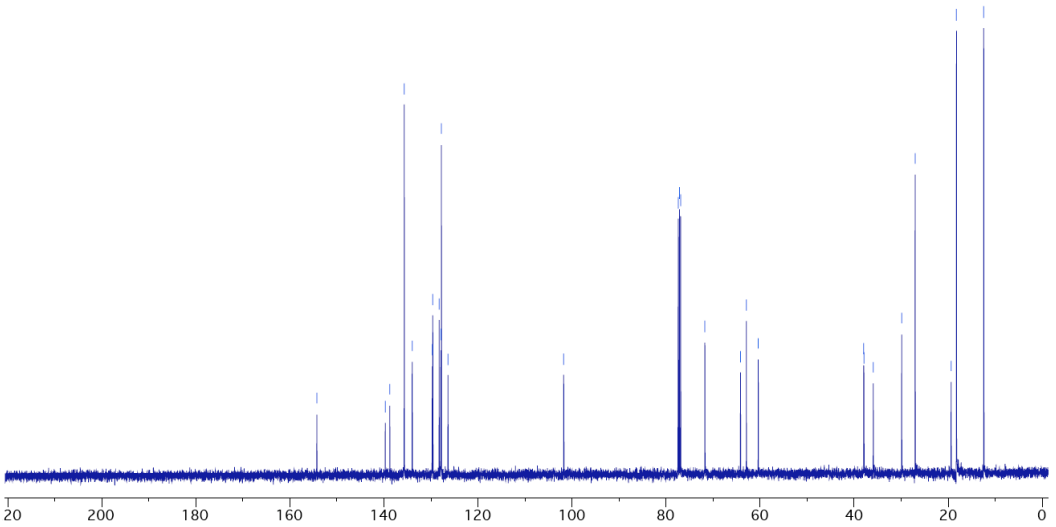
(+)-2-(((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)methyl)phenol (2p).

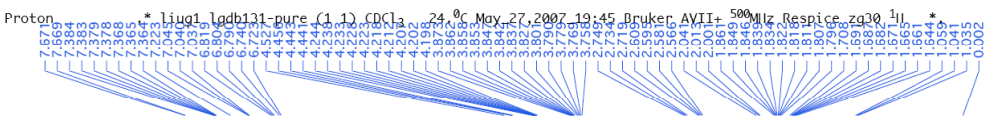


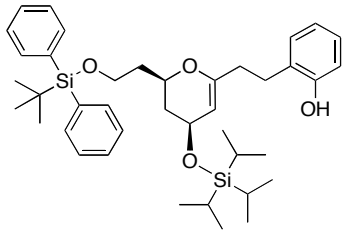
(+)-(2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)ethyl)phenyl)methanol (2f).



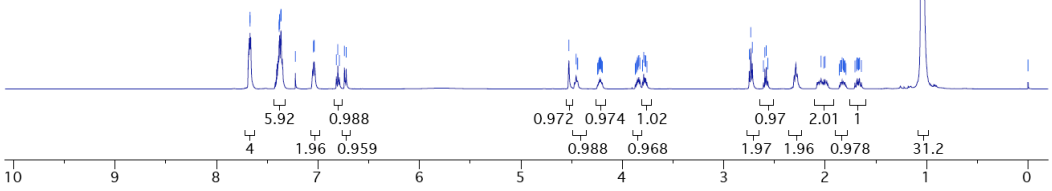


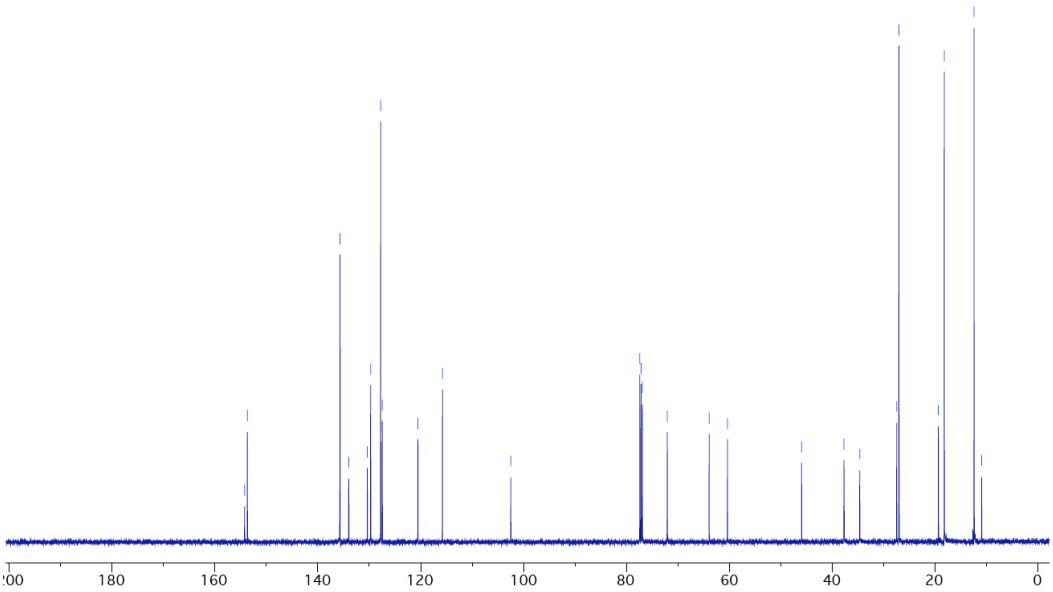


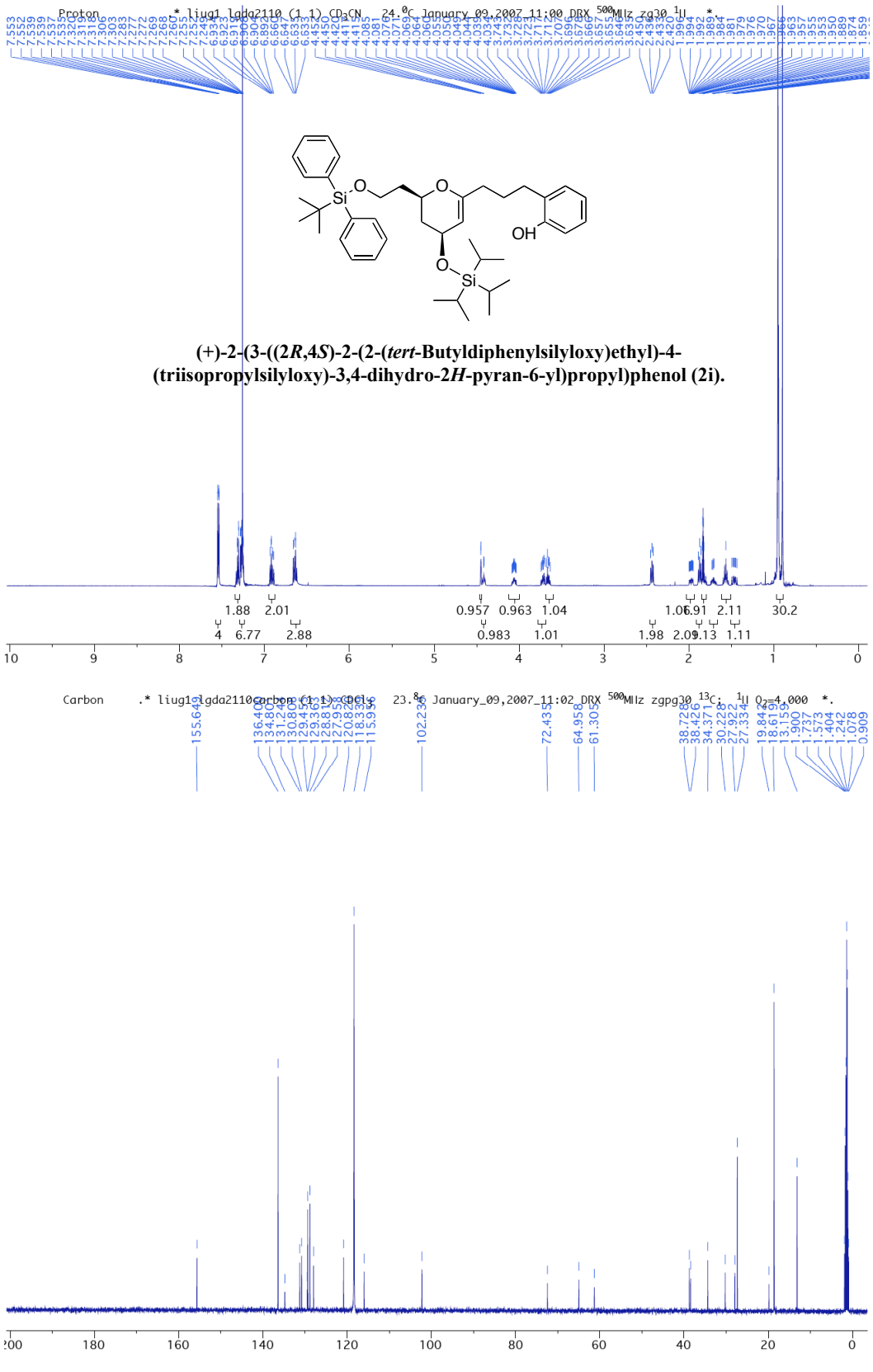




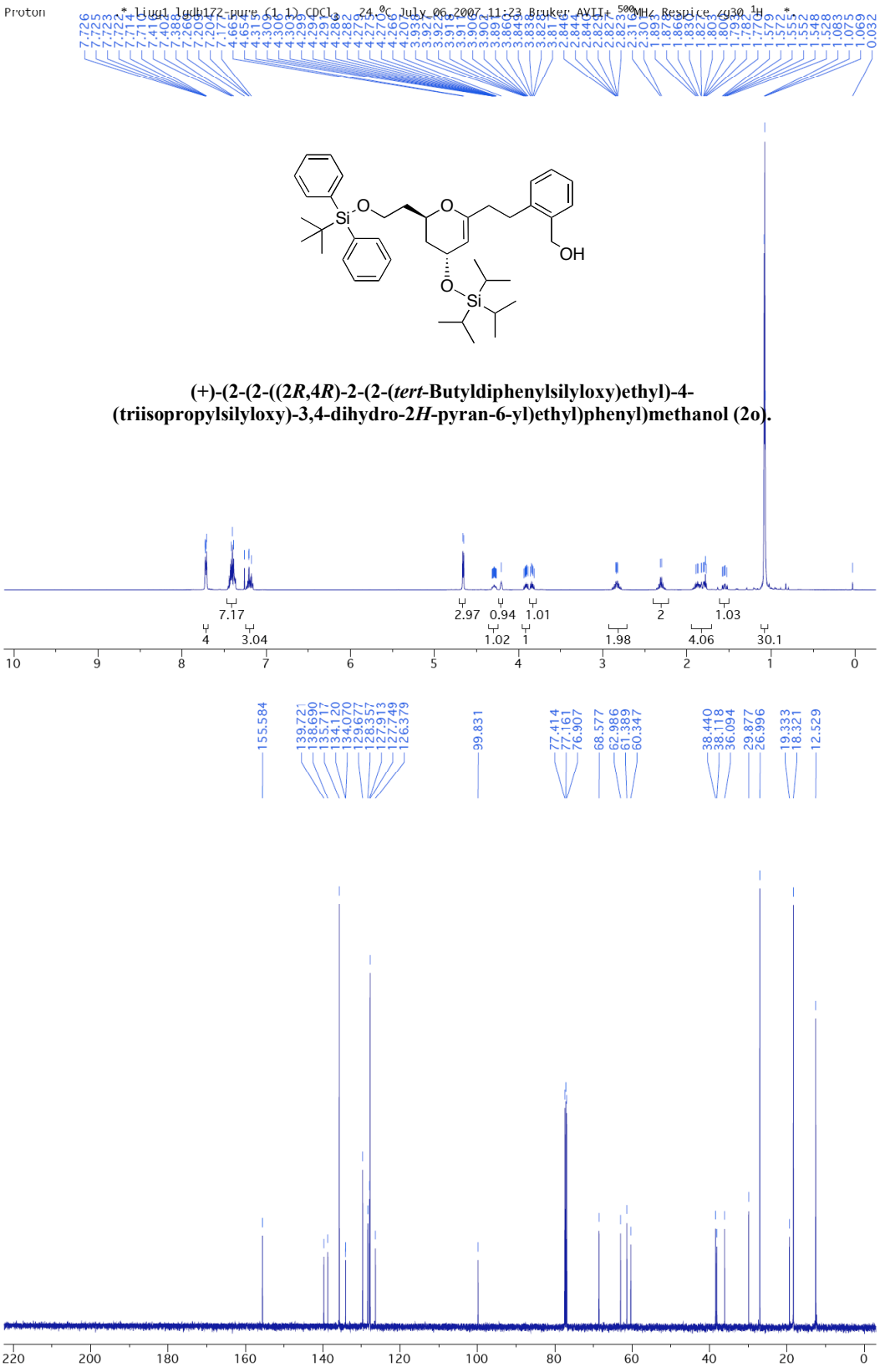
(+)-2-(2-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)ethyl)phenol (2h).



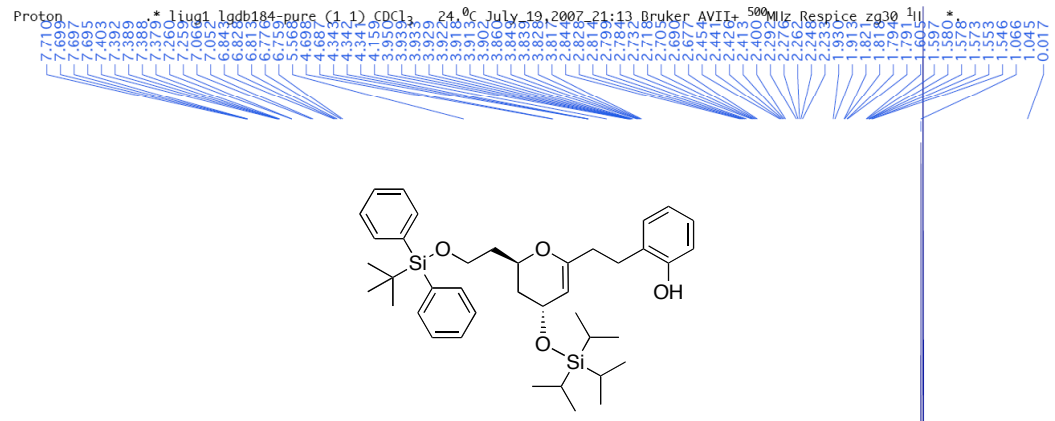




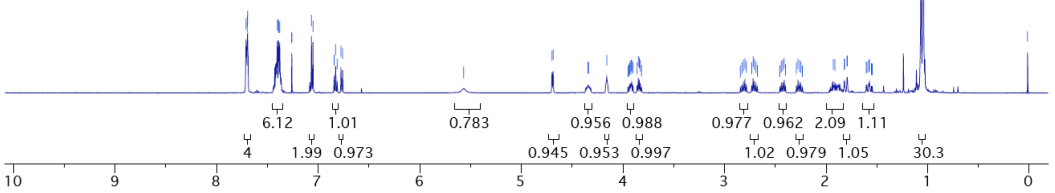
(+)-2-(3-((2*R*,4*S*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)propyl)phenol (2i).

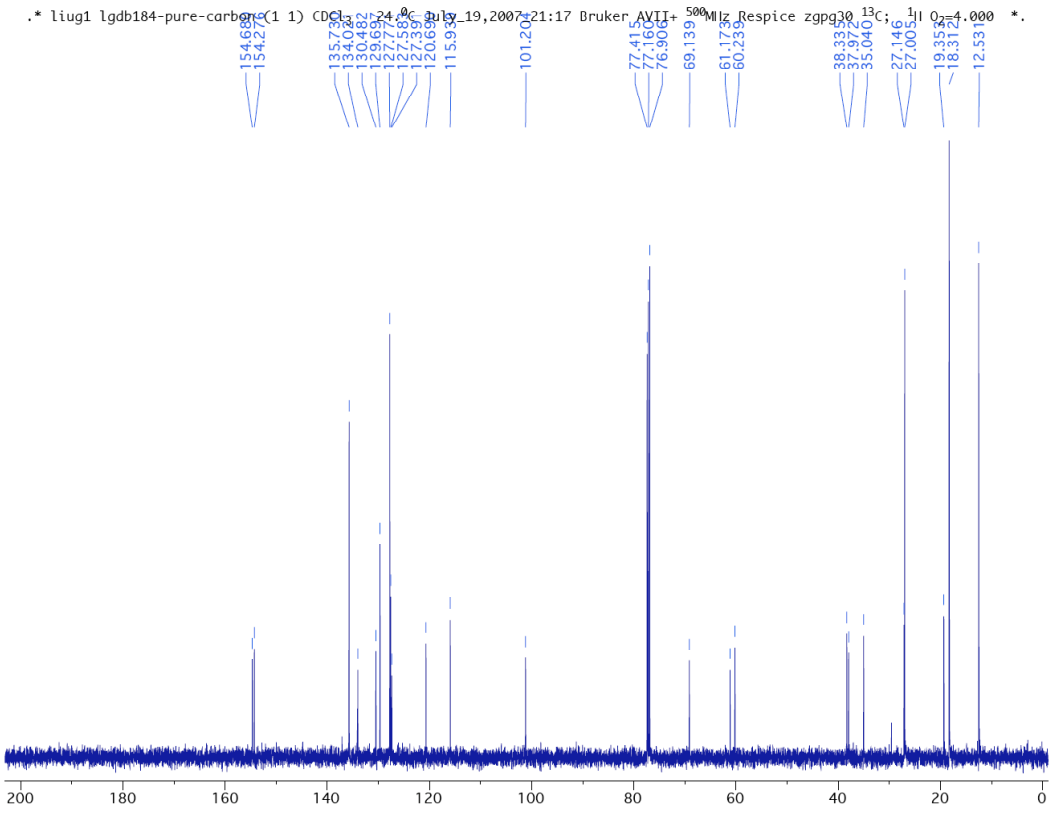


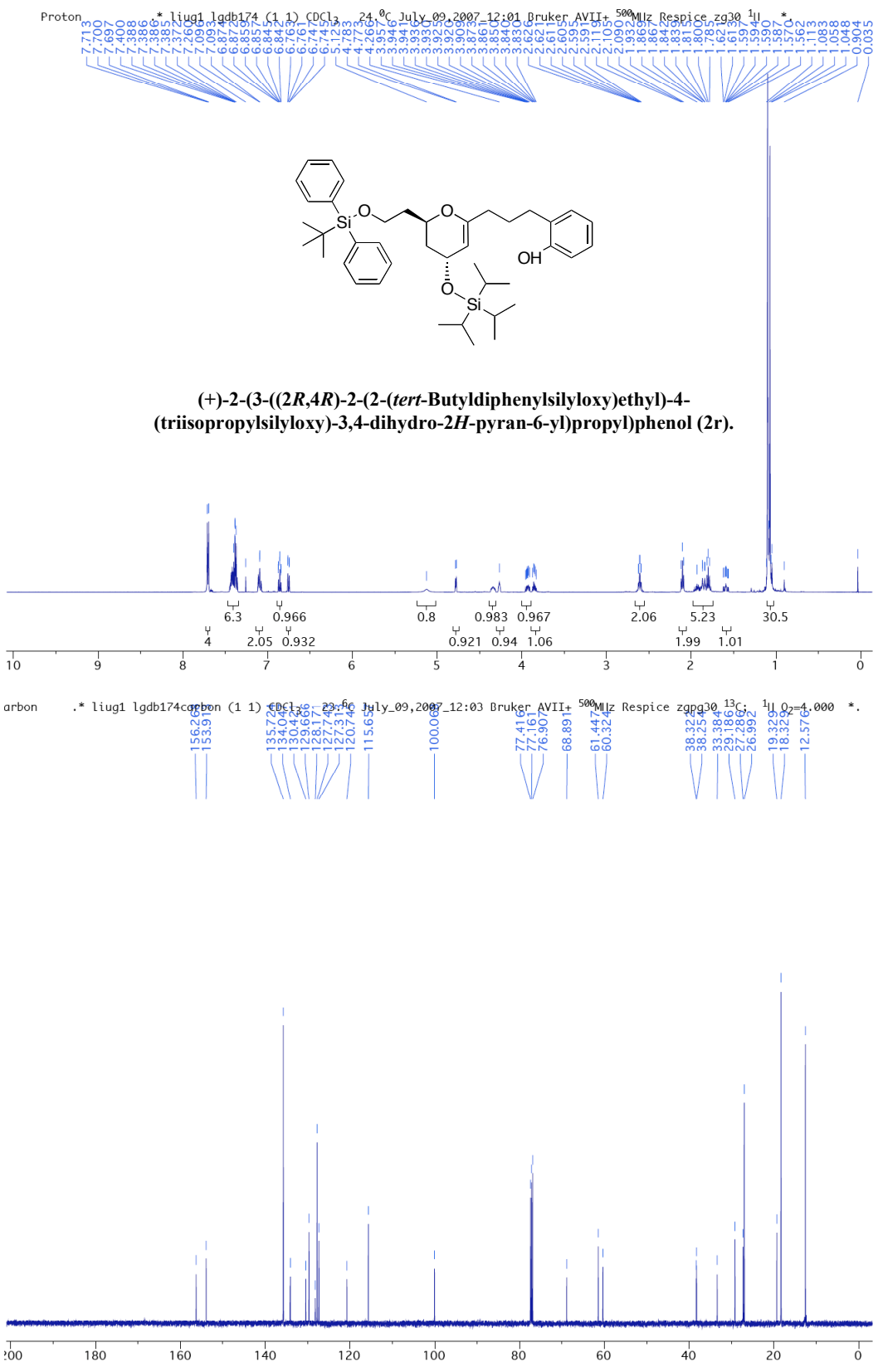
(+)-(2-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)ethyl)phenyl)methanol (2o).



