

Silanediol-Catalyzed Chromenone Functionalization

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Supplemental Section Table of Contents

General Methods	1
Catalyst Preparation	2
General Procedure for the Preparation of Silyl Ketene Acetals	9
General Procedure for the Preparation of Chromenones	9
General Procedure for Addition of Silyl Ketene Acetals to Chromenones	13
General Procedure for the Formation of the N-sulfinyl Imine	16
Determination of the Major Enantiomer	16
Determination of Association Constant	19
References	20
Select HPLC Traces	21
Selected NMR Spectra	33

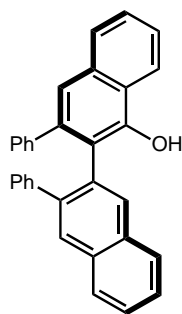
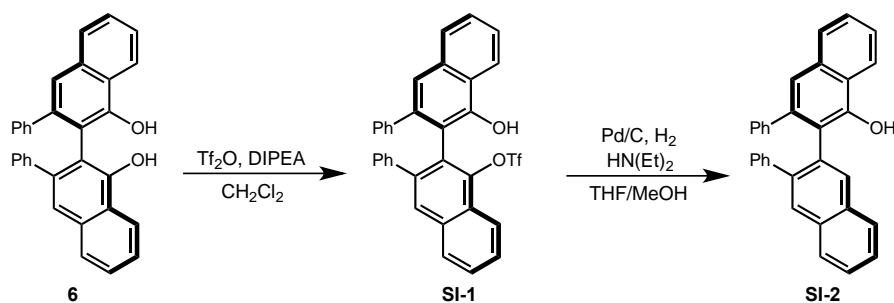
General Methods

Diethyl ether, methylene chloride, tetrahydrofuran, and toluene were purified by passage through a bed of activated alumina. Ethyl acetate, acetone, and hexanes were purchased and used as received. Purification of reaction products was carried out by flash chromatography using Silicycle SiliaFlash P60 silica gel (40 - 63 μ m). Analytical thin layer chromatography was performed on Analtech silica gel HLF uniplates (250 microns, UV254). Visualization was accomplished with UV light and ceric ammonium molybdate or potassium permanganate stains

followed by heating. Melting points (mp) were obtained on a Fisher Scientific Mel-Temp apparatus and are uncorrected. Infrared spectra (IR) were obtained on a Thermo Scientific Nicolet iS5 with iD7 diamond ATR attachment. Proton nuclear magnetic resonances (^1H NMR) were recorded in deuterated solvents on a Bruker Avance AVIII 400 (400 MHz) spectrometer unless otherwise noted. Chemical shifts are reported in parts per million (ppm, δ) using the solvent as internal standard (CDCl_3 , δ 7.26). ^1H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), or quartet (q). Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m) or broad (br). Coupling constants are reported in Hertz (Hz). Proton-decoupled carbon (^{13}C NMR) spectra were recorded on a Bruker Avance AVIII 400 (100 MHz) or a Bruker Avance AVIII 600 (150 MHz) spectrometer and are reported in ppm using the solvent as an internal standard (CDCl_3 , δ 77.0). Electrospray mass spectra (ESI-MS) were obtained using a Bruker MicrOTOF Mass Spectrometer. HPLC analyses were obtained on a Perkin Elmer Series 200 HPLC with multiple wavelength detector. Fluorescence spectra were recorded on a Hitachi F-7000 fluorescence spectrometer. Unless otherwise noted, all other commercially available reagents and solvents were used without further purification.

Catalyst Preparation

Synthesis of SI-2:

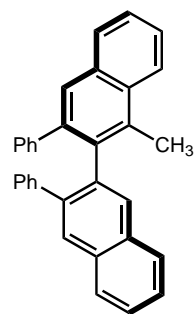
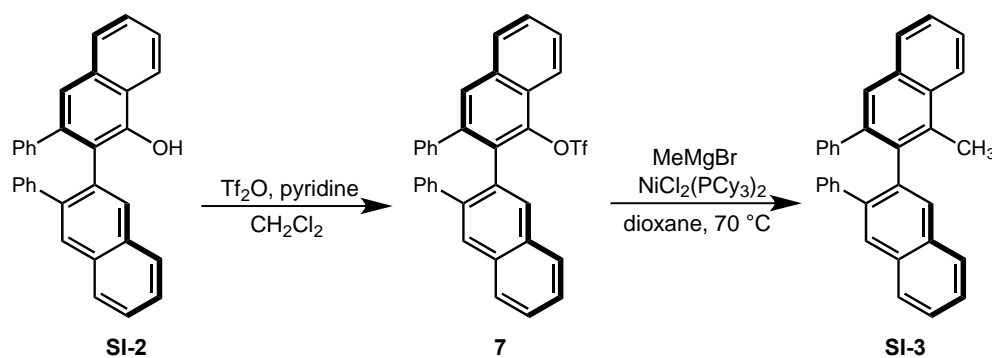


(R)-3,3'-diphenyl-[2,2'-binaphthalen]-1-ol (SI-2): (S)-VANOL (**6**) was prepared from a known synthetic sequence.¹ To a round bottom flask was added (S)-VANOL (**6**) (8.73 g, 19.9 mmol, 1.0 equiv.) followed by the addition of CH_2Cl_2 (87 mL). The reaction flask was then cooled to 0 °C and *N,N*-diisopropylethylamine (3.47 mL, 19.9 mmol, 1.0 equiv.) was added followed by the slow addition of trifluoromethanesulfonic anhydride (3.34 mL, 19.9 mmol, 1.0 equiv.). The reaction mixture was then allowed to stir for 3 h at 0 °C. After 3 h, the reaction was quenched with 2M $\text{HCl}_{(\text{aq})}$ at 0 °C and extracted with CH_2Cl_2 (3x). The combined organic layers were washed with brine, dried with Na_2SO_4 , and concentrated in vacuo. The crude product was then run through a large silica plug using CH_2Cl_2 as the eluent. The resulting solid **SI-1** (11.65 g) was used in the next step of the synthetic sequence without any further purification (see below for ^1H NMR spectrum).

To a flame dried round bottom flask was added slightly impure **SI-1** (11.52 g, 20.18 mmol, 1.0 equiv.) and 10 wt. % Pd/C (3.22 g, 3.03 mmol, 0.15 equiv.). The flask was evacuated and purged with argon, followed by the addition of THF (22 mL), diethyl amine (6.36 mL, 60.54 mmol, 3.0 equiv.) and MeOH (75 mL). The argon from the reaction flask was then evacuated and refilled with H_2 (this cycle was repeated 3x) and the reaction mixture was stirred under a balloon of H_2 for 48 h. After 48 h, the reaction mixture was filtered through Celite using CH_2Cl_2

as the eluent and then the organic layer was washed with 2 M HCl_(aq) (3x), dried with Na₂SO₄, and concentrated in vacuo. The resulting residue was purified via flash column chromatography on silica gel (80:20 hexanes:CH₂Cl₂ to 70:30 hexanes:CH₂Cl₂) to yield the title compound as a yellow solid (7.10 g, 16.8 mmol, 84% over 2 steps). ¹H NMR (400 MHz, CDCl₃) δ 8.34-8.37 (m, 1H), 8.13 (s, 1H), 7.93-7.95 (m, 1H), 7.86-7.88 (m, 1H), 7.76-7.79 (m, 2H), 7.51-7.60 (m, 4H), 7.25 (s, 1H), 7.03-7.12 (m, 2H), 6.90-6.99 (m, 4H), 6.59-6.65 (m, 4H), 6.06 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 149.18, 141.2, 140.9, 140.1, 139.8, 134.0, 133.7, 132.7, 132.2, 131.6, 130.6, 129.6, 129.2, 128.1, 127.8, 127.7, 127.4, 127.0, 126.9, 126.7, 126.6, 126.2, 125.4, 123.3, 122.8, 121.0, 120.5; mp 211-212 °C; IR (neat) 3519, 3055, 2986, 2952, 2305, 2162, 1735, 1701, 1625, 1274, 1132, 748, 701 cm⁻¹; HRMS (ESI): Mass calculated for C₃₂H₂₂ONa⁺ [M+Na]⁺, 445.1563 Found [M+Na]⁺, 445.1558; [α]_D²³ = -220 (c 0.32, CHCl₃).

Synthesis of SI-3:

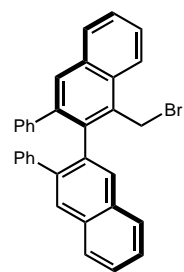
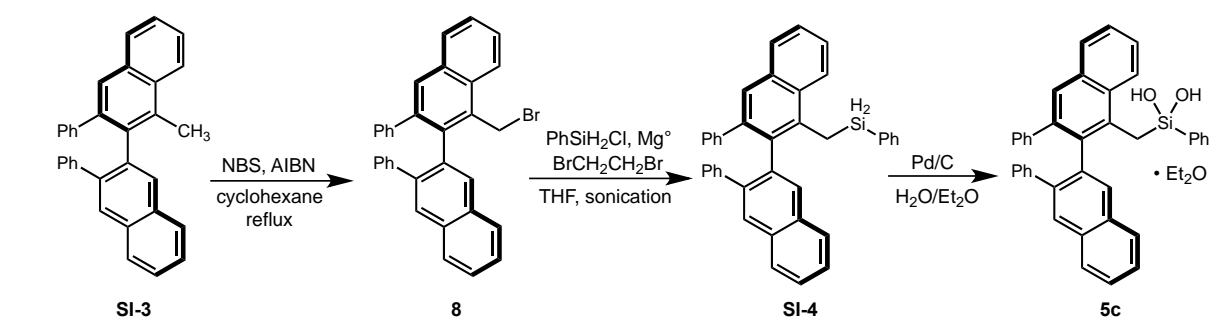


(S)-1-methyl-3,3'-diphenyl-2,2'-binaphthalene (SI-3): To a flame dried round bottom flask was added **SI-2** (5.43 g, 12.85 mmol, 1.0 equiv.), CH₂Cl₂ (45 mL) and pyridine (5.19 mL, 64.25 mmol, 5.0 equiv.). The flask was cooled to 0 °C and trifluoromethanesulfonic anhydride (5.40 mL, 32.13 mmol, 2.5 equiv.) was added slowly. The reaction was then let warm to 23 °C and stir overnight. The reaction flask was then cooled to 0 °C, quenched with 2 M HCl_(aq), and extracted with CH₂Cl₂ (3x). The combined organic layers were washed 2 M HCl_(aq), brine, dried with Na₂SO₄, and concentrated in vacuo. The resulting residue was partially purified via flash column chromatography on silica gel (90:10 hexanes:CH₂Cl₂ to 85:15 hexanes:CH₂Cl₂). The resulting solid **7** (6.96 g) was used as is for the next synthetic step (see below for ¹H NMR spectrum).

To a flame dried two-neck round bottom flask was added slightly impure **7** (6.90 g) and NiCl₂(PCy₃)₂ (883 mg, 1.28 mmol, 0.1 equiv.). The flask was then equipped with a condenser and the reaction system was purged with a continuous flow of N₂. After the reaction system was under N₂ atmosphere, freshly distilled and degassed 1,4-dioxane (115 mL) was added. The reaction flask was cooled to 0 °C and MeMgBr (2.63 M in Et₂O, 14.7 mL, 38.5 mmol, 3 equiv.) was added slowly. The top of the condenser was then equipped with a vent needle and the reaction system was gradually heated to 70 °C allowing for the Et₂O from the MeMgBr solution to evaporate out of the reaction system. The reaction was then stirred for 2 h at 70 °C. After 2 h, the reaction flask was cooled to 0 °C and 2 M HCl_(aq) was added slowly to quench the reaction. The reaction was then diluted with H₂O and extracted with Et₂O (3x). The combined organic

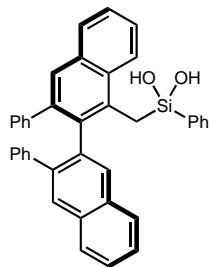
layers were washed with brine, dried with Na_2SO_4 , and concentrated in vacuo. The resulting residue was then run through a large silica plug using CH_2Cl_2 as the eluent and concentrated in vacuo. The crude product was then purified via flash column chromatography on silica gel (97:3 hexanes: CH_2Cl_2 to 95:5 hexanes: CH_2Cl_2) to afford the title compound as a white solid (4.91 g, 11.67 mmol, 90% over 2 steps). ^1H NMR (400 MHz, CDCl_3) δ 8.12 (d, J = 8.4 Hz, 1H), 7.82-7.85 (m, 4H), 7.69 (s, 1H), 7.49-7.59 (m, 5H), 6.90-7.09 (m, 6H), 6.64-6.72 (m, 4H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 141.6, 140.9, 140.2, 140.0, 137.9, 137.6, 133.0, 132.9, 132.8, 132.2, 131.9, 130.0, 129.4, 129.0, 128.7, 127.9, 127.7, 127.5, 127.4, 127.2, 126.4, 126.2, 126.1, 126.0, 125.9, 124.7, 17.6; mp 96-100 °C; IR (neat) 3054, 2987, 2950, 2154, 1735, 1701, 1625, 1591, 1494, 1274, 1265, 1131, 748 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{33}\text{H}_{24}\text{Na}^+$ $[\text{M}+\text{Na}]^+$, 443.1770 Found $[\text{M}+\text{Na}]^+$, 443.1766; $[\alpha]_{\text{D}}^{23}$ = -277 (c 0.16, CHCl_3).

Synthesis of 5c:



(*R*)-1-(bromomethyl)-3,3'-diphenyl-2,2'-binaphthalene (8): To a flame dried round bottom flask was added **SI-3** (4.80 g, 11.41 mmol, 1.0 equiv.), NBS (4.47 g, 25.10 mmol, 2.2 equiv.), AIBN (281 mg, 1.71 mmol, 0.15 equiv.) and cyclohexane (225 mL). The flask was then equipped with a water-cooled condenser and the reaction mixture was refluxed overnight. The reaction was then cooled to 23 °C and filtered through Celite with Et_2O . The resulting solution was then diluted with H_2O and extracted with Et_2O (3x). The organic layers were combined and washed with saturated NaHCO_3 (aq), brine, dried with Na_2SO_4 , and

concentrated in vacuo. The resulting residue was purified via flash column chromatography on silica gel (98:2 hexanes: Et_2O) to afford the title compound as a yellow solid (5.57 g, 11.15 mmol, 98%). ^1H NMR (400 MHz, CDCl_3) δ 8.32 (d, J = 8.1 Hz, 1H), 8.26 (s, 1H), 7.96-7.98 (m, 1H), 7.84-7.87 (m, 2H), 7.69-7.71 (m, 1H), 7.67 (s, 1H), 7.62 (s, 1H), 7.52-7.58 (m, 3H), 7.02-7.09 (m, 2H), 6.88-6.97 (m, 4H), 6.60-6.62 (m, 2H), 6.53-6.55 (m, 2H), 5.25 (d, J = 10.2 Hz, 1H), 4.88 (d, J = 9.9 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 140.7, 140.4, 140.1, 139.7, 139.5, 135.5, 133.5, 133.4, 132.0, 131.5, 131.4, 131.0, 130.7, 129.9, 129.5, 129.3, 129.0, 128.1, 128.0, 127.6, 127.3, 126.9, 126.6, 126.55, 126.53, 126.4, 126.3, 124.8, 31.1; mp 120-124 °C; IR (neat) 3054, 2988, 2949, 2155, 1735, 1701, 1625, 1493, 1274, 1264, 1131, 749, 699 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{33}\text{H}_{23}\text{BrNa}^+$ $[\text{M}+\text{Na}]^+$, 521.0875 Found $[\text{M}+\text{Na}]^+$, 521.0881; $[\alpha]_{\text{D}}^{23}$ = -183 (c 0.52, CHCl_3).



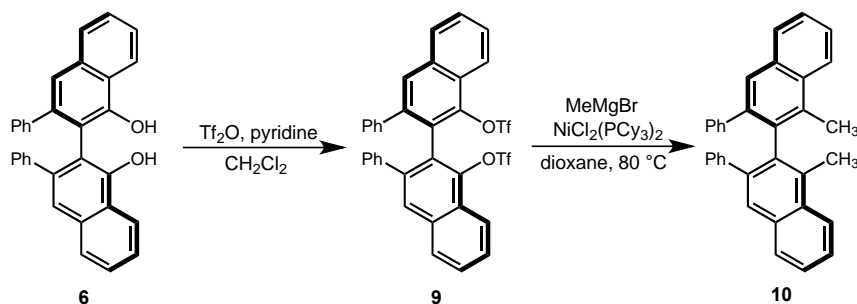
(R)-((3,3'-diphenyl-[2,2'-binaphthalen]-1-yl)methyl)(phenyl)silane-1,2-diol

(5c): To a flame dried round bottom flask was added magnesium powder (182 mg, 7.5 mmol, 3.0 equiv.), THF (5 mL). To a separate flame dried round bottom flask was added **8** (1.25 g, 2.5 mmol, 1.0 equiv.), THF (7.5 mL) and phenylchlorosilane (1.66 mL, 12.5 mmol, 5.0 equiv.). The reaction flask containing the magnesium powder was placed in a sonicator water bath and subjected to sonication at 23 °C. Immediately after beginning sonication, 1,2-dibromoethane (0.11 mL, 1.25 mmol, 0.5 equiv.) was added to the reaction

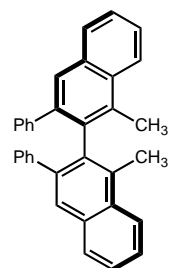
flask followed by the addition of the solution containing **8**, phenylchlorosilane and THF. The reaction mixture was then sonicated for 1 h at 23 °C. After 1 h, the reaction was quenched with saturated $\text{NH}_4\text{Cl}_{(\text{aq})}$, extracted with Et_2O (3x), dried over Na_2SO_4 and concentrated in vacuo. The resulting residue was subjected to flash column chromatography on silica gel (hexanes to 95:5 hexanes: Et_2O). The resulting slightly impure **SI-4** (see ^1H NMR below) was used in the next synthetic sequence.

To a flame dried round bottom flask was added crude **SI-4** and 10 wt. % Pd/C (300 mg, 0.28 mmol, 0.11 equiv.). The reaction mixture was purged with argon followed by the addition of THF (8 mL) and H_2O (0.8 mL). The reaction was then stirred overnight. The mixture was then filtered through Celite, diluted with H_2O and extracted with Et_2O (3x). The combined organic layers were washed with brine, dried with Na_2SO_4 , and concentrated in vacuo. The resulting residue was purified via flash column chromatography on silica gel (hexanes to 60:40 hexanes: Et_2O) to afford the title compound as a white solid (698 mg, 1.25 mmol, 50% over 2 steps). The silanediol exists as a 4:1 complex with Et_2O . ^1H NMR (400 MHz, CDCl_3) δ 8.14-8.16 (m, 1H), 7.78-7.84 (m, 2H), 7.76 (s, 1H), 7.69 (s, 1H), 7.60-7.62 (m, 1H), 7.41-7.54 (m, 7H), 7.32-7.37 (m, 1H), 7.19-7.23 (m, 2H), 6.91-7.09 (m, 6H), 6.77-6.80 (m, 2H), 6.71-6.74 (m, 2H), 2.98 (d, $J = 14.6$ Hz, 1H), 2.77 (d, $J = 14.6$ Hz, 1H), 2.53 (s, 1H), 2.44 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 141.7, 140.7, 140.5, 139.7, 137.4, 136.9, 135.1, 133.9, 133.7, 133.3, 133.0, 132.1, 132.0, 131.4, 130.4, 130.1, 129.4, 129.3, 129.0, 128.0, 127.8, 127.7, 127.5, 127.2, 127.0, 126.5, 126.2, 126.16, 126.15, 126.11, 126.0, 125.3, 21.1; IR (neat) 3517, 3054, 2949, 2163, 1735, 1701, 1493, 1274, 1264, 1131, 763, 748, 715 cm^{-1} ; mp 110-111 °C; HRMS (ESI): Mass calculated for $\text{C}_{39}\text{H}_{30}\text{O}_2\text{SiNa}^+$ $[\text{M}+\text{Na}]^+$, 581.1907 Found $[\text{M}+\text{Na}]^+$, 581.1907; $[\alpha]_D^{23} = -109$ (c 0.24, CHCl_3).

Synthesis of 10:



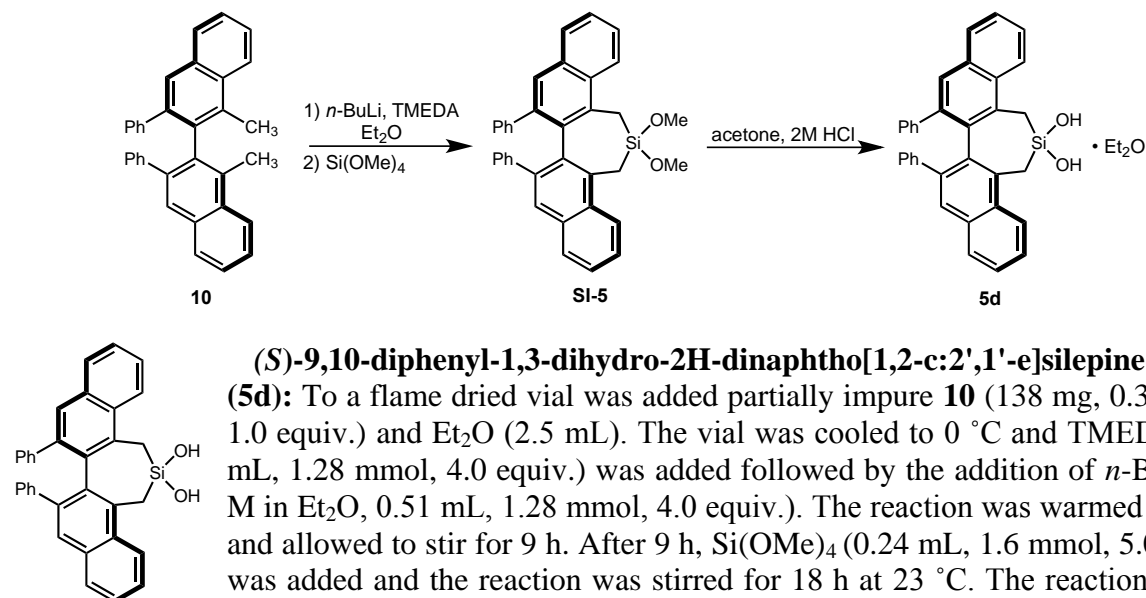
(S)-3,3'-diphenyl-[2,2'-binaphthalene]-1,1'-diyl bis(trifluoromethanesulfonate) (9): To a flame dried round bottom flask was added (S)-VANOL (**6**) (1.0 g, 6.84 mmol, 1.0 equiv.), CH₂Cl₂ (15 mL) and pyridine (3.3 mL, 41.1 mmol, 6.0 equiv.). The flask was cooled to 0 °C and trifluoromethanesulfonic anhydride (4.6 mL, 27.4 mmol, 4.0 equiv.) was added slowly. The reaction was then let warm to 23 °C and stir overnight. The reaction flask was then cooled to 0 °C, quenched with 2 M HCl_(aq), and extracted with CH₂Cl₂ (3x). The combined organic layers were washed 2 M HCl_(aq), brine, dried with Na₂SO₄, and concentrated in vacuo. The resulting residue was partially purified via flash column chromatography on silica gel (90:10 hexanes:CH₂Cl₂ to 85:15 hexanes:CH₂Cl₂). The resulting yellow solid was then triturated with hexanes to afford the title compound as a white solid (4.1 g, 5.8 mmol, 85%). ¹H NMR (400 MHz, CDCl₃) δ 8.34 (d, *J* = 8.4 Hz, 2H), 7.92 (d, *J* = 8.1 Hz, 2H), 7.66-7.77 (m, 6H), 7.09-7.13 (m, 2H), 6.92-6.96 (m, 4H), 6.61-6.63 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 144.8, 140.7, 139.2, 134.8, 130.5, 129.1, 128.6, 128.4, 128.0, 126.9, 126.7, 124.5, 121.9, 118.2 (q, *J*_{CF} = 318.7 Hz); IR (neat) 3054, 2949, 2154, 1736, 1701, 1625, 1591, 1491, 1274, 1132, 796, 699 cm⁻¹; mp 191-194 °C; HRMS (ESI): Mass calculated for C₃₄H₂₀F₆O₆S₂Na⁺ [M+Na]⁺, 725.0498 Found [M+Na]⁺, 725.0472; [α]_D²³ = -18.3 (c 0.68, CHCl₃).



(S)-1,1'-dimethyl-3,3'-diphenyl-2,2'-binaphthalene (10): To a flame dried two-neck round bottom flask was added **9** (500 mg, 0.71 mmol, 1.0 equiv.) and NiCl₂(PCy₃)₂ (49 mg, 0.071 mmol, 0.1 equiv.). The flask was then equipped with a condenser and the reaction system was purged with a continuous flow of N₂. After the reaction system was under N₂ atmosphere, freshly distilled and degassed 1,4-dioxane (3.5 mL) was added. The reaction flask was cooled to 0 °C and MeMgBr (3.0 M in Et₂O, 0.94 mL, 2.84 mmol, 4.0 equiv.) was added slowly. The top of the condenser was then equipped with a vent needle and the reaction system was gradually heated to 80 °C allowing for the Et₂O from the MeMgBr solution to evaporate out of the reaction system. The reaction was then stirred overnight at 80 °C. The reaction flask was cooled to 0 °C and 2 M HCl_(aq) was added slowly to quench the reaction. The reaction was then diluted with H₂O and extracted with Et₂O (3x). The combined organic layers were washed with brine, dried with Na₂SO₄, and concentrated in vacuo. The resulting residue was then run through a large silica plug using CH₂Cl₂ as the eluent and concentrated in vacuo. The crude material was resubjected to the exact same reaction conditions as stated above. After performing the same work-up procedure, the resulting residue was partially purified via flash column chromatography

on silica gel (hexanes to 99:1 hexanes:Et₂O) to give slightly impure **10** (138 mg) (See ¹H-NMR below). The material was then used as is for the next synthetic sequence.

Synthesis of **5d**:



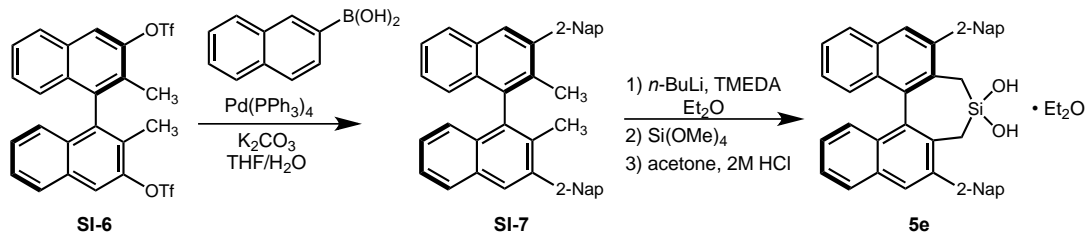
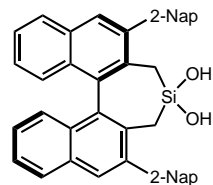
(*S*)-9,10-diphenyl-1,3-dihydro-2H-dinaphtho[1,2-*c*:2',1'-*e*]silepine-2,2-diol

(5d): To a flame dried vial was added partially impure **10** (138 mg, 0.32 mmol, 1.0 equiv.) and Et₂O (2.5 mL). The vial was cooled to 0 °C and TMEDA (0.19 mL, 1.28 mmol, 4.0 equiv.) was added followed by the addition of *n*-BuLi (2.5 M in Et₂O, 0.51 mL, 1.28 mmol, 4.0 equiv.). The reaction was warmed to 23 °C and allowed to stir for 9 h. After 9 h, Si(OMe)₄ (0.24 mL, 1.6 mmol, 5.0 equiv.) was added and the reaction was stirred for 18 h at 23 °C. The reaction mixture

was then filtered through Celite using Et₂O as the eluent and concentrated in vacuo. The material was subjected to flash column chromatography on silica gel (hexanes to 99:1 hexanes:Et₂O) to give slightly impure **SI-5** (20 mg) and used in the next step of the synthetic sequence.

To a flame dried vial was added **SI-5** (20 mg), acetone (1.4 mL) and 2 M HCl_(aq) (0.4 mL). The reaction was then stirred overnight. The vial was then diluted with Et₂O (1 mL) and neutralized to pH 7 using saturated NaHCO_{3(aq)} and then extracted with Et₂O (3x). The combined organic layers were washed with brine, dried with Na₂SO₄, and concentrated in vacuo. The resulting residue was purified via flash column chromatography on silica gel (80:20 hexanes:Et₂O to 20:80 hexanes Et₂O) to afford the title compound as an off-white solid (10.1 mg, 0.02 mmol, 3% over three steps). The silanediol exists as a 2:1 complex with Et₂O. ¹H NMR (400 MHz, CDCl₃) δ 8.21 (d, *J* = 8.5 Hz, 2H), 7.80 (d, *J* = 8.1 Hz, 2H), 7.57-7.61 (m, 2H), 7.49-7.53 (m, 2H), 7.42 (s, 2H), 7.02-7.06 (m, 2H), 6.88-6.92 (m, 4H), 6.43-6.45 (m, 4H), 3.08 (d, *J* = 13.9 Hz, 2H), 2.37-2.41 (m, 4H); ¹³C NMR (150 MHz, CDCl₃) δ 141.3, 139.8, 135.5, 134.1, 133.6, 130.5, 129.6, 129.2, 127.3, 126.4, 126.2, 126.0, 124.2, 17.5; IR (neat) 3515, 3054, 2984, 1735, 1701, 1493, 1264, 1133, 736, 704 cm⁻¹; mp 257-260 °C; HRMS (ESI): Mass calculated for C₃₄H₂₆O₂SiNa⁺ [M+Na]⁺, 517.1594 Found [M+Na]⁺, 517.1588; [α]_D²³ = -84.1 (c 0.29, CHCl₃).

