

Enantiospecific generation and trapping reactions of aryne atropisomers

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Synthetic procedures and characterization data

General information and Complementary optimization studies

Reactions were generally carried out under an argon atmosphere in oven-dried reaction vessels in anhydrous solvents. All reagents were weighed and handled in air at room temperature unless otherwise mentioned, and all commercially available reagents and solvents were used as received unless otherwise mentioned. Anhydrous methanol was obtained by refluxing over magnesium turning and then distilled. Anhydrous hexane was obtained by refluxing over the benzophenone sodium dianion (purple color) and then distilled. Anhydrous dichloromethane, diethyl ether, tetrahydrofuran and toluene were dried by filtration over solid dehydrating agents using a commercial solvent purification system. Anhydrous acetonitrile and dimethylformamide were obtained directly from commercial sources. The reactions were monitored by TLC visualized by UV (254 nm) and/or with an ethanolic solution of *p*-anisaldehyde and sulfuric acid. Purifications were routinely performed using flash chromatography with 40-63 μm silica gel generally eluted with a mixture ethyl acetate/petroleum ether (bp 40–60°C) or ethyl acetate/cyclohexane. NMR data were generally recorded in deuterated chloroform using as internal standards the residual chloroform signal for ^1H NMR ($\delta = 7.26$ ppm) and the deuterated solvent signal for ^{13}C NMR ($\delta = 77.16$ ppm). Chemical shifts (δ) are in ppm, coupling constants (J) are in Hertz (Hz) and the classical abbreviations are used to describe the signal multiplicities. Melting points were measured with an air-flow apparatus. Specific rotations were recorded at 25 °C and 589 nm. The ratios of enantiomers were determined by HPLC analyses at 25 °C using chiral stationary phases at the ChirBase platform (see <http://chirbase.u-3mrs.fr>). High-resolution mass spectra were recorded in triplicate at the Spectropole (<http://fr-chimie.univ-amu.fr/spectropole/>). Circular dichroism spectroscopy was performed at the Spectropole (<http://fr-chimie.univ-amu.fr/spectropole/>).

The so-called Soós's quinine thiourea catalyst was prepared according to the procedure described by Soós,¹ and the known racemic and enantio-enriched bromophenol (*aS*)-**3a** was prepared as described by Wang and co-workers, using 15 mol% of the Soós catalyst, with similar yields and enantioselectivity.²

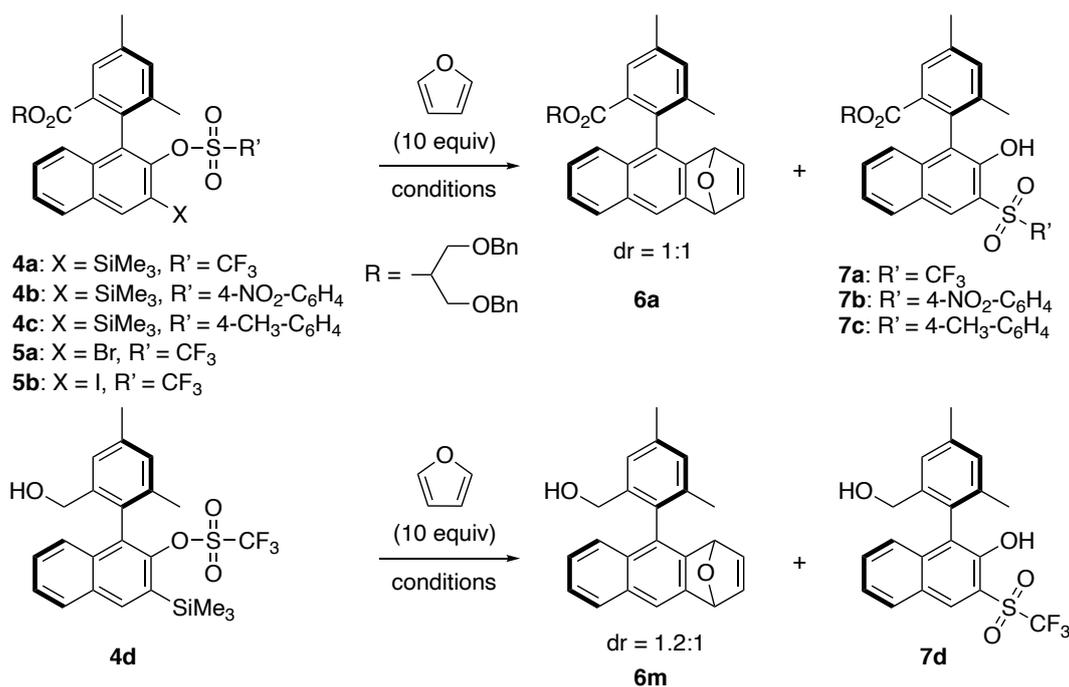
All molecules in the main text and this document are represented with their correct and verified absolute configuration.