(+)-2-(2-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)ethyl)phenol (2q).

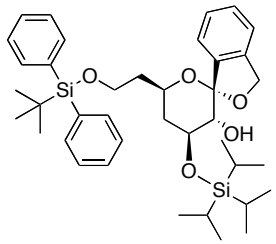




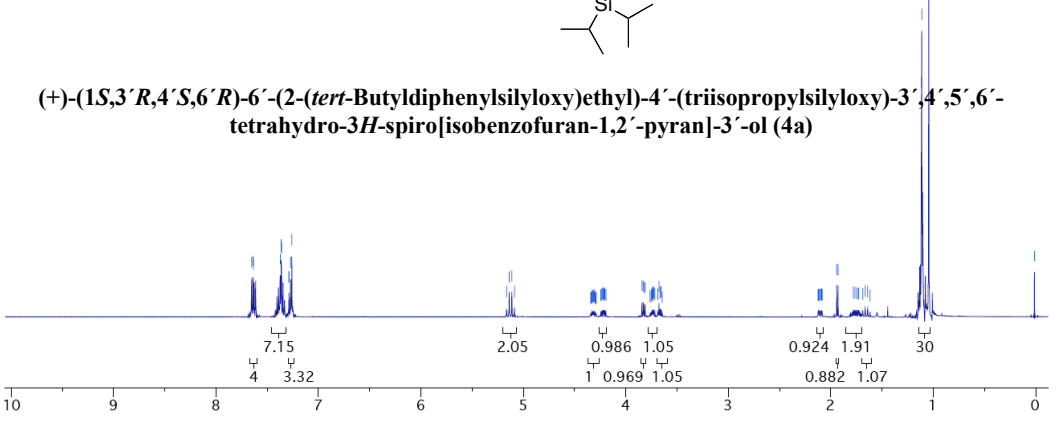


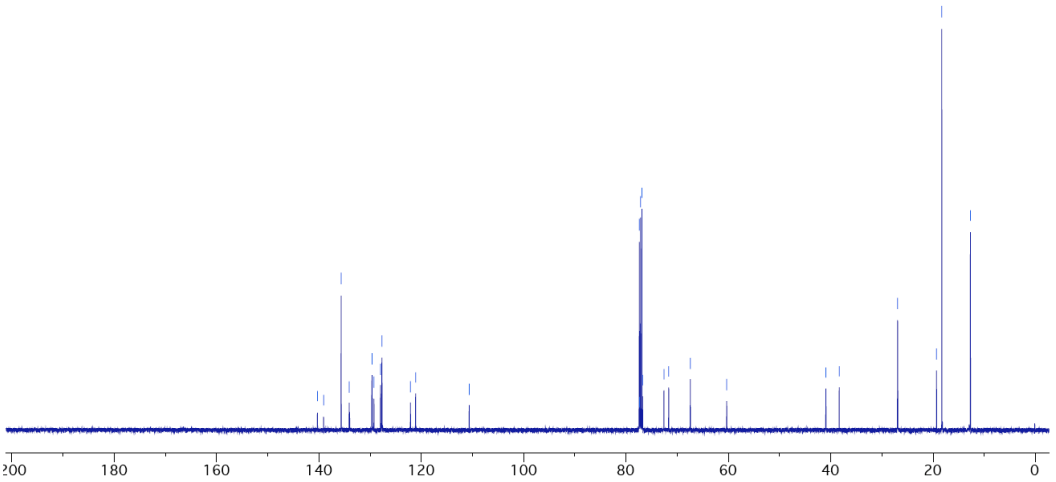
(+)-2-(3-((2*R*,4*R*)-2-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4-(triisopropylsilyloxy)-3,4-dihydro-2*H*-pyran-6-yl)propyl)phenol (2r).

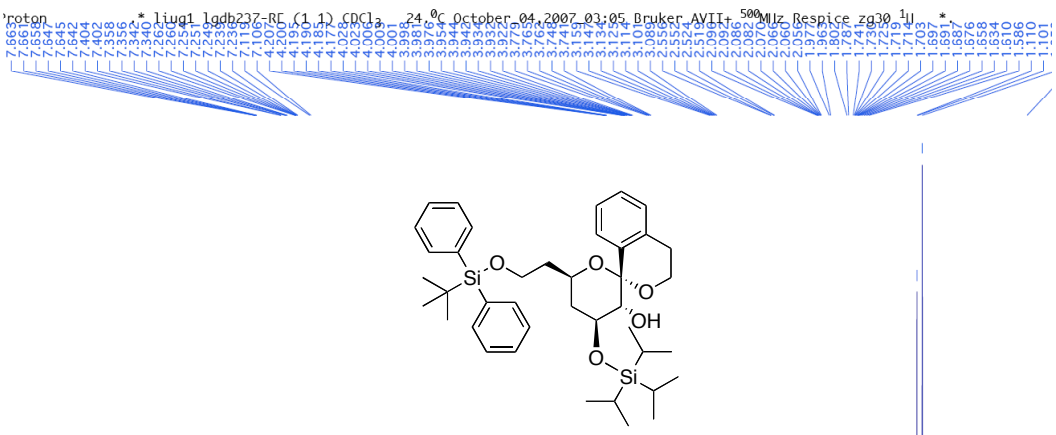
C. SPIROCYCLIZATION WITH RETENTION OF CONFIGURATION ($Ti[OiPr]_4$) (4a–r)



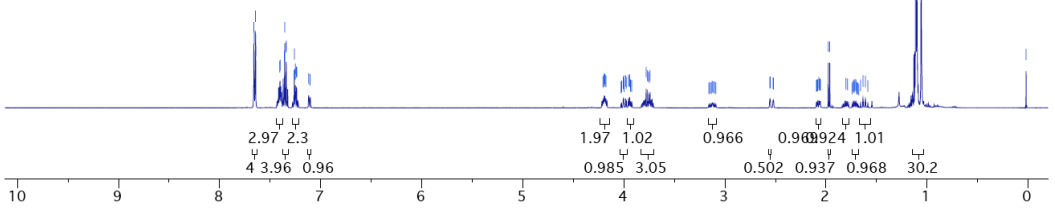
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (4a)

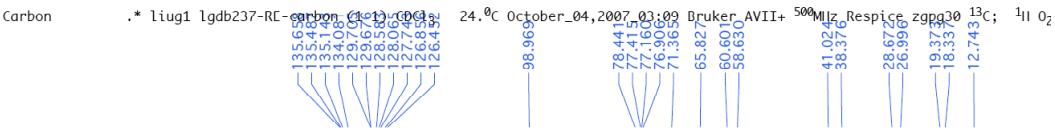


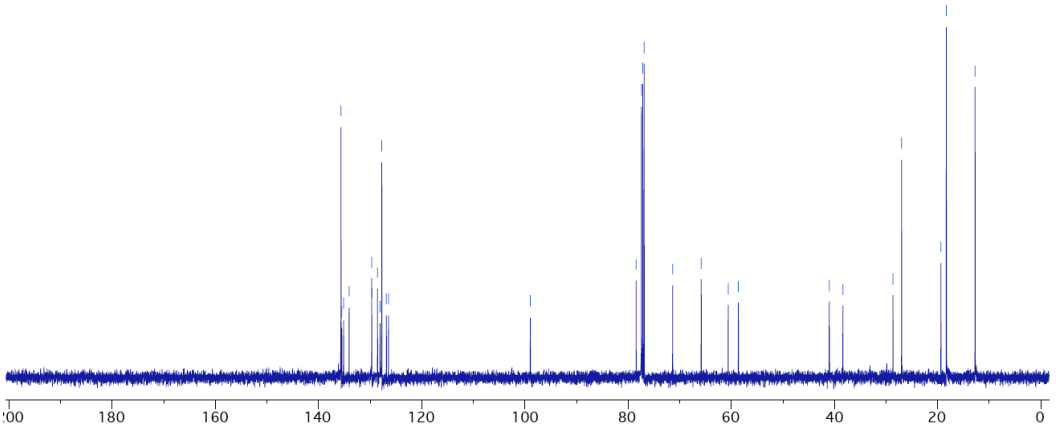


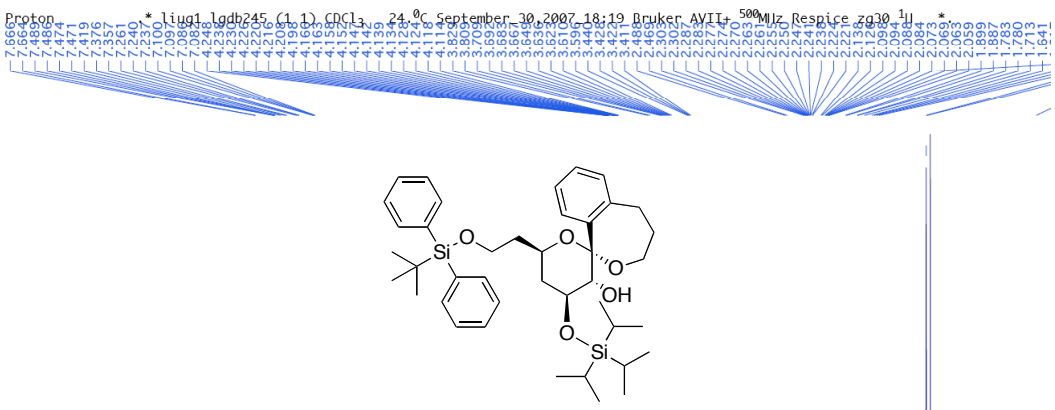


(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (4b)

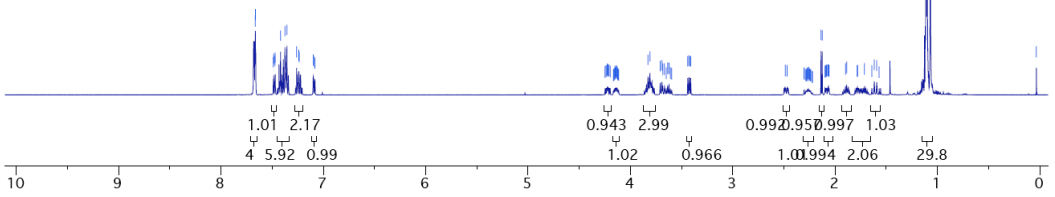


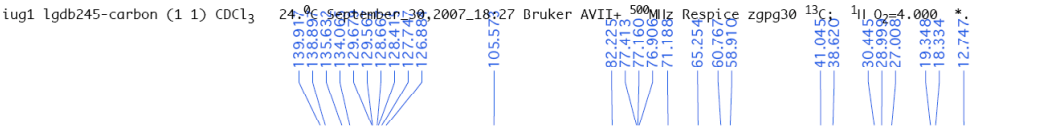


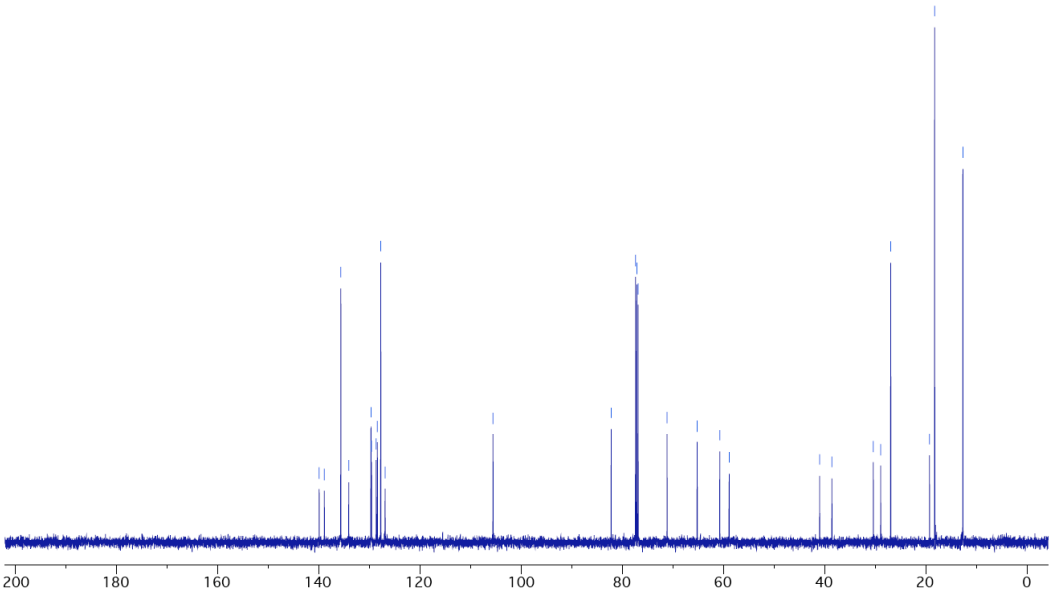


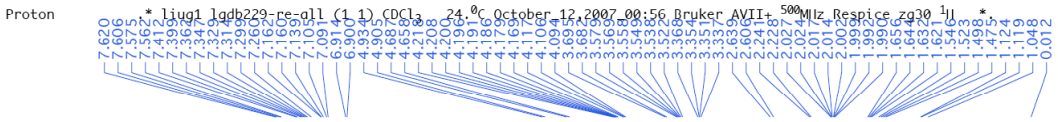


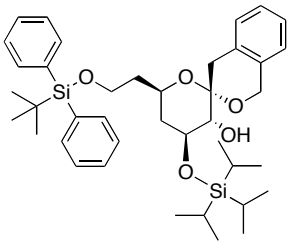
(+)-(1*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (4c)



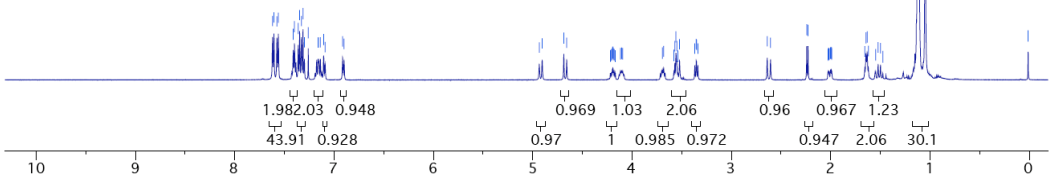


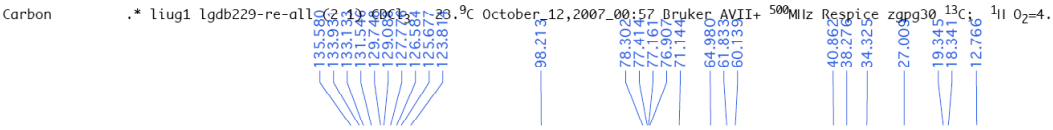


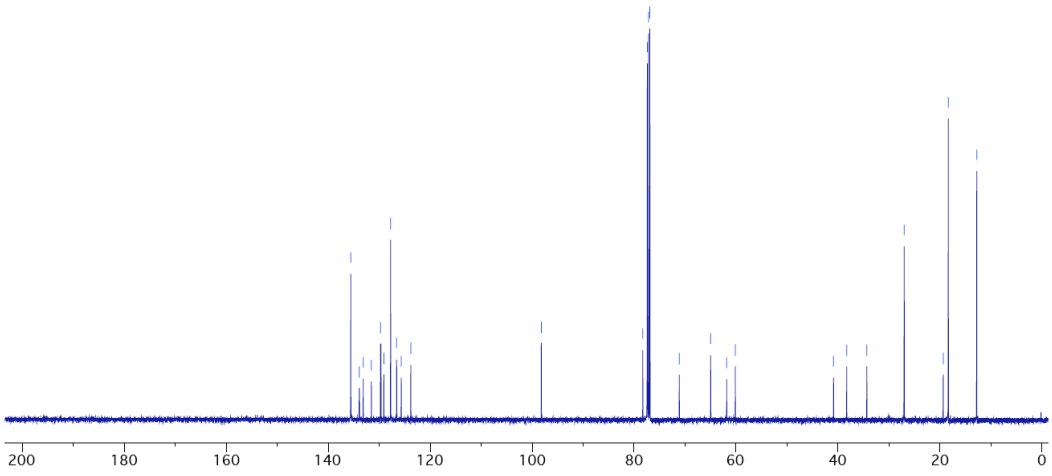


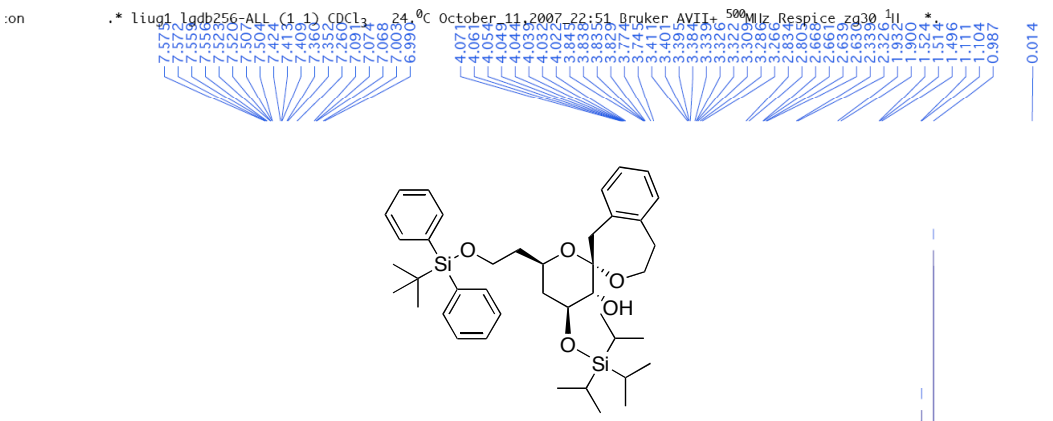


(+)-(2′*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-3,2′-pyran]-3′-ol (4d)