Synthesis of 5e:

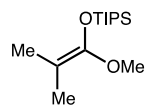
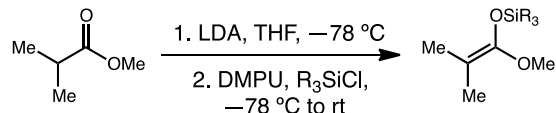
**(R)-2,6-di(naphthalen-2-yl)-3,5-dihydro-4H-dinaphtho[2,1-c:1',2'-e]silepine-4,4-diol (5e):**

SI-6 was prepared according to a known synthetic sequence.² To a flame dried round bottom flask was added **SI-6** (3.50 g, 6.05 mmol, 1.0 equiv.), 2-naphthylboronic acid (2.50 g, 14.52 mmol, 2.4 equiv.), Pd(PPh₃)₄ (699 mg, 0.605 mmol, 0.1 equiv.) and K₂CO₃ (5.02 g, 36.3 mmol, 6.0 equiv.). The reagents were dissolved in THF (25 mL) and H₂O (25 mL) and the reaction was refluxed overnight. The reaction was then cooled to 23 °C and diluted with H₂O (50 mL) and extracted with Et₂O (3x). The combined organic layers were washed with brine, dried with Na₂SO₄, and concentrated in vacuo. The resulting solid was subjected to flash column chromatography on silica gel (hexanes to 95:5 hexanes:Et₂O) to give **SI-7** and was used directly in the next reaction.

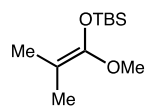
To a flame dried round bottom flask was added **SI-7**, Et₂O (90 mL), and TMEDA (4.5 mL, 30.25 mmol, 5.0 equiv.). The flask was cooled to 0 °C and *n*-BuLi (2.5 M in Et₂O, 12.1 mL, 30.25 mmol, 5.0 equiv.) was slowly added. The reaction was warmed to 23 °C and allowed to stir for 24 h. After 24 h, Si(OMe)₄ (8.9 mL, 60.5 mmol, 10.0 equiv.) was added and the reaction was stirred overnight at 23 °C. The reaction mixture was then filtered through Celite using Et₂O as the eluent and concentrated in vacuo. The material was run through a large silica gel plug using Et₂O as the eluent, concentrated and then subjected to flash column chromatography on silica gel (hexanes to 80:20 hexanes:Et₂O) to give 1.26 g of crude product, which was used directly in the next synthetic step.

To a flame dried round bottom flask was added crude material (1.26 g) and acetone (225 mL), then the reaction was cooled to 0 °C. 2 M HCl_(aq) was added slowly and the reaction was allowed to warm to 23 °C and stir overnight. The flask was then diluted with Et₂O and neutralized to pH 7 using saturated NaHCO_{3(aq)} and then extracted with Et₂O (3x). The combined organic layers were washed with brine, dried with Na₂SO₄, and concentrated in vacuo. The resulting residue was purified via flash column chromatography on silica gel (90:10 hexanes:Et₂O to 60:40 hexanes Et₂O) to afford the title compound as a white solid (742 mg, 1.25 mmol, 21% over three steps). The silanediol exists as a 2:1 complex with Et₂O. ¹H NMR (400 MHz, CDCl₃) δ 7.79-7.97 (m, 12H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.42-7.47 (m, 4H), 7.36-7.40 (m, 2H), 7.24-7.28 (m, 2H), 7.15-7.17 (m, 2H), 2.26 (d, *J* = 13.8 Hz, 2H), 2.18 (s, 2H), 1.86 (d, *J* = 13.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 140.2, 139.8, 134.2, 133.4, 133.0, 132.42, 132.41, 131.6, 129.2, 128.6, 128.4, 128.1, 128.0, 127.7, 126.6, 126.5, 126.2, 125.3, 18.9; IR (neat) 3422, 3056, 2981, 2952, 2249, 1731, 1701, 1626, 1493, 1275, 908, 749 cm⁻¹; mp 301-305 °C; HRMS (ESI): Mass calculated for C₄₂H₃₀O₂SiNa⁺ [M+Na]⁺, 617.1907 Found [M+Na]⁺, 617.1916; [α]_D²³ = -79.5 (c 0.44, CHCl₃).

General Procedure for the Preparation of Silyl Ketene Acetals

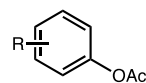
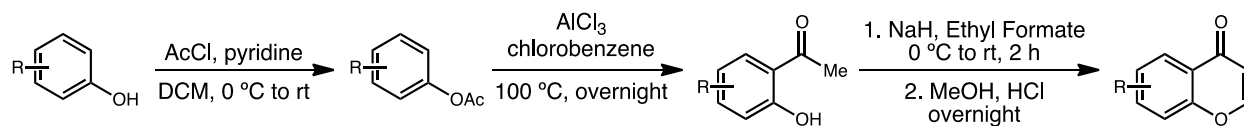


(3a) Triisopropyl((1-methoxy-2-methylprop-1-en-1-yl)oxy)silane was prepared according to an established procedure.³ A 250 mL round bottom flask equipped with a stir bar was flame dried under vacuum and purged with N₂(g). The flask was placed under positive pressure of argon gas and fitted with a rubber septa. The reaction vessel was charged with 50 mL of anhydrous THF and diisopropyl amine (4.2 mL, 30 mmol, 1.2 equiv), and cooled to 0 °C. A solution of 1.3 M *n*-BuLi (21.2 mL, 27.5 mmol, 1.1 equiv) in hexanes was added dropwise to the reaction mixture and stirred for 20 minutes at 0 °C. The reaction was cooled to –78 °C and methyl isobutyrate (2.87 mL, 25 mmol, 1.0 equiv) was added over a 10-minute period. The reaction was stirred for 30 mins at –78 °C, followed by the addition 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU) (4.53 mL, 37.5 mmol, 1.5 equiv) and triisopropylsilyl chloride (6.42 mL, 30 mmol, 1.2 equiv). The reaction stirred at –78 °C for 30 min then warmed to room temperature for 1 h. Solvent was removed under reduced pressure and the resulting mixture was taken up in 200 mL of pentane, washed sequentially with water (1 x 100 mL), saturated CuSO₄ (1 x 100 mL), saturated NaHCO₃ (1 x 100 mL), and brine (1 x 100 mL). The organic layer was dried over anhydrous Na₂SO₄, and concentrated under reduced pressure, resulting in an oil which was purified via fractional distillation to yield the title compound (5.62 g, 21.7 mmol, 87% yield) as a clear colorless liquid. ¹H NMR (400 MHz, CDCl₃): δ 3.56 (s, 3H), 1.57 (s, 6H), 1.09–1.18 (21H). All spectral data matched that previously reported.⁴

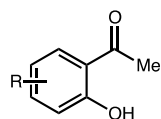


(3b) tert-Butyl((1-methoxy-2-methylprop-1-en-1-yl)oxy)dimethylsilane Using the method above, the title compound (4.04 g, 18.7 mmol, 75% yield) was obtained as a clear colorless liquid. ¹H NMR (400 MHz, CDCl₃): δ 3.51 (s, 3H), 1.57 (s, 3H), 1.53 (s, 3H), 0.96 (s, 9H), 0.14 (s, 6H). All spectral data matched that previously reported.⁵

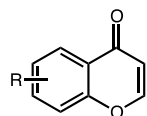
General Procedure for the Preparation of Chromenones



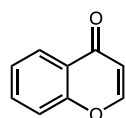
Phenols were purchased and used as received. The corresponding phenol was dissolved in dichloromethane (1.3 M) in a flame-dried flask that was cooled to 0 °C. Pyridine (1.3 eq) was added to the flask immediately followed by acetyl chloride (1.2 eq). The flask was warmed to room temperature and the reaction mixture stirred until complete as indicated by TLC (approx. 3 hours). The reaction mixture was washed with water, 3M HCl (aq), water, NaHCO₃ (sat. aq) and finally dried with Na₂SO₄. The solvent was removed under reduced pressure and pure material was isolated after column chromatography in nearly quantitative yield.⁶



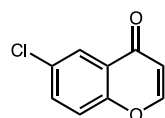
2'-hydroxyacetophenones were either purchased and used as received or synthesized according to a modified procedure.⁶ Acylated phenols were dissolved in a flame-dried flask in chlorobenzene (0.8 M). The flask was fitted with a septum and a positive flow of nitrogen with a vent needle flowing into a flask of NaHCO_3 (sat. aq) to quench any HCl gas released during the course of the reaction. The flask was cooled to 0 °C and aluminum trichloride was slowly added in portions. After the addition, the flask was placed in an oil bath and slowly warmed to 100 °C and allowed to stir overnight. Then, the reaction was cooled to room temperature, dichloromethane added to solubilize the mixture, and the flask cooled to °C. Cold 3M HCl was added drop wise to quench the reaction which was then future diluted with dichloromethane. The organic phase was washed with water, dried with Na_2SO_4 , and solvent removed. The pure acetophenone was isolated via flash column chromatography.



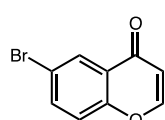
Chromenones were prepared according to a modified procedure or purchased and used as received.⁷ The corresponding 2'-hydroxyacetophenone (1 eq) was placed in a flame-dried flask with stir bar in 0.5 M ethyl formate and cooled to 0 °C. NaH (60% in mineral oil, 6 eq) was added portion-wise to the cooled solution over 2 hours. If necessary for stirring, minimal amounts of dry THF were added to the flask in portions as needed. After addition of all of the NaH, the solution was warmed to room temperature and quenched with methanol (10 eq). Concentrated HCl (50 eq) was then added slowly and allowed to stir overnight at room temperature. The reaction was then diluted with ethyl acetate, washed with water, NaHCO_3 (sat. aq.), and brine, dried with Na_2SO_4 , and concentrated under vacuum to afford the crude chromenone. The chromenones were then recrystallized with ethyl acetate/hexanes or dichloromethane/hexanes to afford pure material.



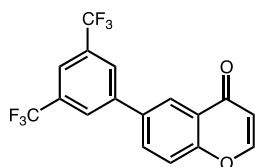
(1a) 4H-chromen-4-one: was purchased and used as received.



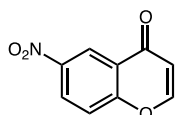
(1b) 6-chloro-4H-chromen-4-one: was purchased and used as received.



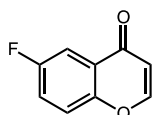
(1c) 6-bromo-4H-chromen-4-one: was synthesized from the 2'-1-(5-bromo-2-hydroxyphenyl)ethanone (purchased) (25 mmol) according to the standard procedure above. 4.75 g (84% yield) of pure chromenone was isolated as a white solid via recrystallization from ethyl acetate/hexanes. All spectral data matched previous reports.⁸ ^1H NMR (400 MHz, CDCl_3) δ 8.33 (d, J = 2.4 Hz, 1H), 7.85 (d, J = 6 Hz, 1H), 7.75 (dd, J = 8.8, 2.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 1H), 6.35 (d, J = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.3, 155.5, 155.4, 136.9, 128.6, 126.3, 120.3, 118.9, 113.2.



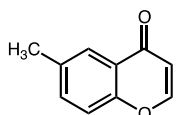
(1d) 6-(3,5-bis(trifluoromethyl)phenyl)-4H-chromen-4-one: Compound **1c** was subjected to typical Suzuki coupling conditions: **1c** (250 mg, 1.11 mmol, 1 eq), 3,5-bis(trifluoromethyl)phenyl boronic acid (343 mg, 1.33 mmol, 1.2 eq), Pd(PPh₃)₄ (65 mg, 0.056 mmol, 0.05 eq), and K₂CO₃ (920 mg, 6.66 mmol, 6 eq) were dissolved in H₂O (5 mL) and THF (5 mL) and refluxed overnight. After cooling, the mixture was diluted with 2 M HCl (aq), extracted with diethyl ether (20 mL x 3), washed with brine (20 mL), and dried with Na₂SO₄. After removal of the solvent under reduced pressure, crude **1d** was isolated after silica gel flash column chromatography (100% hexanes to 20% ethyl acetate: hexanes). **1d** was isolated as a white solid in 65% yield (260 mg). Mp 190-195 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.46 (d, *J* = 2.4 Hz, 1H), 8.08 (s, 2H), 7.94-7.90 (m, 3H), 7.62 (d, *J* = 8.8 Hz, 1H), 6.42 (d, *J* = 6.4, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 177.3, 156.8, 155.6, 141.5, 135.5, 132.6 (q, *J*_{CF} = 333 Hz), 132.5, 127.4, 125.4, 124.5, 123.3 (q, *J*_{CF} = 270 Hz), 121.7 (p, *J*_{CF} = 37 Hz), 119.6, 113.4. IR: 3063, 2981, 1655, 1615, 1472, 1379, 1276, 1162, 1133, 1114, 1083, 897, 832, 680 cm⁻¹; HRMS (ESI): Mass calculated for C₁₇H₈F₆NaO₂⁺ [M+Na]⁺ 381.0321, Found [M+Na]⁺ 381.0312.



(1e) 6-nitro-4H-chromen-4-one: was purchased and used as received.

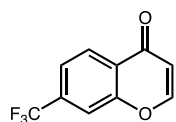


(1f) 6-fluoro-4H-chromen-4-one: was synthesized from the 2'-1-(5-fluoro-2-hydroxyphenyl)ethanone (purchased) (10 mmol) according to the standard procedure above. Observed spectral data matched previous reports.⁹ 0.902 g (55% yield first crop) of pure chromenone was isolated as a white solid via recrystallization from DCM/hexanes. Mp 163-166 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.86-7.83 (m, 2H), 7.49-7.45 (m, 1H), 7.42-7.37 (m, 1H), 6.33 (d, *J* = 6 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 176.8 (d, *J*_{CF} = 2 Hz), 159.6 (d, *J*_{CF} = 247 Hz), 155.5, 152.8 (d, *J*_{CF} = 2 Hz), 126.1 (d, *J*_{CF} = 7 Hz), 122.1 (d, *J*_{CF} = 25 Hz), 120.4 (*J* = 8 Hz), 112.3, 110.7 (d, *J* = 24 Hz); IR: 3084, 3037, 1640, 1617, 1574, 1478, 1397, 1313, 1202, 1170, 1134, 1026, 918, 893, 704, 548 cm⁻¹; HRMS (ESI): Mass calculated for C₉H₅FNaO₂⁺ [M+Na]⁺ 187.0166, Found [M+Na]⁺ 187.0166.



(1g) 6-methyl-4H-chromen-4-one: was synthesized according to a known procedure similar to the general procedure above.¹⁰ p-cresol (1 eq, 10 mmol) was dissolved in dry toluene (2 mL, 5 M) in a flame-dried flask and cooled to 0 °C. Acetyl chloride (0.711 mL, 10 mmol, 1 eq) was added slowly. After stirring for 5 minutes, a positive flow of nitrogen with a vent needle flowing into a flask of NaHCO₃ (sat. aq) to quench any HCl gas released during the course of the reaction. AlCl₃ (2.67 g, 20 mmol, 2 eq) was added in portions to the cooled reaction mixture. The flask was then warmed to 120 °C and heated for 10 hours. After this time, the flask was cooled to room and hydrolyzed with crushed ice. The organic layer was extracted with dichloromethane and dried with Na₂SO₄. After the solvent was removed under reduced pressure, the pure 1-(2-hydroxy-5-methylphenyl)ethanone (0.470 g, 32% yield) was isolated via silica gel flash column chromatography (100% hexanes to 80/20 hexanes/ethyl ether). Spectral data matched previous reports. Mp 80-82 °C; ¹H NMR (400 MHz, CDCl₃) δ 12.08 (s, 1H), 7.29 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 2.62 (s,

3H), 2.31 (s, 3H); 1-(2-hydroxy-5-methylphenyl)ethanone (1.33 g, 8.85 mmol) was then subjected to the general chromenone formation procedure as stated above. 6-methyl-4H-chromen-4-one was isolated as a white solid from recrystallization with dichloromethane/hexanes (1.03 g, 72% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.98 (s, 1H), 7.82 (dd, J = 6, 1.2 Hz, 1H), 7.47-7.45 (m, 1H), 7.34 (dd, J = 8.8, 2 Hz, 1H), 6.30 (dd, J = 6.3, 2 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 177.7, 155.1, 154.8, 135.2, 134.9, 125.1, 124.5, 117.9, 112.8, 20.9; IR: 2980, 2915, 1644, 1620, 1480, 1431, 1314, 1198, 835, 809 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{10}\text{H}_8\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$ 183.0417, Found $[\text{M}+\text{Na}]^+$ 183.0416.

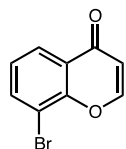


(1h)

7-(trifluoromethyl)-4H-chromen-4-one:

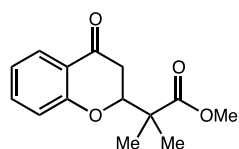
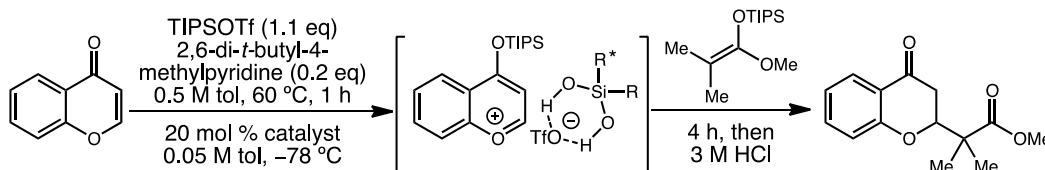
2-Hydroxy-4-

(trifluoromethyl)benzoic acid (1.0 g, 4.85 mmol, 1 eq) was dissolved in 10 mL dry THF in a flame dried flask. The flask was cooled to 0 °C and MeLi (1.6 M in ether, 10.3 mL, 16.49 mmol, 3.4 eq) was added dropwise. The mixture was allowed to come to room temperature and stir overnight. The solution was diluted with 10 mL of EtOAc and cooled to 0 °C. 10 mL of 12 M HCl was added to the flask. The solution was extracted with EtOAc (20 mL x 3), washed with brine (20 mL), and dried with Na_2SO_4 . After removal of the solvent under reduced pressure. The residue was isolated after silica gel flash plug with 100% EtOAc to afford the 1-(2-hydroxy-4-(trifluoromethyl)phenyl)ethanone in 96% yield (947 mg).¹¹ The acetophenone was then subjected to the standard procedure above to afford **1h** in 63% yield (600 mg) as a white solid. Mp 66-69 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.33 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 6 Hz, 1H), 7.75 (s, 1H), 7.64 (dd, J = 8.4, 1.2 Hz, 1H), 6.40 (d, J = 6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.5, 156.0, 155.9, 135.4 (q, J_{CF} = 33 Hz), 127.3, 127.1, 123.1 (q, J_{CF} = 271 Hz), 121.6 (q, J_{CF} = 33 Hz), 116.2 (q, J_{CF} = 39 Hz), 113.6. IR: 3098, 2980, 2889, 1654, 1631, 1436, 1348, 1311, 1169, 1122, 1089, 1018, 875, 822, 686 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{10}\text{H}_5\text{F}_3\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$ 237.0134, Found $[\text{M}+\text{Na}]^+$ 237.0131.

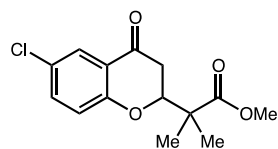


(1i) 8-bromo-4H-chromen-4-one: was synthesized from 2-bromophenol (4 mL, 35 mmol) according to the general procedure above to afford 7.35 g of 2-bromophenyl acetate (98% yield) ^1H NMR (400 MHz, CDCl_3) δ 7.62-7.59 (m, 1H), 7.35-7.31 (m, 1H), 7.14-7.10 (m, 2H), 2.35 (s, 3H); 2-bromophenyl acetate, crude from part 1 (3 g, 13.95 mmol), was then reacted with aluminum trichloride according to the general procedure to afford 1-(3-bromo-2-hydroxyphenyl)ethanone in 20% yield (0.610 g) as a crude mixture. 610 mg (2.83 mmol) of crude 1-(3-bromo-2-hydroxyphenyl)ethanone was then subjected to the general chromenone formation procedure to afford 240 mg of 8-bromo-4H-chromen-4-one (38% yield) after one recrystallization from dichloromethane/hexanes. ^1H NMR (400 MHz, CDCl_3) δ 8.16 (dd, J = 8, 1.6 Hz, 1H), 7.94 (d, J = 6 Hz, 1H), 7.91 (dd, J = 8, 1.6 Hz, 1H), 7.29 (t, J = 8 Hz, 1H), 6.39 (d, J = 6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 177.7, 155.1, 154.8, 135.2, 134.9, 125.1, 124.5, 117.9, 112.8, 20.9. Spectral data matched previously reported data.⁸

General Procedure for Addition of Silyl Ketene Acetals to Chromenones

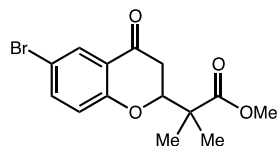


(4a) methyl 2-methyl-2-(4-oxochroman-2-yl)propanoate: An 8 mL vial with stir bar was flame dried under vacuum, cooled to room temperature under vacuum, and backfilled with argon gas. Chromone (14.6 mg, 0.1 mmol, 1 eq) and 2,6-di-*tert*-butyl-4-methylpyridine (6.2 mg, 0.03 mmol, 0.3 eq) was weighed out and placed in the vial. The vial was then placed under vacuum again and backfilled with argon. 200 μ L of dry toluene (0.5 M) was added to the vial. Freshly distilled triisopropylsilyl trifluoromethanesulfonate (29.5 μ L, 0.11 mmol, 1.1 eq) was added via microliter syringe to the solution and the vial was placed in a 60 $^{\circ}$ C oil bath for one hour. After the reaction time, the vial was cooled to room temperature and further diluted with 1.3 mL of toluene. The vial was then cooled to -78° C in an acetone/dry ice bath. After an appropriate amount of time to allow the reaction to come to temperature had passed, a solution of silanediol catalyst in 0.5 mL toluene (12.6 mg, 0.02 mmol, 0.2 eq) was added slowly down the side of the vial. The reaction mixture was stirred for 10 minutes before addition of the silyl ketene acetal (125 μ L of a 1 M solution in toluene, 0.125 mmol, 1.25 eq) slowly down the side of the vial. After 4 hours at -78° C, the reaction was quenched with 200 μ L of 3 M HCl (aqueous) (6 eq) at -78° C. The solution is allowed to warm to room temperature overnight. Then, the crude reaction mixture was extracted with ethyl acetate (5 mL), washed with water (5 mL), dried with Na_2SO_4 , and solvent removed under vacuum. The crude mixture was then dissolved in CDCl_3 and 1,3,5-trimethoxybenzene was added as an internal standard for ^1H NMR yields. The product was then isolated via silica gel flash column chromatography (100% hexanes to 80/20 hexanes/ethyl acetate) or preparative TLC plates for HPLC analysis (80/20 hexanes/ethyl acetate solvent system). HPLC samples are occasionally filtered through an alumina plug to remove any undesired silanol by-products. The desired product **4a** was 76% by ^1H NMR yield. ^1H NMR (400 MHz, CDCl_3) δ 7.88-7.86 (m, 1H), 7.48-7.44 (m, 1H), 7.01 (t, J = 7.2 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 4.64 (dd, J = 14, 2.4 Hz, 1H), 3.73 (s, 3H), 2.82-2.75 (m, 1H), 2.62-2.58 (m, 1H), 1.37 (s, 1H), 1.28 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 192.3, 175.6, 161.7, 136.1, 127.1, 121.6, 120.9, 118.0, 81.8, 52.3, 46.3, 38.5, 20.9, 20.7; IR: 2981, 2889, 1729, 1687, 1607, 1463, 1392, 1303, 1221, 1133, 1115, 1078, 990, 870, 764 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{14}\text{H}_{16}\text{NaO}_4^+$ $[\text{M}+\text{Na}]^+$ 271.0941, Found $[\text{M}+\text{Na}]^+$ 271.0934; HPLC: 30.46:69.54 e.r., Chiralpak AD-H column, 98:2 (Hexanes: isopropanol), 1 mL/min, 254 nm, t_r (minor): 11.4 min, t_r (major): 13.8 min. $[\alpha]_D^{23}$ = 13.0 (c 0.135, CHCl_3).



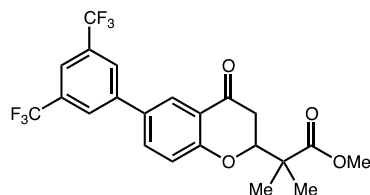
(4b) methyl 2-(6-chloro-4-oxochroman-2-yl)-2-methylpropanoate: ^1H NMR yield: 70%; Mp 100-102 $^{\circ}$ C; ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, J = 2.4 Hz, 1H), 7.40 (dd, J = 9.2, 2.8 Hz, 1H), 6.92 (d, J = 8.8 Hz, 1H), 4.63 (dd, J = 14, 2.4 Hz, 1H), 3.73 (s, 3H), 2.81-2.73 (m, 1H), 2.64-2.59 (m, 1H), 1.36 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 191.0, 175.3, 159.9, 135.8, 127.1, 126.3, 121.6, 119.6, 82.0, 52.3, 46.1, 38.1, 20.8, 20.6; IR: 3068, 2981, 2913,

1717, 1684, 1599, 1470, 1423, 1270, 1157, 1140, 1082, 994, 829, 770, 535 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{14}\text{H}_{15}\text{ClNaO}_4^+$ $[\text{M}+\text{Na}]^+$ 305.0551, Found $[\text{M}+\text{Na}]^+$ 305.0544; HPLC: 29.71:70.29 e.r., Chiralpak AD-H column, 98:2 (Hexanes: isopropanol), 1 mL/min, 254 nm, t_r (minor): 9.0 min, t_r (major): 11.9 min. $[\alpha]_D^{23} = 17.1$ (c 0.175, CHCl_3).



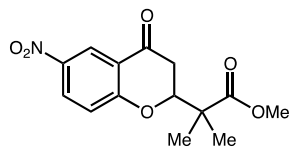
(4c) methyl 2-(6-bromo-4-oxochroman-2-yl)-2-methylpropanoate:

^1H NMR yield under standard conditions with 0.1 mmol scale: 73%; This reaction was also run on a 0.3 mmol scale to confirm that the ^1H NMR yields obtained were accurate: ^1H NMR yield: 86%; Isolated yield of a white solid after silica gel flash column chromatography (100% hexanes to 20/80 ethyl acetate/hexanes): 80%; Mp 115-116 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.97 (d, $J = 2.4$ Hz, 1H), 7.49 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.87 (d, $J = 8.8$ Hz, 1H), 4.62 (dd, $J = 14, 4.4$ Hz, 1H), 3.73 (s, 3H), 2.81-2.73 (m, 1H), 2.64-2.59 (m, 1H), 1.36 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 191.1, 175.4, 160.5, 138.7, 129.5, 122.2, 120.1, 114.3, 82.1, 52.4, 46.2, 38.2, 20.9, 20.7; IR: 3069, 2981, 2914, 2889, 1717, 1684, 1599, 1471, 1435, 1423, 1388, 1271, 1220, 1191, 1158, 1140, 1083, 994, 829, 770, 686 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{14}\text{H}_{15}\text{BrNaO}_4^+$ $[\text{M}+\text{Na}]^+$ 349.0046, Found $[\text{M}+\text{Na}]^+$ 349.0032 HPLC: 27.57:72.43 e.r., Chiralpak AD-H column, 98:2 (Hexanes: isopropanol), 1 mL/min, 220 nm, t_r (minor): 9.1 min, t_r (major): 12.4 min. $[\alpha]_D^{23} = 24.7$ (c 0.290, CHCl_3). After recrystallization with isopropanol:hexanes: 33% isolated yield with 74% ee HPLC: 13.04:86.96 e.r., Chiralpak AD-H column, 98:2 (Hexanes: isopropanol), 1 mL/min, 220 nm, t_r (minor): 9.7 min, t_r (major): 13.2 min. $[\alpha]_D^{23} = 56.1$ (c 0.19, CHCl_3).



(4d) methyl 2-(6-(3,5-bis(trifluoromethyl)phenyl)-4-oxochroman-2-yl)-2-methylpropanoate:

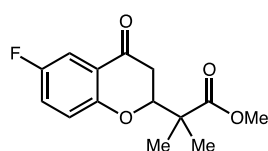
^1H NMR yield starting material: 67%; ^1H NMR yield product: 12%; Mp 127-130 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 8.13 (d, $J = 2.4$ Hz, 1H), 7.98 (s, 2H), 7.84 (s, 1H), 7.74 (dd, $J = 8.4, 2.4$ Hz, 1H), 7.13 (d, $J = 8.8$ Hz, 1H), 4.72 (dd, $J = 14.4, 2.8$ Hz, 1H), 3.76 (s, 3H), 2.89-2.82 (m, 1H), 2.72-2.67 (m, 1H), 1.41 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 191.9, 175.4, 162.0, 141.8, 134.5, 132.4 (q, $J_{\text{CF}} = 33$ Hz), 131.7, 126.8, 126.8, 125.6, 123.4 (q, $J_{\text{CF}} = 271$ Hz), 121.2, 121.1, (p, $J_{\text{CF}} = 4$ Hz), 119.3, 82.2, 52.4, 46.3, 38.4, 20.9, 20.8; IR: 2981, 2889, 1719, 1691, 1612, 1504, 1464, 1380, 1332, 1272, 1185, 1171, 1125, 1081, 1057, 893, 837, 680 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{22}\text{H}_{18}\text{F}_6\text{NaO}_4^+$ $[\text{M}+\text{Na}]^+$ 483.1001, Found $[\text{M}+\text{Na}]^+$ 483.0992; HPLC: 21.96:78.04 e.r., Chiralpak AD-H column, 98:2 (Hexanes: isopropanol), 1 mL/min, 220 nm, t_r (minor): 7.1 min, t_r (major): 10.4 min. $[\alpha]_D^{23} = 30.4$ (c 0.080, CHCl_3).