A selection of results from the optimization study is presented in Table S1.

(1) Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. Highly Enantioselective Conjugate Addition of Nitromethane to Chalcones Using Bifunctional Cinchona Organocatalyst. *Org. Lett.* **2005**, *7*, 1967–1969.

(2) Yu, C.; Huang, H.; Li, X.; Zhang, Y.; Wang, W. Dynamic Kinetic Resolution of Biaryl Lactones via a Chiral Bifunctional Amine Thiourea-Catalyzed Highly Atropo- enantioselective Transesterification. *J. Am. Chem. Soc.* **2016**, *138*, 6956–6959.

Table S1. Highlights of the optimization study.

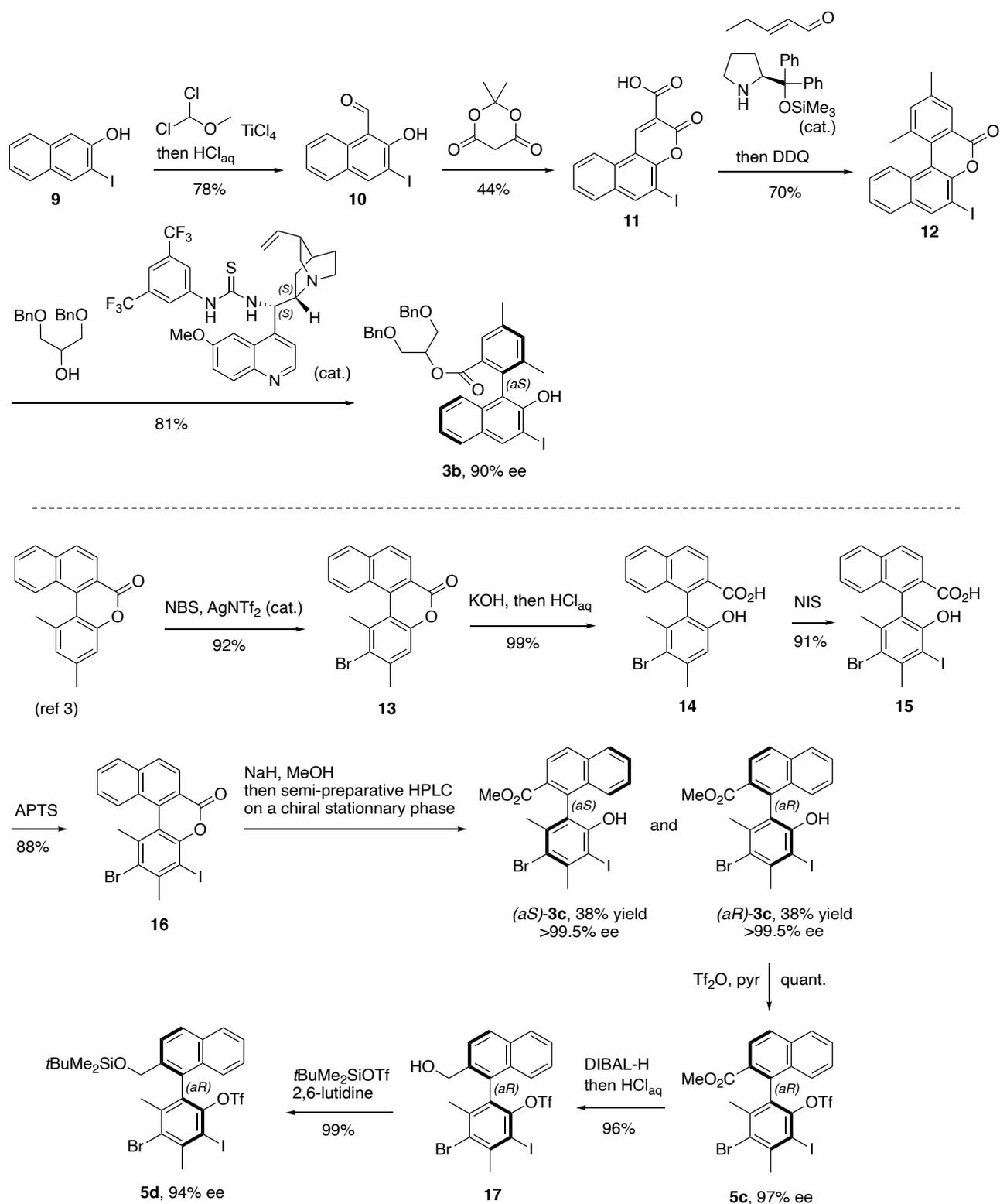


entry	precursor	conditions	yield of 6 ^[a]	ratio 6:7 ^[b]
1	<i>rac</i> - 4a	TBAF (3 equiv), CH ₃ CN, 25 °C, 0.5 h	42%	1:1
2	<i>rac</i> - 4a	TBAF (3 equiv), THF, 25 °C, 0.5 h	43%	1:1
3	<i>rac</i> - 4a	TBAF (3 equiv), hexane, 25 °C, 3 h	40%	1.7:1
4	<i>rac</i> - 4a	KF / 18-crown-6 (1.5 equiv), THF, 25 °C, 12 h	35%	1:1.3
5	<i>rac</i> - 4a	KF / 18-crown-6 (1.5 equiv), hexane, 25 °C, 72 h	58%	2:1
6	<i>rac</i> - 4a	CsF (3 equiv), CH ₃ CN, 30 °C, 3 h	30%	1:1.4
7	<i>rac</i> - 4a	CsF (3 equiv), CH ₃ CN, 0 °C, 8 h	41%	1:1
8	<i>rac</i> - 4a	CsF (3 equiv), PhCN, 20 °C, 12 h	nr	nd