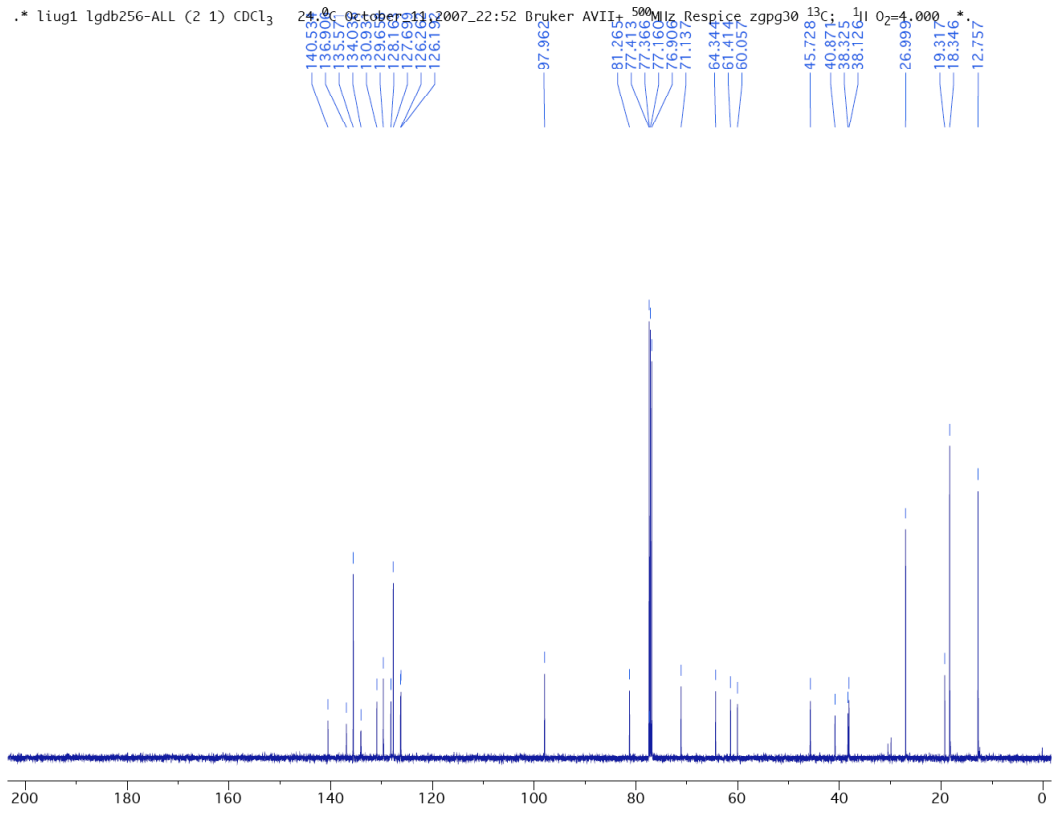


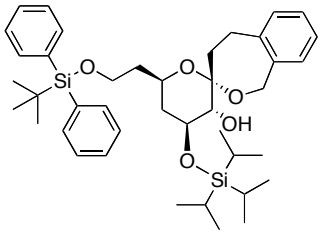




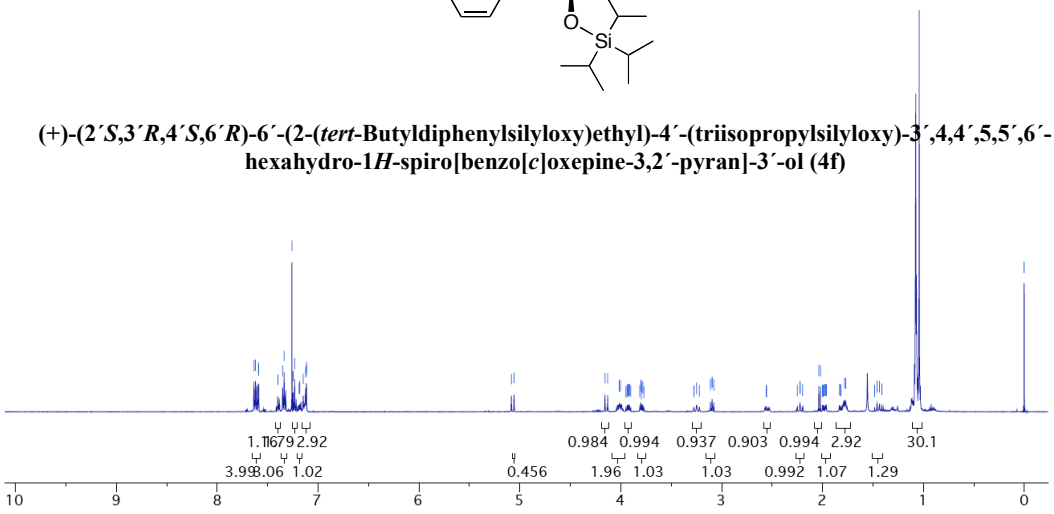


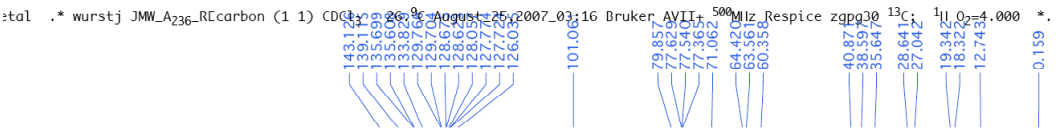
(+)-(2*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*d*]oxepine-2,2′-pyran]-3′-ol (4e)

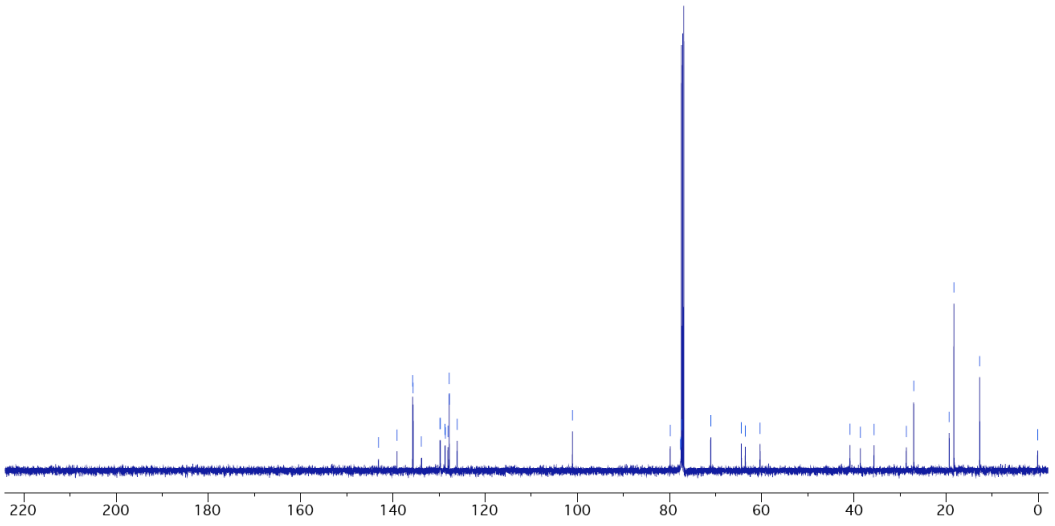


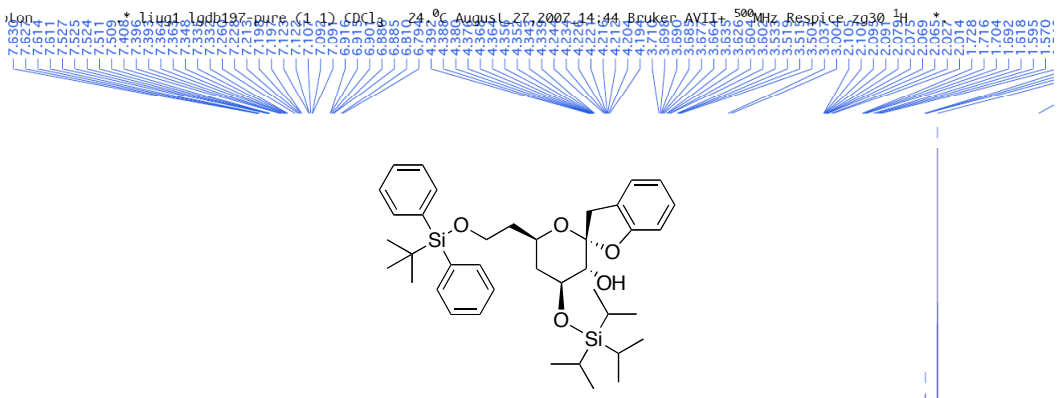


(+)-(2′*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*c*]oxepine-3,2′-pyran]-3′-ol (4f)

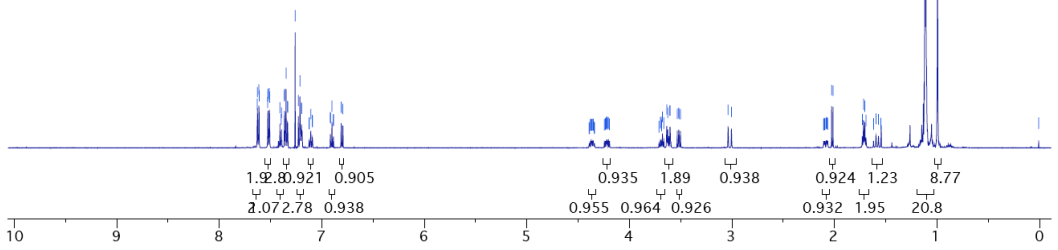


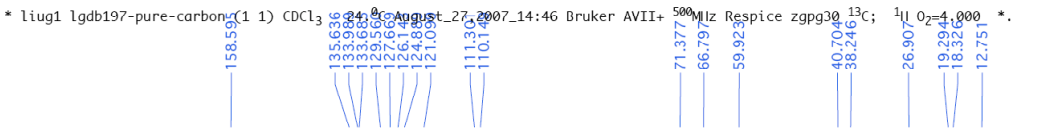


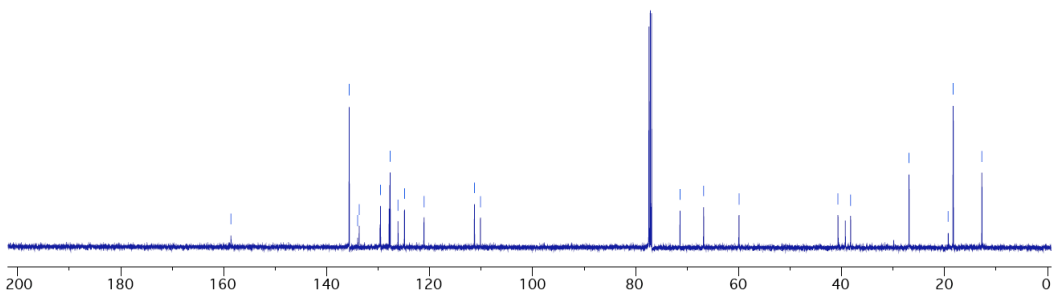


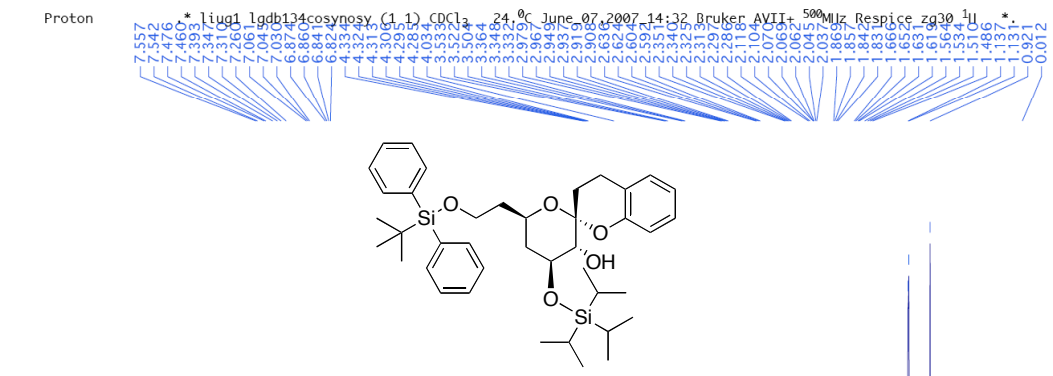


(+)-(2*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[benzofuran-2,2′-pyran]-3′-ol (4g)

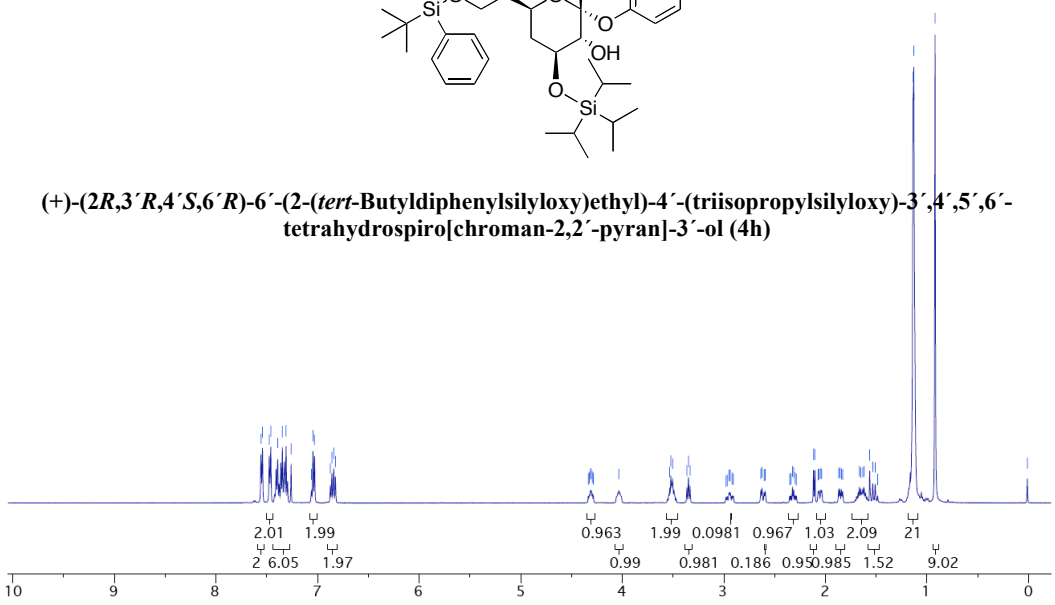


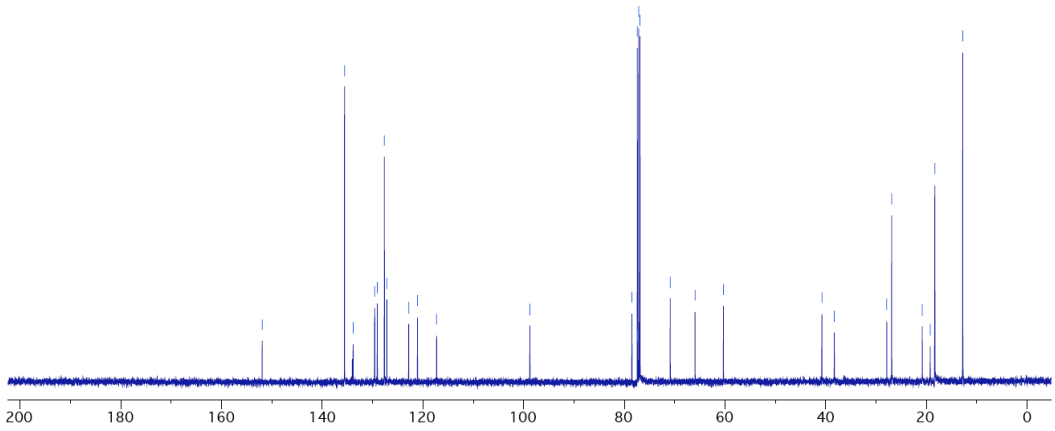


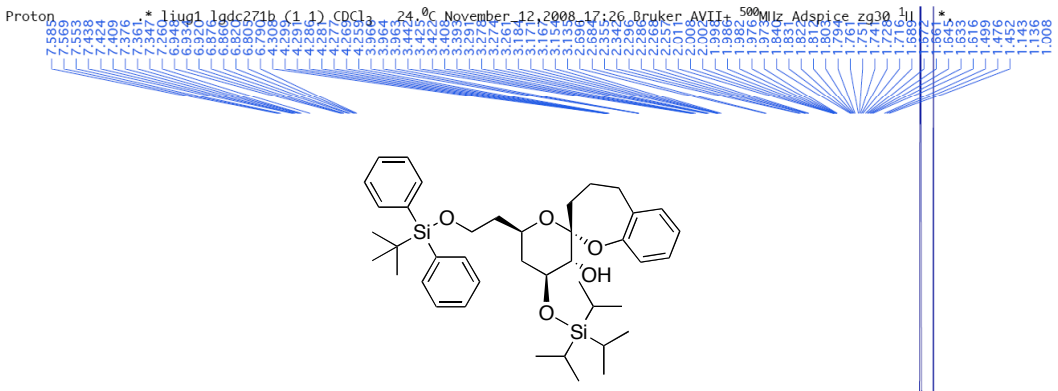




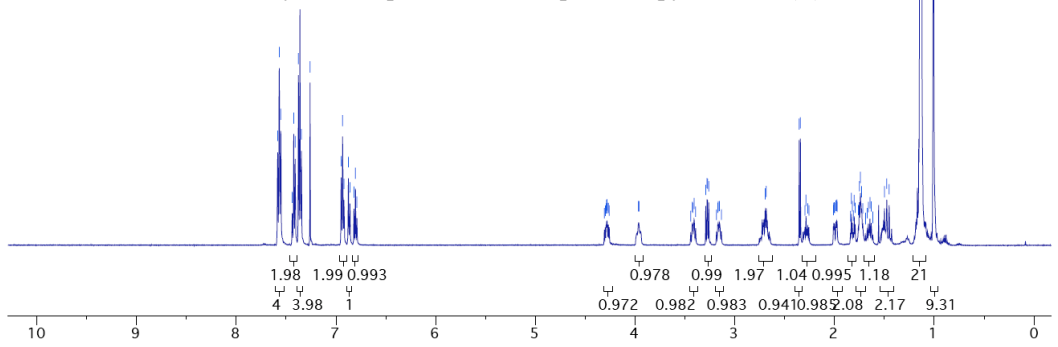
(+)-(2*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[chroman-2,2′-pyran]-3′-ol (4h)

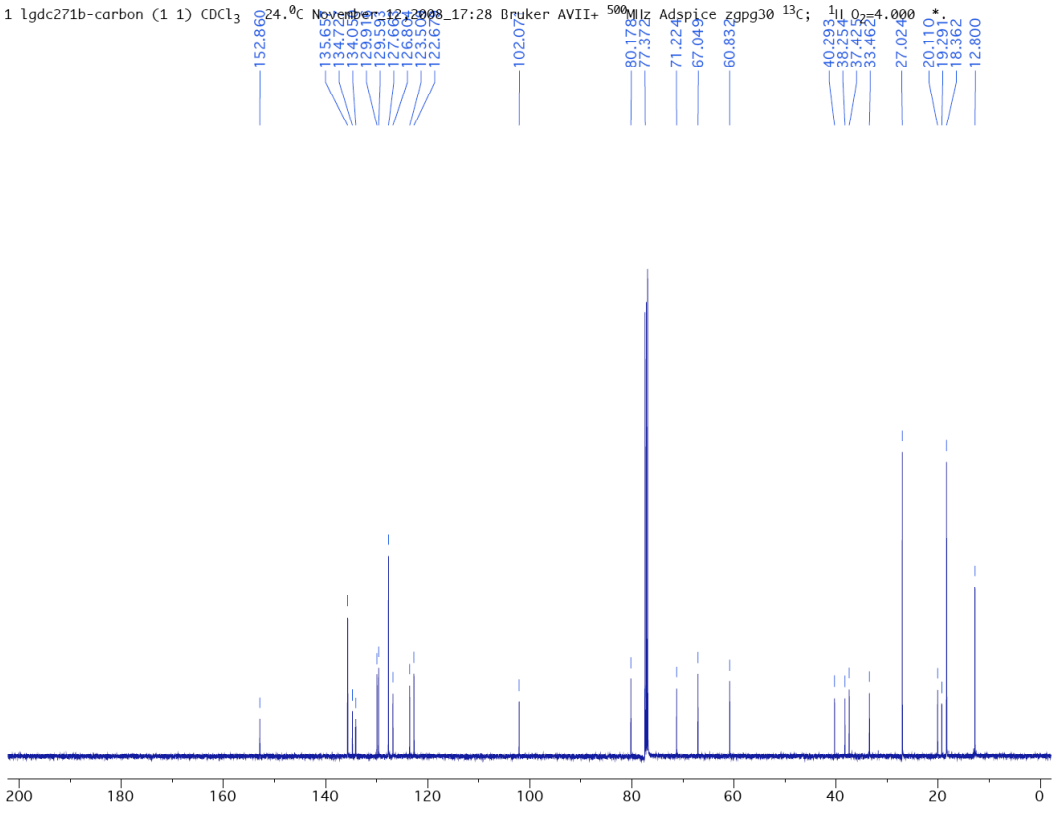


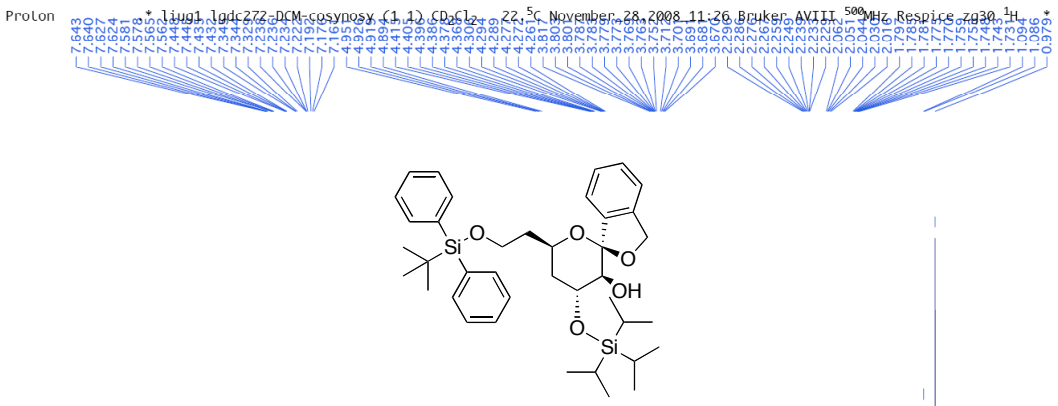




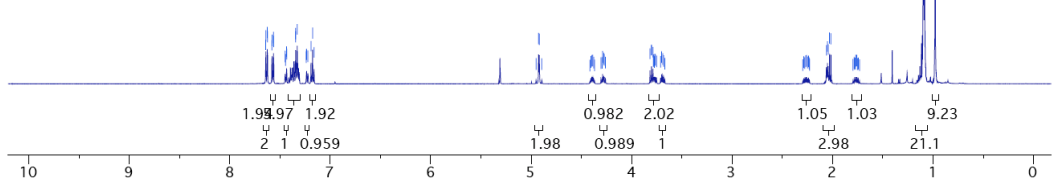
(+)-(2*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*b*]oxepine-2,2′-pyran]-3′-ol (4i)