(4e) methyl 2-(6-nitro-4-oxochroman-2-yl)-2-methylpropanoate:

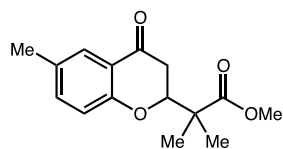
^1H NMR yield starting material: 50%; ^1H NMR yield product: 27%; Mp 96-103 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 8.76 (d, $J = 2.8$ Hz, 1H), 8.32 (dd, $J = 9.2, 2.8$ Hz, 1H), 7.10 (d, $J = 8.8$ Hz, 1H), 4.76 (dd, $J = 14, 2.8$ Hz, 1H), 3.75 (s, 3H), 2.88-2.71 (m, 2H), 1.40 (s, 3H), 1.31 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 189.9, 174.9, 165.2, 142.2, 130.3, 123.5, 120.3, 119.2, 82.6, 52.4, 46.0, 37.9, 20.8, 20.6; IR: 2981, 2914, 2889, 1717, 1685, 1600, 1574, 1472, 1436, 1424, 1388, 1370, 1271, 1191, 1140, 1083, 994, 830, 770 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{14}\text{H}_{15}\text{NNaO}_6^+$ $[\text{M}+\text{Na}]^+$ 316.0792, Found $[\text{M}+\text{Na}]^+$ 316.0792; HPLC: 25.88:74.12 e.r., Chiralpak AD-H column, 98:2 (Hexanes: isopropanol), 1 mL/min, 220 nm, t_r (minor): 25.5 min, t_r (major): 32.2 min. $[\alpha]_D^{23} =$

–23.1 (c 0.295, CHCl₃).



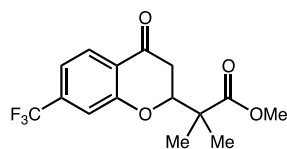
(4f) methyl 2-(6-fluoro-4-oxochroman-2-yl)-2-methylpropanoate:

¹H NMR yield: 80%; Mp 52–53 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.51 (ddd, *J* = 8.2, 3.2, 1.2 Hz, 1H), 7.19 (td, *J* = 8.8, 3.2 Hz, 1H), 6.94 (dd, *J* = 9.2, 4.4 Hz, 1H), 4.62 (dd, *J* = 14, 2.4), 3.73 (s, 3H), 2.81–2.73 (m, 1H), 2.64–2.59 (m, 1H), 1.37 (s, 3H), 1.28 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 191.6 (d, *J*_{CF} = 1 Hz), 175.5, 157.9 (d, *J*_{CF} = 2 Hz), 157.4 (d, *J*_{CF} = 241 Hz), 123.6 (d, *J*_{CF} = 2 Hz), 121.3 (d, 7 Hz), 119.6 (d, 7 Hz), 112.0 (*J*_{CF} = 23 Hz), 82.1, 52.4, 46.2, 38.2, 20.9, 20.7; IR: 2982, 2951, 1723, 1690, 1618, 1481, 1435, 1269, 1194, 1133, 995, 830, 710, 545 cm^{–1}; HRMS (ESI): Mass calculated for C₁₄H₁₅FN₄⁺ [M+Na]⁺ 289.0847, Found [M+Na]⁺ 289.0844; HPLC: 30.54–69.46 e.r., (Hexanes: isopropanol), 1 mL/min, 220 nm, *t*_r (minor): 13.3 min, *t*_r (major): 19.4 min. [α]_D²³ = 13.6 (c 0.33, CHCl₃).



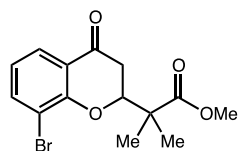
(4g) methyl 2-methyl-2-(6-methyl-4-oxochroman-2-yl)propanoate:

¹H NMR yield: 53%; Mp 79–82 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.66–7.75 (m, 1H), 7.28–7.26 (m, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 4.60 (dd, *J* = 14, 2.4 Hz, 1H), 3.72 (s, 3H), 2.80–2.75 (m, 1H), 2.59–2.55 (m, 1H), 2.29 (s, 3H), 1.36 (s, 3H), 1.27 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 192.6, 175.7, 159.8, 137.2, 131.0, 126.6, 120.5, 117.8, 81.8, 52.3, 46.3, 38.5, 20.9, 20.8, 20.5; IR: 2921, 2927, 1730, 1685, 1614, 1488, 1468, 1393, 1291, 1253, 1134, 1075, 992, 830, 583, 541 cm^{–1}; HRMS (ESI): Mass calculated for C₁₅H₁₈NaO₄⁺ [M+Na]⁺ 285.1097, Found [M+Na]⁺ 285.1096; HPLC: 42.15:57.85 e.r., Chiralpak AD-H column, 98:2 (Hexanes: isopropanol), 1 mL/min, 254 nm, *t*_r (minor): 10.3 min, *t*_r (major): 14.8 min. [α]_D²³ = 2.9 (c 0.335, CHCl₃).



(4h) methyl 2-methyl-2-(4-oxo-7-(trifluoromethyl)chroman-2-yl)propanoate:

¹H NMR yield: 90%; Mp 61–64 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.99–7.97 (m, 1H), 7.26–7.24 (m, 2H), 4.700 (dd, *J* = 14, 2.4 Hz, 1H), 3.75 (s, 3H), 2.87–2.79 (m, 1H), 2.70–2.65 (m, 1H), 1.39 (s, 3H), 1.30 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 191.4, 175.3, 161.4, 137.3 (q, *J*_{CF} = 33), 128.1, 123.2 (q, *J*_{CF} = 272 Hz), 123.0, 118.0 (q, *J*_{CF} = 5 Hz), 115.7 (q, *J*_{CF} = 5 Hz), 82.3, 52.5, 46.2, 38.4, 20.9, 20.8; IR: 2981, 2889, 1730, 1699, 1625, 1437, 1332, 1208, 1165, 1123, 1072, 994, 882, 830, 723 cm^{–1}; HRMS (ESI): Mass calculated for C₁₅H₁₅F₃NaO₄⁺ [M+Na]⁺ 339.0815, Found [M+Na]⁺ 339.0817; HPLC: 34.18–65.82 e.r., Chiralcel OJ column, 99:1 (Hexanes: isopropanol), 1 mL/min, 220 nm, *t*_r (minor): 10.0 min, *t*_r (major): 13.9 min. [α]_D²³ = 9.5 (c 0.155, CHCl₃).

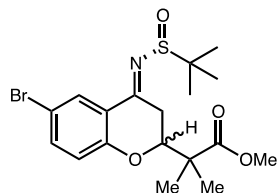


(4i) methyl 2-(8-bromo-4-oxochroman-2-yl)-2-methylpropanoate:

¹H NMR yield: 62%; ¹H NMR (400 MHz, CDCl₃) δ 7.82 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.70 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 4.70 (dd, *J* = 14, 2.4 Hz, 1H), 3.75 (s, 3H), 2.85–2.77 (m, 1H), 2.67–2.62 (m, 1H), 1.43 (s, 3H), 1.32 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 191.5, 175.4, 158.0, 139.2, 126.4, 122.3, 122.1, 112.0, 82.7, 52.5, 46.4, 38.2, 21.0, 20.6; IR: 2980, 2889, 1727, 1693, 1593, 1462, 1429, 1391, 1289, 1240, 1133, 1062, 991, 733 cm^{–1}; HRMS (ESI): Mass calculated for C₁₄H₁₅BrNaO₄⁺ [M+Na]⁺ 349.0046, Found [M+Na]⁺ 349.0039; HPLC: 40.05–50.95 e.r., Chiralpak AD-H column, 99.5:0.5 (Hexanes: isopropanol), 1 mL/min, 220 nm, *t*_r (minor): 19.3

min, t_r (major): 34.8 min. $[\alpha]_D^{23} = 1.6$ (c 0.17, CHCl_3).

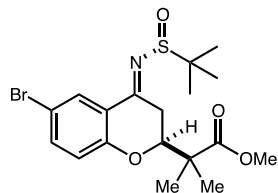
General Procedure for the Formation of the N-sulfinyl Imine



(11) methyl 2-((*E*)-6-bromo-4-(((*R*)-*tert*-butylsulfinyl)imino)chroman-2-yl)-2-methylpropanoate: Using a modified known procedure,¹² racemic ketone (**4c**) (100 mg, 0.3 mmol) and (*R*)-2-methylpropane-2-sulfinamide (37.0 mg, 0.3 mmol, 1 eq) were placed in a flame-dried flask with stirbar and dissolved in 5 mL dry THF (0.06 M). 157.7 mg of $\text{Ti}(\text{OMe})_4$ (0.9 mmol, 3 eq) was added to the flask and it was fitted with a

reflux condenser under a nitrogen atmosphere and refluxed for 48 hours. The volume of THF was monitored and more added as necessary to maintain stirring of the solution. After the reaction time, the flask was cooled to room temperature, quenched with brine (2 mL) and filtered through Celite with ethyl acetate. The filtrate was diluted with water (10 mL) extracted with EtOAc (10 mL x 3), washed brine (10 mL), and dried with Na_2SO_4 . The mixture of diastereomers was isolated via silica gel flash column chromatography (100% hexanes to 30% ethyl acetate:hexanes) to yield 104.9 mg of product as a yellow solid (80% yield). Mp 106-110 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.02 (dd, $J = 4.5, 2.5$ Hz, 1H), 7.44 (dd, $J = 8.5, 2.4$ Hz, 1H), 6.80 (dd, $J = 8.7, 1.5$ Hz, 1H), 4.44-4.38 (m, 1H), 4.04 (dd, $J = 16.6, 2.5$ Hz, 0.5H), 3.73 (s, 3H), 3.66 (dd, $J = 17, 2$ Hz, 0.61H), 2.82 (dd, $J = 17, 14$ Hz, 0.53H), 2.59 (dd, $J = 16.5, 14$ Hz, 0.4H), 1.34-1.33 (m, 12H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 175.7, 175.5, 168.8, 168.8, 158.1, 158.0, 136.9, 136.8, 129.1, 129.1, 122.5, 122.4, 120.1, 114.1, 114.1, 80.7, 80.4, 58.5, 58.3, 52.4, 46.2, 31.0, 30.1, 22.8, 22.8, 21.3, 21.0, 20.4, 20.3; IR: 2981, 2950, 1728, 1610, 1585, 1464, 1415, 1363, 1266, 1219, 1129, 1067, 997, 822, 662 cm^{-1} ; HRMS (ESI): Mass calculated for $\text{C}_{18}\text{H}_{24}\text{BrNNaO}_4\text{S}^+$ $[\text{M}+\text{Na}]^+$ 452.0502, Found $[\text{M}+\text{Na}]^+$ 452.0502; HPLC: OD-H 97:3 (Hexanes: isopropanol), 1 mL/min, 220 nm, t_r (major): 6.66 min, t_r (minor): 8.22 min.

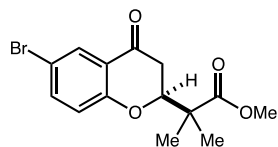
Determination of the Major Enantiomer



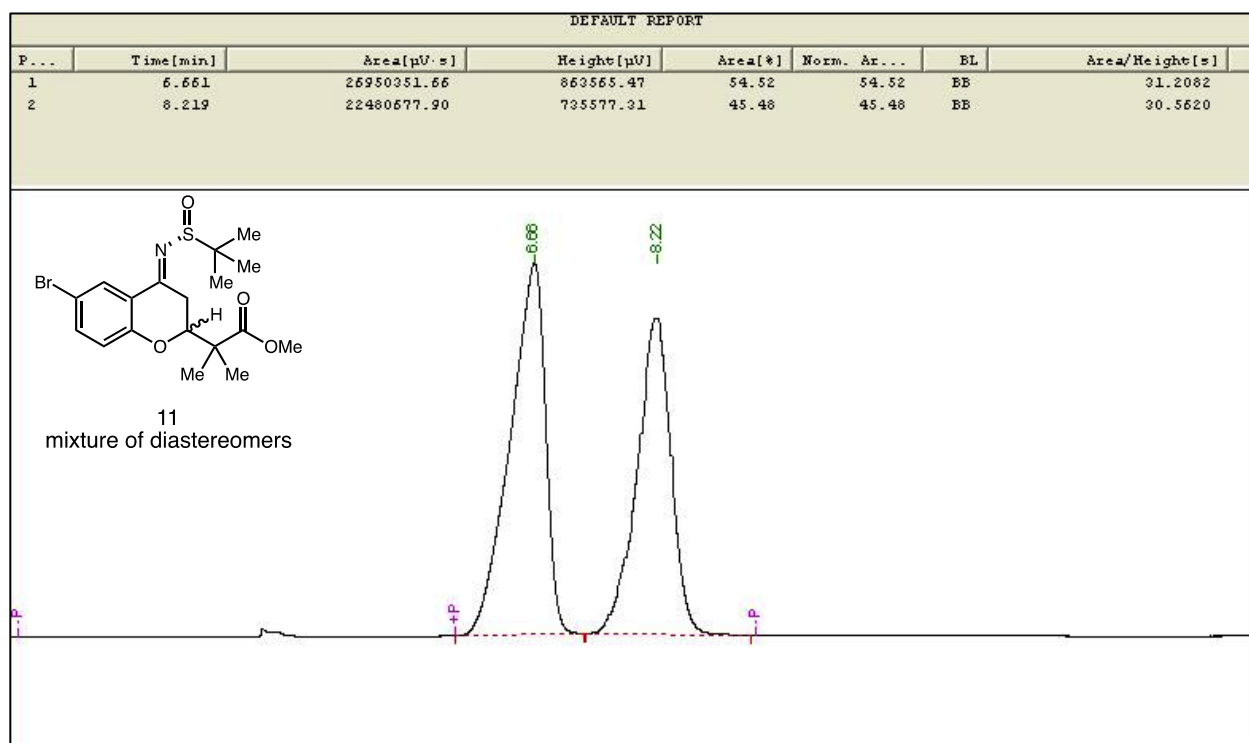
(11a) methyl 2-(((*S,E*)-6-bromo-4-(((*R*)-*tert*-butylsulfinyl)imino)chroman-2-yl)-2-methylpropanoate: This diastereomer was isolated via slow evaporation as it was not separable by column chromatography in our hands. The mixture of diastereomers (**11**) was dissolved in a minimal amount of DCM and layered with hexanes.

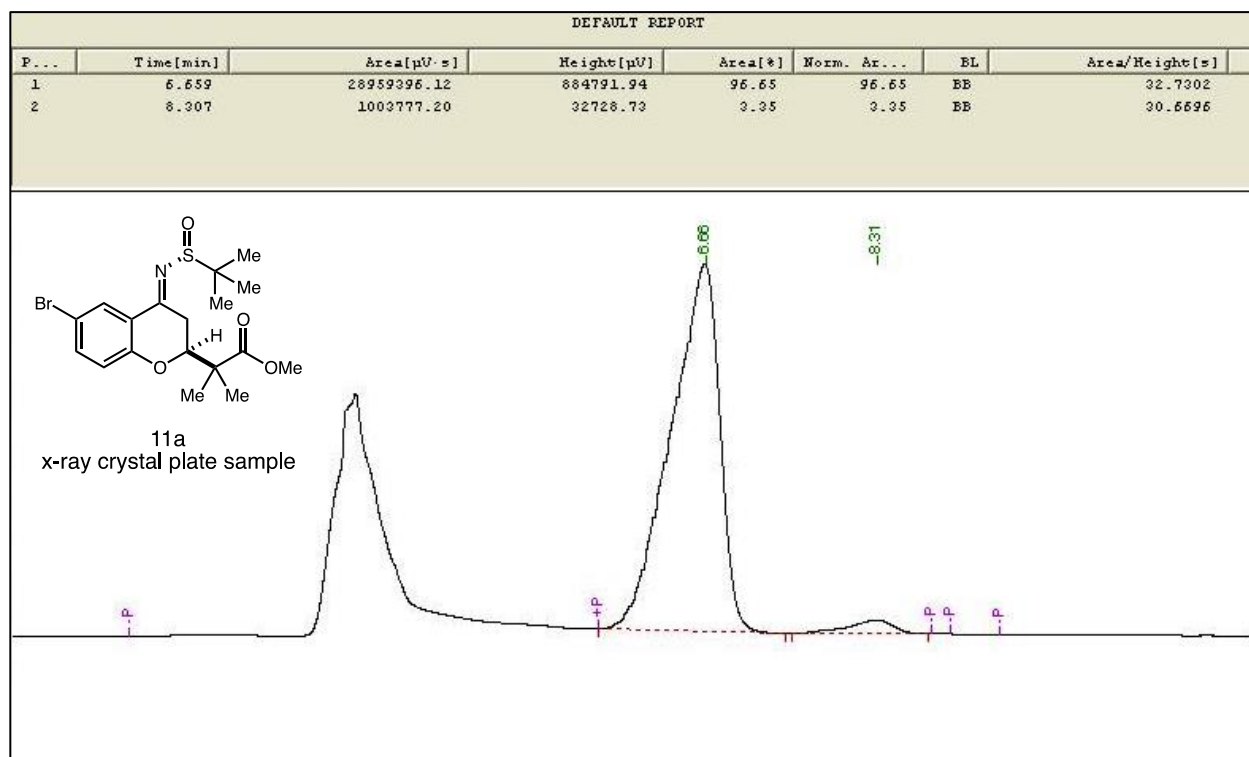
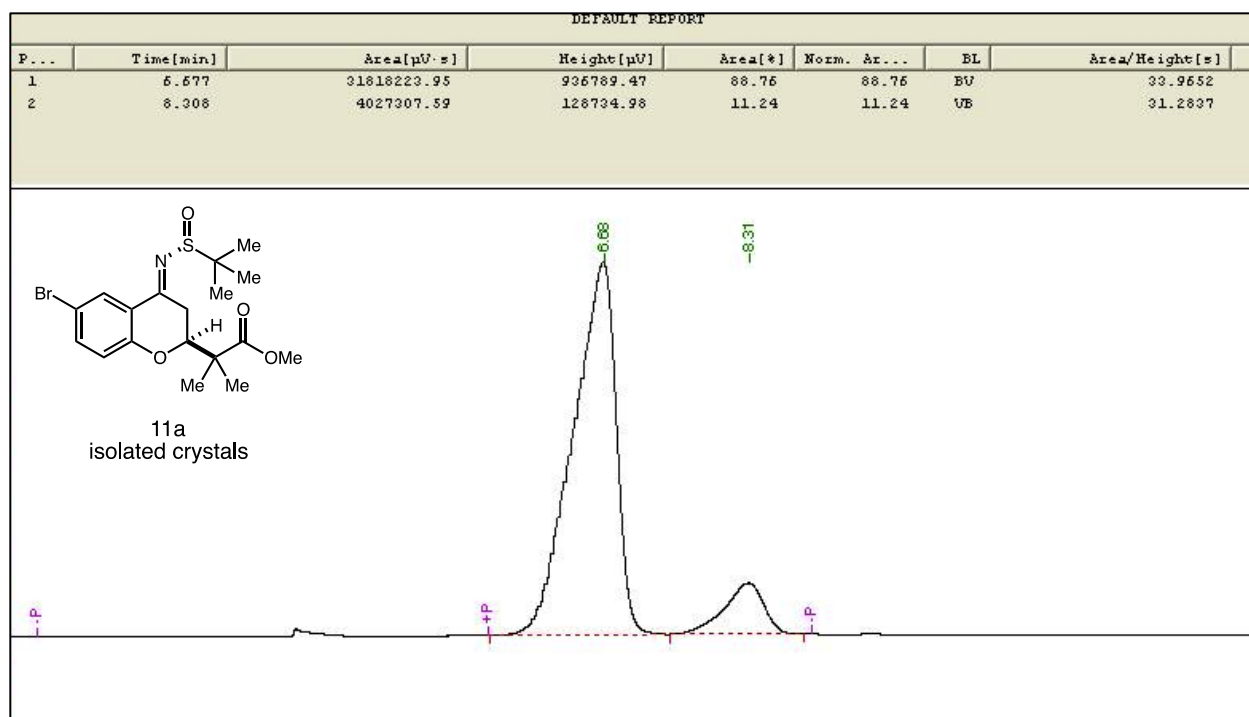
The vial was allowed to sit open to air for slow evaporation over several days. Clear, yellow squares eventually crystallized in the bottom of the vessel which contained a minimal amount of the other diastereomer. These were carefully extracted from the mixture and characterized via NMR and X-ray crystallography to determine the stereochemistry at the 2-position. This isolated diastereomer was subjected to HPLC analysis to confirm that it was indeed majority one diastereomer. The crystal plate used to determine the stereochemistry was also subjected to HPLC analysis to confirm that the isolated diastereomers were identical (this HPLC trace contains grease due to the adhesive used for obtaining the X-ray data; the exact crystal used for data collection broke in transport and could not be subjected to HPLC analysis). X-ray analysis indicated that the crystal used for obtaining the data was only one enantiomer. Mp 116-122 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.01 (d, $J = 2.8$ Hz, 1H), 7.44 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.80 (d, $J = 8.8$ Hz, 1H); 4.40 (dd, $J = 14, 2$ Hz, 1H); 3.73 (s, 3H), 3.66 (dd, $J = 17.2, 2.4$ Hz, 1H), 2.83 (dd, $J = 17.2, 14$ Hz, 1H); 1.34-1.33 (m, 12H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 175.7, 168.8, 158.1, 136.8, 129.2, 122.4, 120.1, 114.1, 80.4, 58.5, 52.4, 46.2, 31.0,

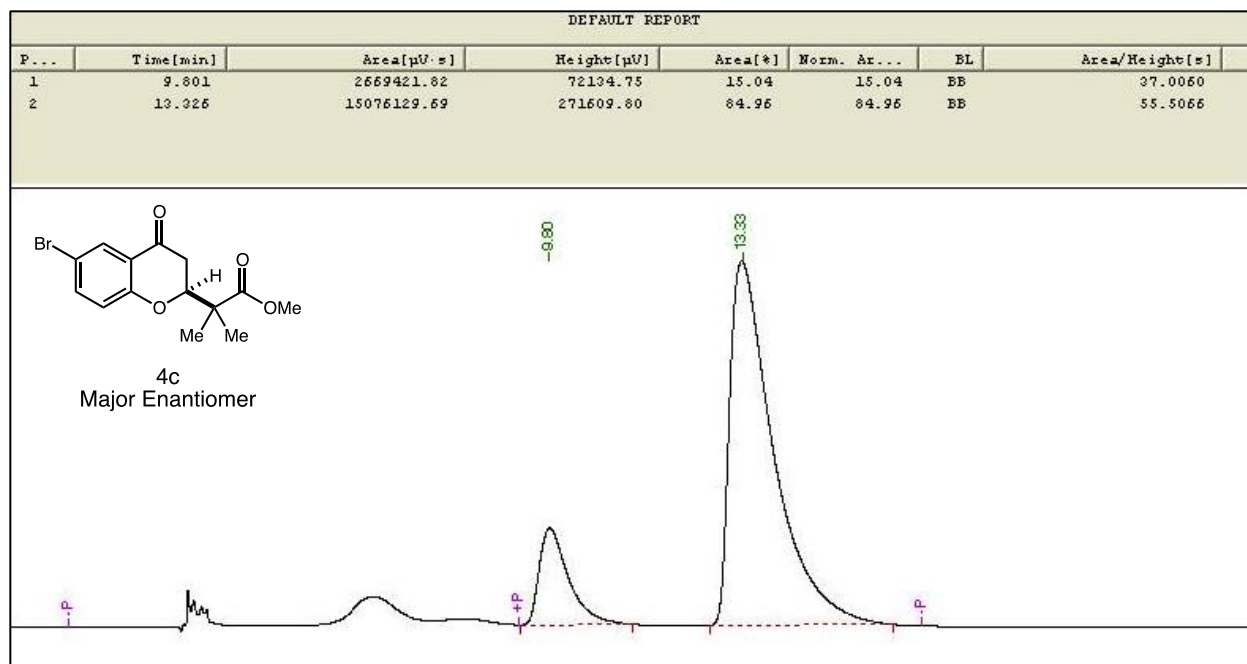
22.8, 22.8, 21.0, 20.4; HPLC: 88.76-11.24 e.r., Chiralpak OD-H 97:3 (Hexanes: isopropanol), 1 mL/min, 220 nm, t_r (major): 6.68 min, t_r (major): 8.30 min.



(4c) (S)-methyl 2-(6-bromo-4-oxochroman-2-yl)-2-methylpropanoate: The isolated diastereomer (**11a**) (13.7 mg, 0.032 mmol) was dissolved in methanol (1.0 mL, 0.3 M). HCl was added slowly (0.1 mL, 12 M) and allowed to stir at room temperature for 30 minutes. The product was neutralized with NaHCO_3 (aq) extracted with dichloromethane, washed with water, and dried with Na_2SO_4 to afford pure, crude **4c** (94% yield, 9.8 mg). This product was then subjected to prep TLC for HPLC analysis to demonstrate that this was the major enantiomer obtained during the silanediol-catalyzed addition of silyl ketene acetals to the chromenone salts.







Determination of Association Constant

The association constant of silanediol **5a** (host) and tetrabutylammonium triflate (TBAOTf) (guest) was determined by fluorescence titrations.^{13,14} Chloroform was purified to remove any stabilizers and distilled from CaH₂ prior to use. Commercially available TBAOTf was dried under reduced pressure for 1-day prior to use. The titration experiments were carried out with a host solution (3 mL, 5 × 10⁻⁵ M in CHCl₃) in a quartz cell and fluorescence spectra recorded upon the addition of aliquots of the stock solution of guest ion in CHCl₃ with a microsyringe. Titration data in the appropriate wavelength range were analyzed with multi-wavelength curve fitting. The sum of the square deviation is defined as equation 1.

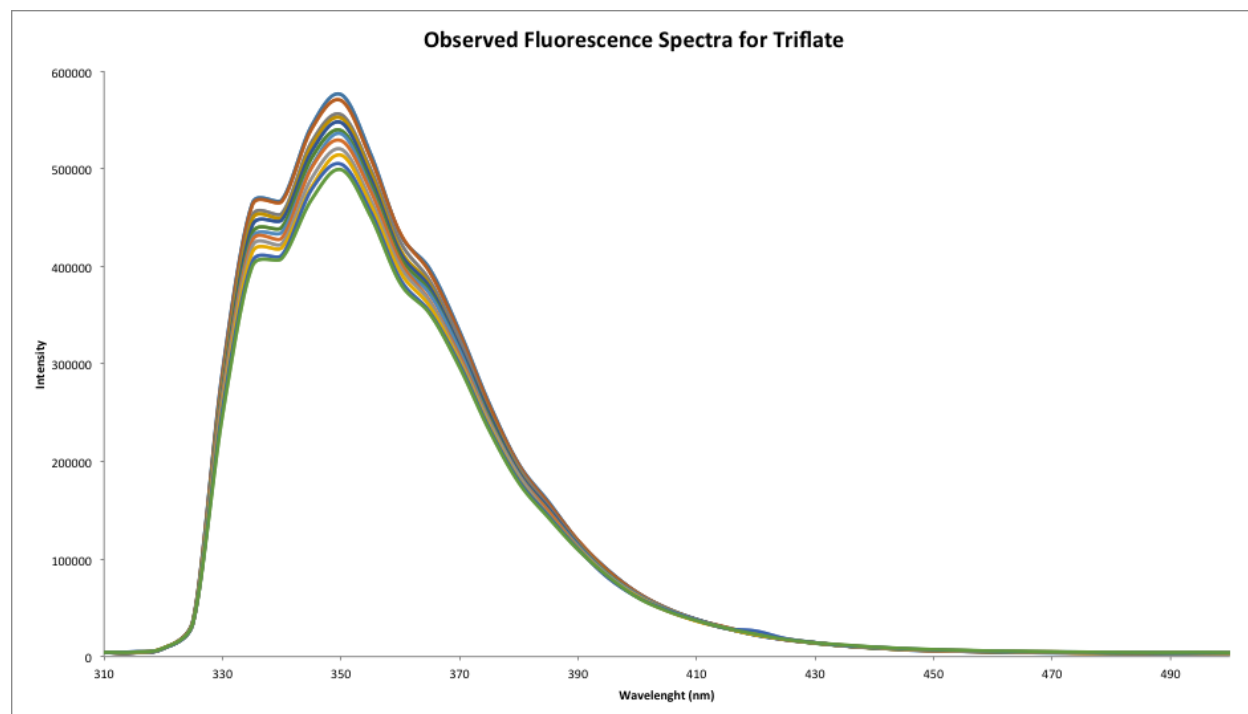
$$\text{Equation 1: } \chi^2 = \sum_{\lambda} \sum_{\alpha} (I_{\lambda\alpha}^{\text{obsd}} - I_{\lambda\alpha}^{\text{calcd}})^2$$

Where $I_{\lambda\alpha}^{\text{obsd}}$ and $I_{\lambda\alpha}^{\text{calcd}}$ observed and calculated absorbance or fluorescence intensity of host in the presence of α equiv of anions at λ nm emission $I_{\lambda\alpha}^{\text{calcd}}$ can be calculated as equation 2.

$$\text{Equation 2: } I_{\lambda\alpha}^{\text{calcd}} = I_{\lambda 0} + (I_{\lambda \infty} - I_{\lambda 0}) \frac{(\alpha+1)[H]_t + \frac{1}{K_{11}} - \sqrt{(\alpha-1)^2[H]_t^2 + \frac{2(\alpha+1)}{K_{11}}[H]_t + \frac{1}{K_{11}^2}}}{2[H]_t}$$

In which $I_{\lambda 0}$ and $I_{\lambda \infty}$ are the fluorescence intensities of host and the complex respectively; $[H]_t$ is the total concentration of host; K_{11} is the associate constant during the complexation. The association constant and the sets of $I_{\lambda 0}$ and $I_{\lambda \infty}$ were calculated by non-linear least-squares treatment based on the Powell algorithm to minimize χ^2 with a self-written software on a 32-bit Windows PC. The titration experiments were duplicated independently 4 times and the mean value and the standard deviation are reported.