9	<i>rac</i> - 4a	CsF (3 equiv), <i>t</i> BuCN, 20 °C, 12 h	nr	nd
10	<i>rac</i> - 4a	CsF (3 equiv), DMF, 20 °C, 24 h	21%	1:3.4
11	<i>rac</i> - 4b	CsF (3 equiv), CH ₃ CN, 20 °C, 24 h	<10%	< 1:5, 43% ^[c]
12	<i>rac</i> - 4c	CsF (3 equiv), CH ₃ CN, 20 °C, 72 h	<2%	< 1:30, 54% ^[c]
13	<i>rac</i> - 4d	CsF (3 equiv), CH ₃ CN, 20 °C, 12 h	37%	1.1:1, 33% ^[c]
14	<i>rac</i> - 5a	Mg turnings, THF, 65 °C under microwaves, 1 h	<5%	nd
15	<i>rac</i> - 5a	Mg turnings, THF, 80 °C under microwaves, 2 h	22%	> 30:1
16	<i>rac</i> - 5a	Mg turnings, THF, 80 °C under microwaves, 8 h	60%	> 30:1

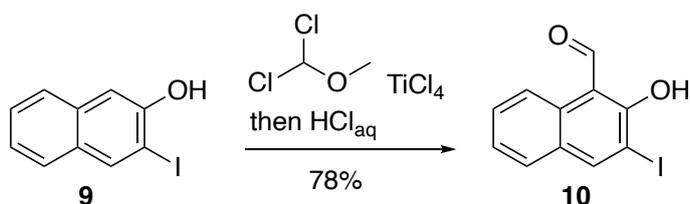
17	<i>rac-5b</i>	<i>i</i> PrMgCl (2 equiv), hexane, -30 °C, 24 h	nr	nd
18	<i>rac-5b</i>	MeMgCl (2 equiv), hexane, -30 °C, 24 h	nr	nd
19	<i>rac-5b</i>	MeMgCl (2 equiv), THF, -10 °C, 24 h	<5%	nd
20	<i>rac-5b</i>	MeMgCl (3 equiv), hexane, 30 °C, 24 h	<15%	>30:1
21	<i>rac-5b</i>	Me ₃ SiCH ₂ MgCl (2 equiv), hexane, -30 °C, 24 h	nr	nd
22	<i>rac-5b</i>	Me ₃ SiCH ₂ MgCl (14 equiv), Et ₂ O, 0 °C, 3 h	85%	> 50:1

[a] Isolated yield after purification. [b] Determined by ¹H NMR analysis from the crude reaction mixtures. [c] Isolated yield of **7** after purification. nr = no reaction, nd = not determined.