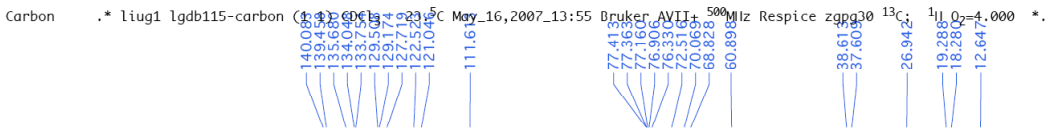


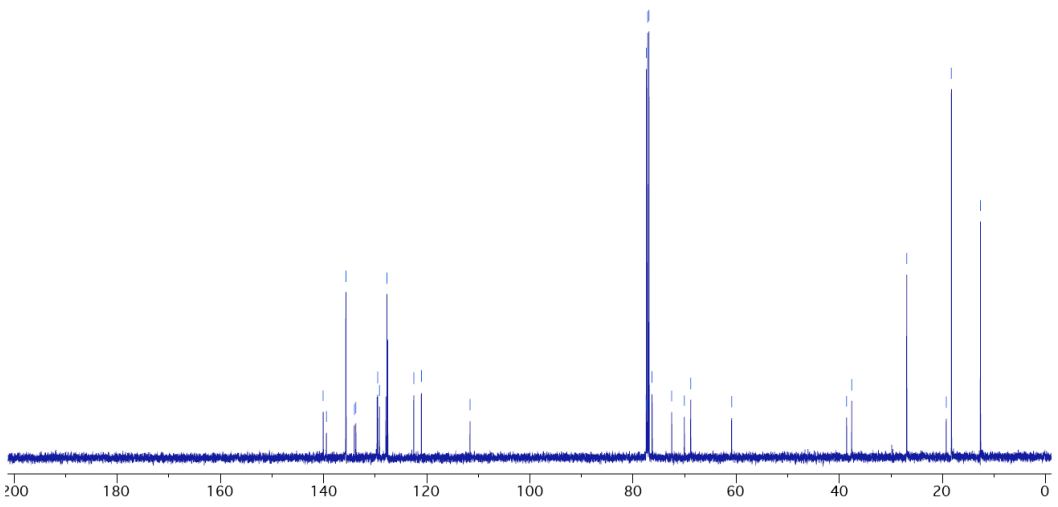


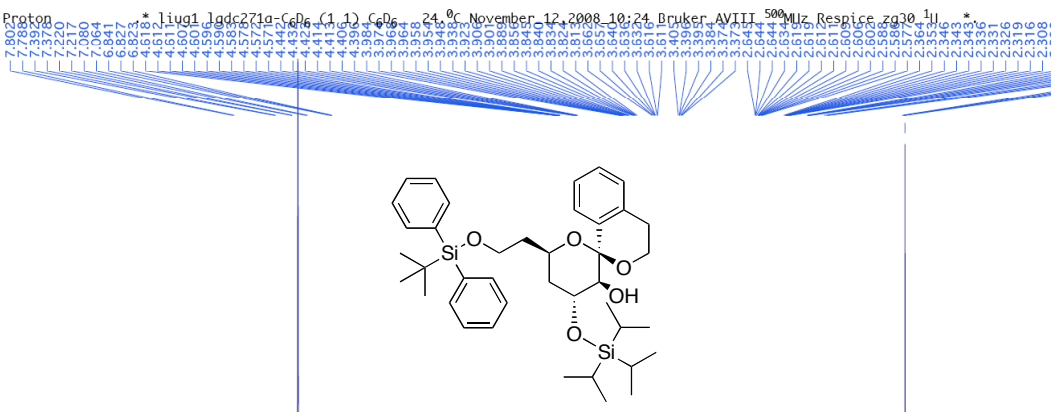


(+)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (4j)

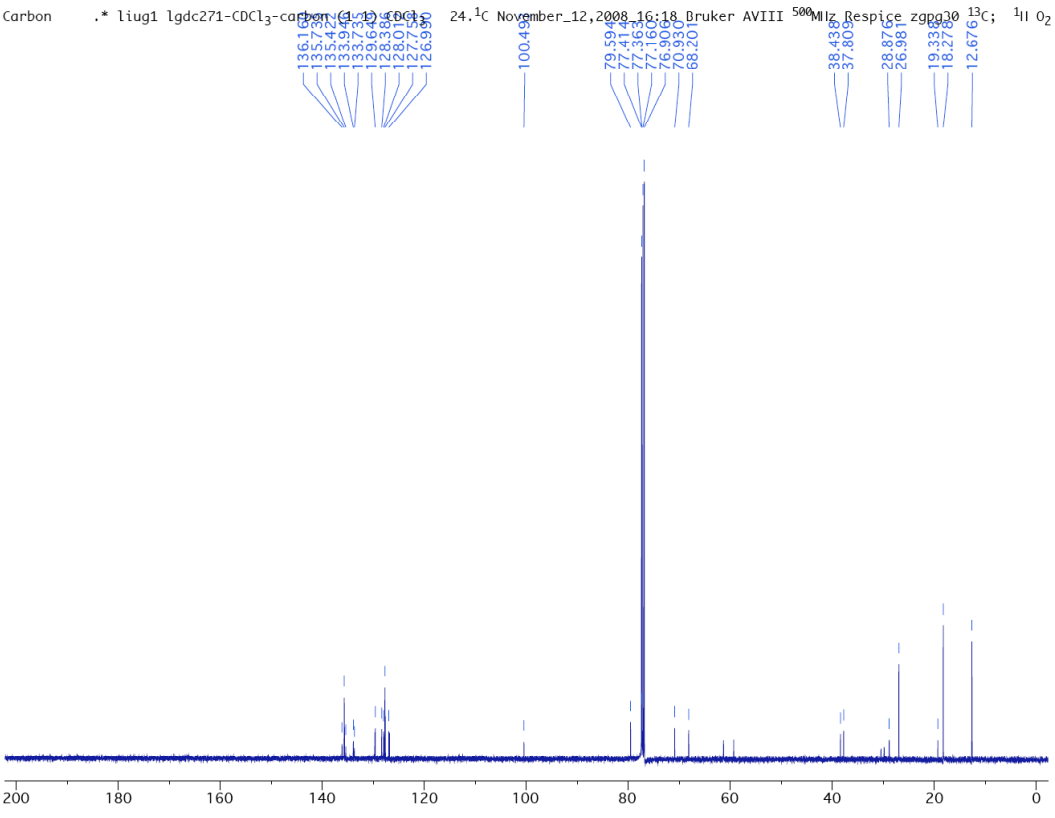


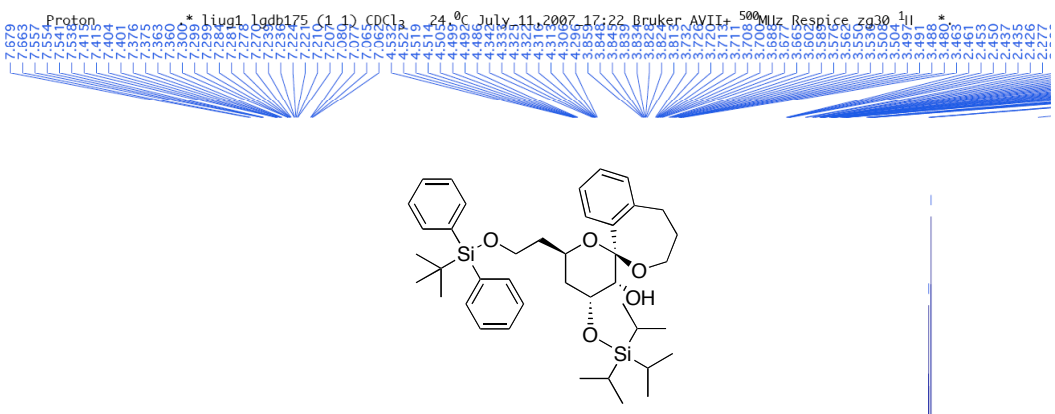




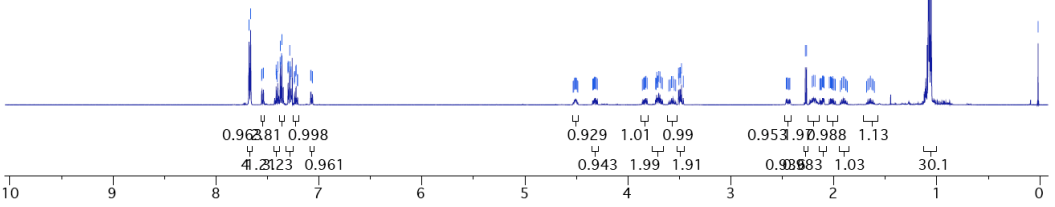


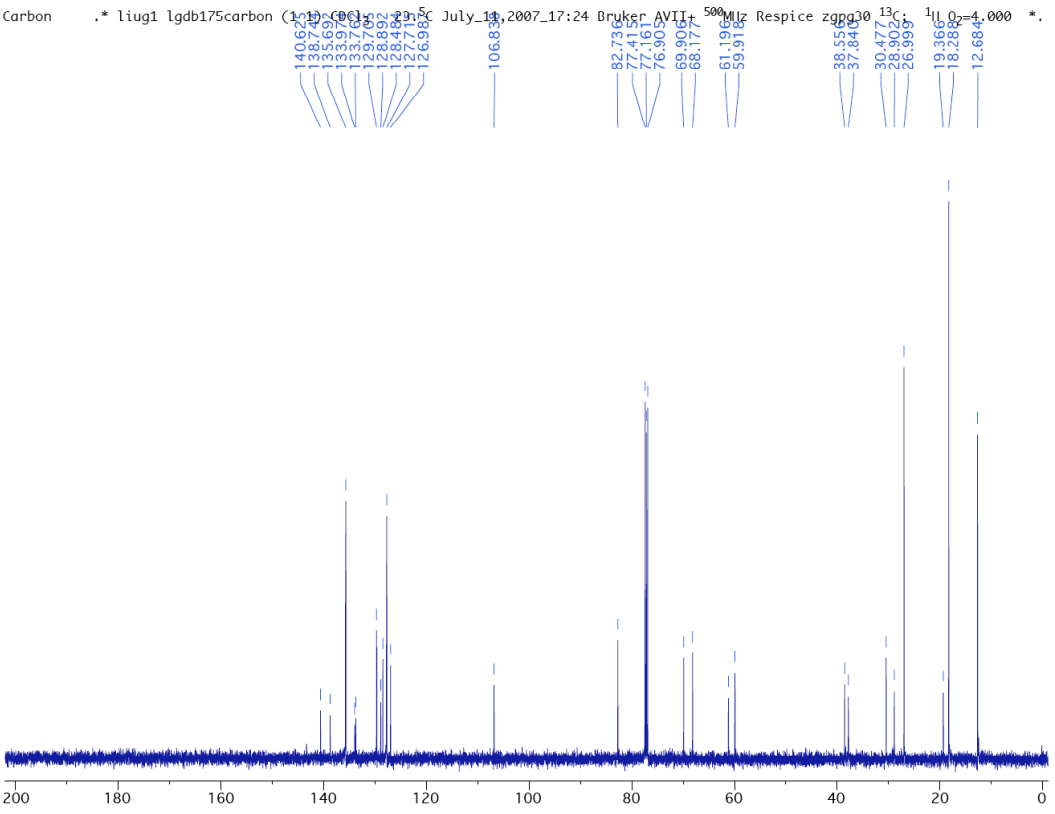
(+)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (4k)

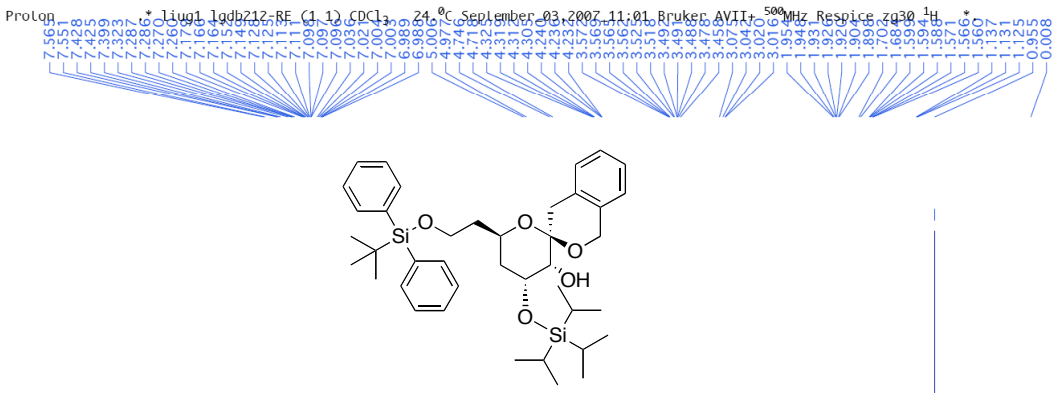




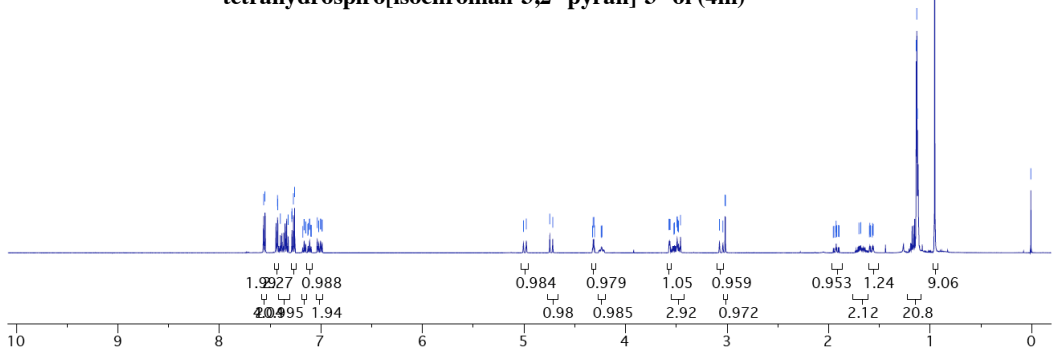
(+)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*c*]oxepine-1,2′-pyran]-3′-ol (4l)

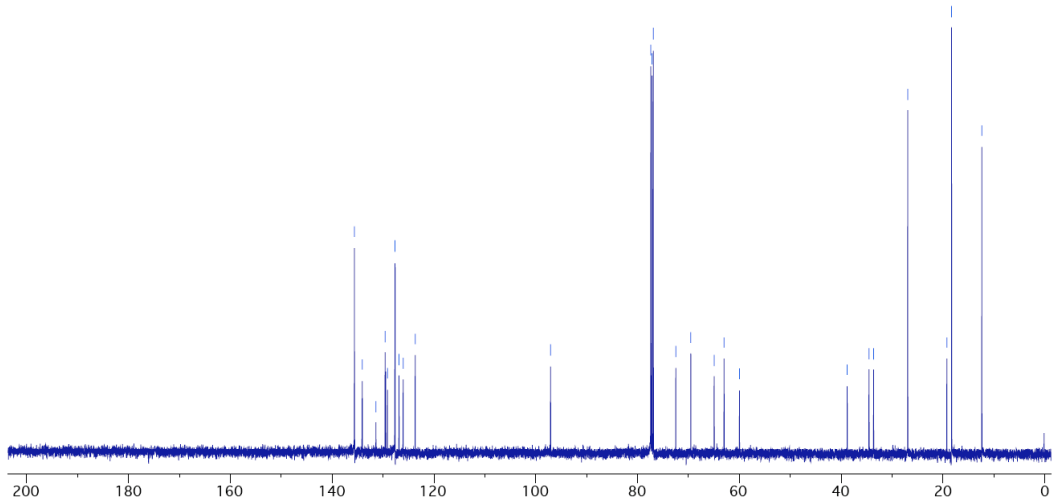


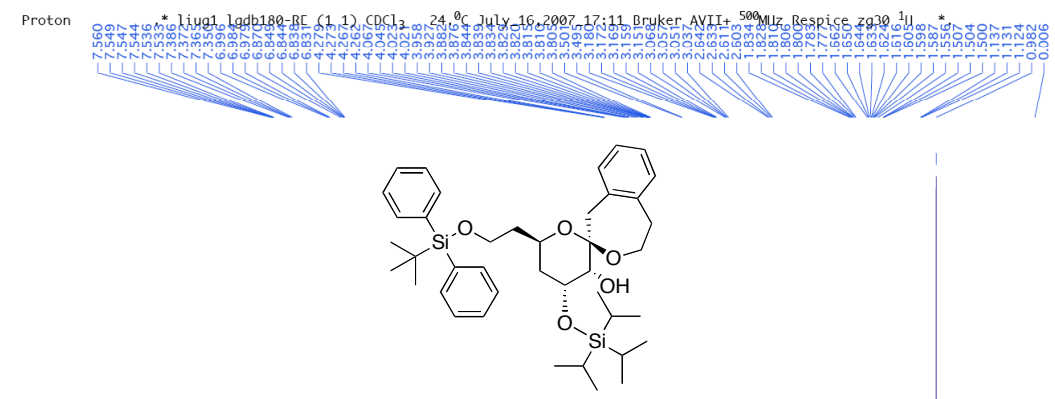




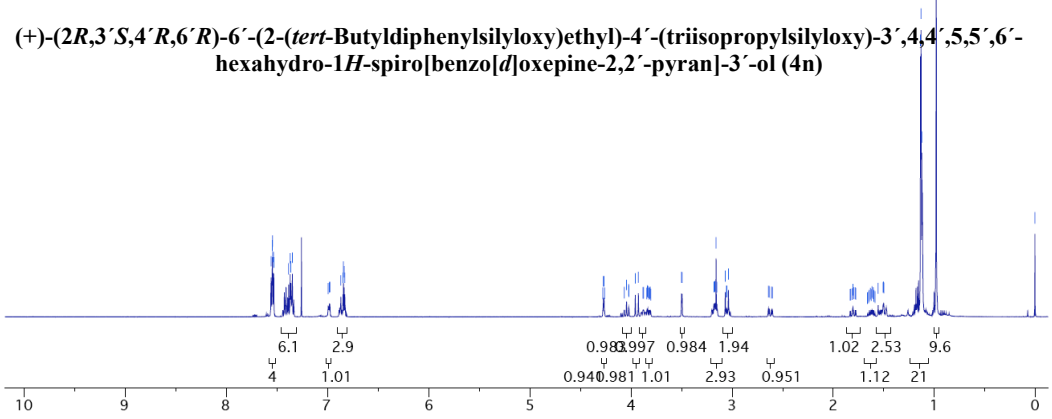
(+)-(2′*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-3,2′-pyran]-3′-ol (4m)