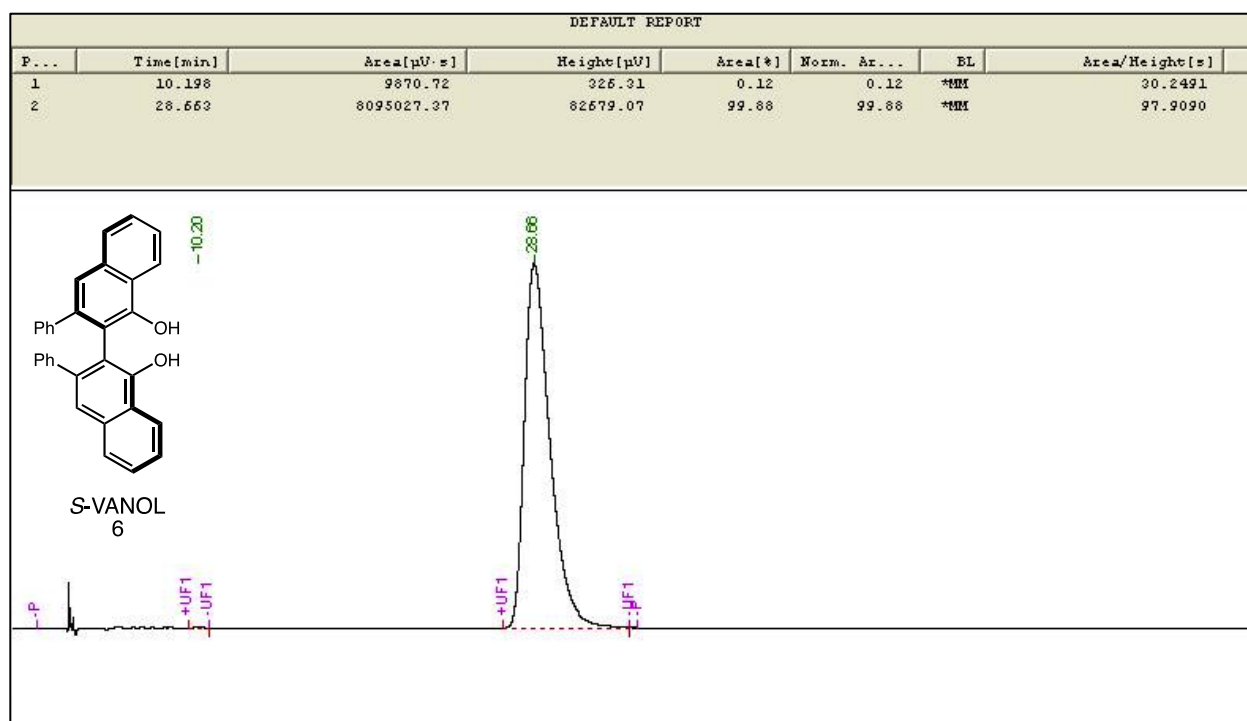
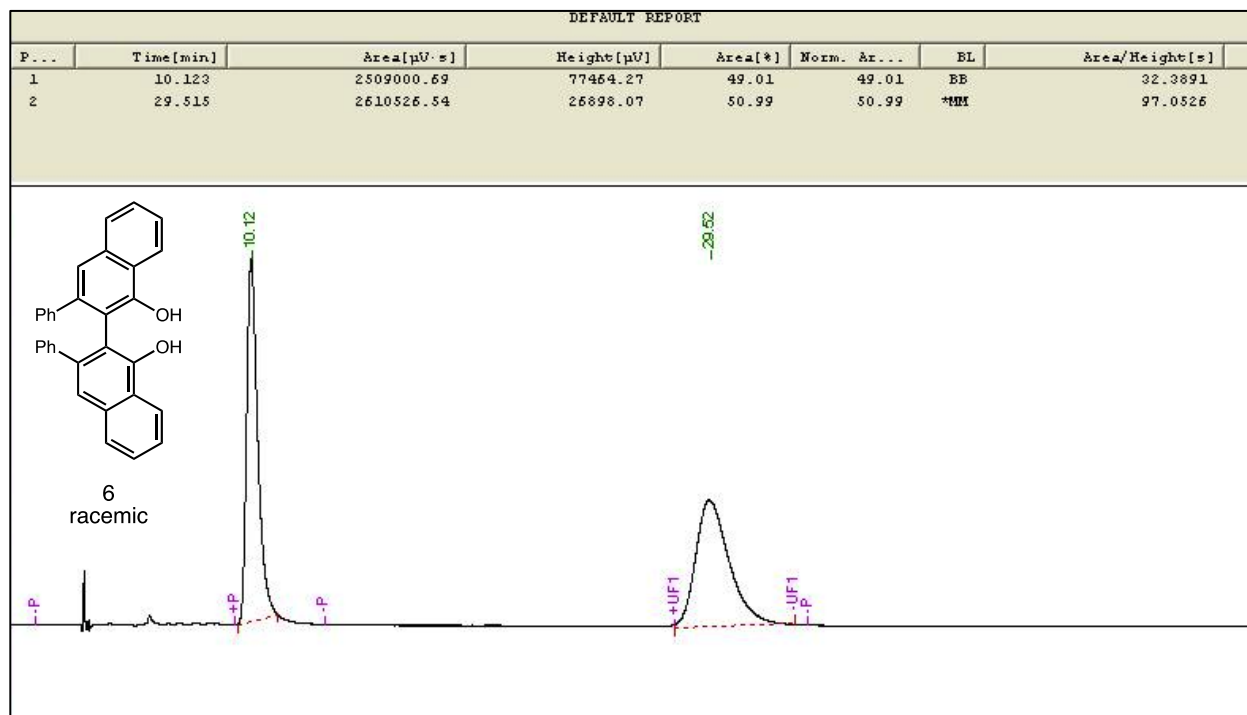
Representative fluorescence spectra upon the addition of TBAOTf to silanediol **5a** in CHCl_3 :

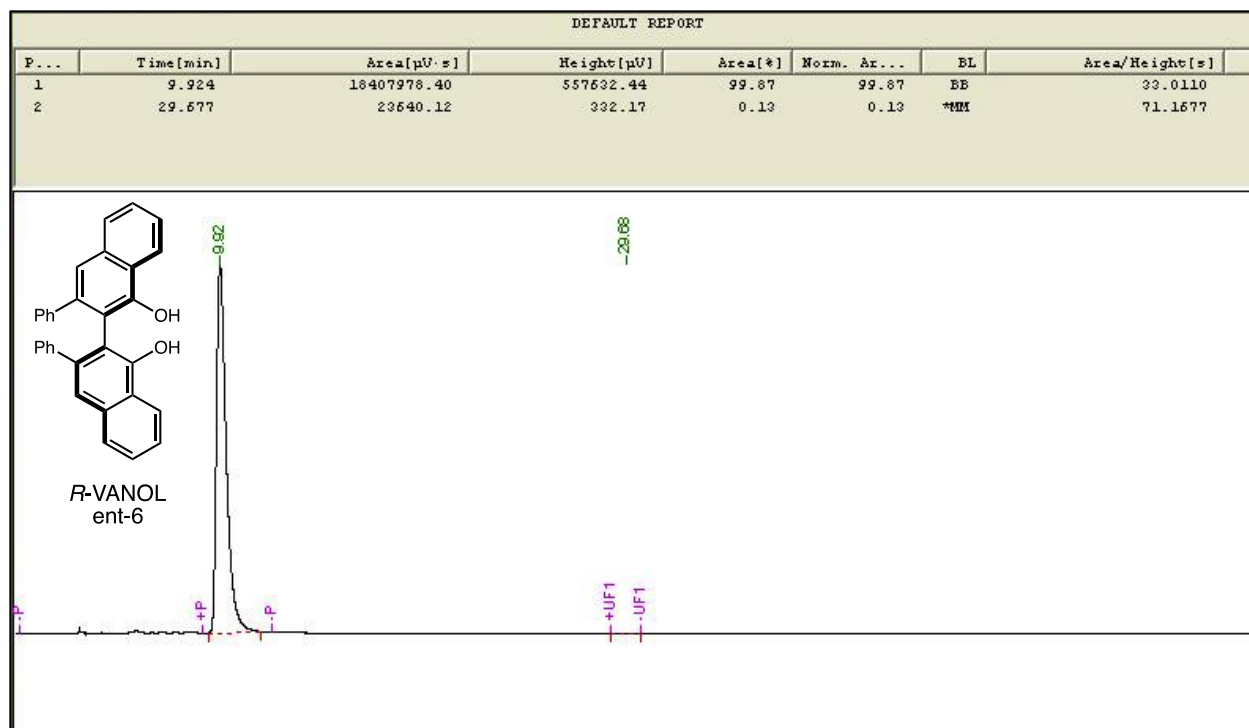


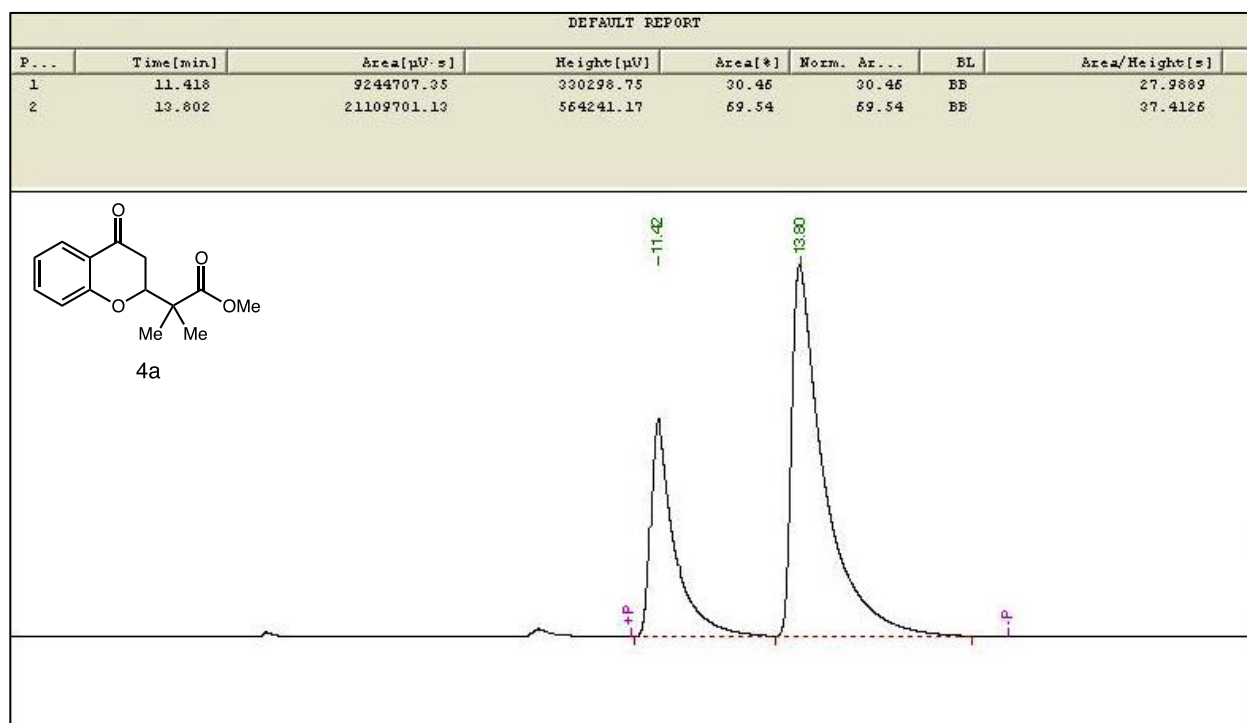
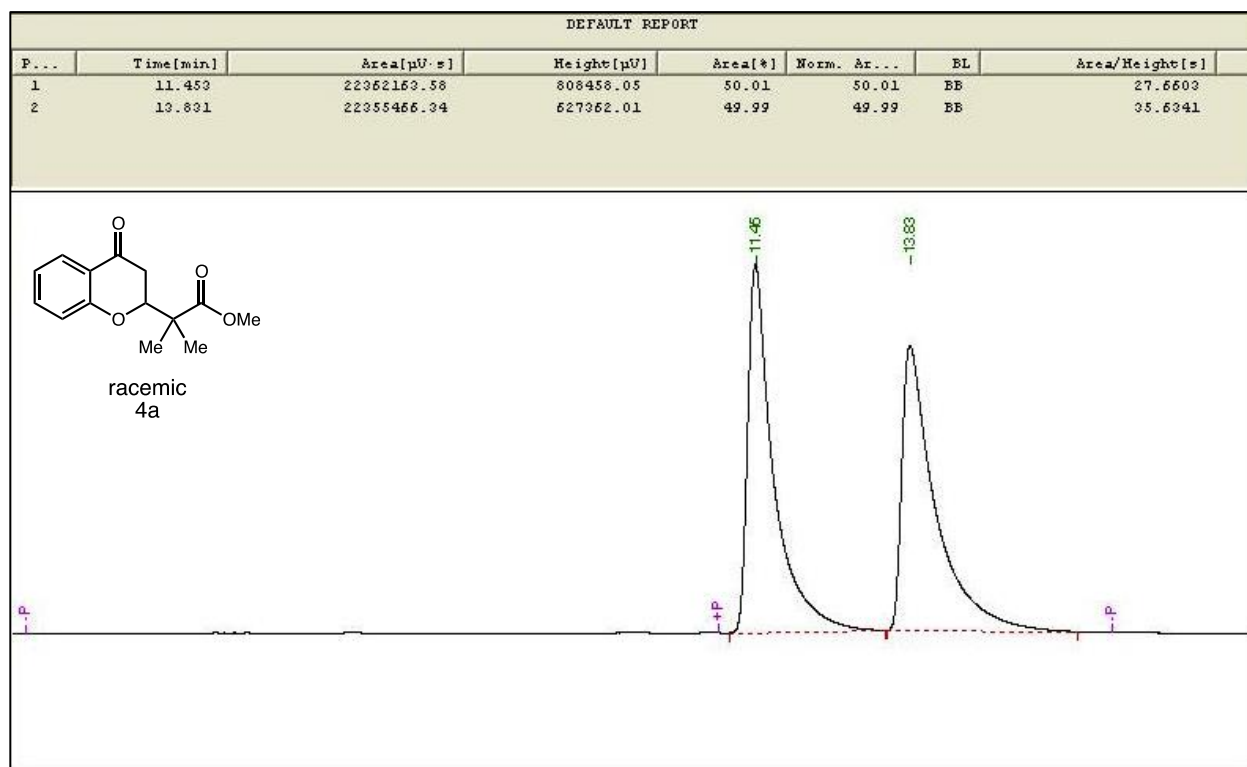
References

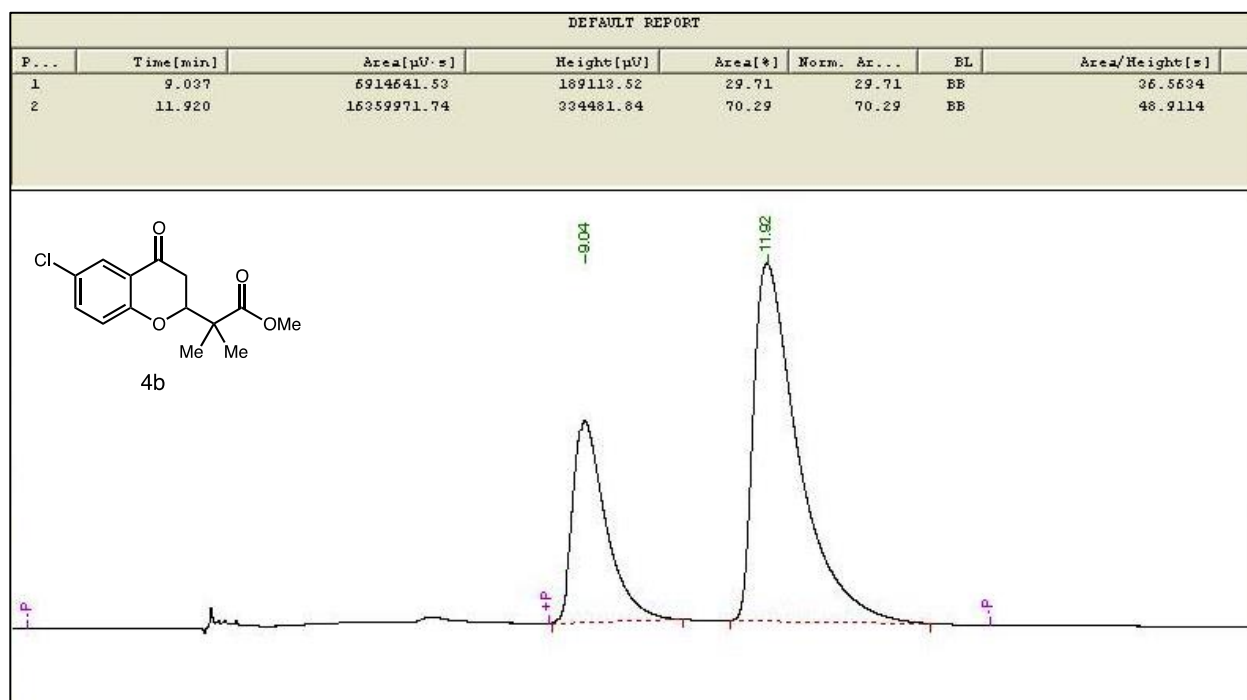
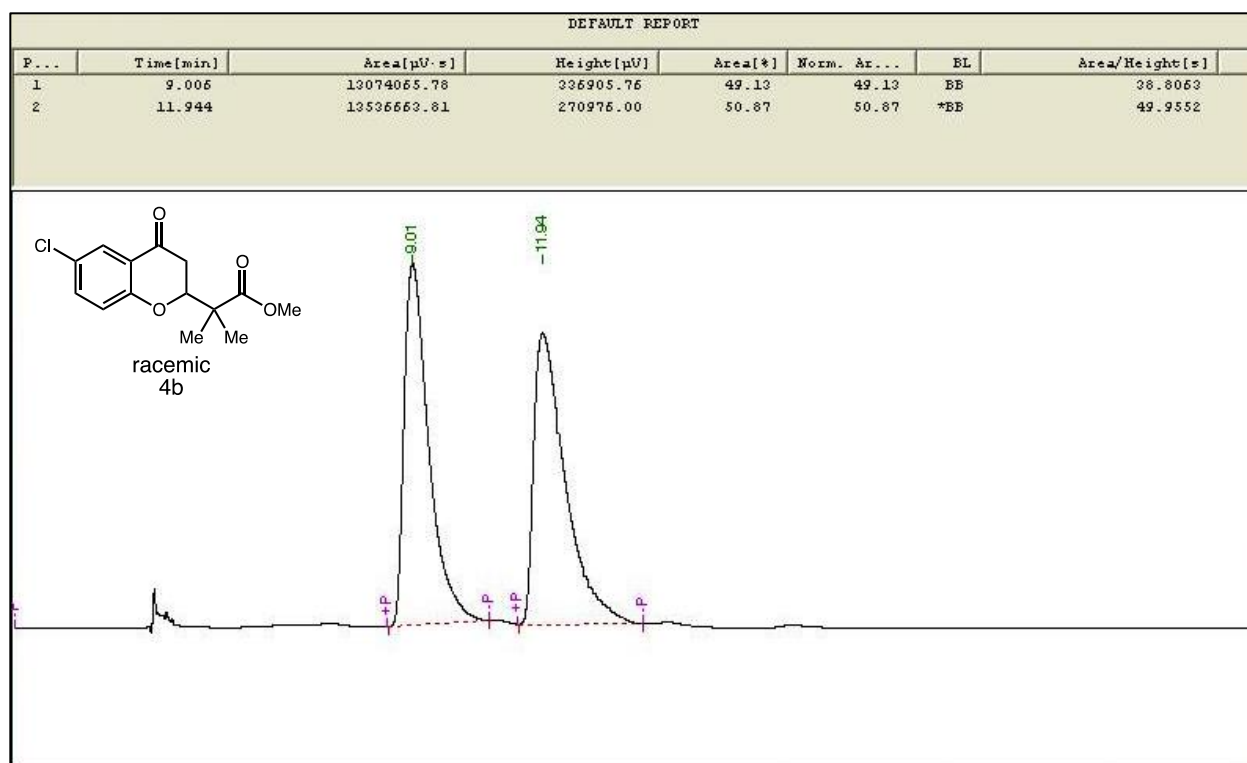
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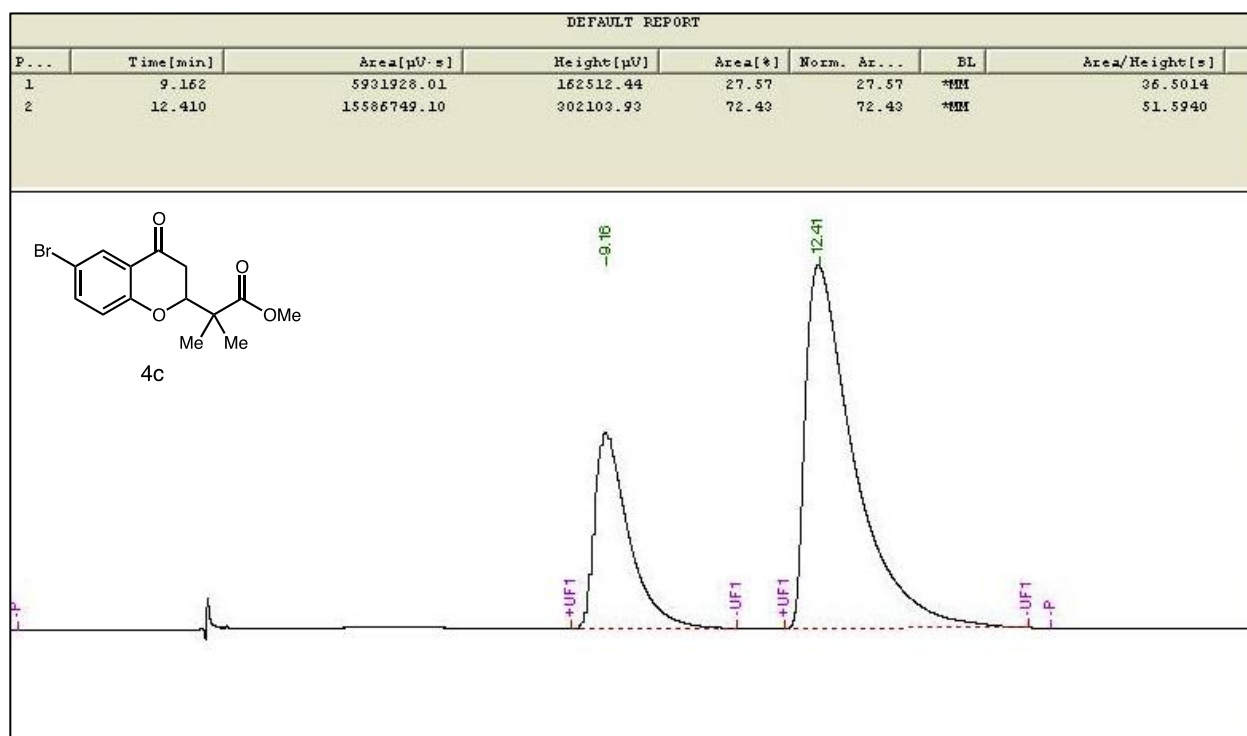
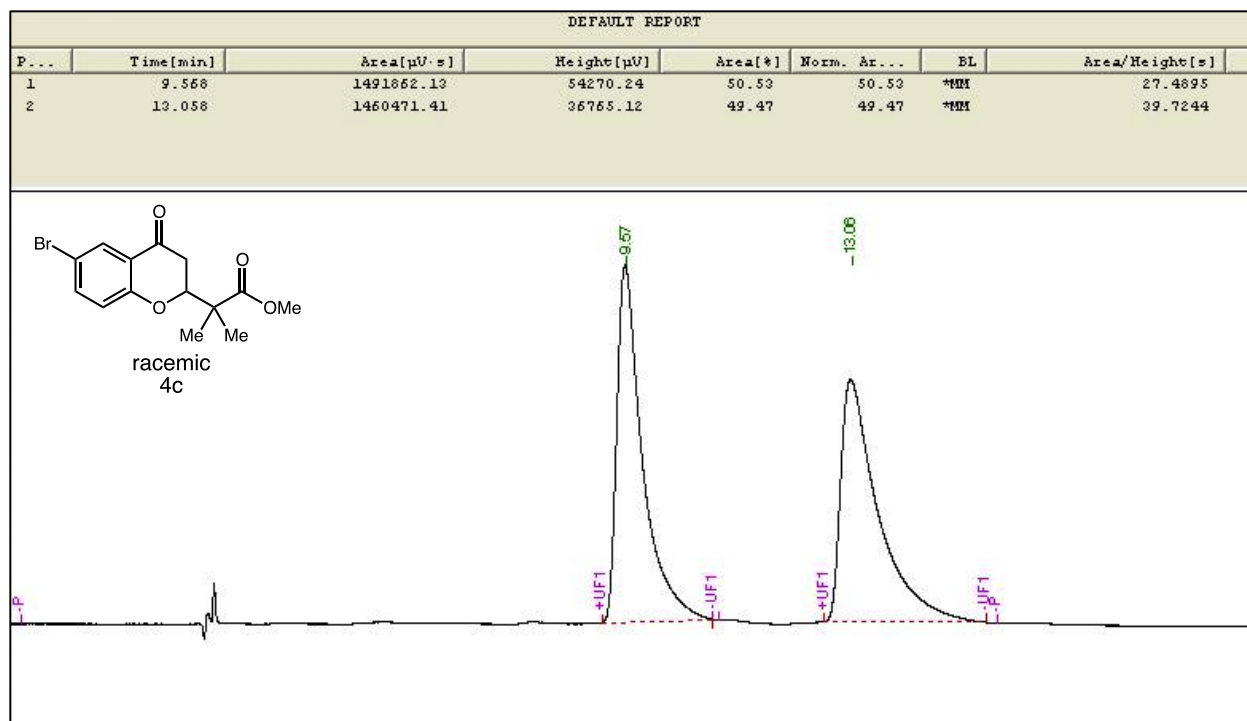
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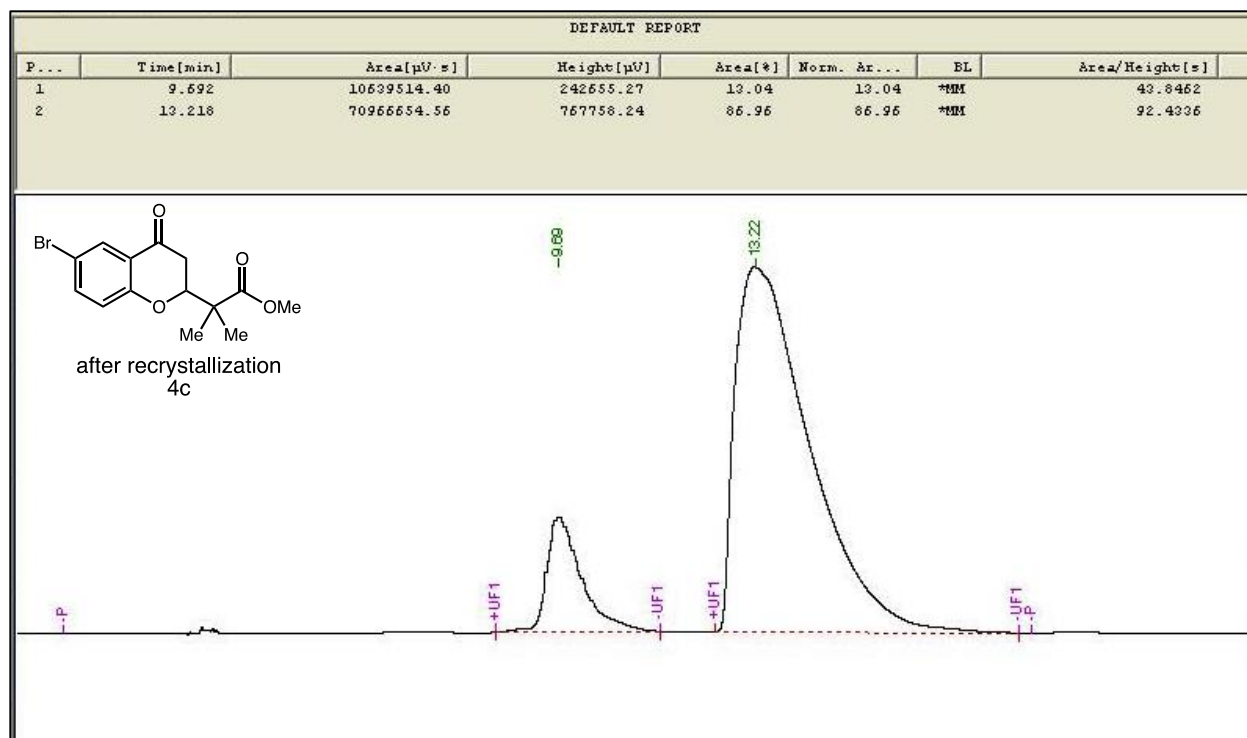