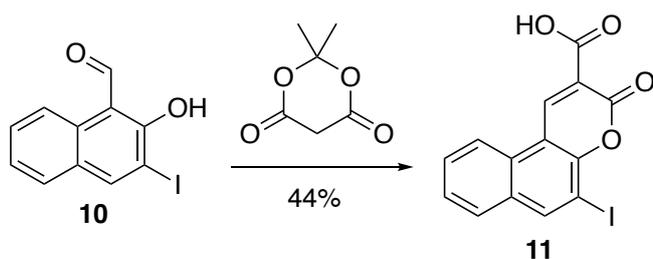
Procedures and characterization data for all new compounds



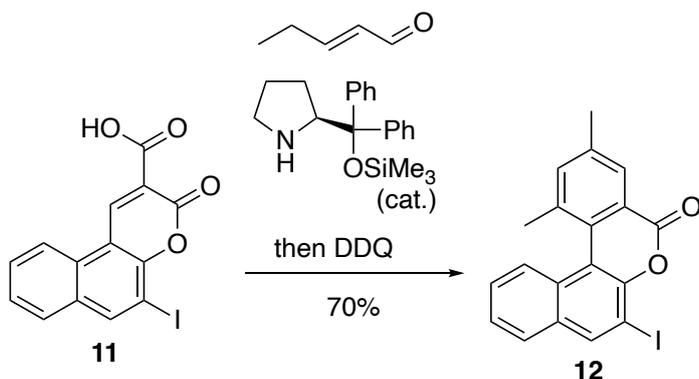
Scheme S1. Highlights of the syntheses of **3b** (top), **5c** and **5d** (bottom).



A solution of TiCl_4 (2.0 mL, 18.2 mmol) and dichloromethyl(methyl)ether (0.82 mL, 9.1 mmol) in anhydrous dichloromethane (10 mL) was stirred at 0 °C for 15 min. A solution of the 3-iodonaphthalen-2-ol (**9**, 2.43 g, 9.0 mmol) in CH_2Cl_2 (30 mL) was added dropwise over 1 hour, the reaction mixture was warmed to room temperature and stirred for 14 h, whereupon 1 N HCl (10 mL) was added under vigorous stirring. The aqueous layer was extracted with CH_2Cl_2 (3 \times 10 mL), and the combined organic layers were dried with anhydrous Na_2SO_4 , filtered and concentrated under reduced pressure to afford the crude product. This material was purified by flash chromatography eluted with hexane/EtOAc = 20:1 to afford the pure product as a white solid (**10**, 2.09 g, 78%). **HRMS** (ESI+) m/z calcd for $\text{C}_{11}\text{H}_8\text{IO}_2^+$ $[\text{M}+\text{H}]^+$ 298.9563, found 298.9567; **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 14.00 (s, 1H), 10.69 (s, 1H), 8.56 (s, 1H), 8.35 (d, $J = 8.4$ Hz, 1H), 7.74 (d, $J = 8.1$ Hz, 1H), 7.69 (ddd, $J = 7.6, 7.2, 0.8$ Hz, 1H), 7.48 (ddd, $J = 7.8, 7.3, 1.0$ Hz, 1H); **$^{13}\text{C}\{^1\text{H}\}$ NMR** (101 MHz, CDCl_3) δ 193.0 (CH), 162.9 (C), 148.3 (CH), 132.8 (C), 129.8 (CH), 129.5 (C), 128.7 (CH), 125.3 (CH), 118.7 (CH), 111.3 (C), 87.8 (C).