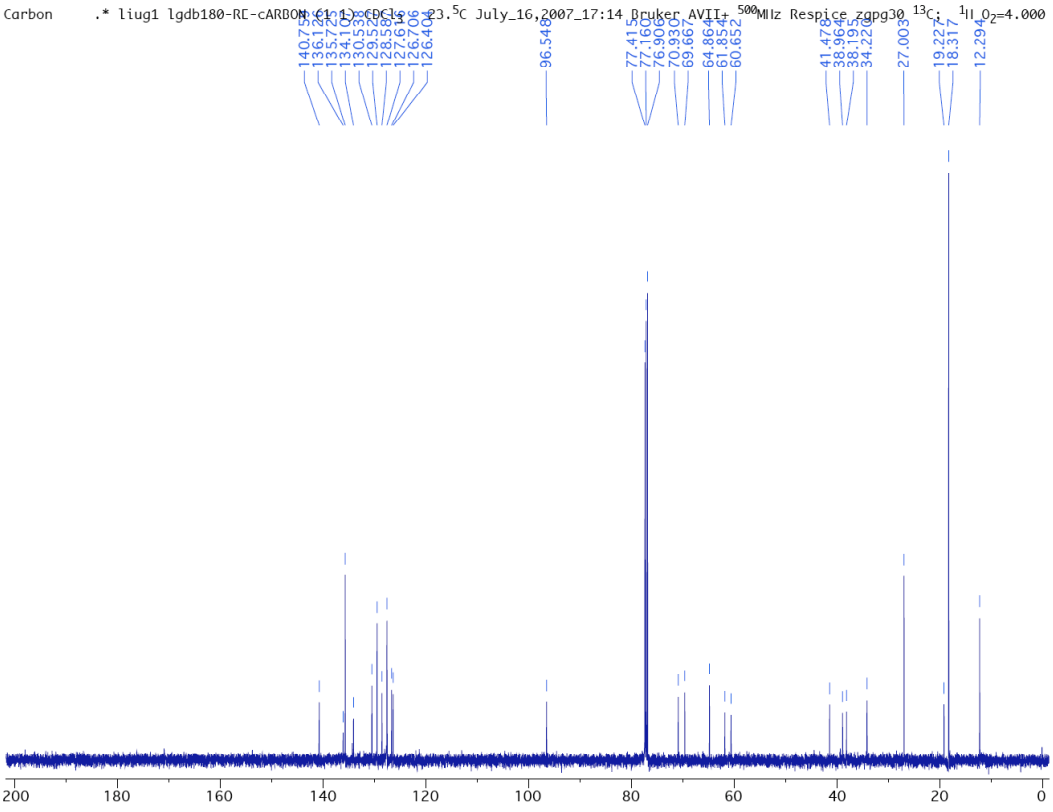


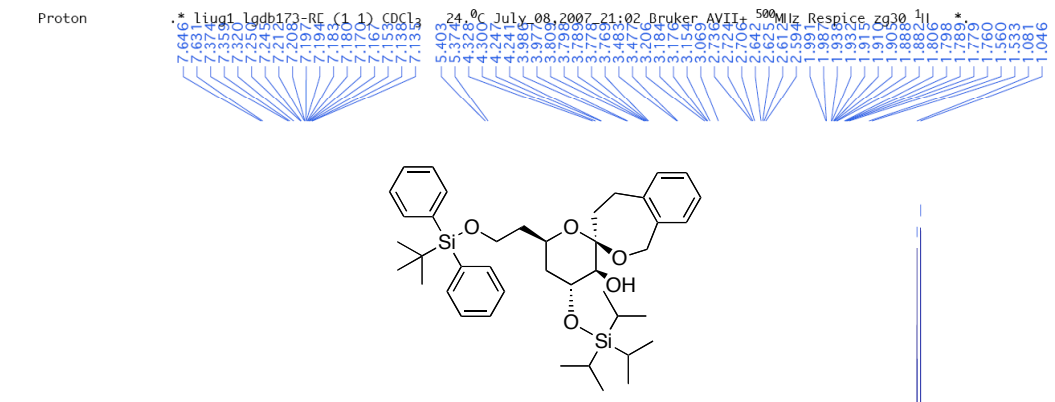




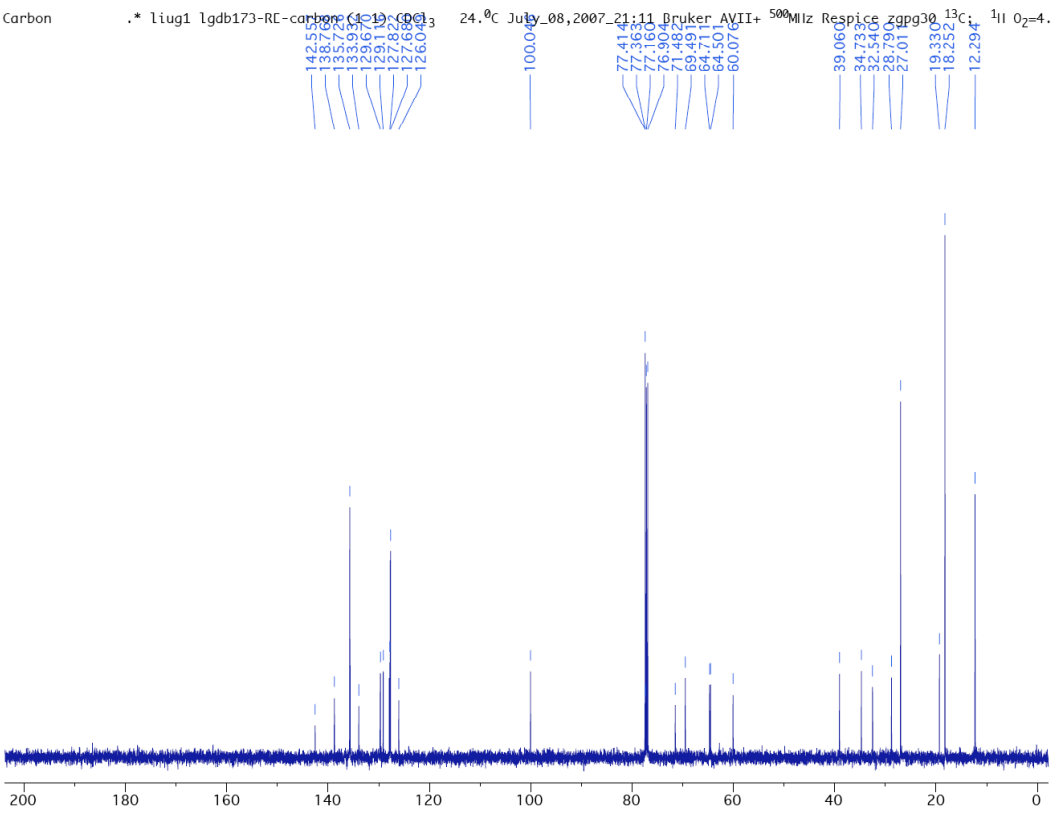
(+)-(2*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*d*]oxepine-2,2′-pyran]-3′-ol (4n)

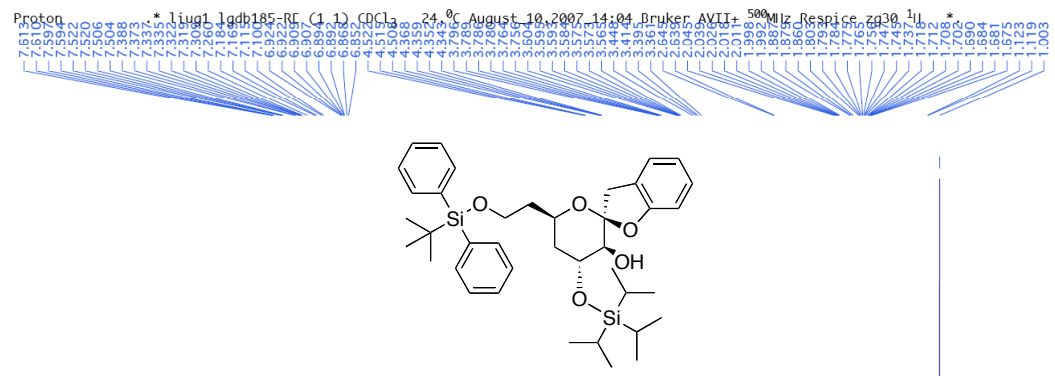




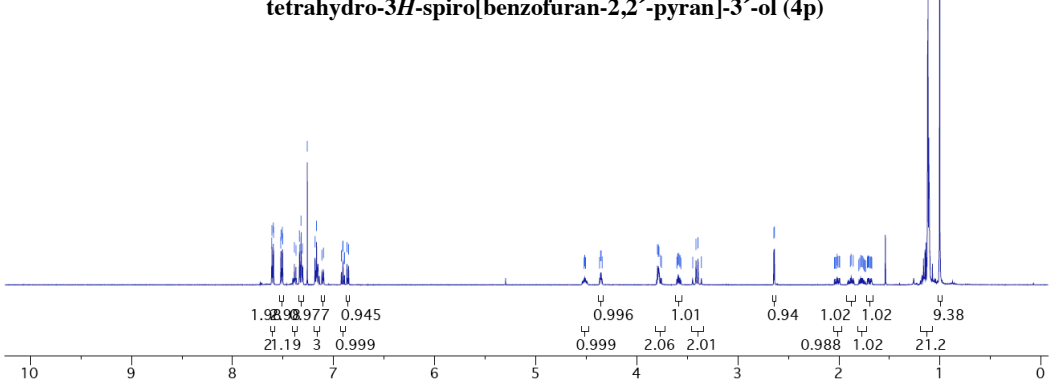


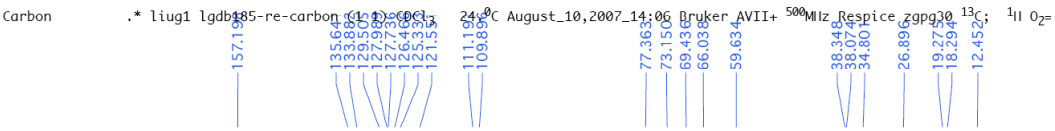
(+)-(2′*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*c*]oxepine-3,2′-pyran]-3′-ol (4o).

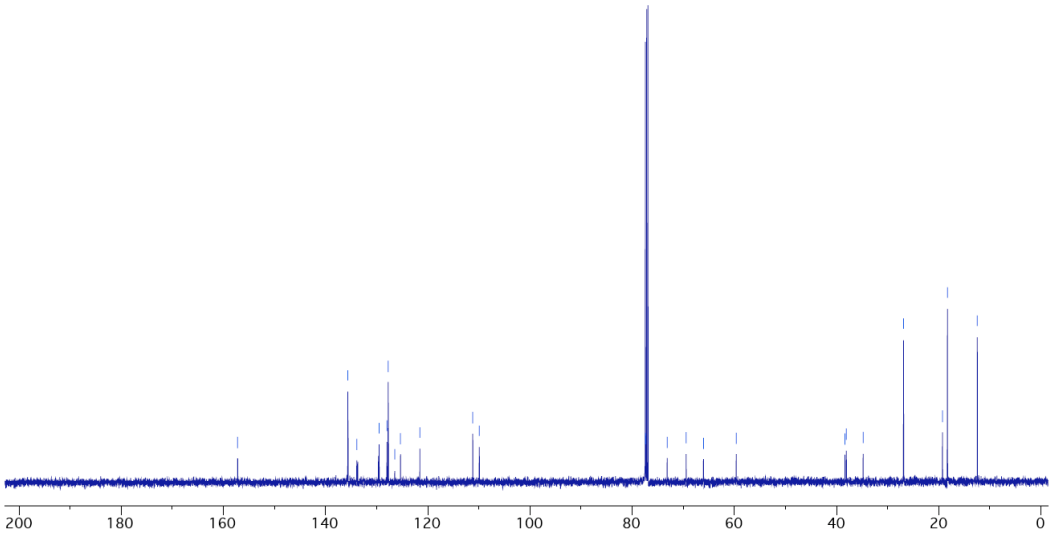


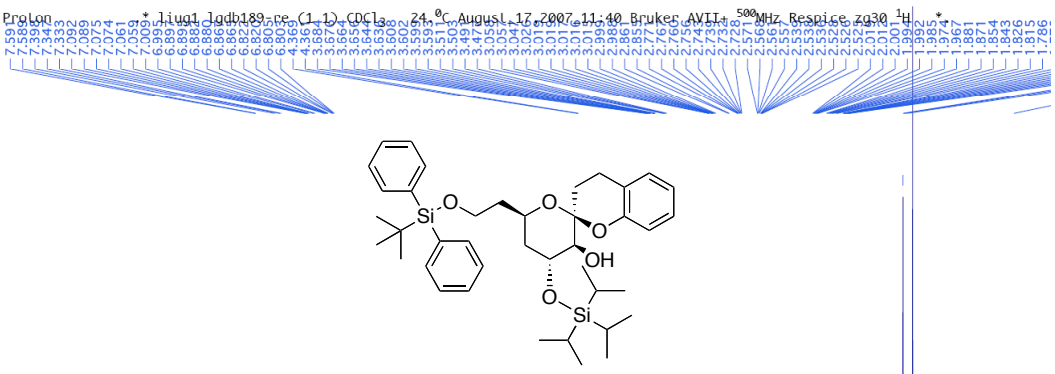


(+)-(2*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[benzofuran-2,2′-pyran]-3′-ol (4p)

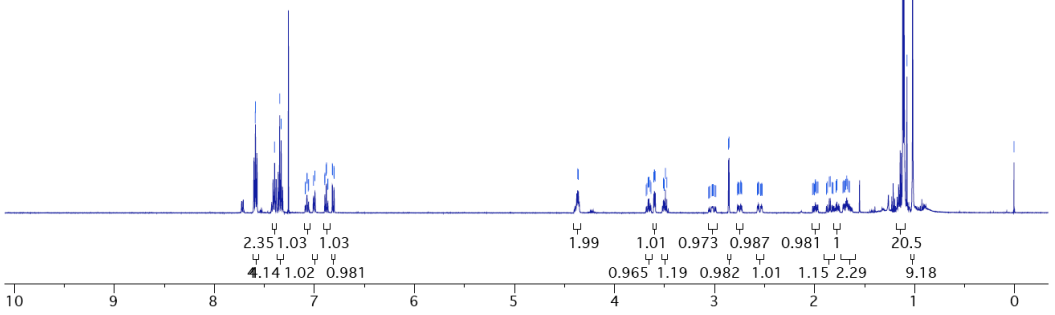


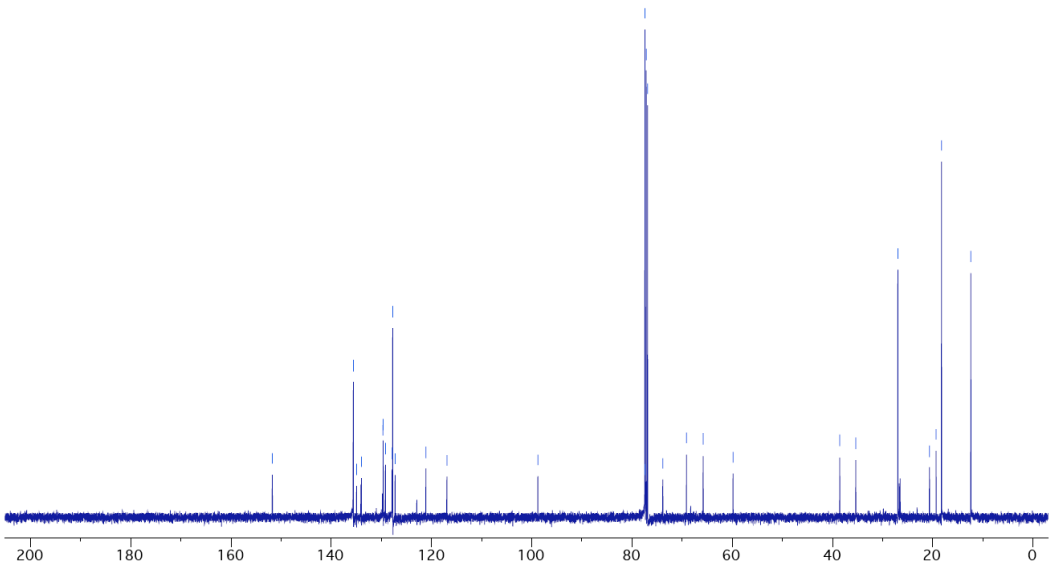


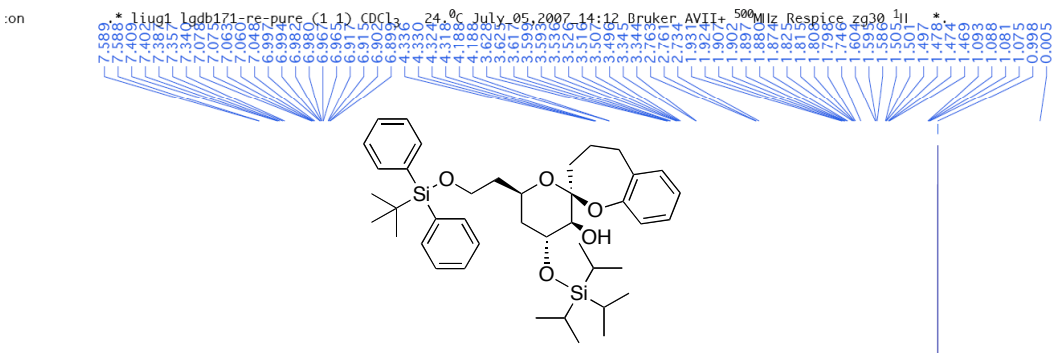




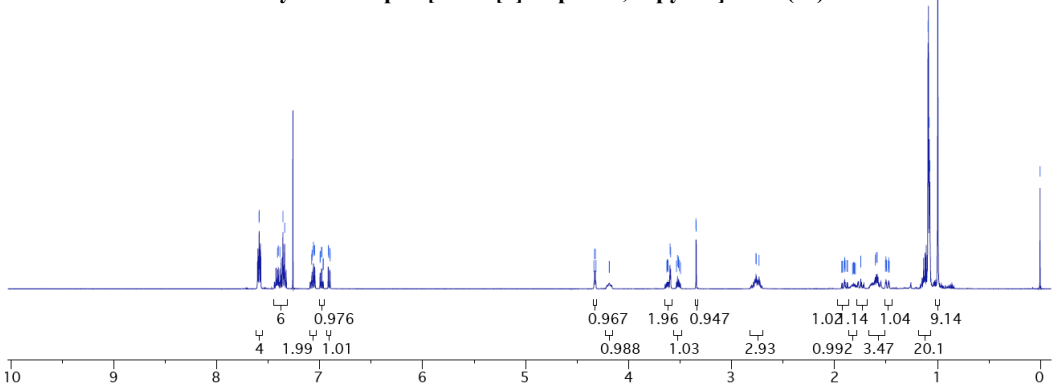
(+)-(2*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[chroman-2,2′-pyran]-3′-ol (4q).