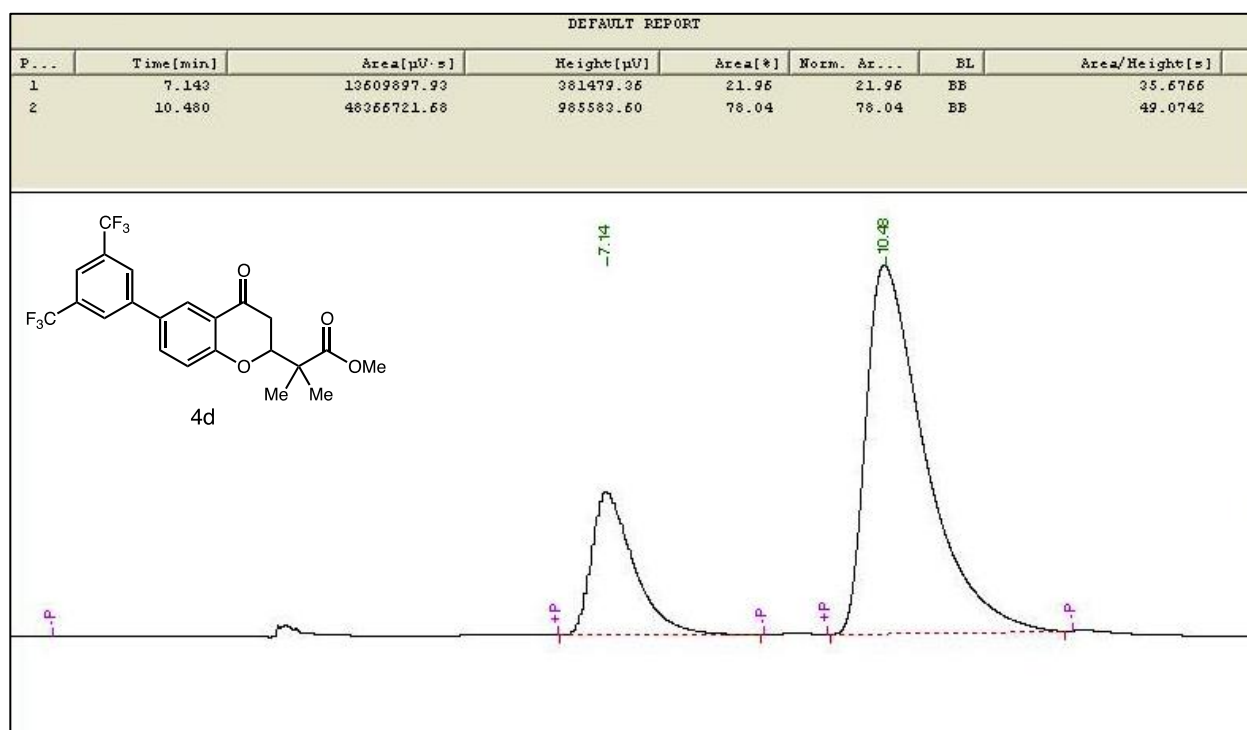
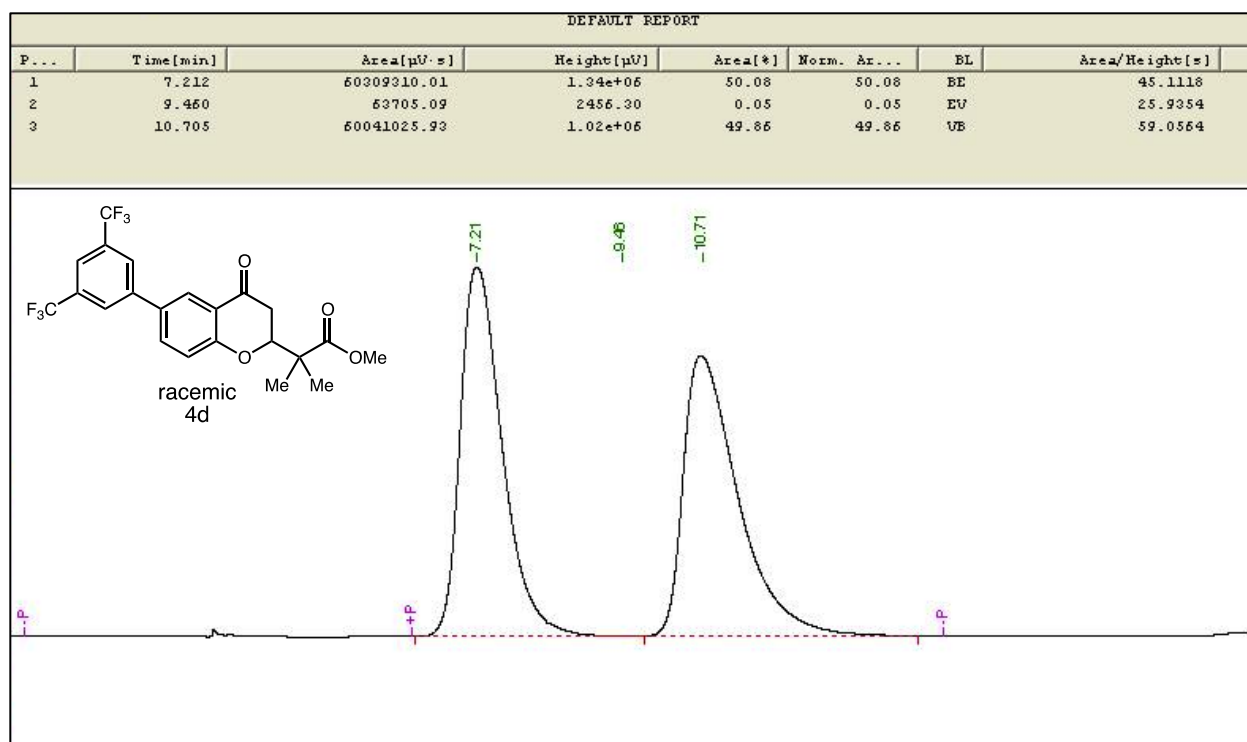


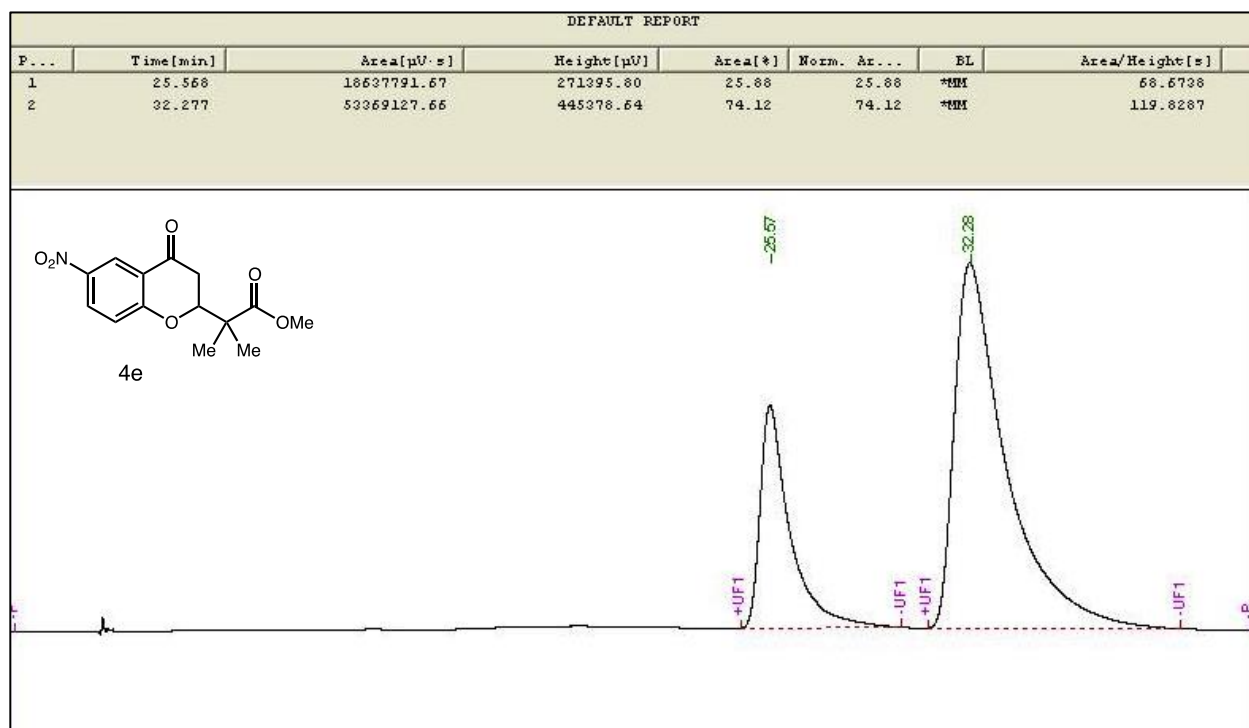
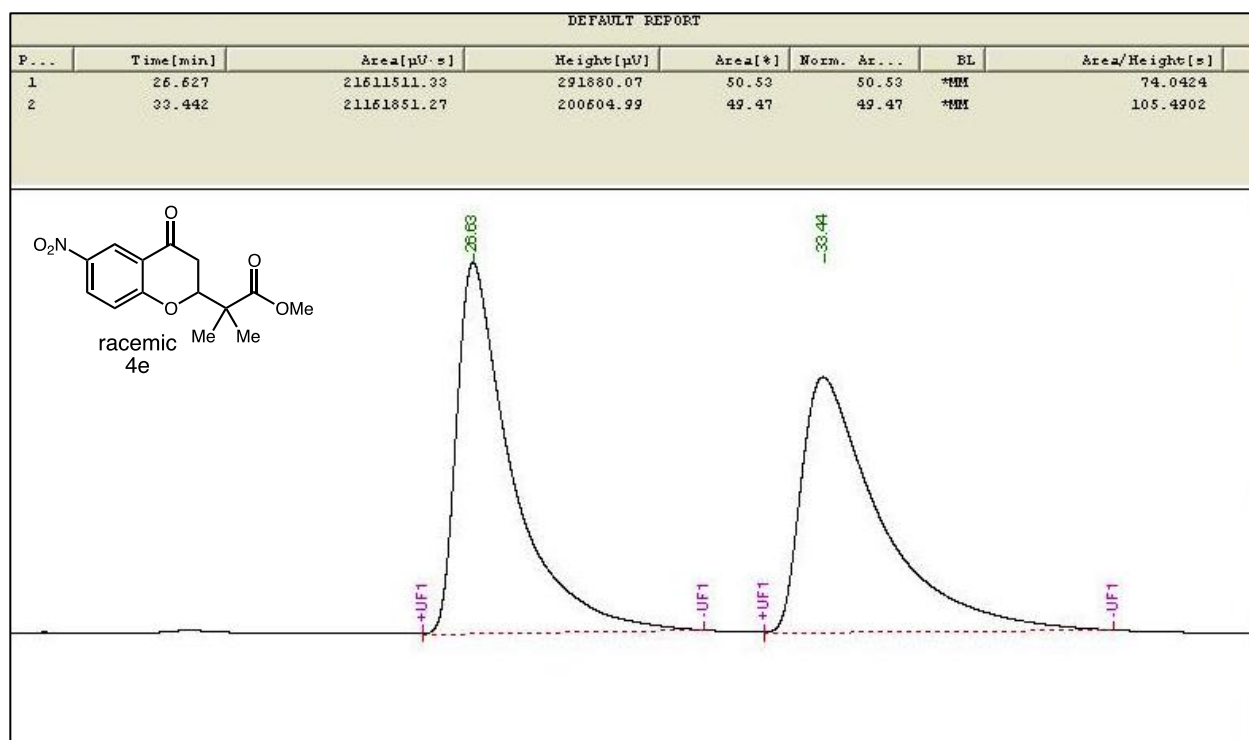


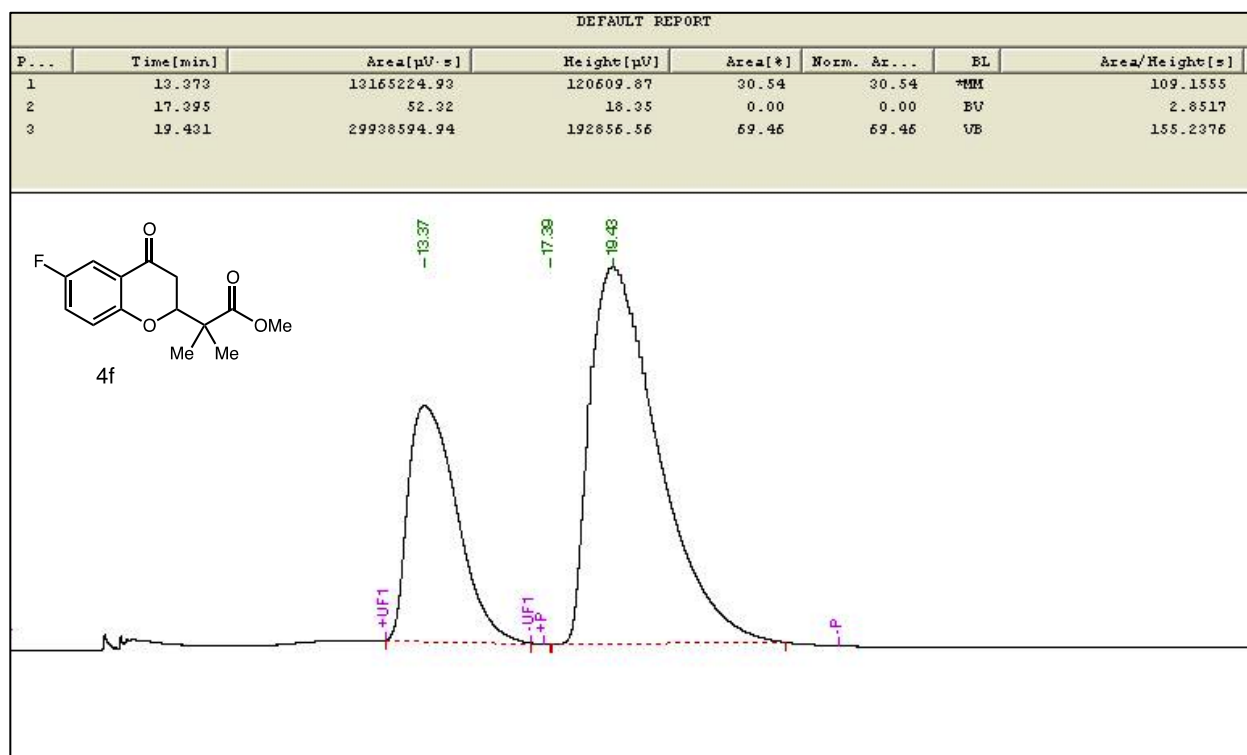
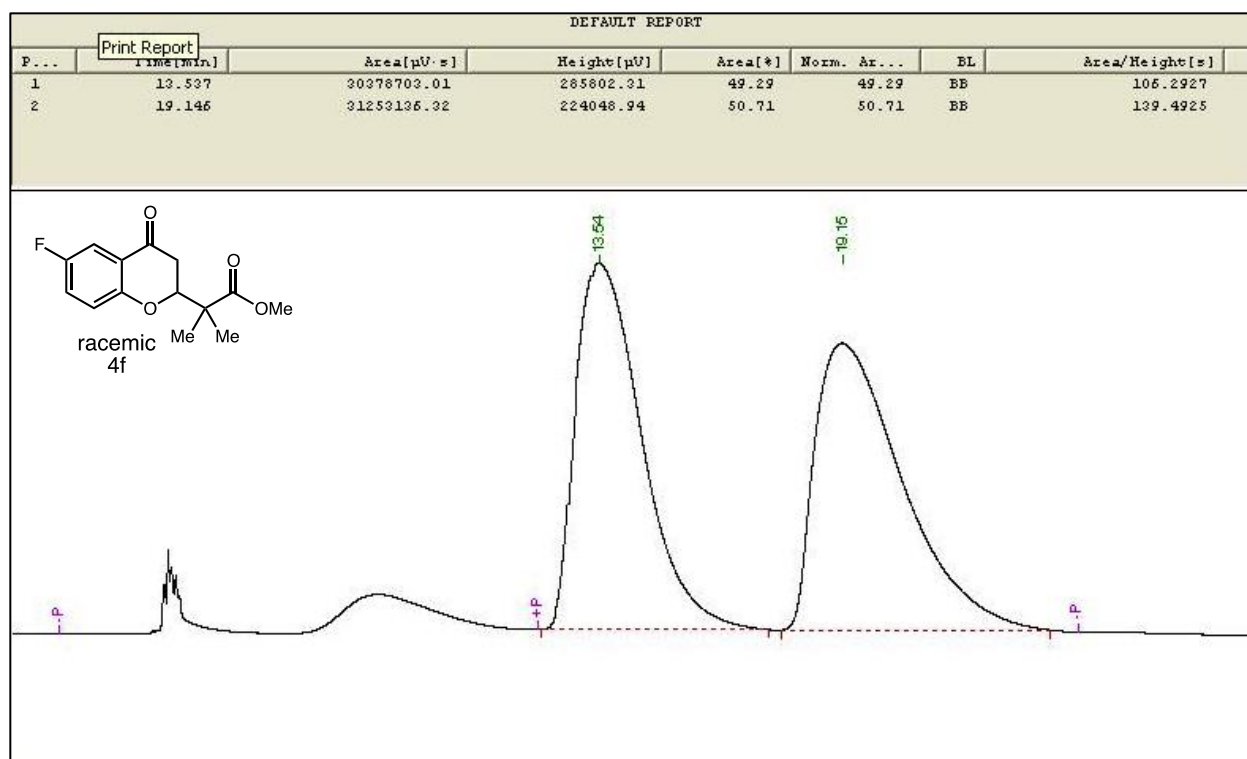


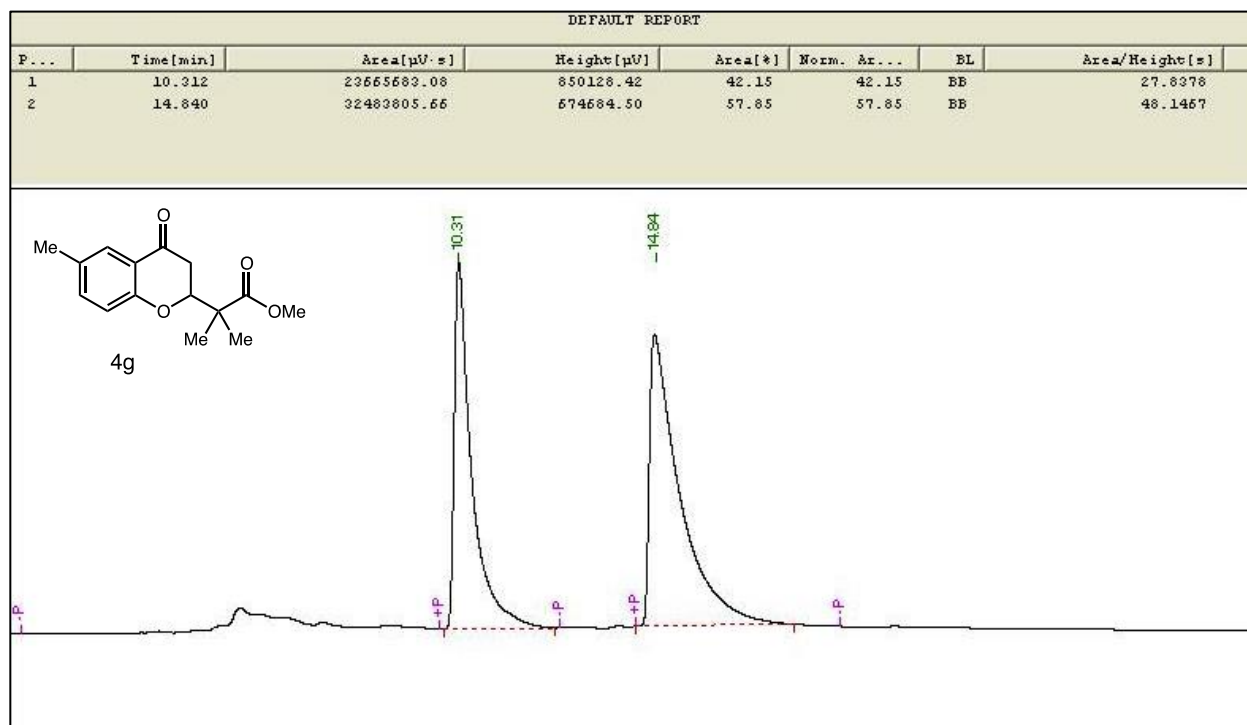
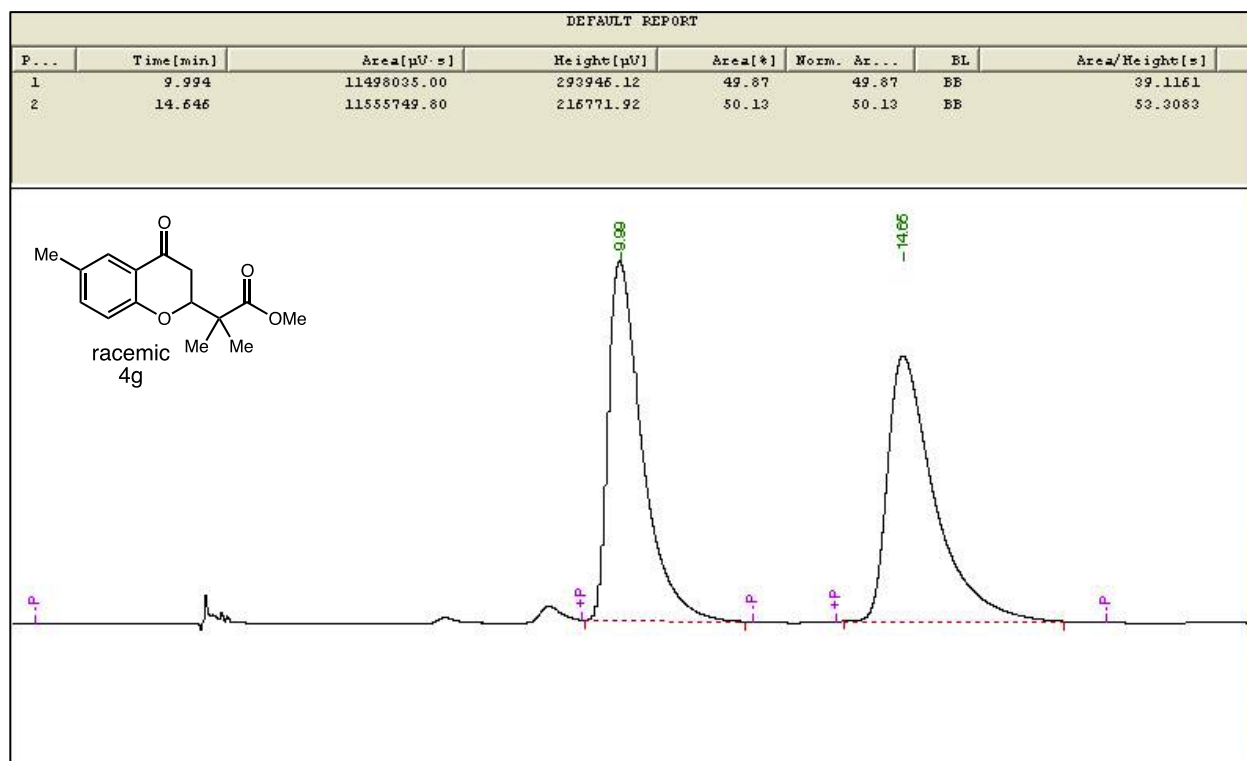


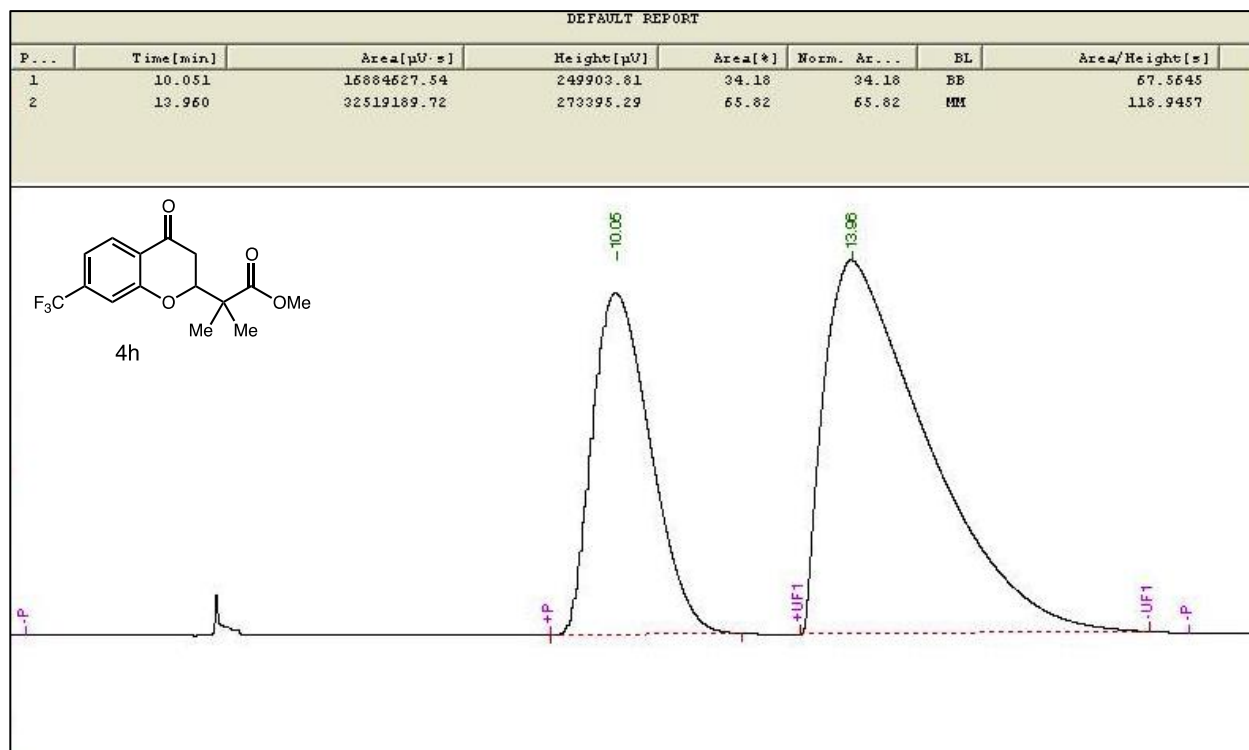
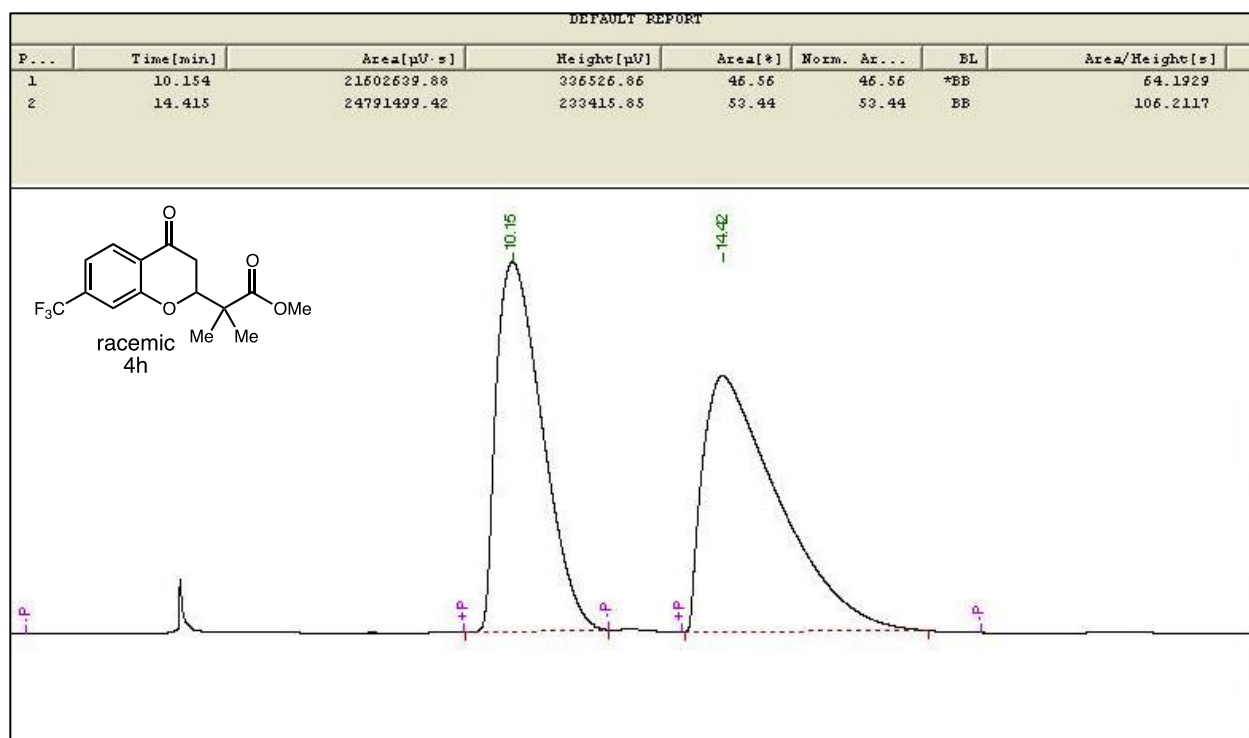