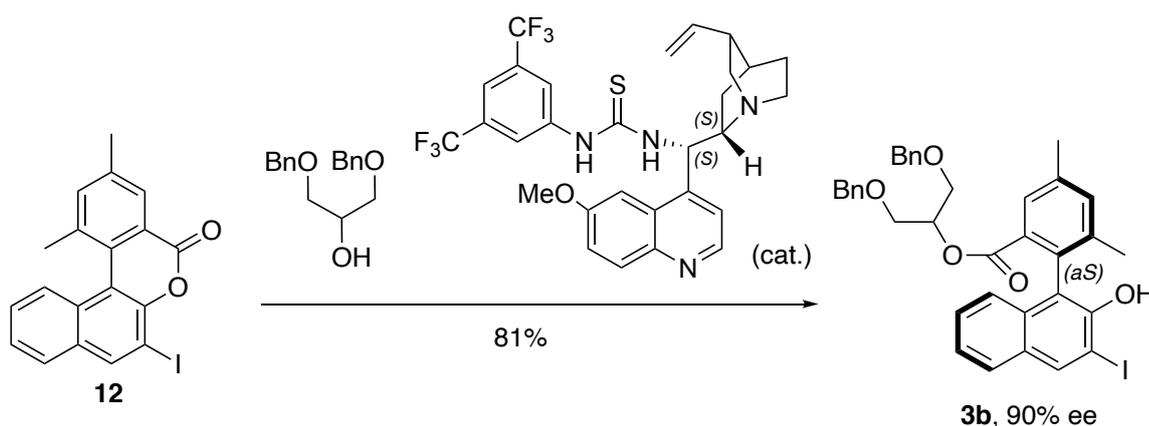


To an ethanolic solution (30 mL) of **10** (3.50 g, 11.7 mmol) and Meldrum's acid (1.72 g, 11.9 mmol) was added pyridine (0.2 mL, 2.5 mmol) and the mixture was refluxed for 4 h. The yellow solid formed during the reaction was filtered off to give directly the desired product (**11**, 1.89 g, 44%) requiring no additional purification. **Mp**: 284–286 °C (amorphous); **HRMS** (ESI+) m/z calcd for $\text{C}_{14}\text{H}_8\text{IO}_4^+$ $[\text{M}+\text{H}]^+$ 366.9462, found 366.9456; **$^1\text{H NMR}$** (400 MHz, d_6 -DMSO) δ 13.39 (broad s, 1H), 9.27 (s, 1H), 8.85 (s, 1H), 8.54 (d, $J = 8.0$ Hz, 1H), 8.00 (d, $J = 8.1$ Hz, 1H), 7.76 (dd, $J = 7.6, 7.5$ Hz, 1H), 7.64 (dd, $J = 7.6, 7.5$ Hz, 1H); **$^{13}\text{C}\{^1\text{H}\}$ NMR** (101 MHz, d_6 -DMSO) δ 164.0 (C), 156.2 (C), 153.1 (C), 144.4 (CH), 143.5 (CH), 131.1 (C), 129.2 (CH), 128.8 (C), 128.0 (CH), 126.8 (CH) 122.3 (C), 117.9 (C), 112.5 (C), 84.5 (CH).

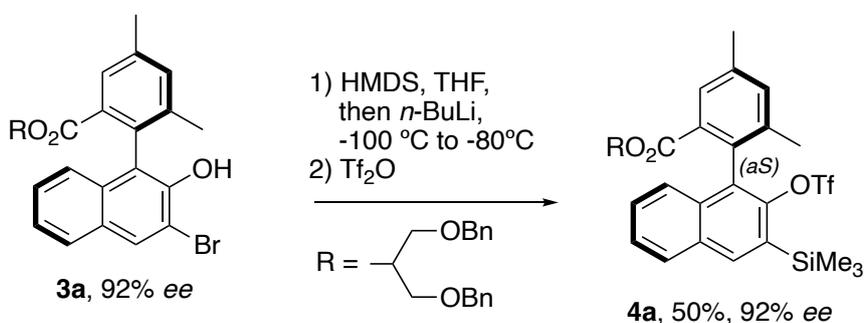


A mixture of the carboxylic acid **11** (365 mg, 1.00 mmol), (*E*)-2-pentenal (147 μL , 1.5 mmol) and (*S*)-diphenylprolinol(trimethylsilyl) ether (0.20 mmol, 65 mg) was stirred in 5 mL