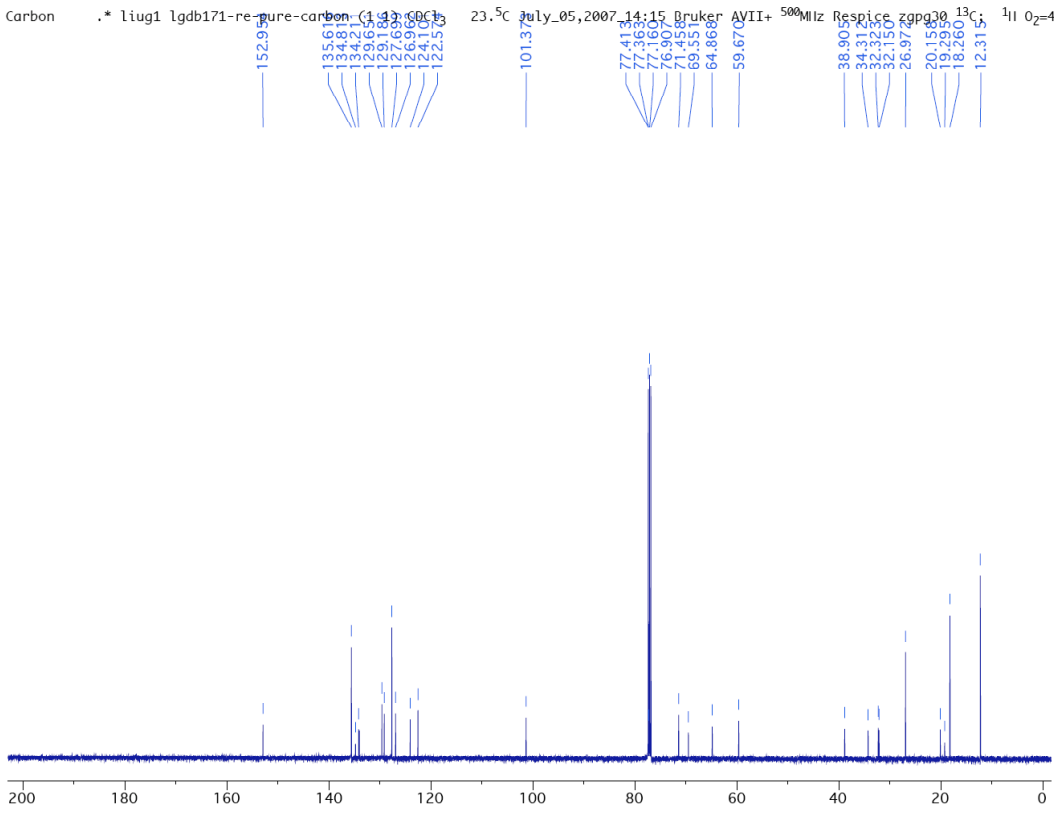




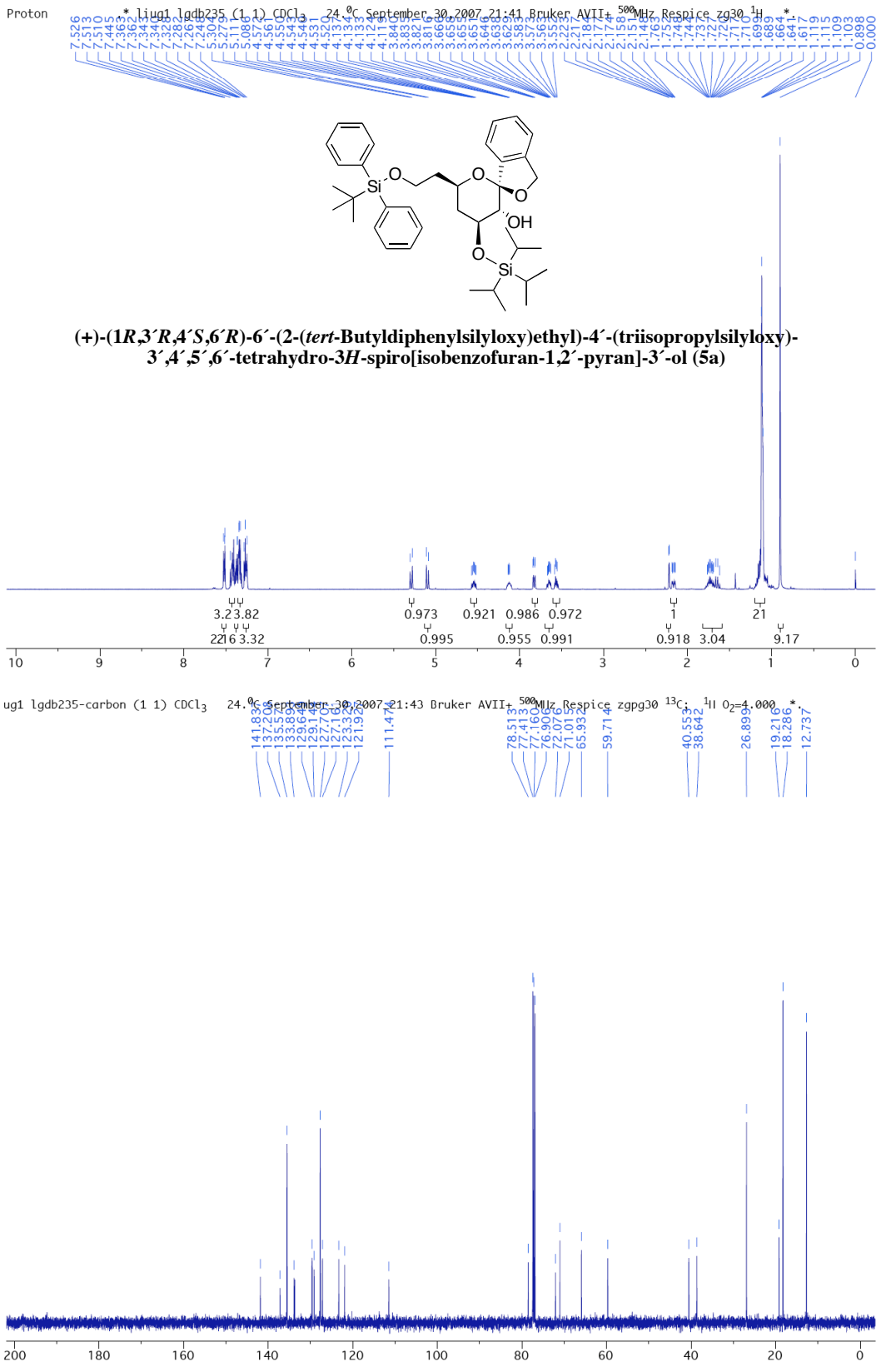


(+)-(2*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*b*]oxepine-2,2′-pyran]-3′-ol (4r)

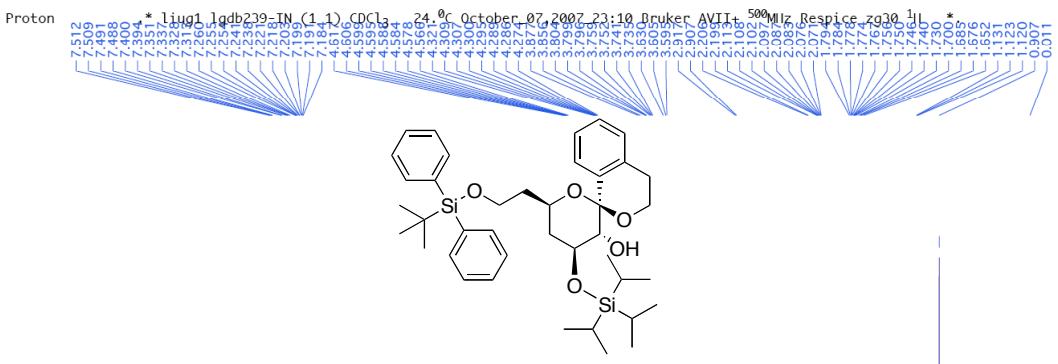




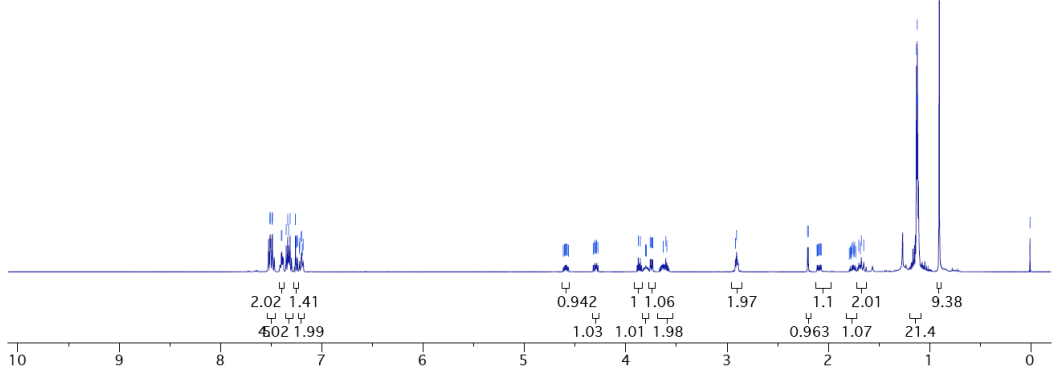
D. SPIROCYCLIZATION WITH INVERSION OF CONFIGURATION (MEOH OR ACOH) (5a–r)

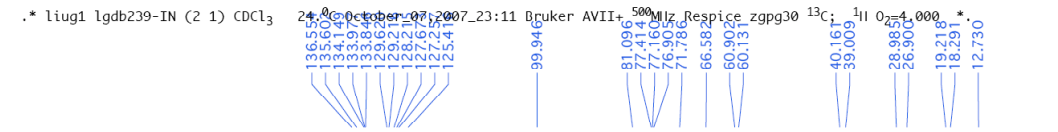


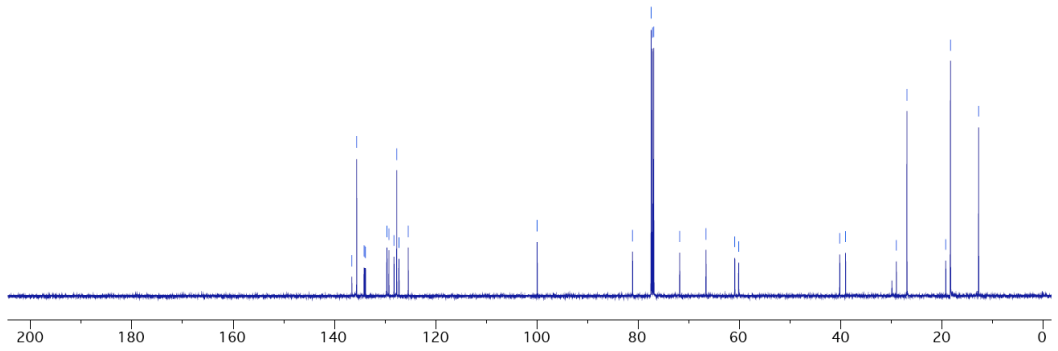
(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (5a)

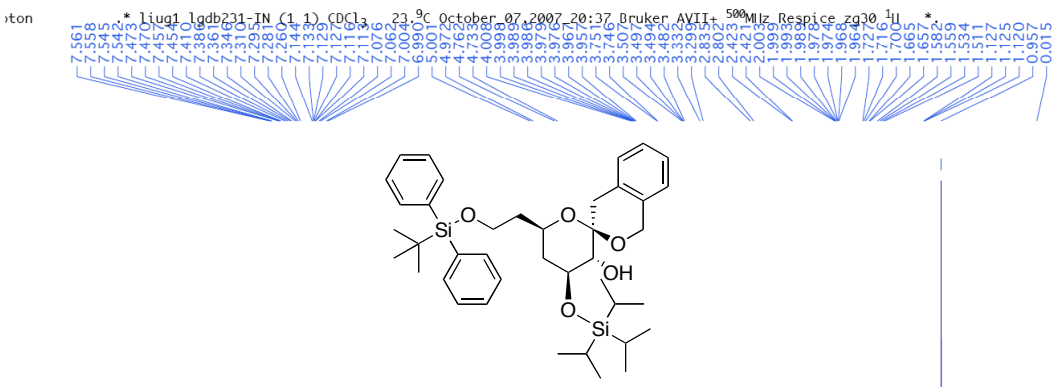


(+)-(1*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-1,2′-pyran]-3′-ol (5b)

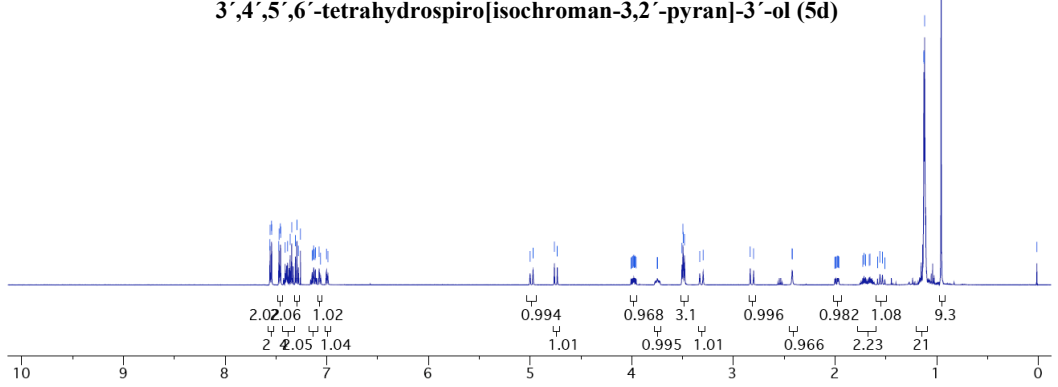


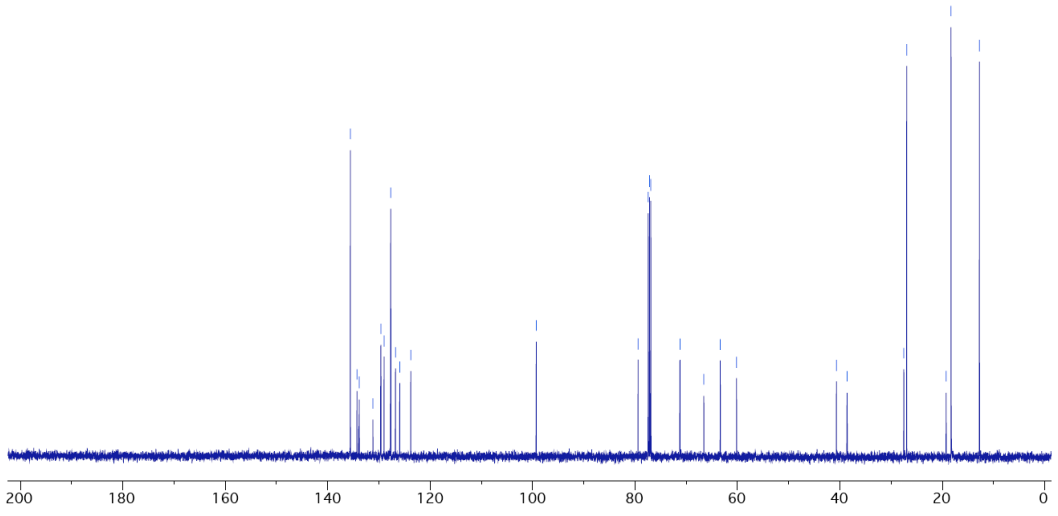


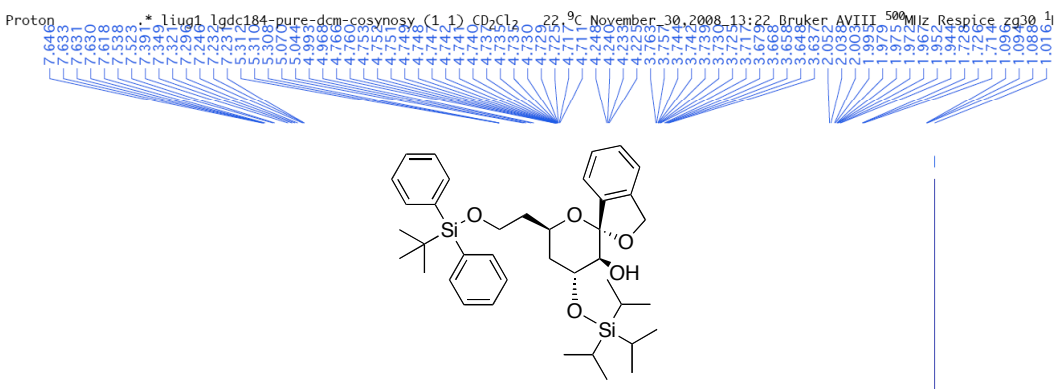




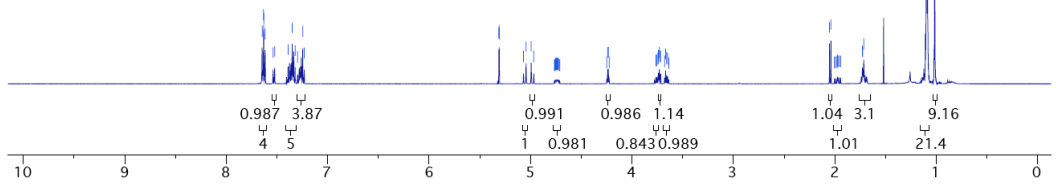
(+)-(2′*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-3,2′-pyran]-3′-ol (5d)

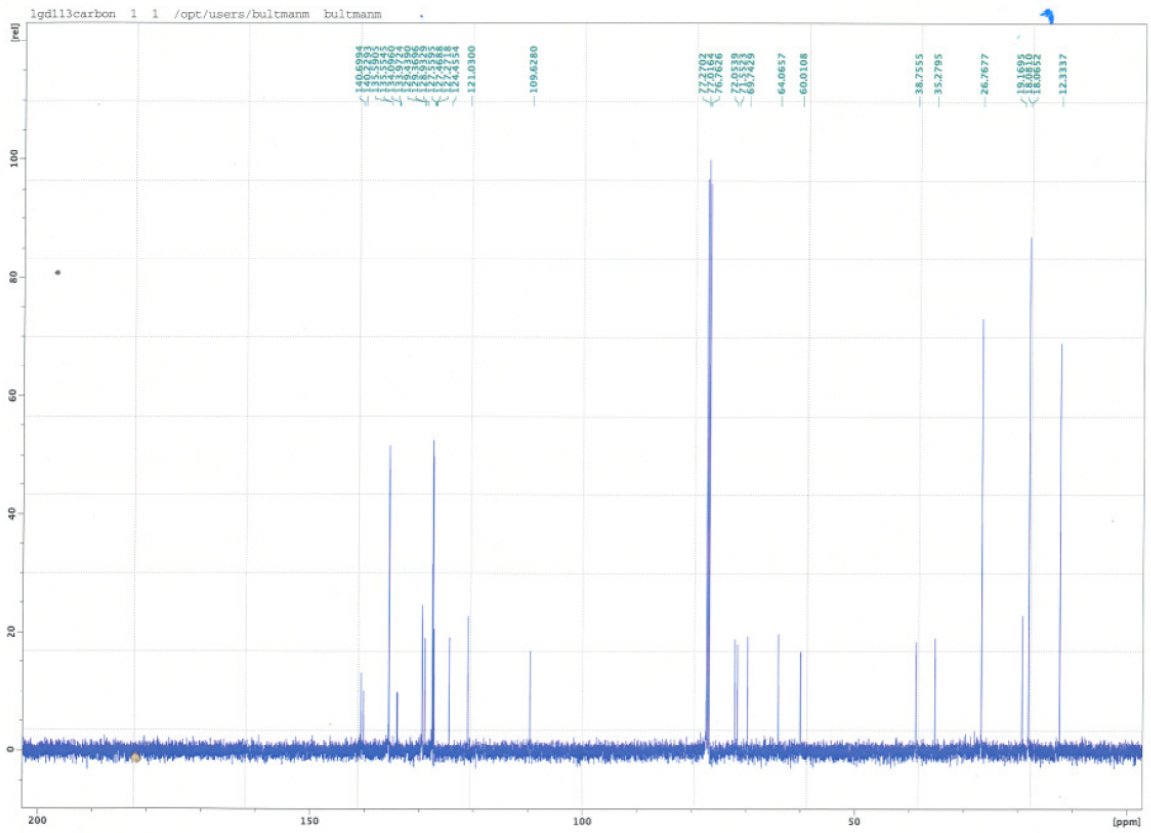


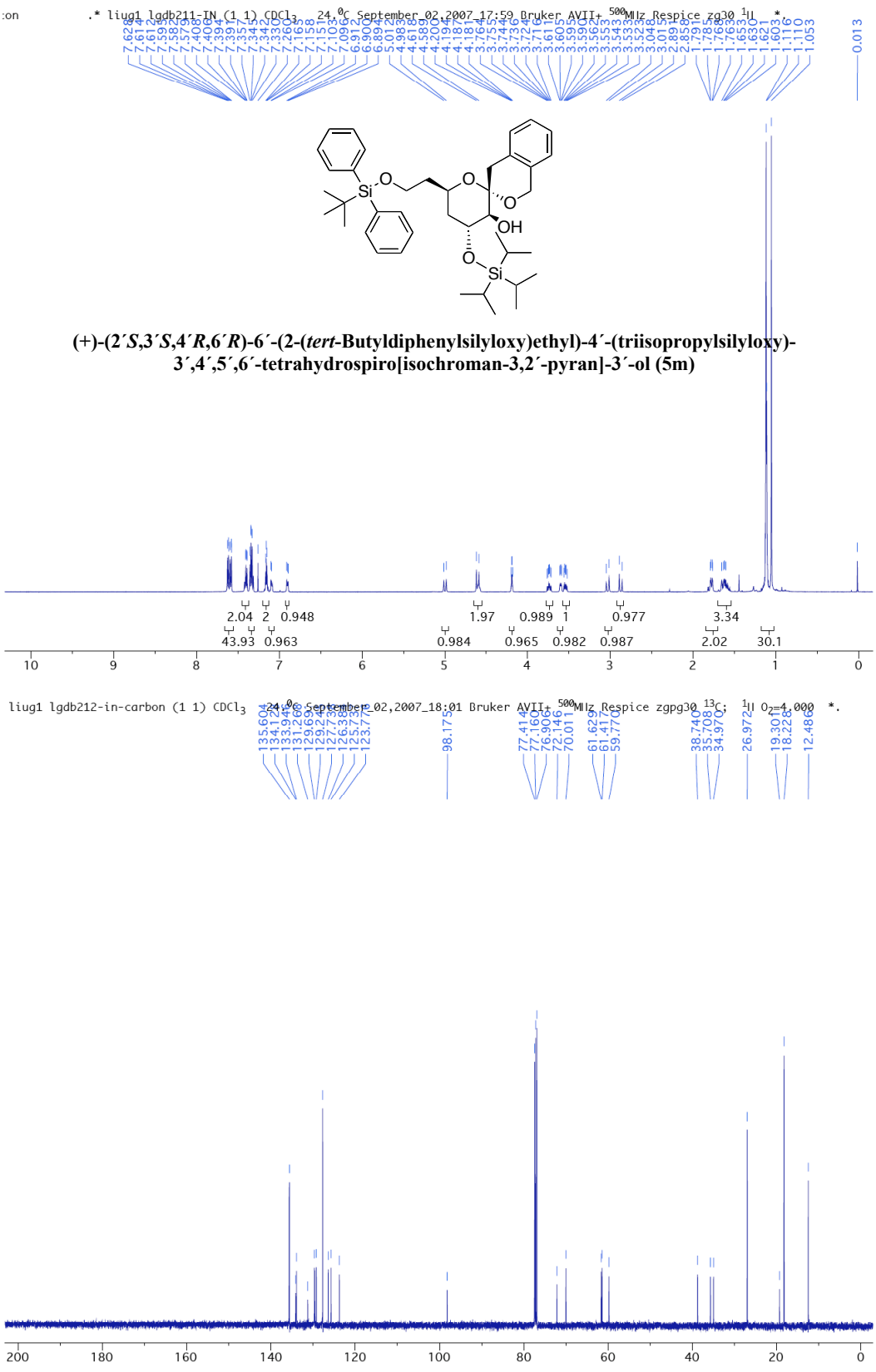




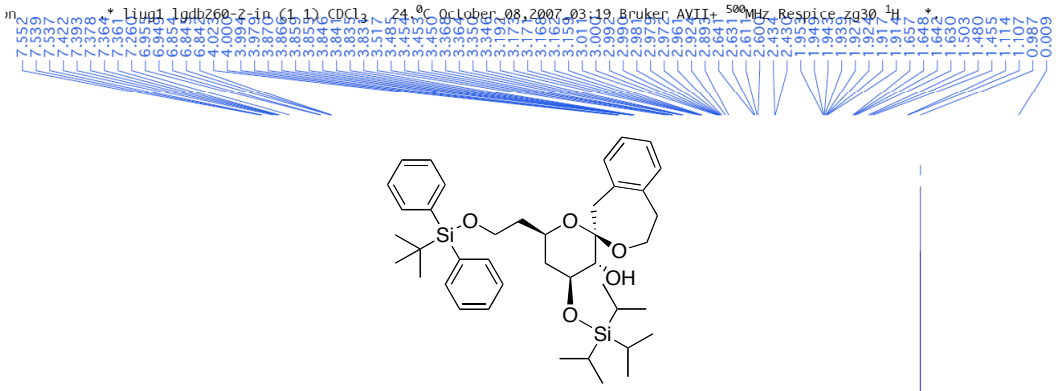
(+)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′-ol (5j)