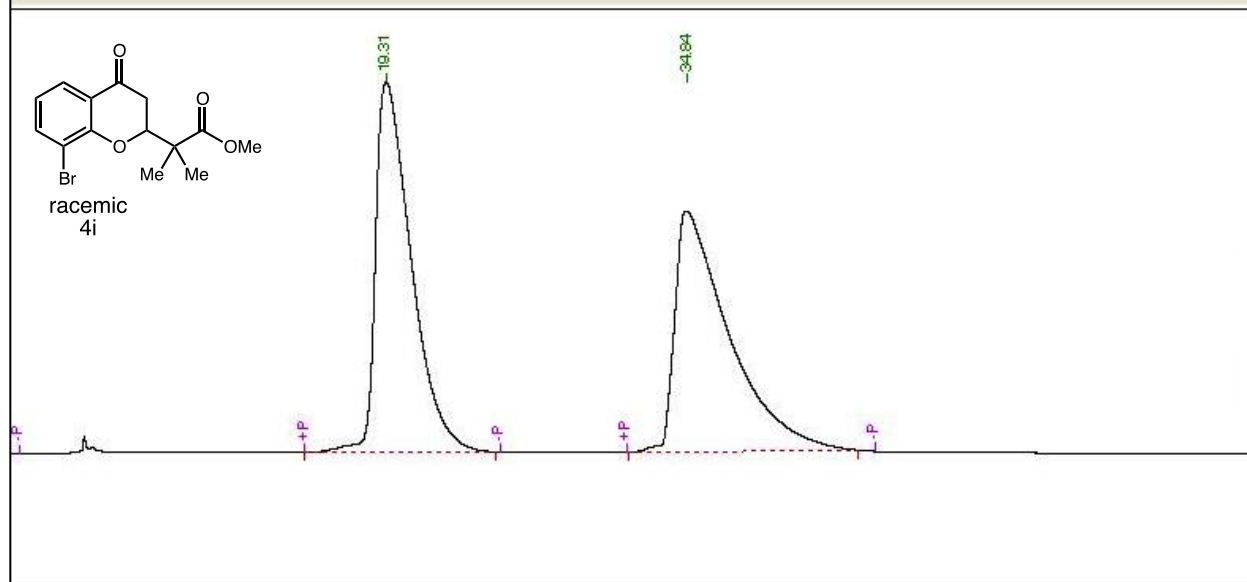




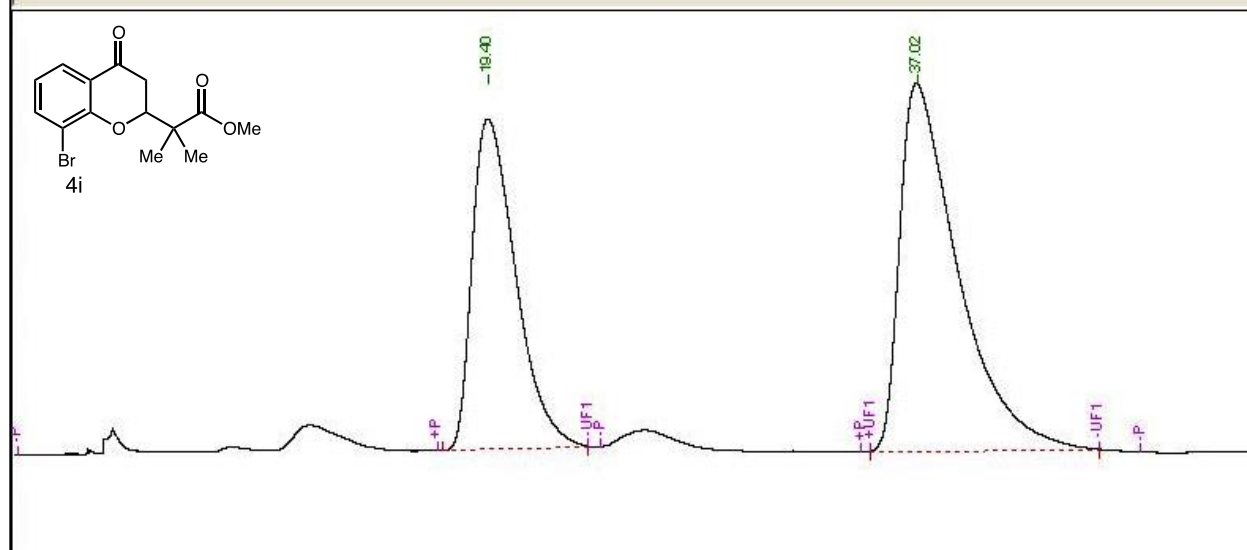




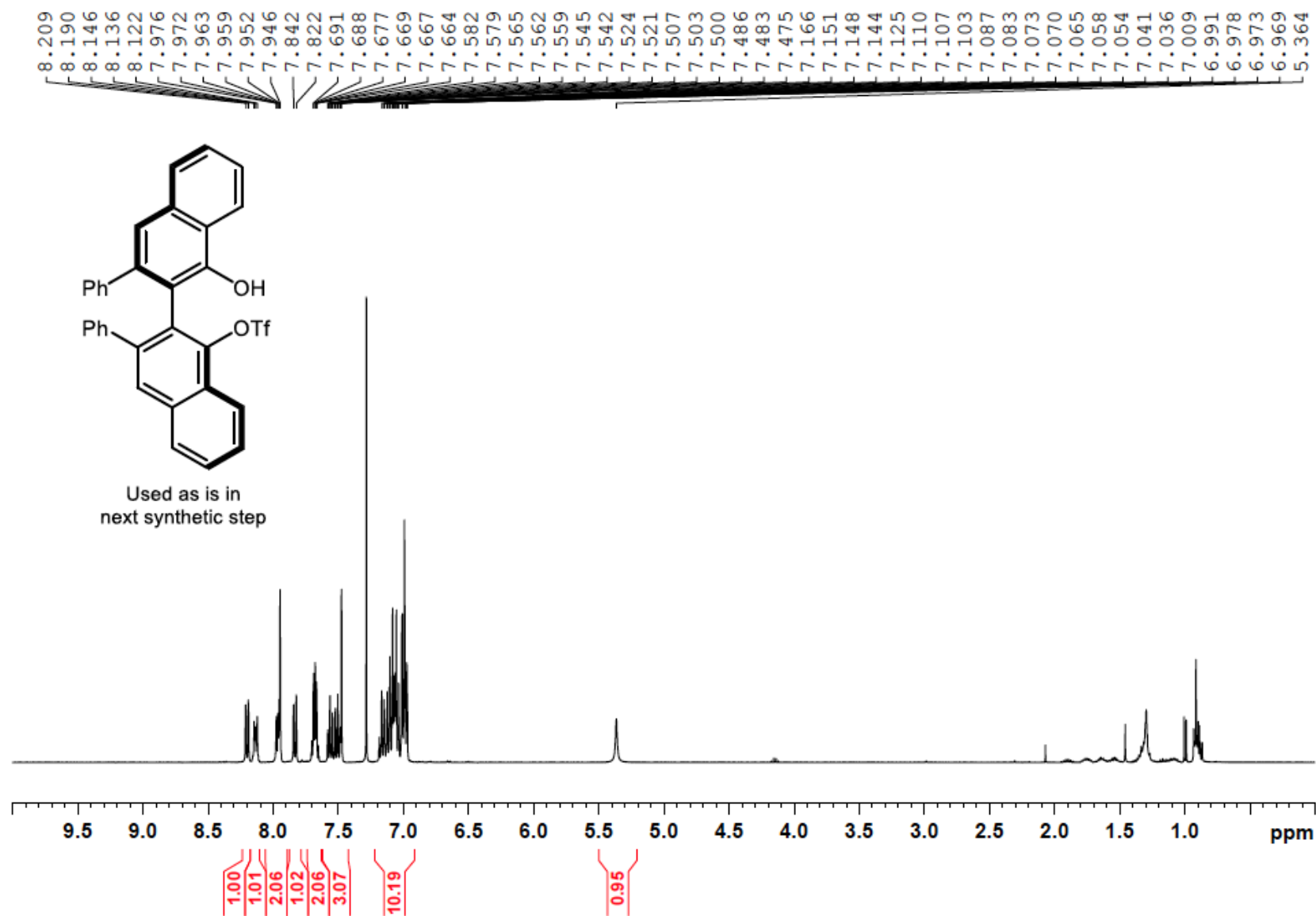
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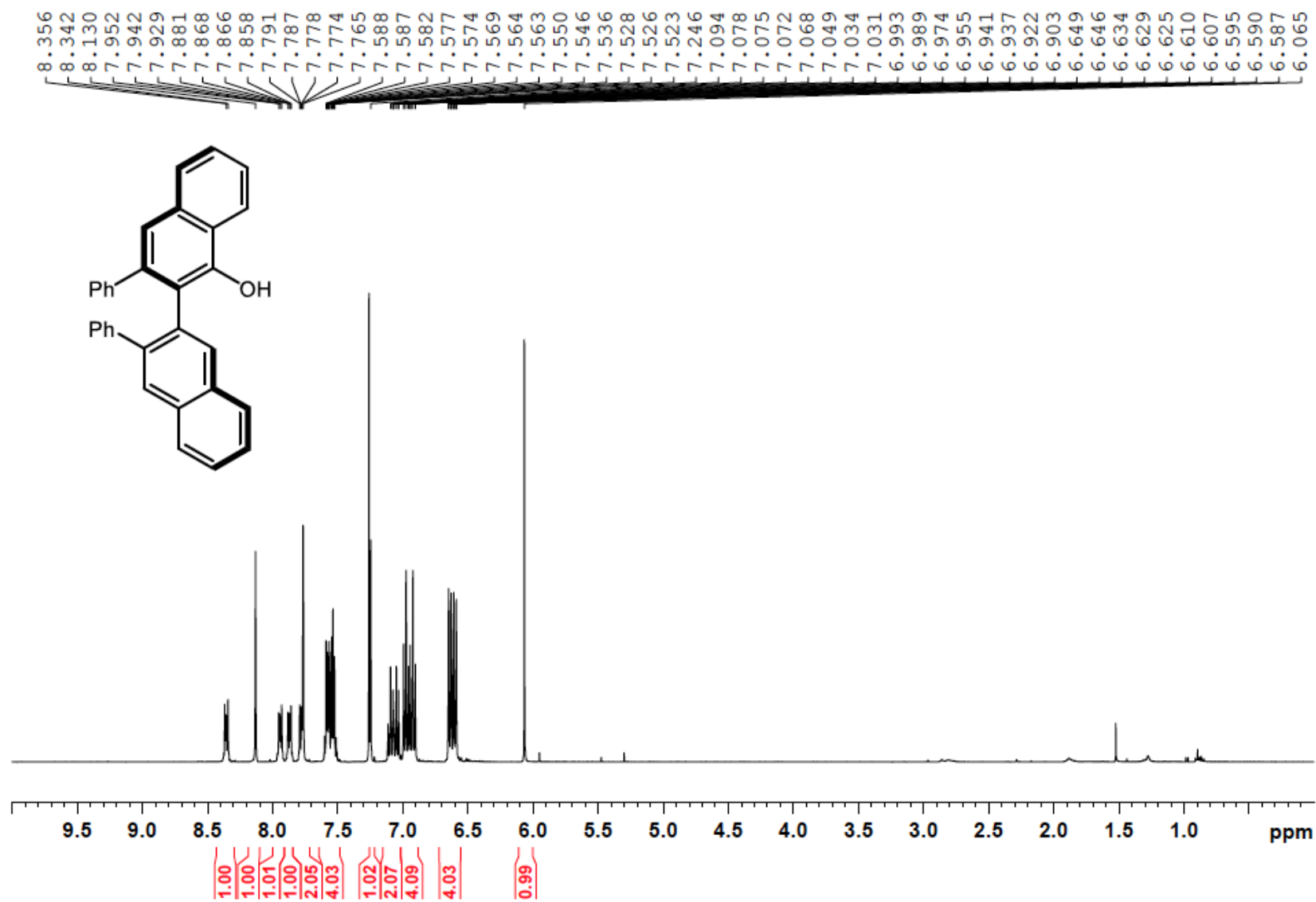


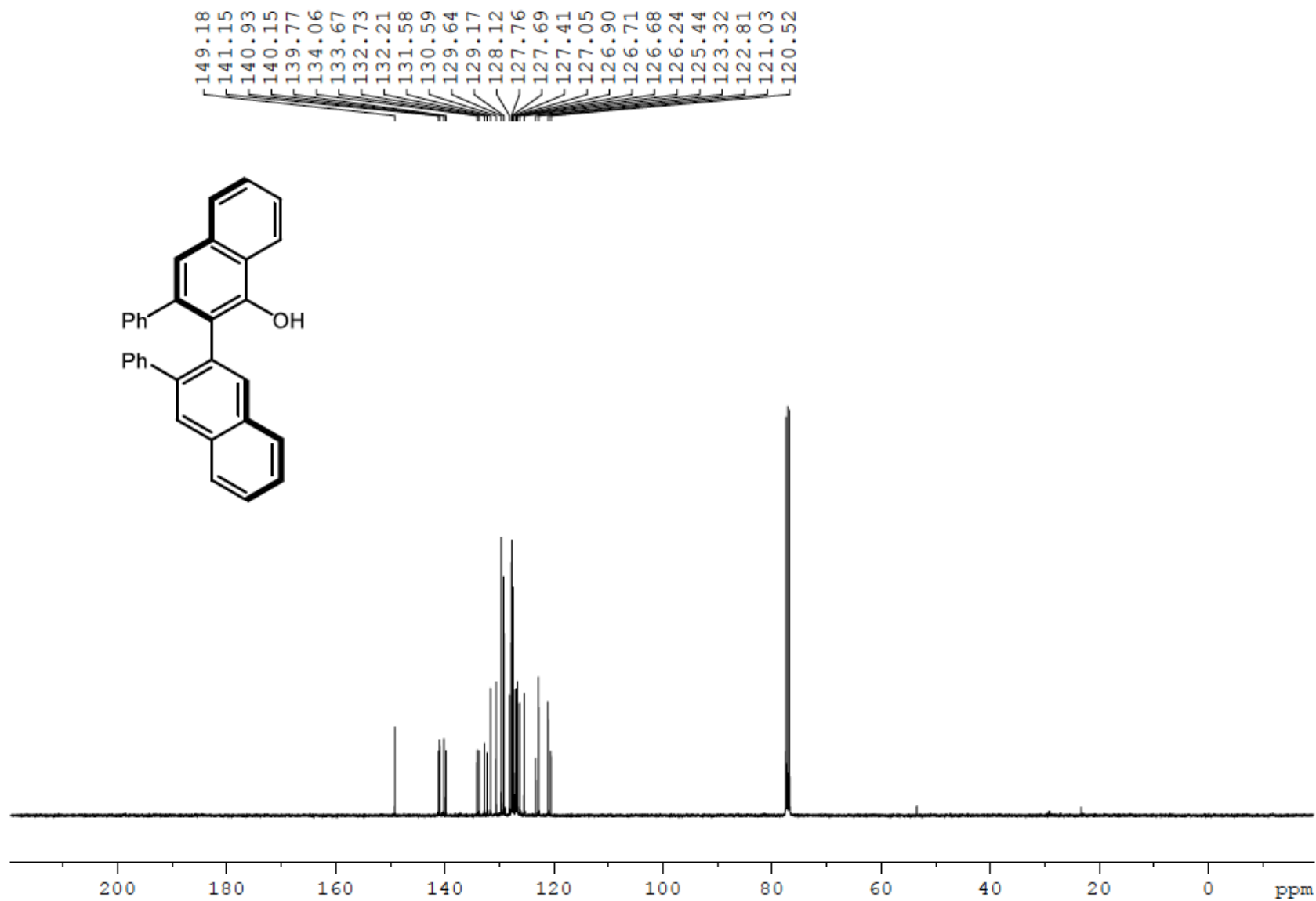
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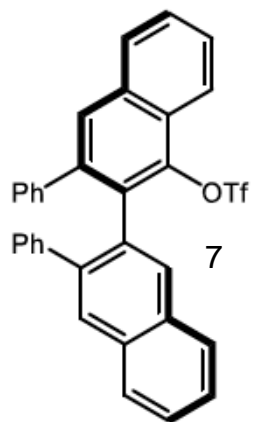


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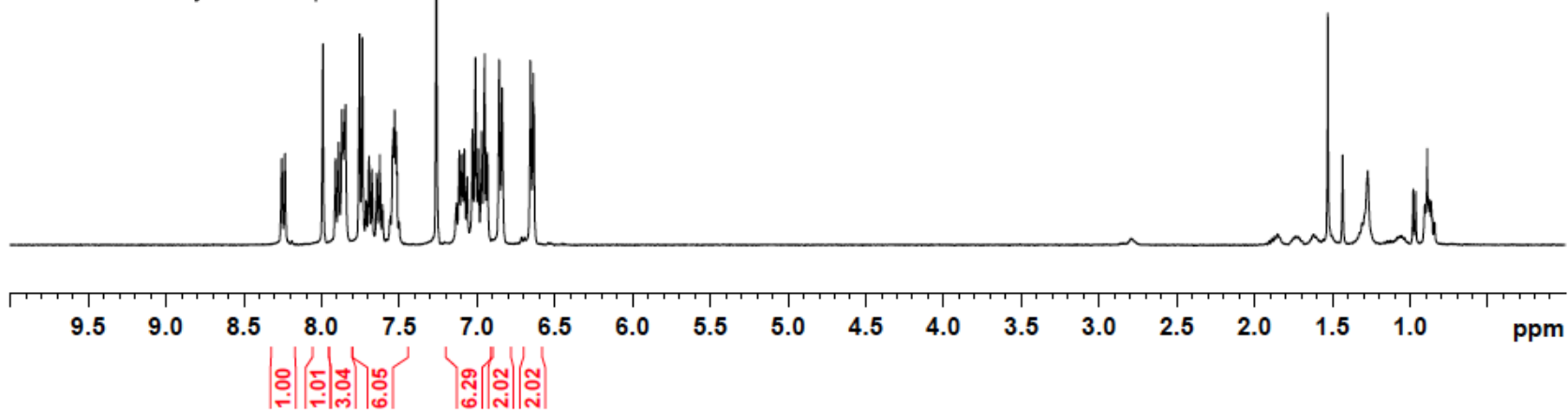