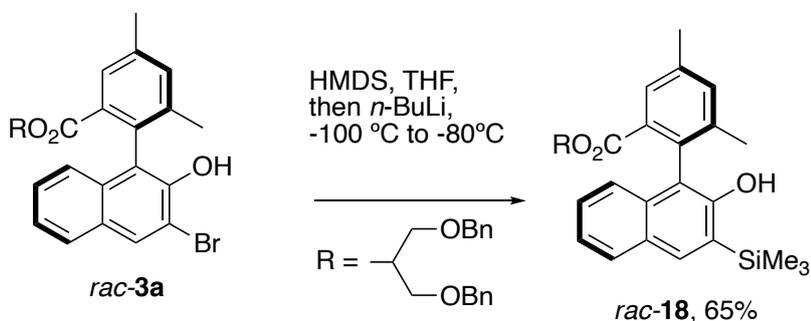
chloroform at 40 °C for 3 h. Then, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 480 mg, 2.1 mmol) was added to the reaction mixture that was stirred for an additional 8 h at 40 °C. Silica gel (1.2 g) was added to the cooled reaction mixture and all volatiles were removed under vacuum. Purification of the resulting material by flash chromatography eluted with hexane/dichloromethane/diethyl ether 20:4:1 afforded the Bringmann's lactone as a white solid (**12**, 279 mg, 70%). **Mp** 220–221 °C (amorphous); **HRMS** (ESI+) *m/z* calcd for C₁₉H₁₄IO₂⁺ [M+H]⁺ 401.2229, found 401.2229; **¹H NMR** (400 MHz, CDCl₃) δ 8.46 (s, 1H), 8.13 (s, 1H), 7.80 (d, *J* = 8.3 Hz, 1H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.55–7.45 (m, 3H), 2.53 (s, 3H), 2.28 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 161.7 (C), 147.8 (C), 140.1 (CH), 139.1 (CH), 139.0 (C), 135.9 (C), 132.2 (C), 131.5 (C), 129.2 (CH), 128.2 (CH), 127.3 (CH), 127.2 (CH), 126.6 (CH), 125.8 (CH), 124.7 (C), 114.7 (C), 83.9 (C), 23.6 (CH₃), 21.2 (CH₃).



A mixture of the lactone **12** (40 mg, 0.10 mmol), 1,3-bis(benzyloxy)propan-2-ol (33 mg, 0.12 mmol) and the Soós quinine catalyst (9 mg, 0.015 mmol) in 1.0 mL trifluorotoluene was stirred for 4 days at 23 °C, concentrated, and directly purified by silica gel chromatography, eluted with hexane/EtOAc = 20:1 to afford **3b** (54.3 mg, 81% yield) as a colorless oil. **HRMS** (ESI+) *m/z* calcd for C₃₆H₃₇NIO₅ [M+NH₄]⁺ 690.1711, found 690.1710; **¹H NMR** (400 MHz, CDCl₃) δ 8.15 (s, 1H), 7.67 (s, 1H), 7.52 (dd, *J* = 7.0, 2.4 Hz, 1H), 7.32–7.11 (m, 11H), 7.08–7.02 (m, 2H), 6.92–6.90 (m, 1H), 5.29 (s, 1H), 4.93 (p, *J* = 5.6 Hz, 1H), 4.30 (broad s, 2H), 4.07 (broad s, 2H), 3.15 (dd, *J* = 10.5, 4.7 Hz, 1H), 3.07 (dd, *J* = 10.5, 5.9 Hz, 1H), 2.92 (dd, *J* = 10.3, 5.4 Hz, 1H), 2.68 (dd, *J* = 10.3, 5.8 Hz, 1H), 2.38 (s, 3H), 1.81 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 167.0 (C), 148.3 (C), 139.4 (C), 138.8 (C), 138.3 (C), 138.2 (CH), 138.1 (C), 135.2 (CH), 133.4 (C), 132.9 (C), 130.8 (C), 130.4 (C), 129.4 (CH), 128.4 (2CH), 128.4 (2CH), 127.7 (2CH), 127.7 (CH), 127.6 (CH), 127.6 (2CH), 127.2 (CH), 127.0 (CH), 124.4 (CH), 124.1 (CH), 120.6 (C), 87.1 (C), 73.2 (CH₂), 73.0 (CH₂), 71.8 (CH), 68.5 (CH₂), 68.1 (CH₂), 21.2 (CH₃), 19.9 (CH₃); **HPLC** Chiralpak IF column, heptane/ethanol = 90:10, 1 mL/min, 220 nm, retention time: *t*_{major} = 8.74 min, *t*_{minor} = 11.73 min, 90% ee; **Specific rotation** [α]_D²⁵ = 4.6 (*c* = 1.0, CHCl₃). Repeating this experiment with minor variations at various scales (up to 2 g) consistently afforded **3b** in 40–81% yield with 75–91% ee. The absolute configuration of the major enantiomer of **3b** was determined as (*aS*) by comparison of the HPLC data and chiroptical properties of the products **6a** derived from **3a** and **3b** (see Schemes 2 and 3).