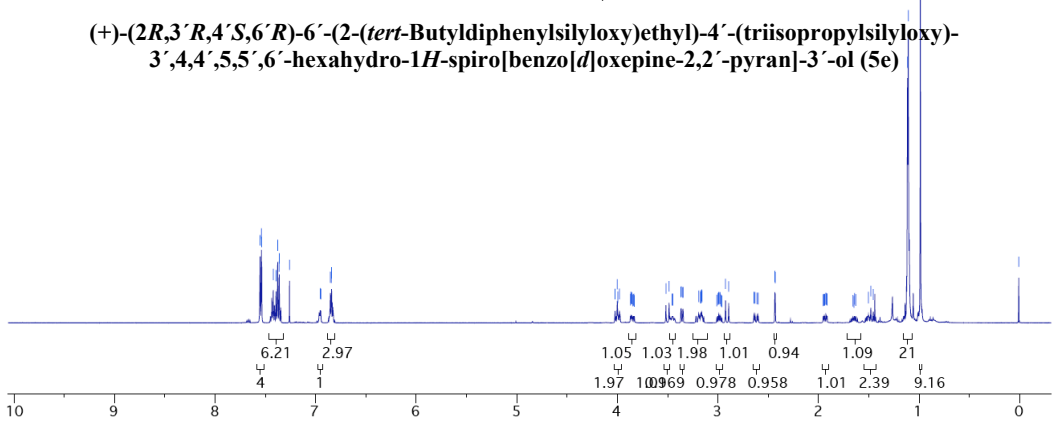


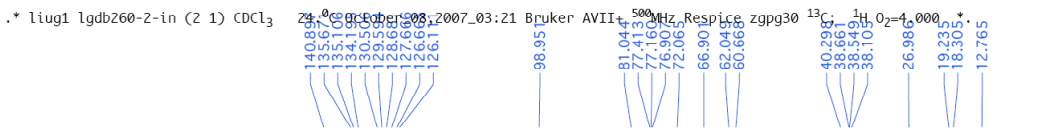


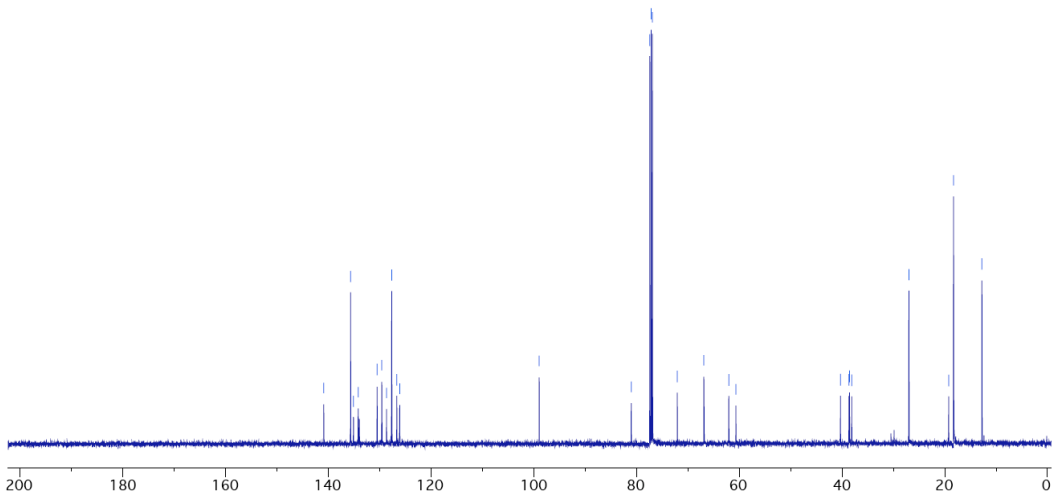
(+)-(2′*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[isochroman-3,2′-pyran]-3′-ol (5m)

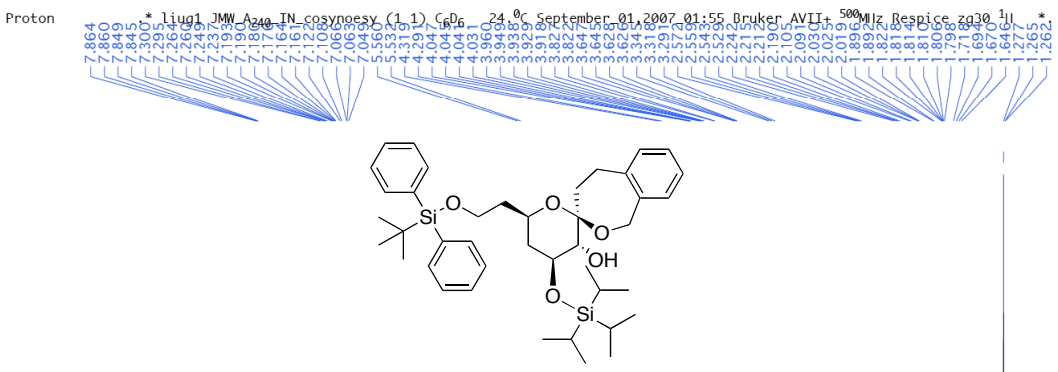


(+)-(2*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*d*]oxepine-2,2′-pyran]-3′-ol (5e)

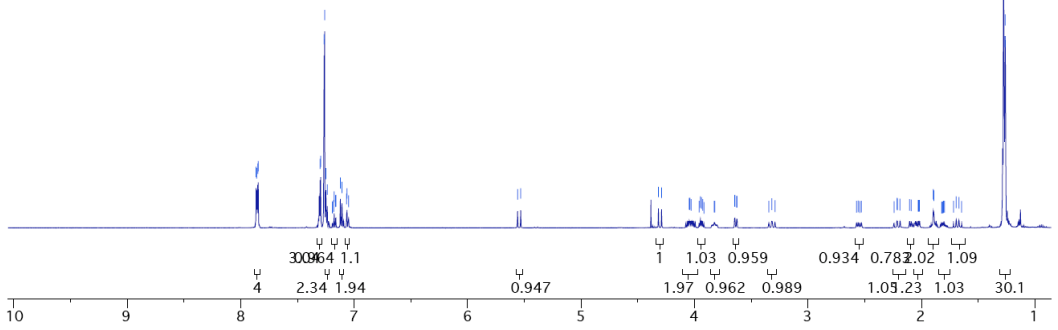


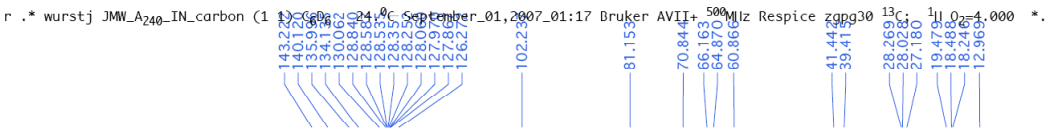


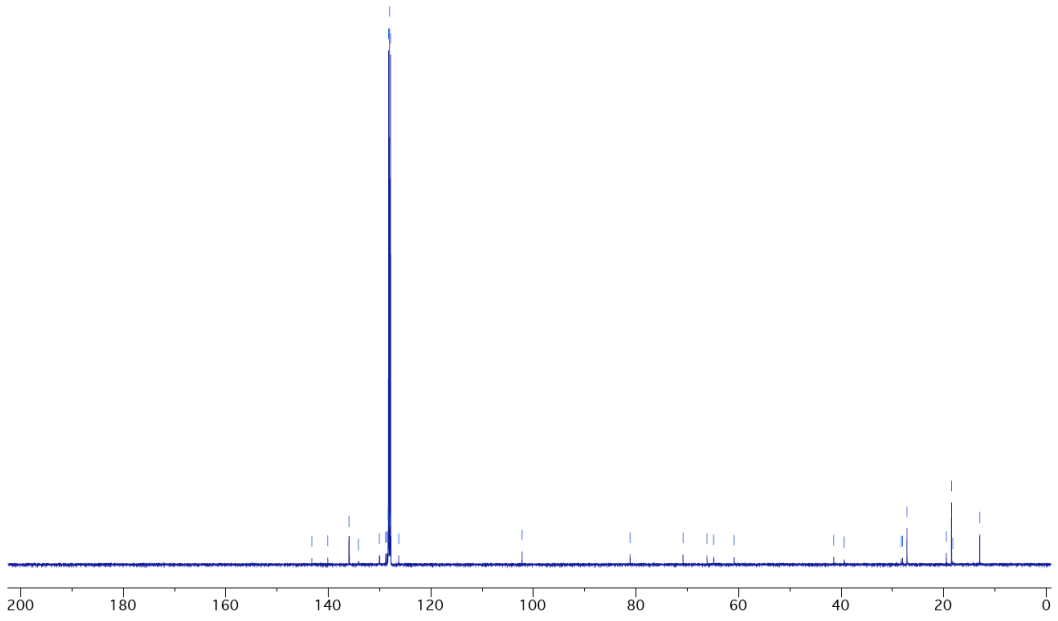


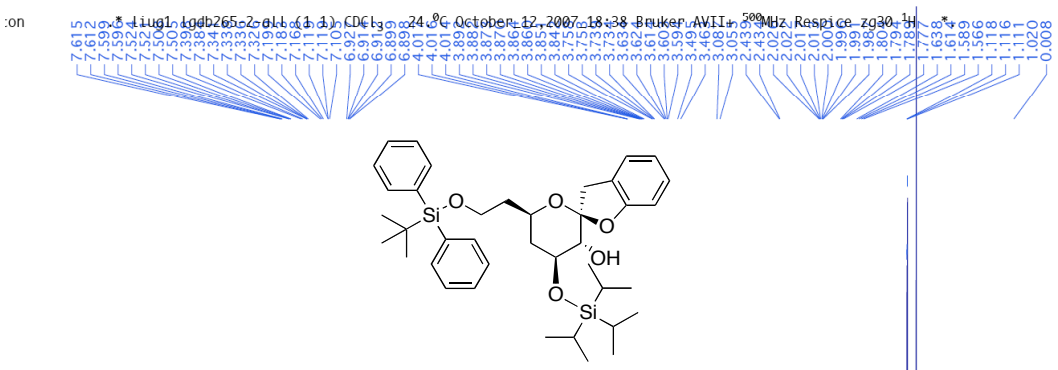


(+)-(2′*R*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*c*]oxepine-3,2′-pyran]-3′-ol (5f)

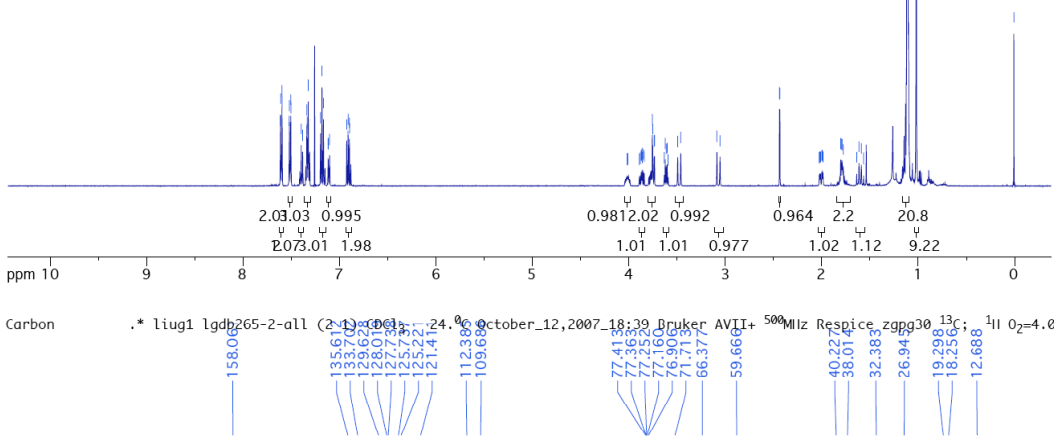


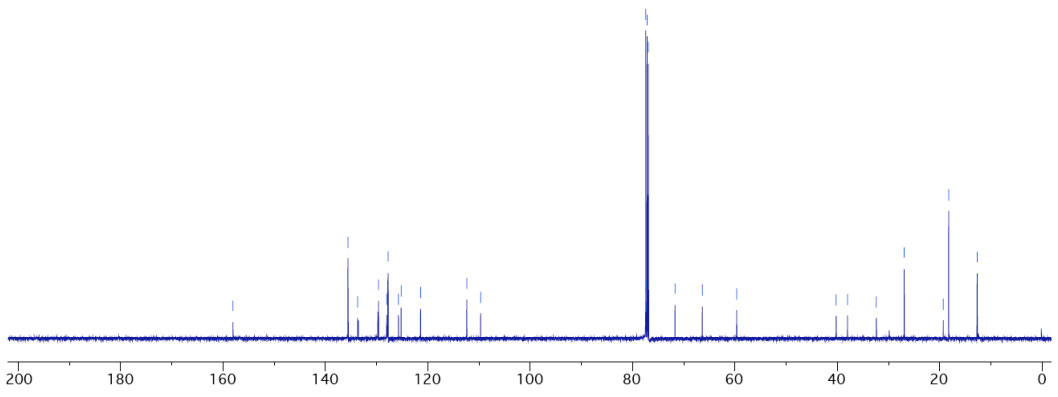


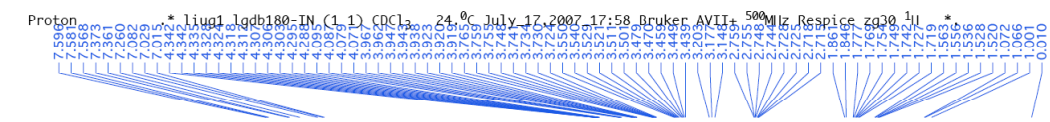


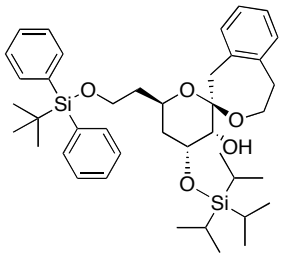


(+)-(2*S*,3′*R*,4′*S*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[benzofuran-2,2′-pyran]-3′-ol (5g)