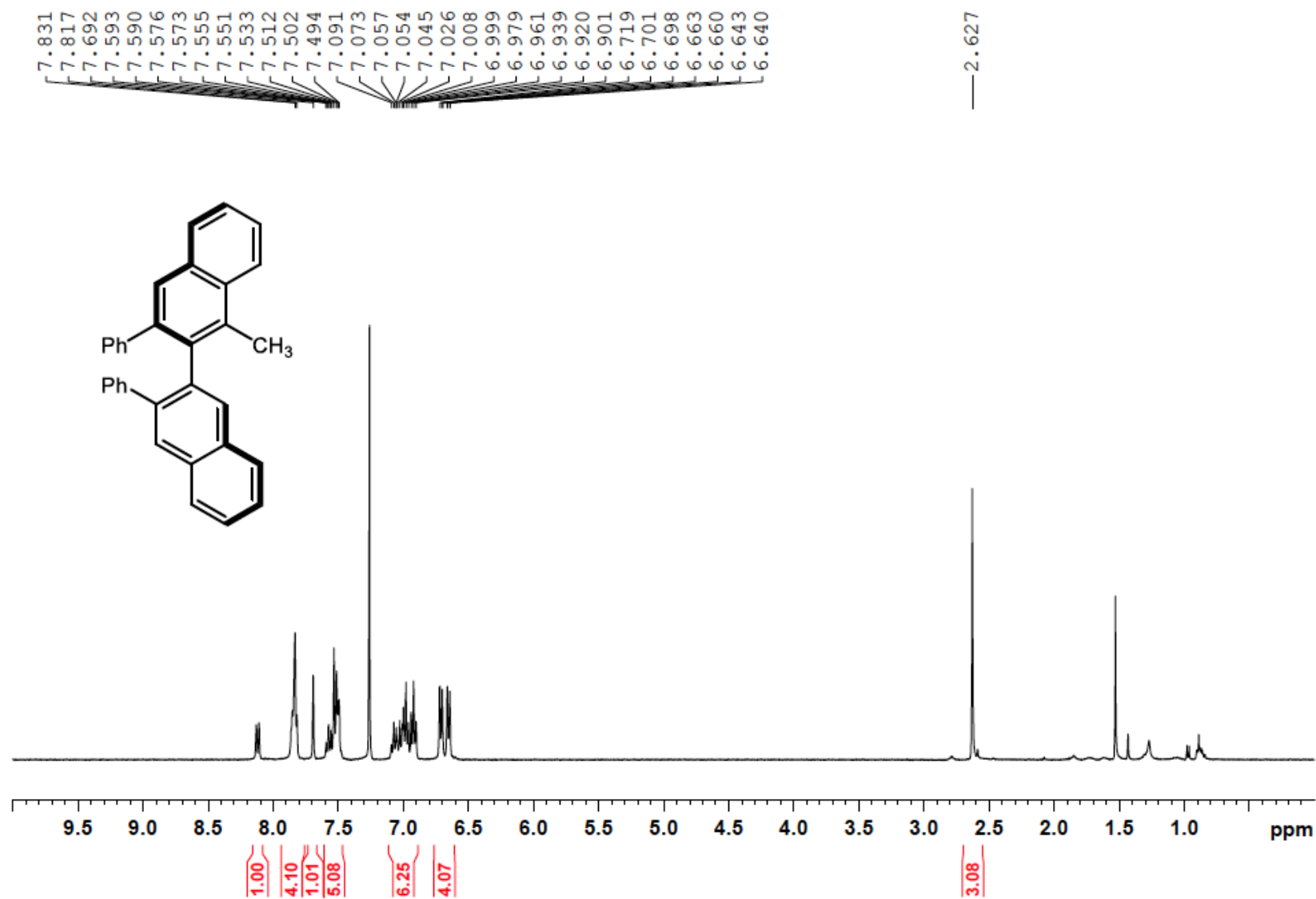


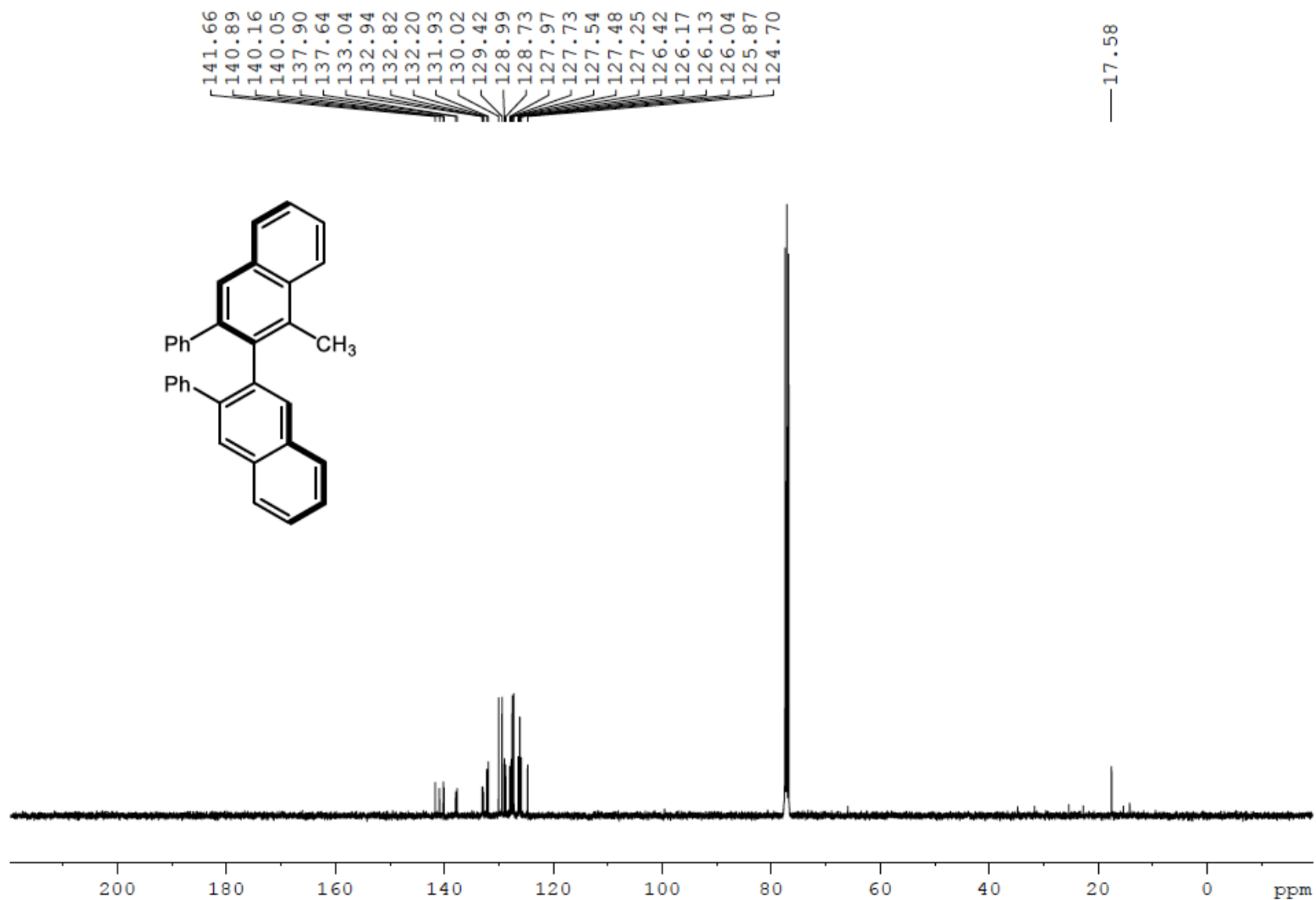


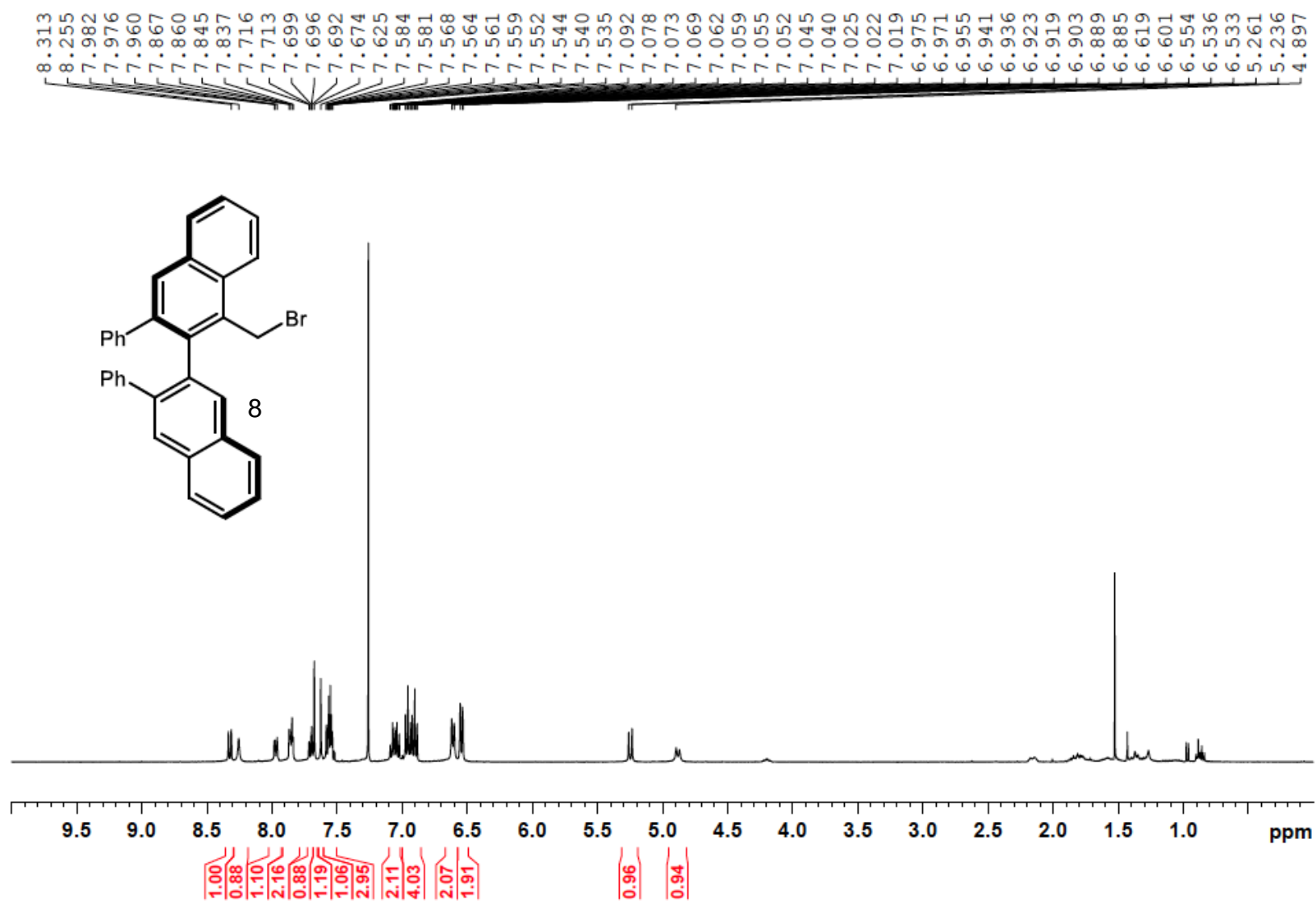


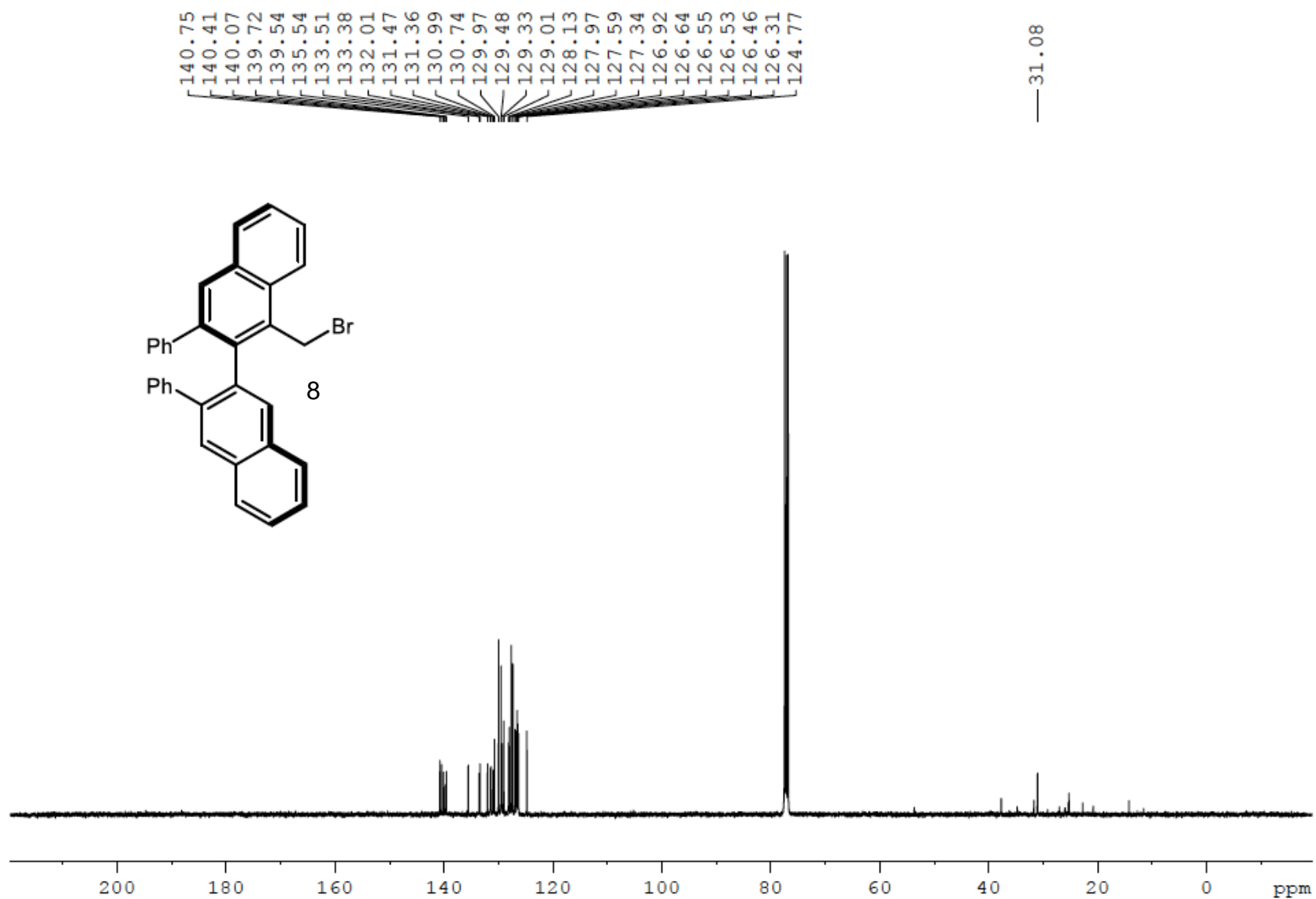
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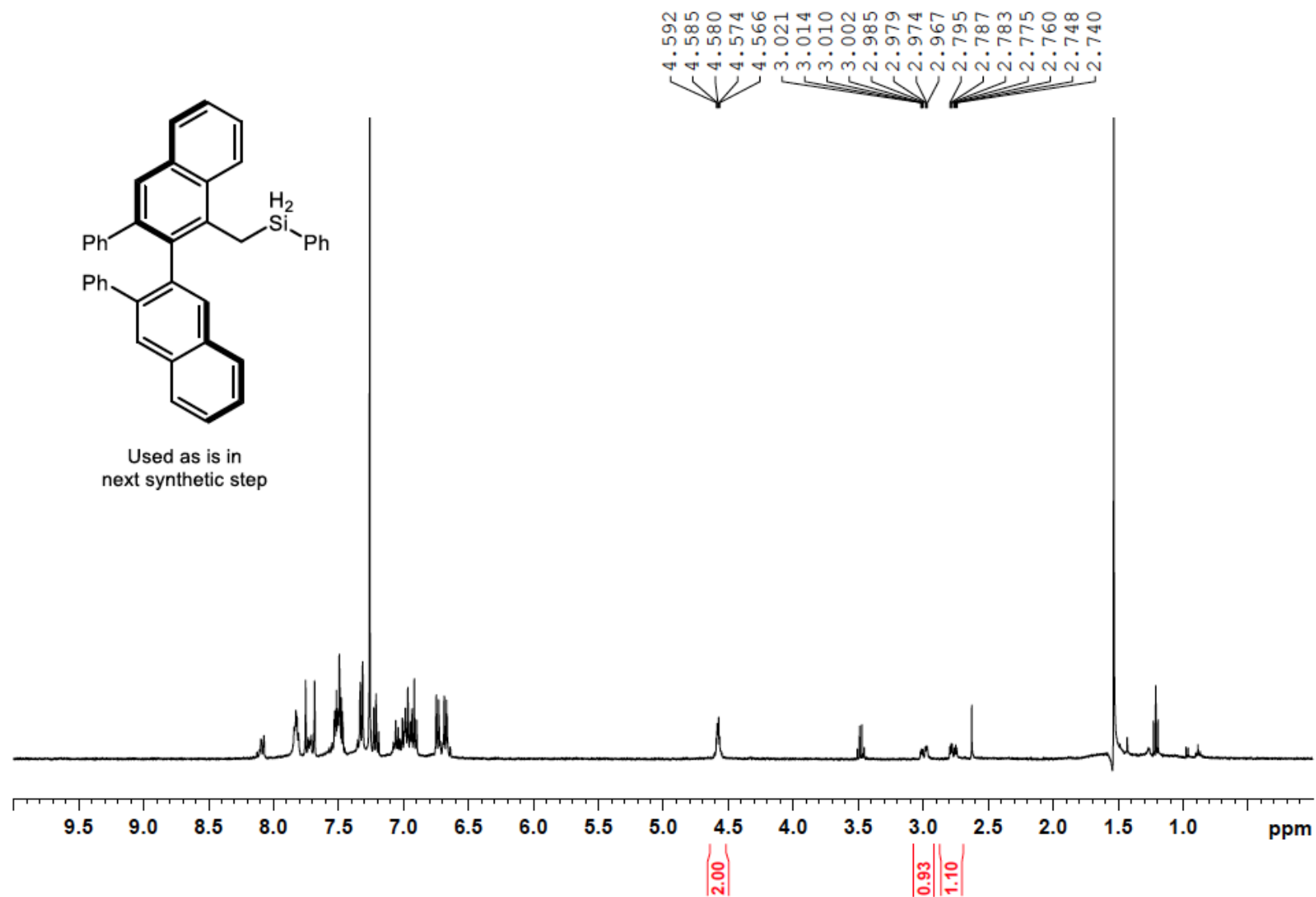


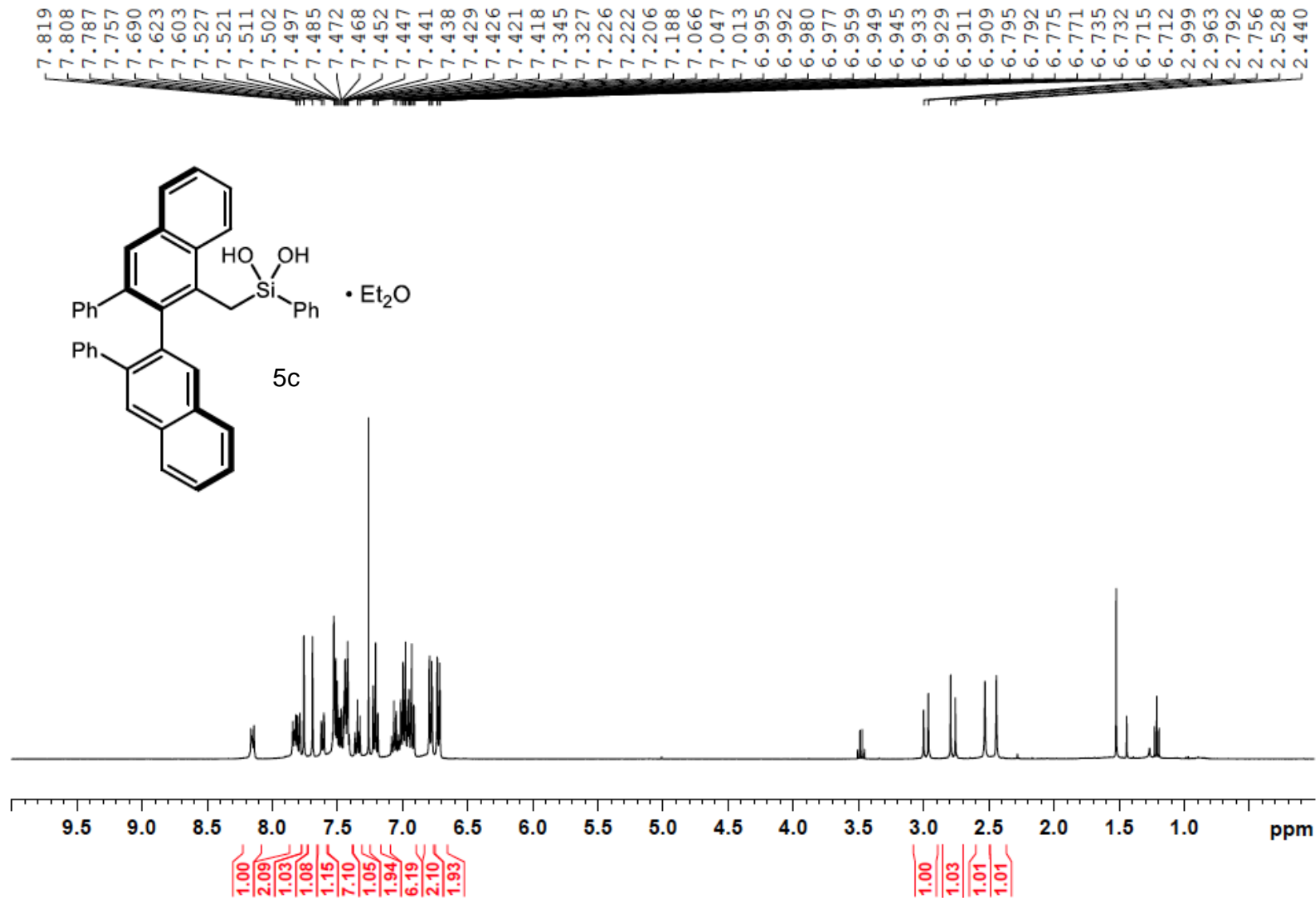


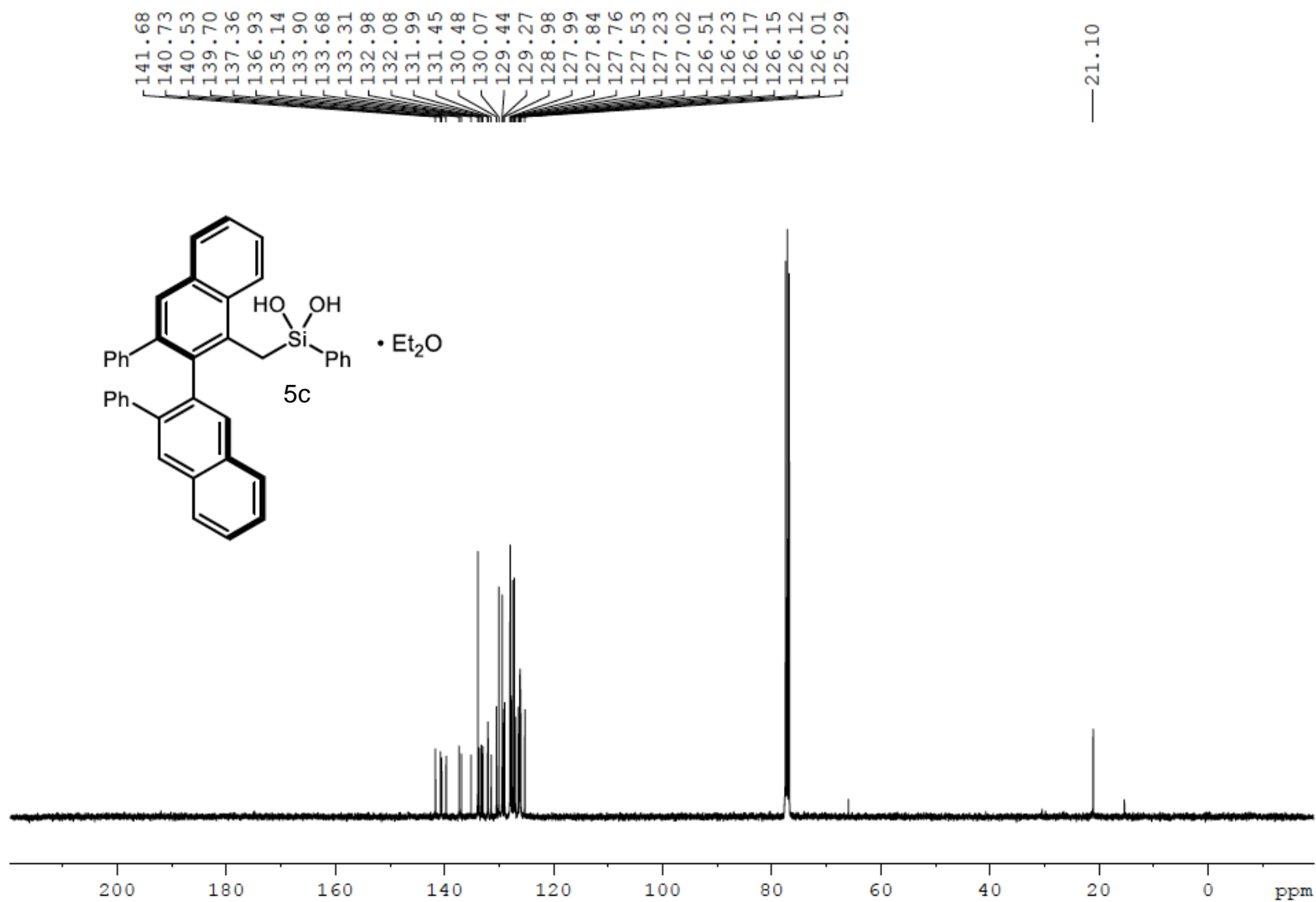


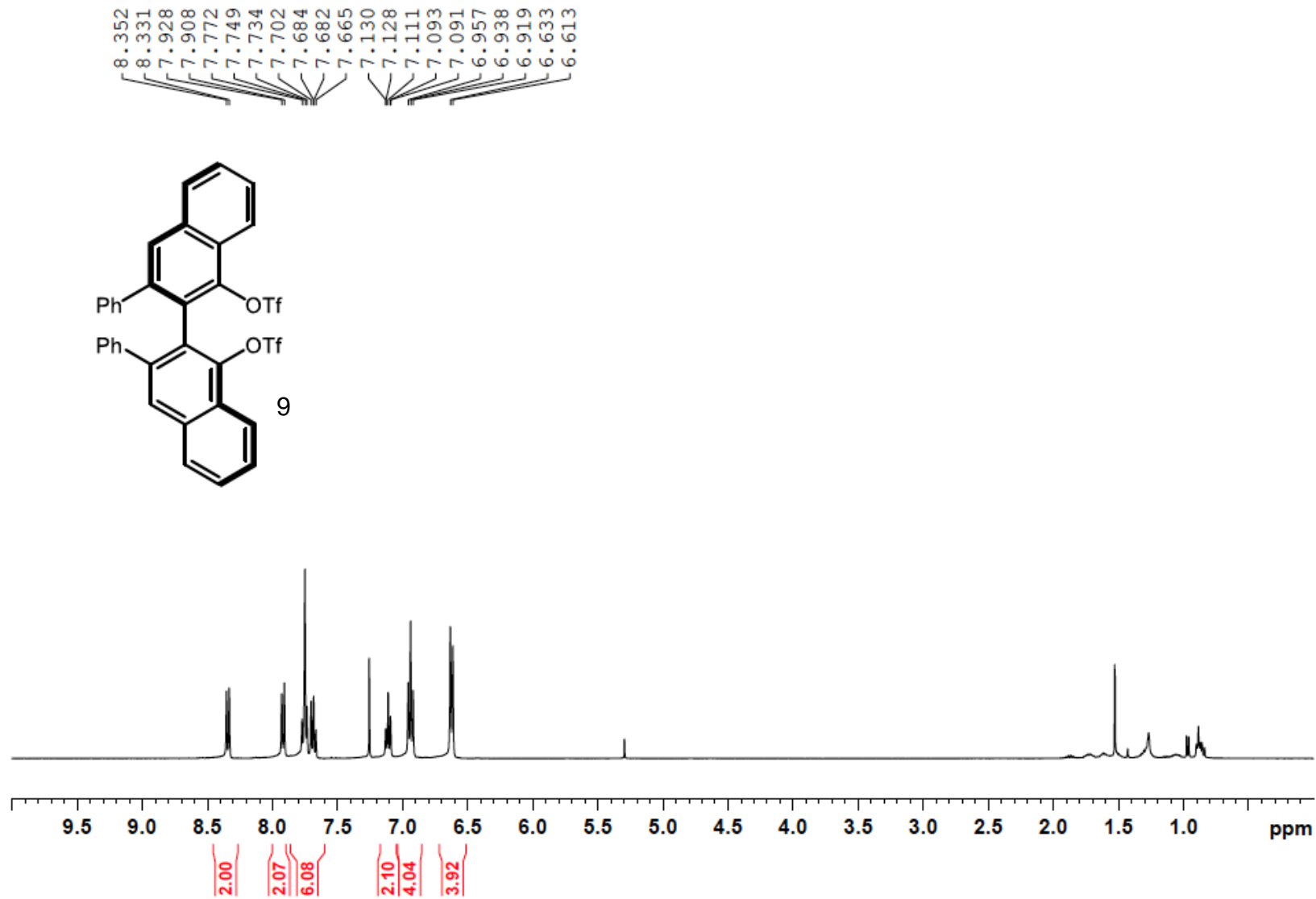


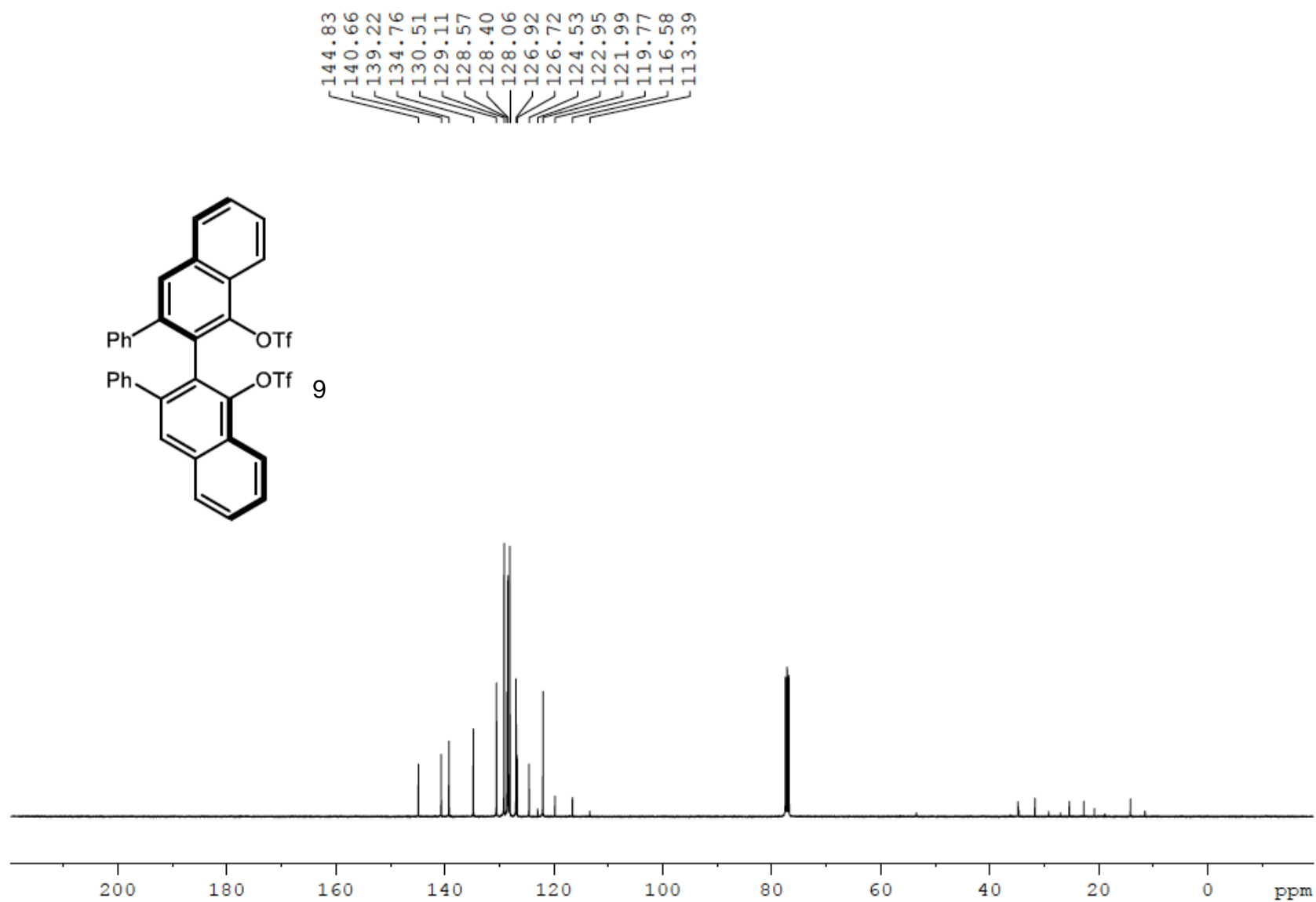


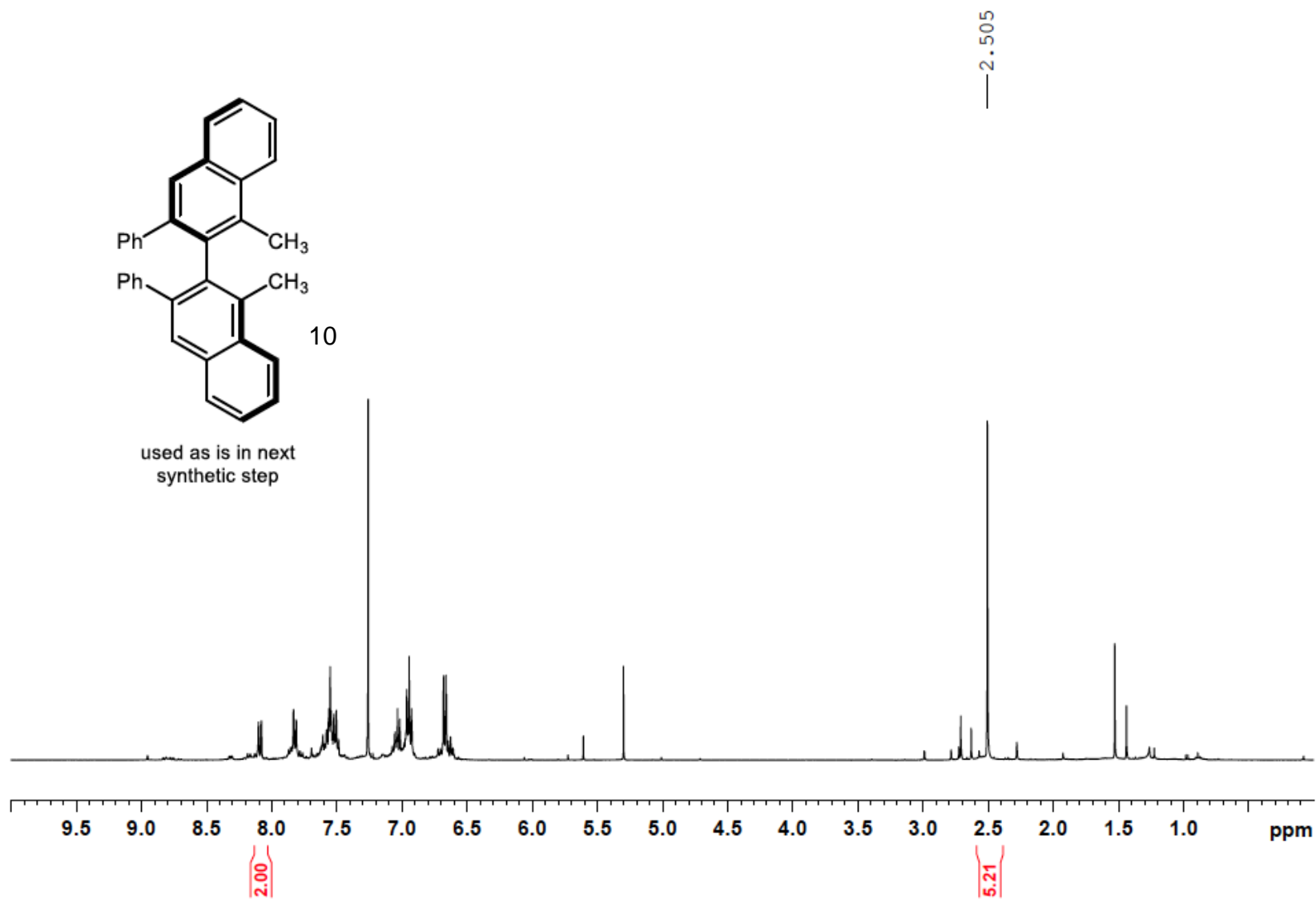


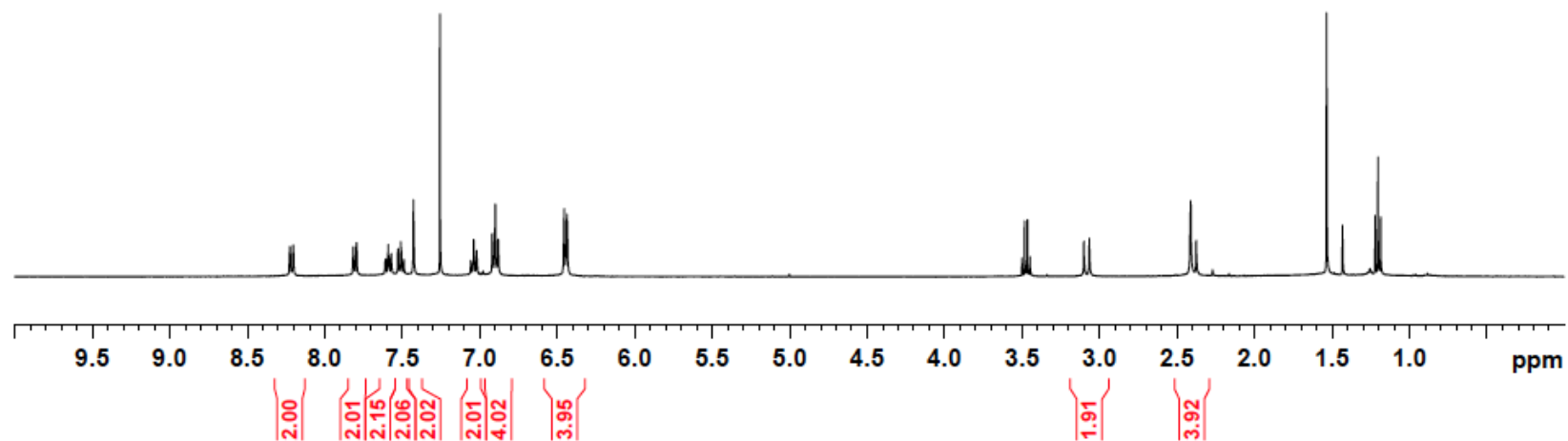
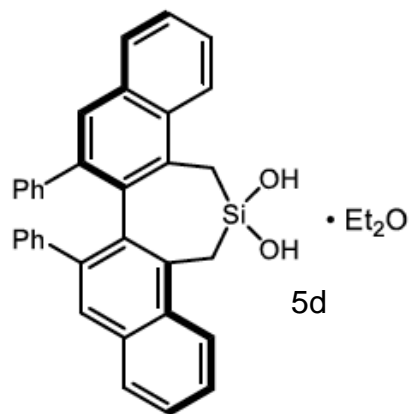
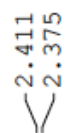
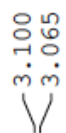
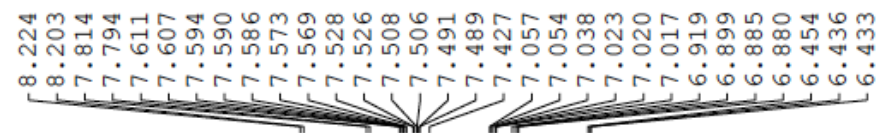