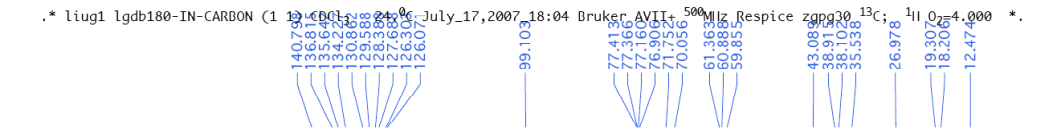


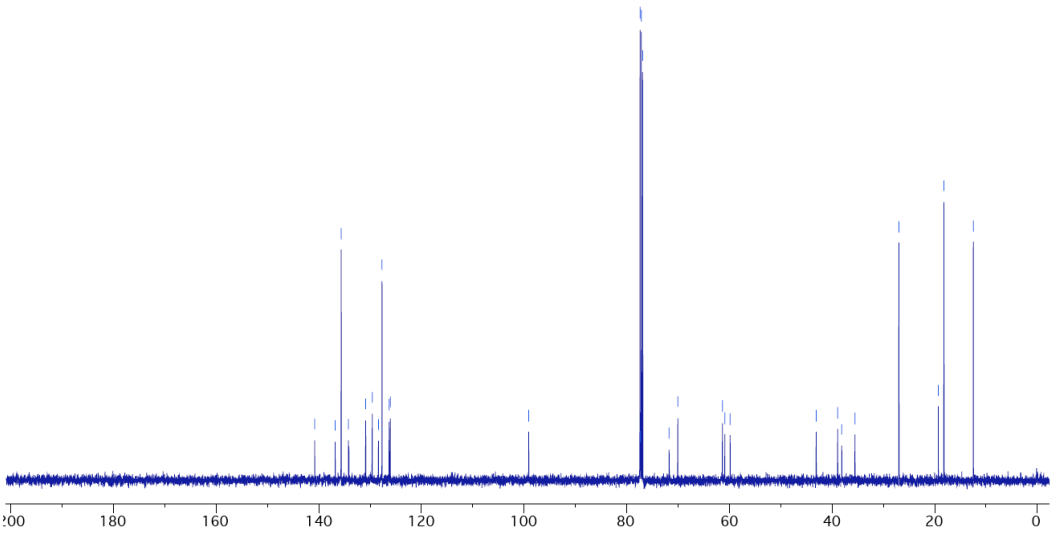


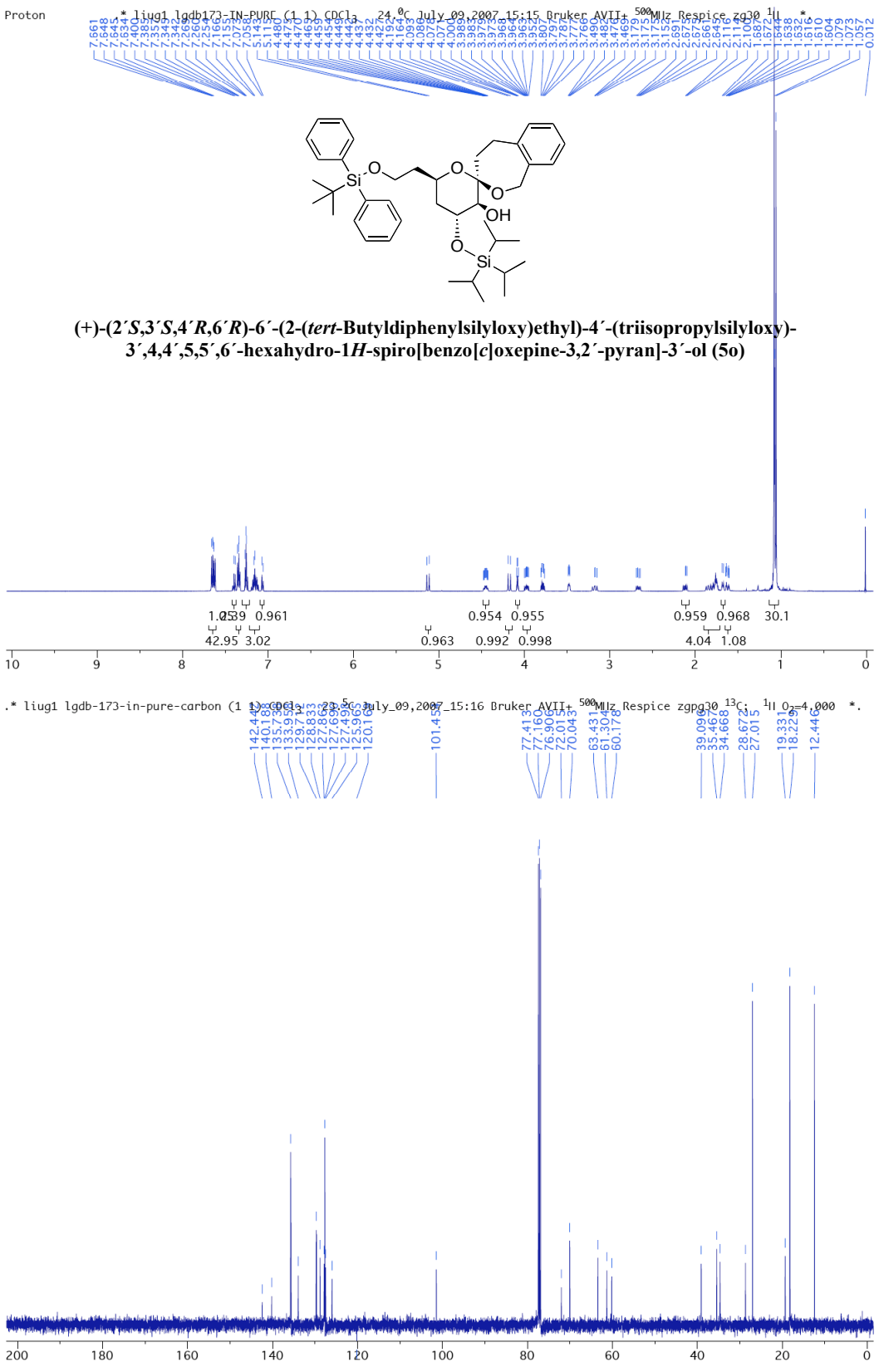




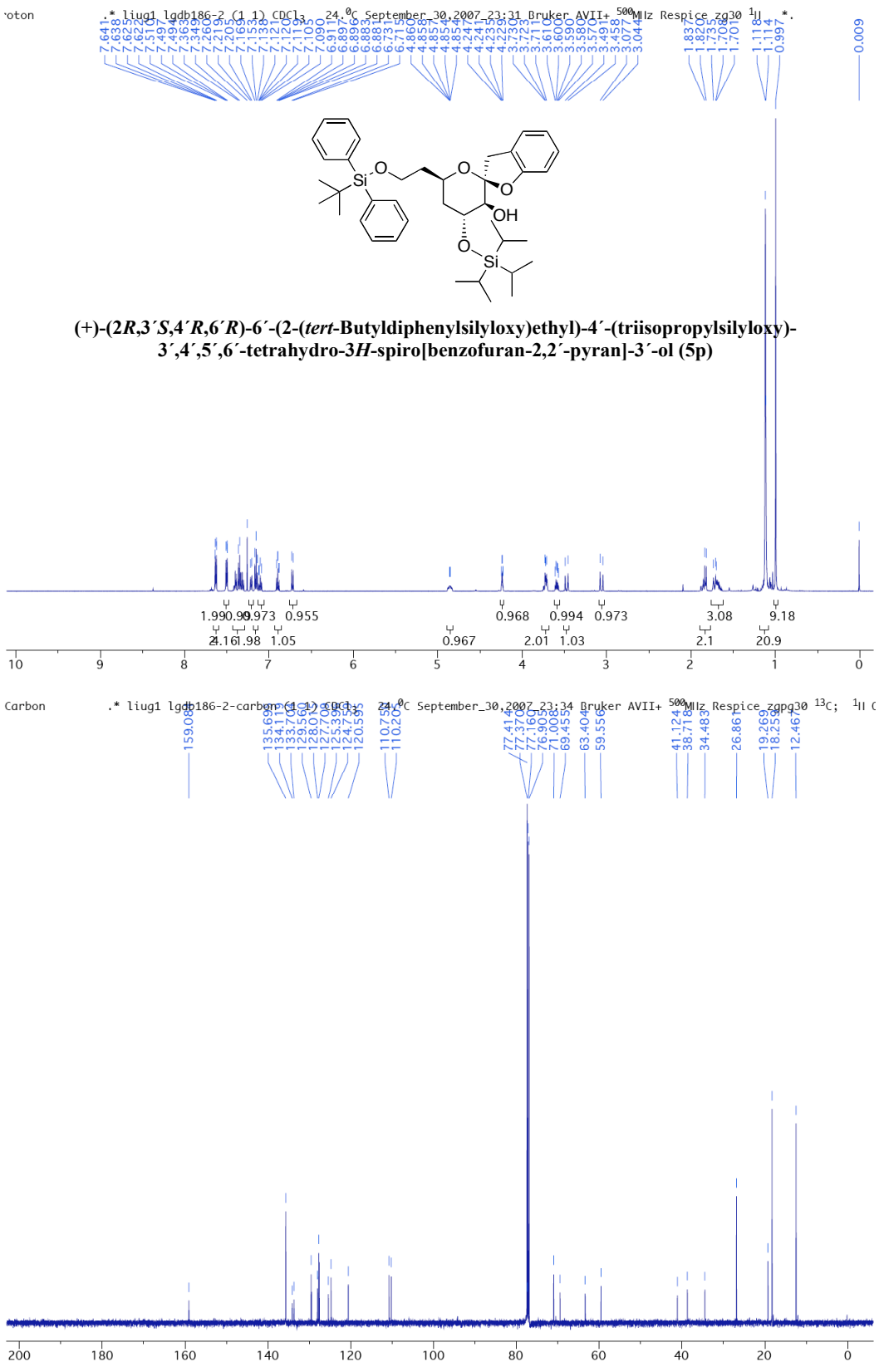
(+)-(2*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*d*]oxepine-2,2′-pyran]-3′-ol (5n)



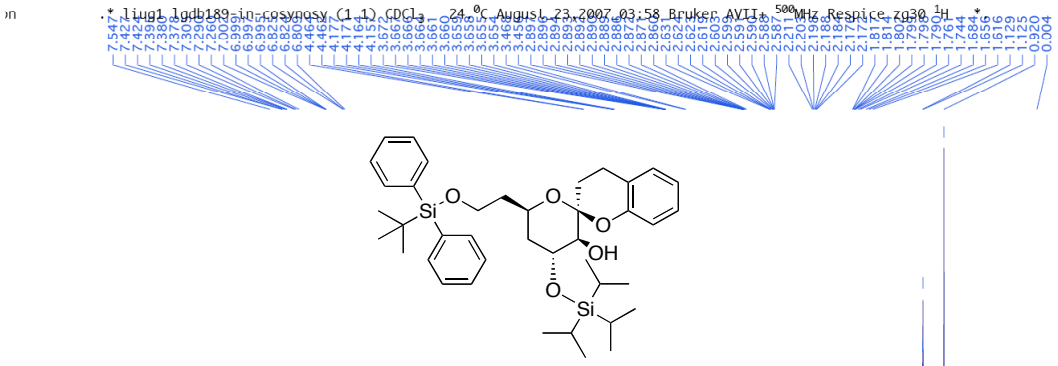




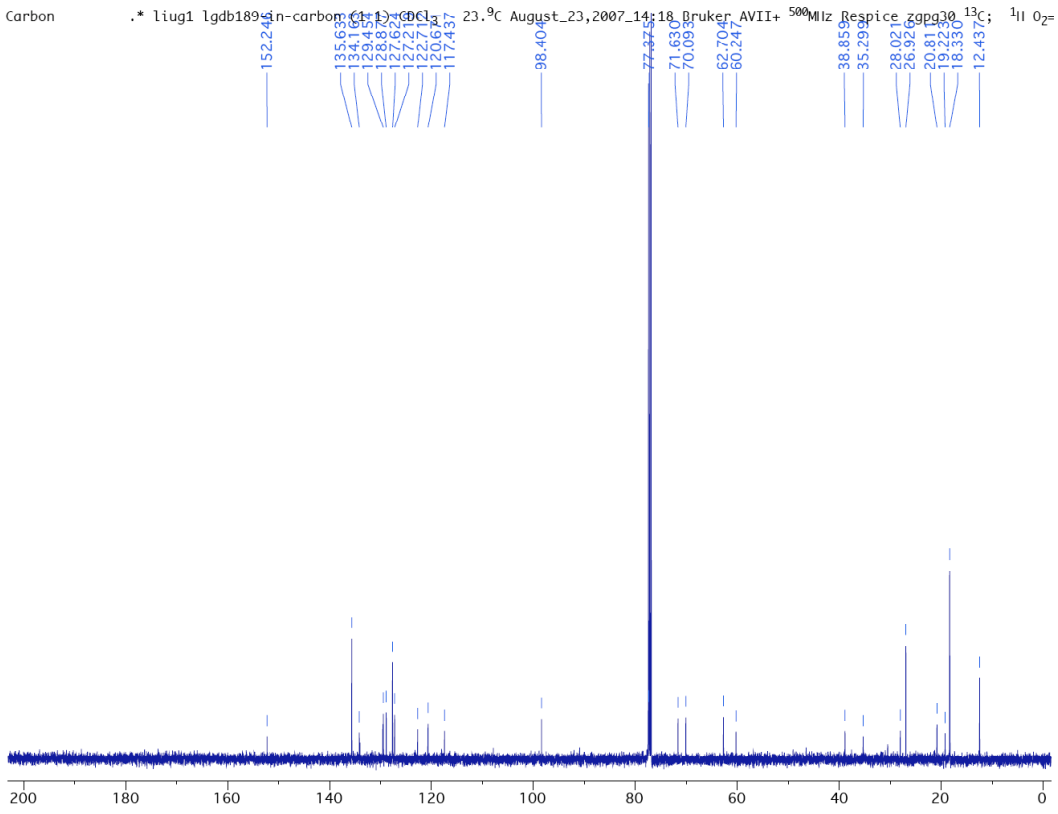
(+)-(2′*S*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-1*H*-spiro[benzo[*c*]oxepine-3,2′-pyran]-3′-ol (5o)

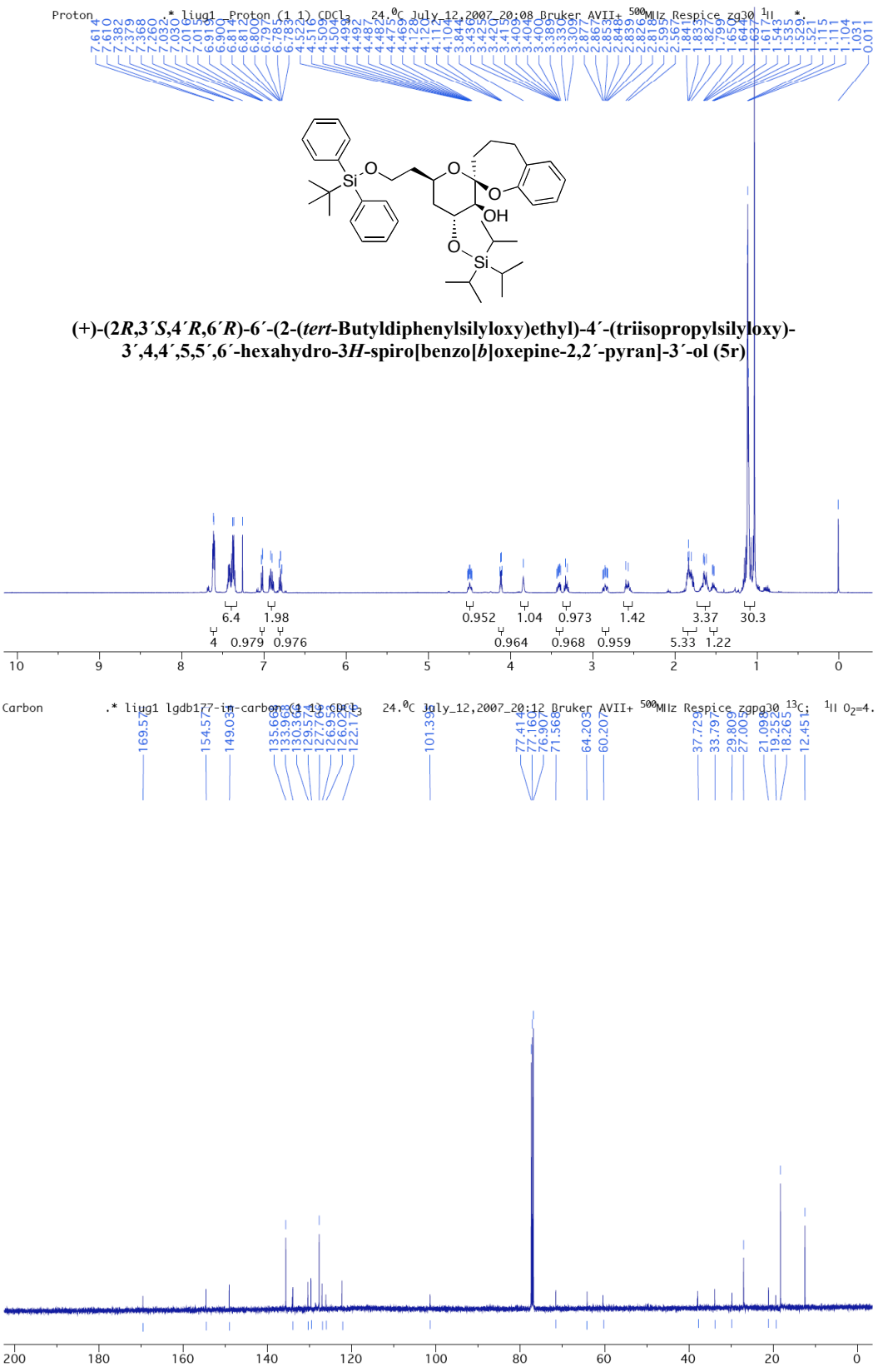


(+)-(2*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[benzofuran-2,2′-pyran]-3′-ol (5p)



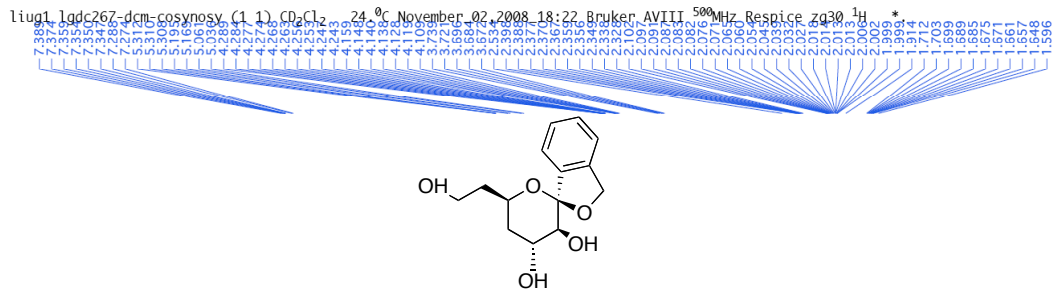
(+)-(2*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4′,5′,6′-tetrahydrospiro[chroman-2,2′-pyran]-3′-ol (5q)



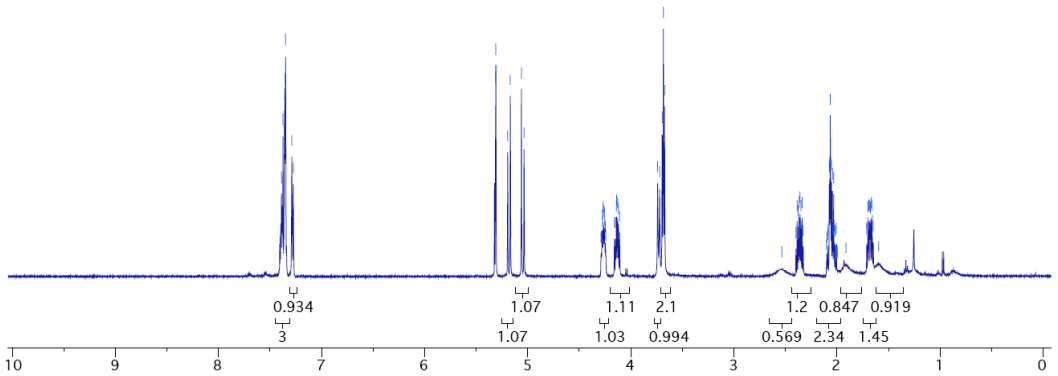


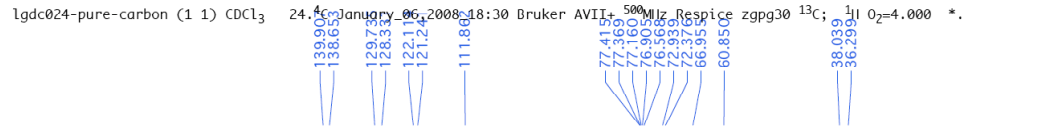
(+)-(2*R*,3′*S*,4′*R*,6′*R*)-6′-(2-(*tert*-Butyldiphenylsilyloxy)ethyl)-4′-(triisopropylsilyloxy)-3′,4,4′,5,5′,6′-hexahydro-3*H*-spiro[benzo[*b*]oxepine-2,2′-pyran]-3′-ol (5r)

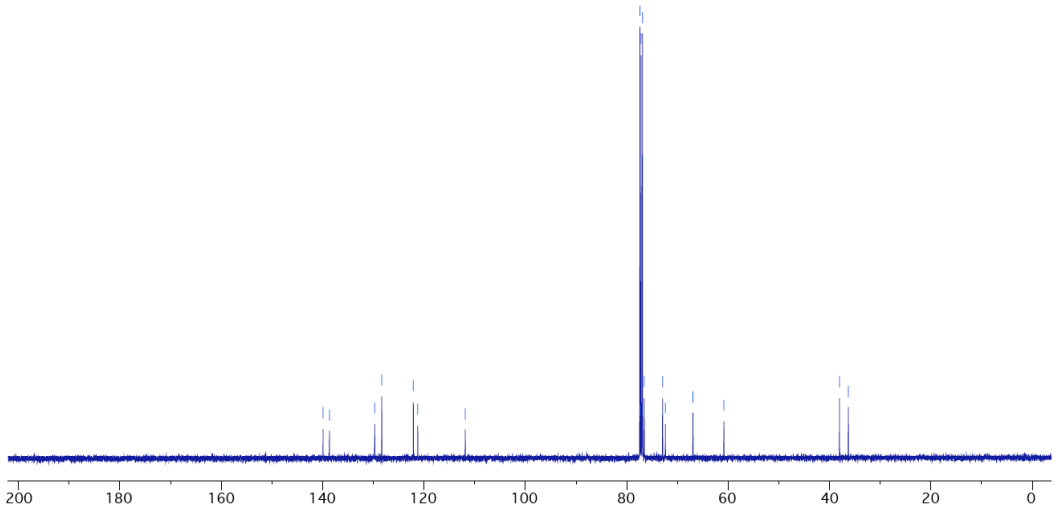
E. DESILYLATION OF SPIROKETALS (7, 8)

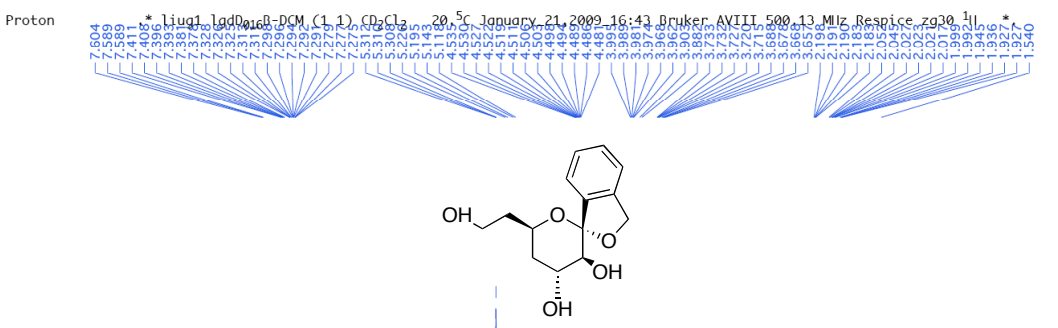


(+)-(1*R*,3′*S*,4′*R*,6′*R*)-6′-(2-hydroxyethyl)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′,4′-diol (7)









(+)-(1*S*,3′*S*,4′*R*,6′*R*)-6′-(2-hydroxyethyl)-3′,4′,5′,6′-tetrahydro-3*H*-spiro[isobenzofuran-1,2′-pyran]-3′,4′-diol (8)