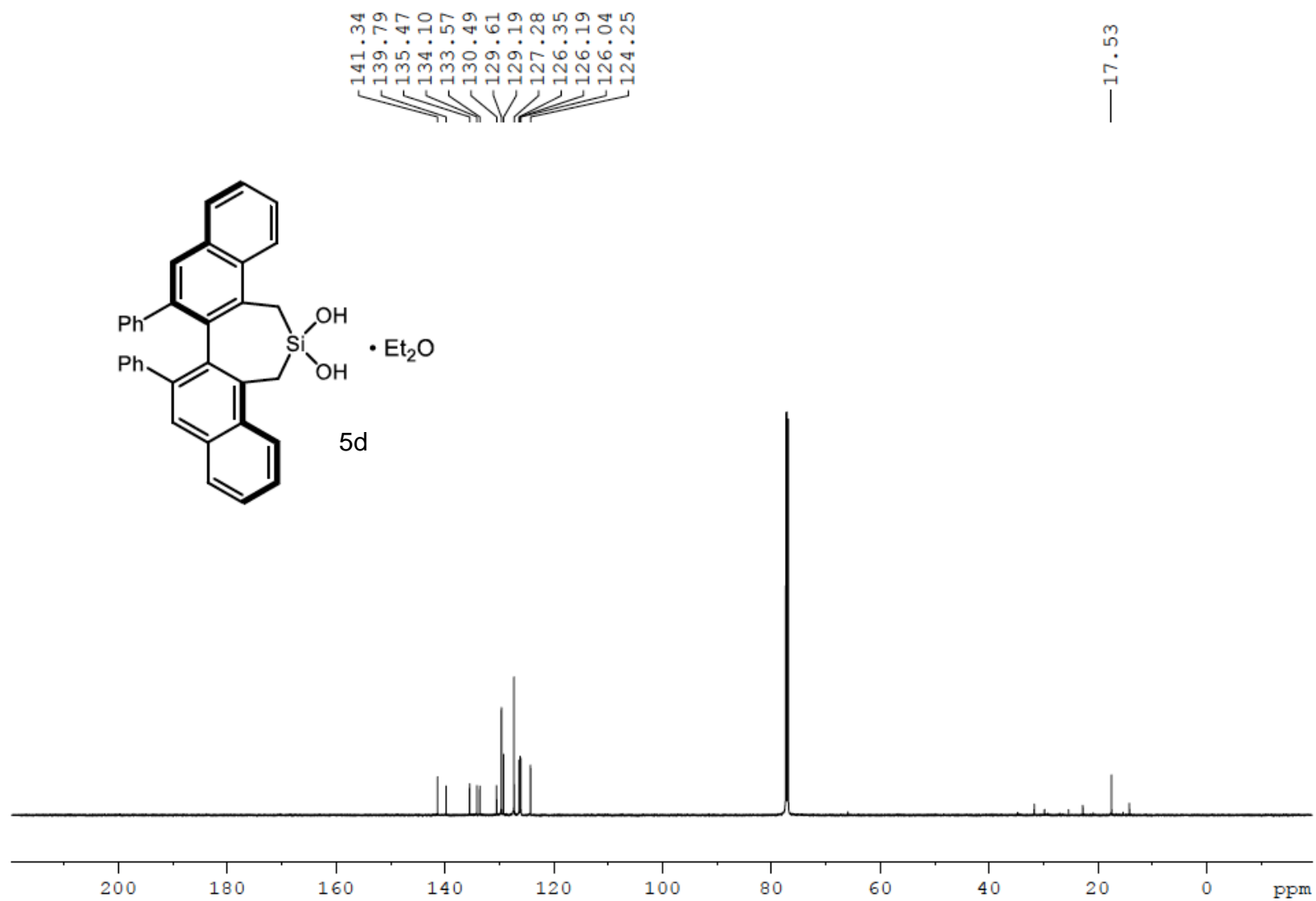


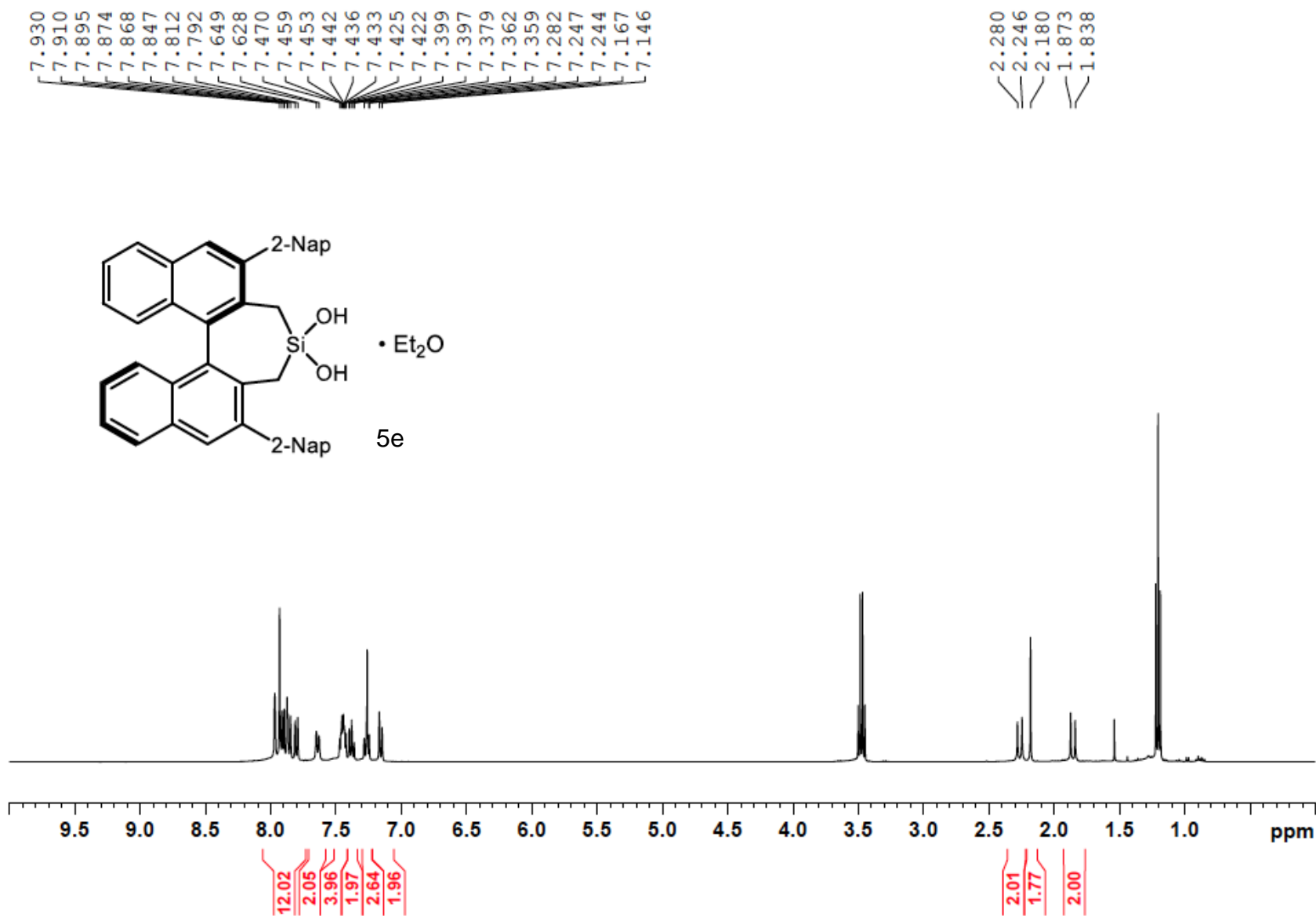


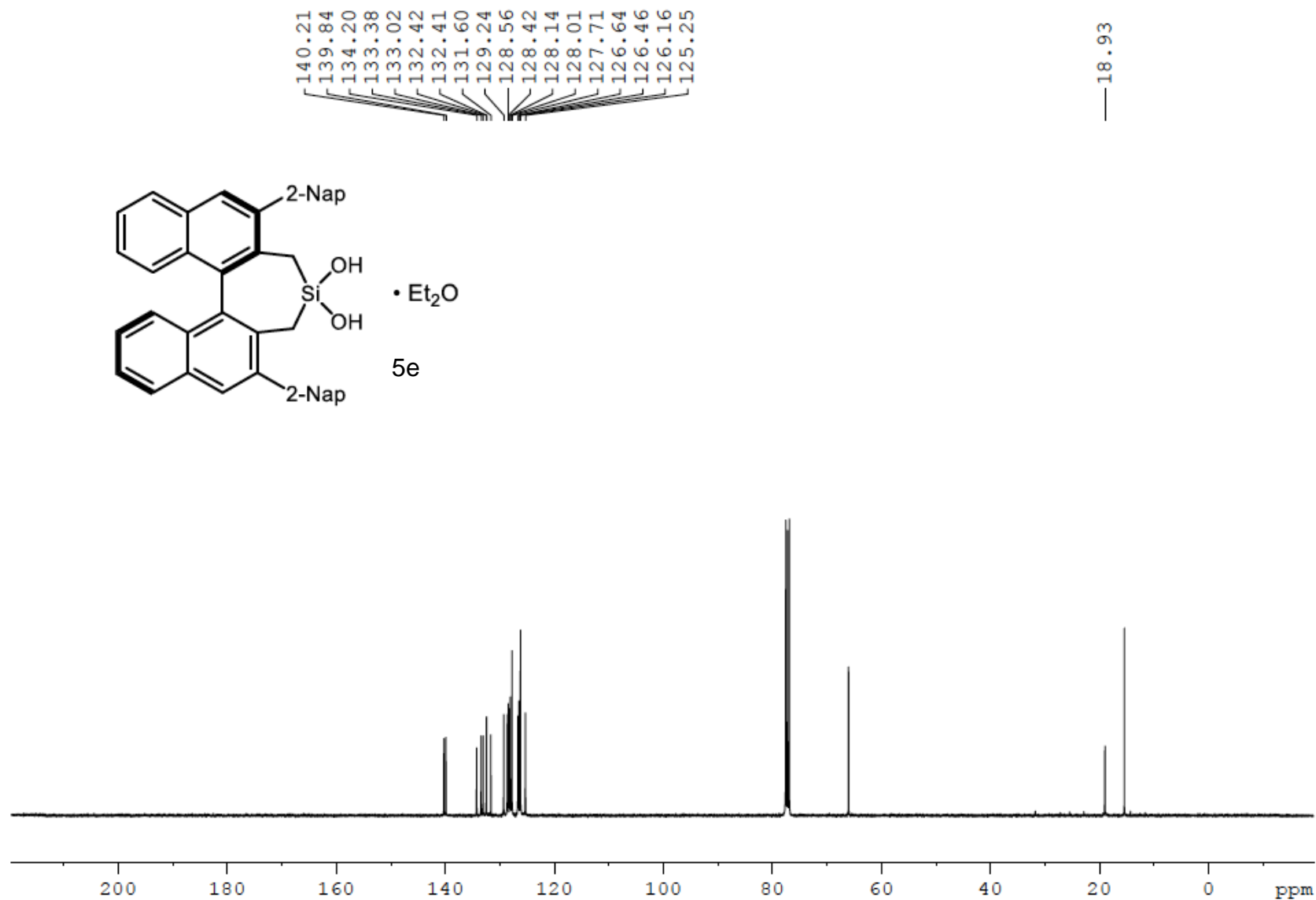


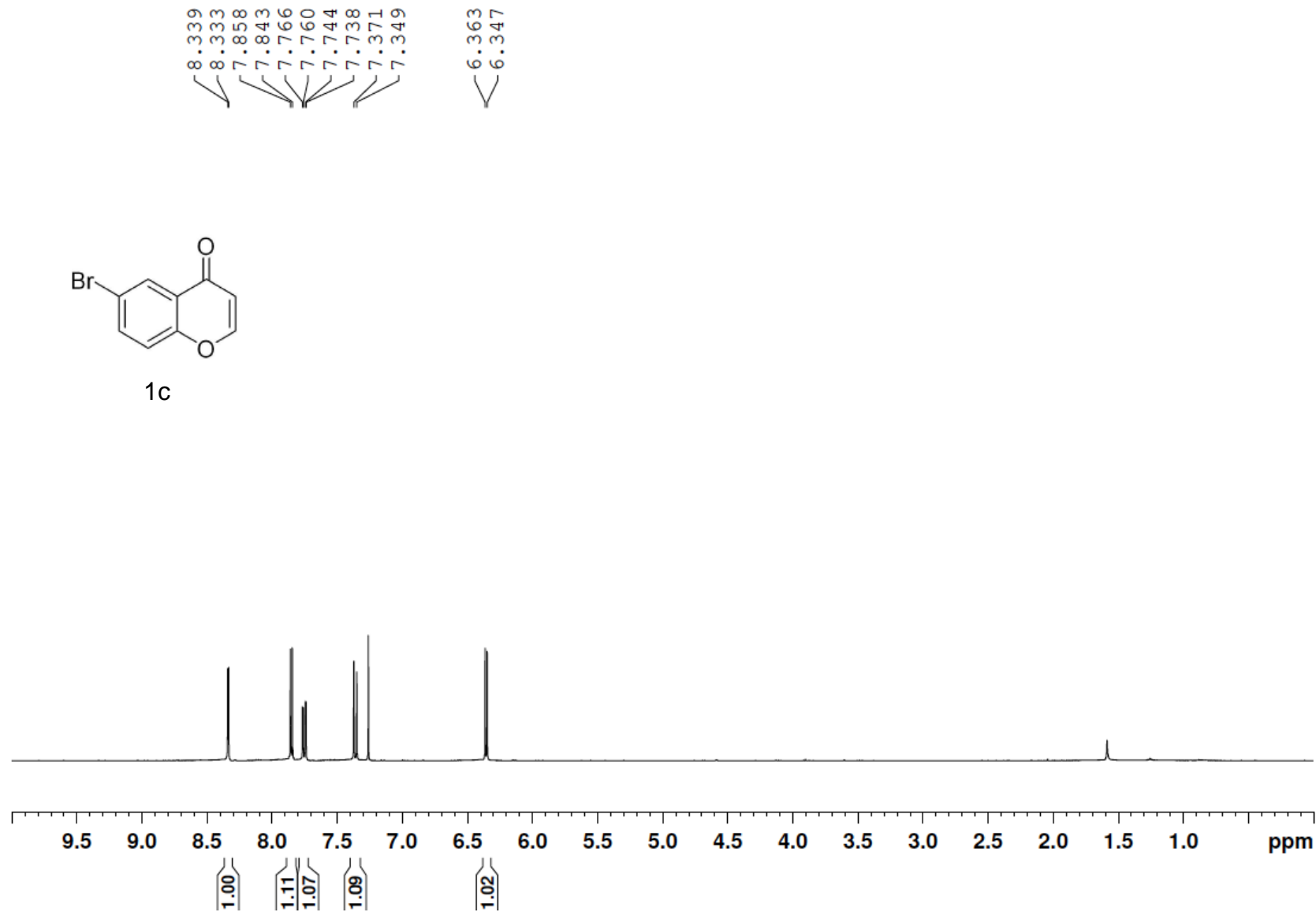


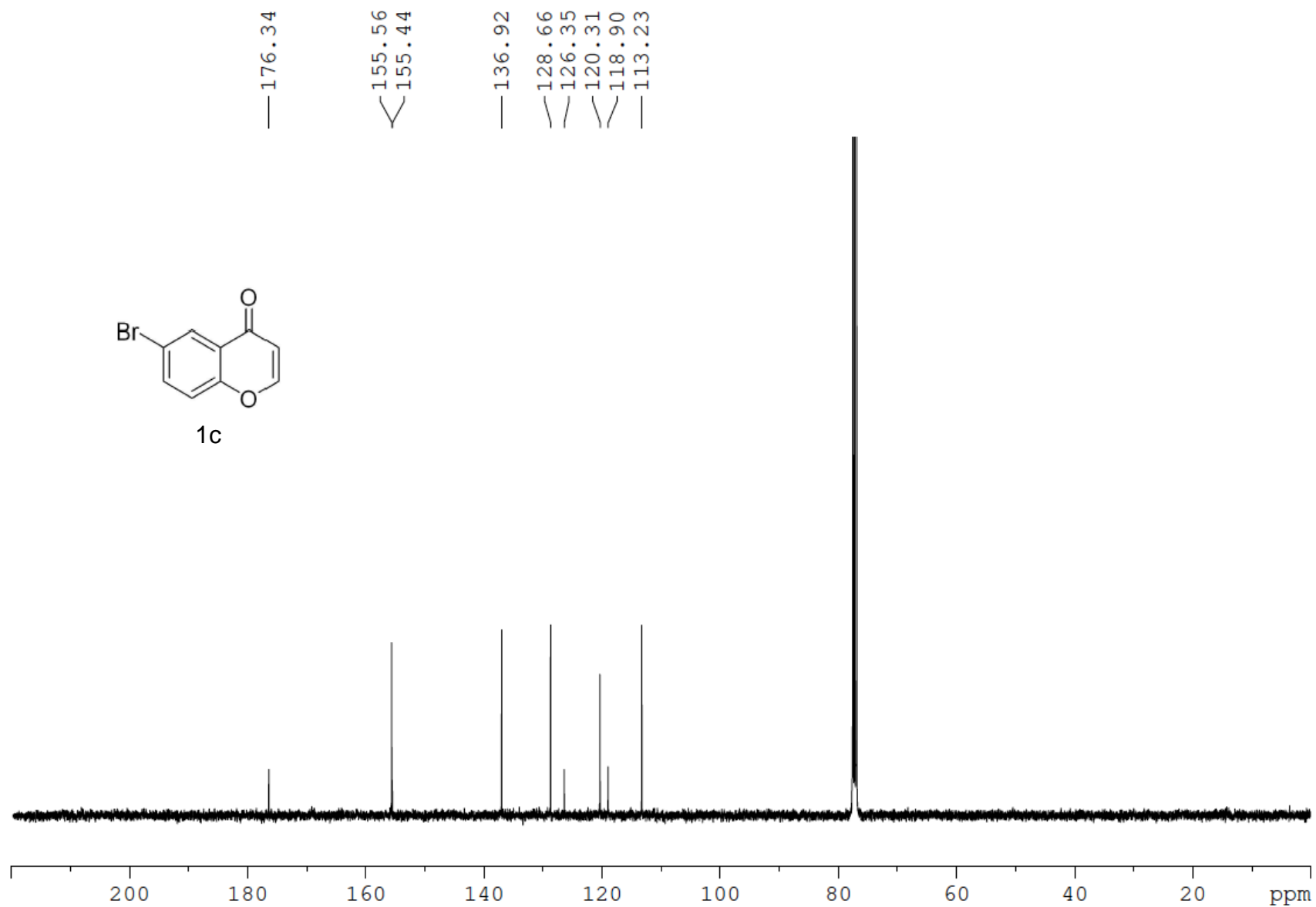


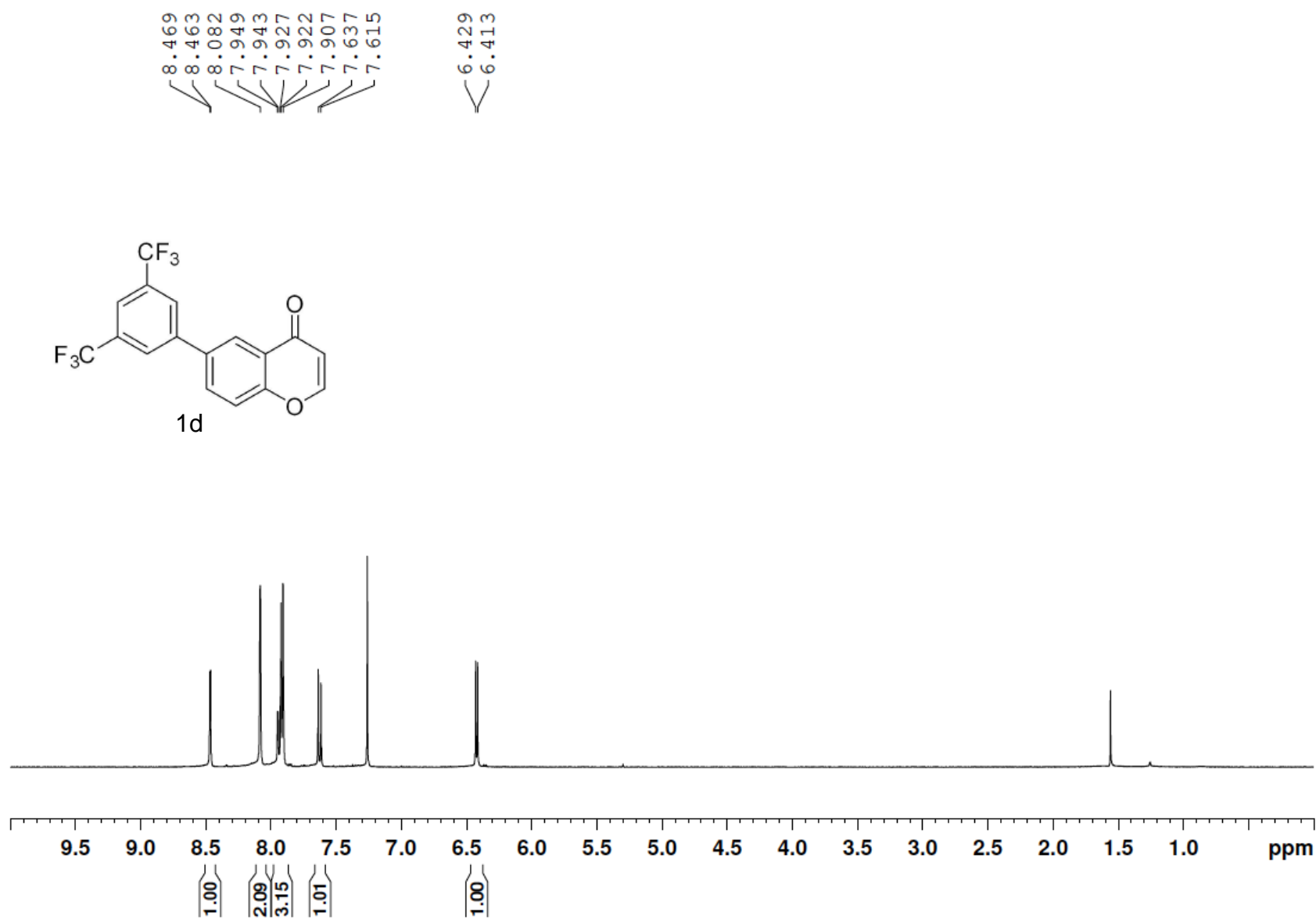


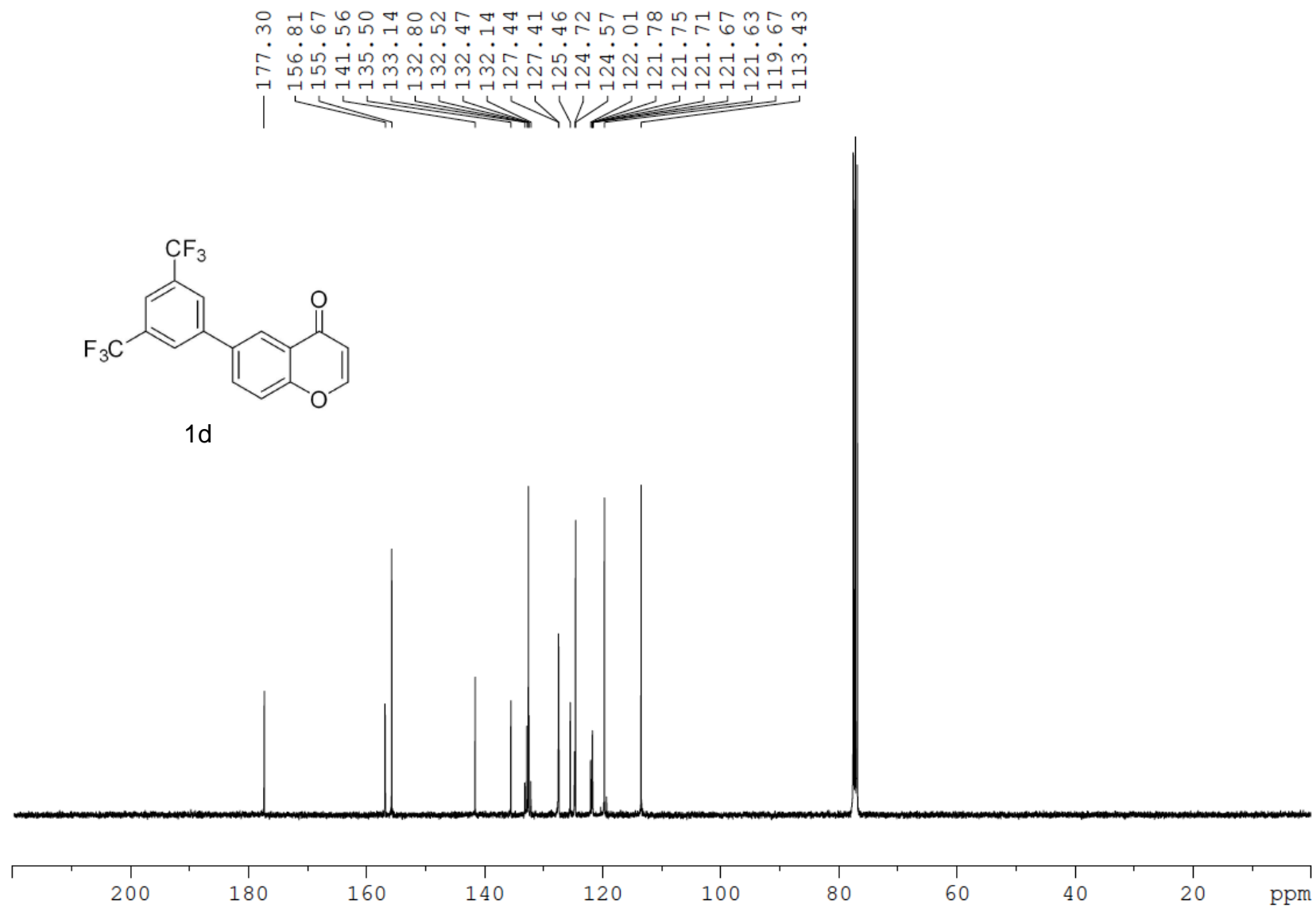


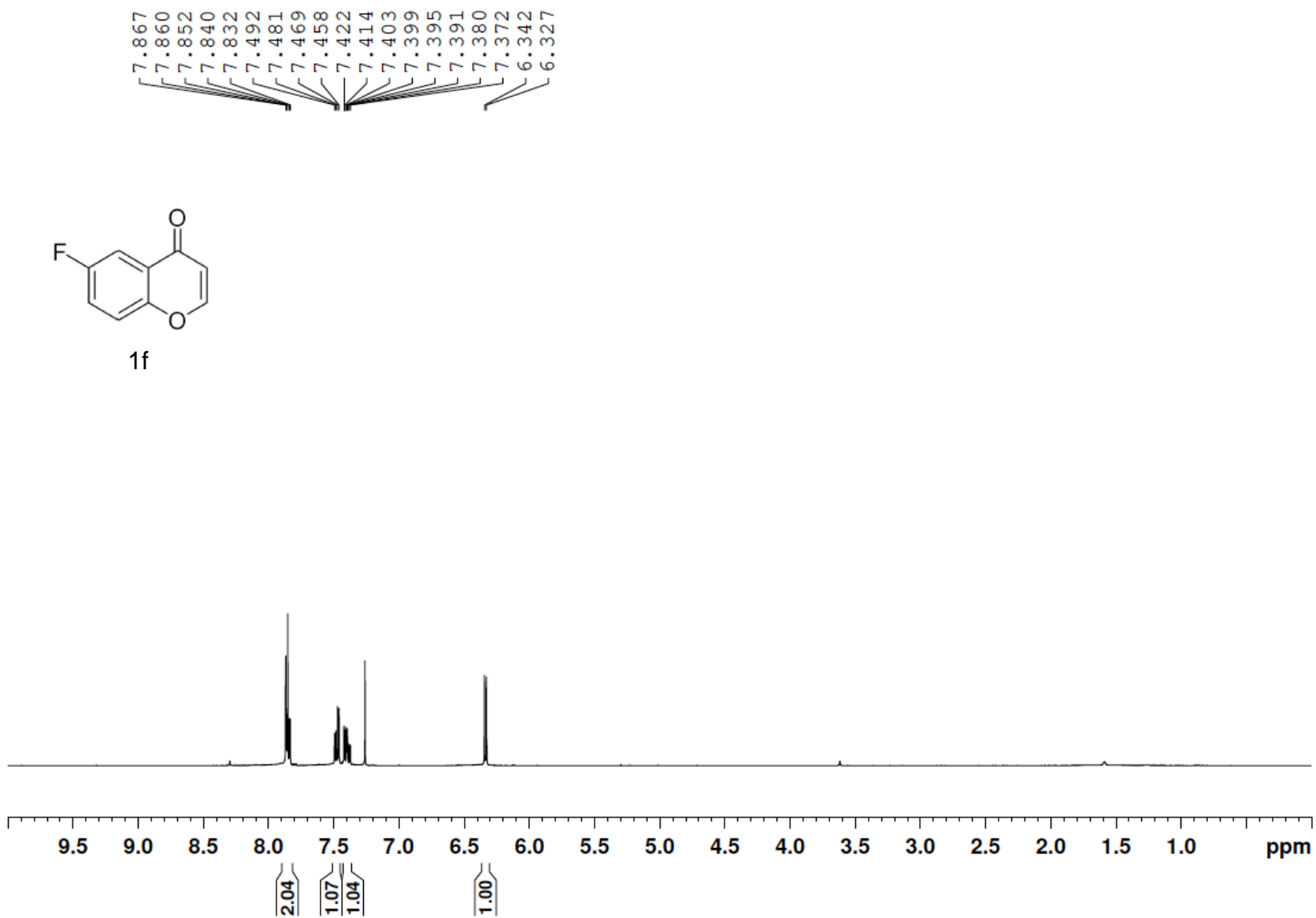


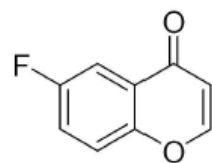












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