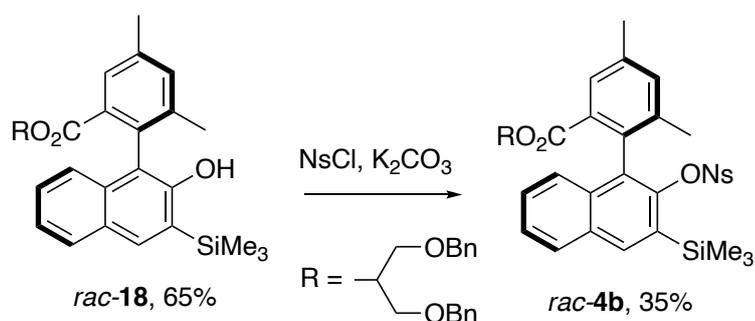


To a solution of **3a** (190 mg, 0.304 mmol) in THF (3.0 mL) was added hexamethyldisilazane (0.13 mL, 0.62 mmol) at room temperature and the resulting mixture was stirred 2 h at 60 °C. After evaporating the solvent and HMDS under reduced pressure, the residue was dissolved in THF (3.0 mL) and the resulting solution was cooled down to -100 °C. *n*-BuLi (2.5 M in hexanes, 0.24 mL, 0.60 mmol) was slowly added at -100 °C and the temperature was allowed to warm to -80 °C over 20 min. After cooling to -100 °C again, Tf₂O (0.11 mL, 0.65 mmol) was added dropwise to the reaction mixture, and the stirring was continued until the temperature reached -65 °C (20 min). Then, 5 mL of a cold saturated aqueous solution of NaHCO₃ were added to the reaction mixture that was allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic extracts were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluted with petroleum ether/EtOAc = 40:1 to afford **4a** (115 mg, 50%) as a colorless oil. **HRMS** (ESI+) *m/z* calcd for C₄₀H₄₅NF₃O₇SSi⁺ [M+NH₄]⁺ 768.2633, found 768.2633; **¹H NMR** (400 MHz, CDCl₃) δ 8.05 (s, 1H), 7.85 (m, 2H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.36–7.19 (m, 13H), 5.04 (p, *J* = 5.0 Hz, 1H), 4.37 (s, 2H), 4.30 (s, 2H), 3.36 (dd, *J* = 10.2, 5.5 Hz, 1H), 3.29 (dd, *J* = 10.3, 5.0 Hz, 1H), 3.24 (dd, *J* = 10.3, 5.2 Hz, 1H), 3.06 (dd, *J* = 10.3, 5.2 Hz, 1H), 2.47 (s, 3H), 1.90 (s, 3H), 0.48 (s, 9H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 166.1 (C), 147.5 (C), 139.2 (C), 138.5 (C), 138.3 (2C), 137.9 (CH), 135.1 (CH), 134.4 (C), 132.5 (C), 132.1 (C), 132.0 (C), 131.2 (C), 130.9 (C), 129.5 (CH), 128.4 (2CH), 128.3 (2CH), 128.3 (CH), 127.7 (CH), 127.6 (2CH), 127.6 (CH), 127.6 (2CH), 127.6 (CH), 126.8 (CH), 126.3 (CH), 118.1 (q, ¹*J*_{C-F} = 320.7 Hz, CF₃), 73.1 (CH₂), 73.0 (CH₂), 71.5 (CH), 68.4 (CH₂), 68.3 (CH₂), 21.2 (CH₃), 20.2 (CH₃), 0.4 (3CH₃); **¹⁹F NMR** (376 MHz, CDCl₃) δ -74.0; **HPLC**: (S,S) Whelk-O1, heptane/isopropanol = 95:5, 1 mL/min, 220 nm, retention time: *t*_{major} = 10.61 min, *t*_{minor} = 12.48, 92% *ee*; **Specific rotation** [α]_D²⁵ = 12.3 (*c* = 1.00, CHCl₃).

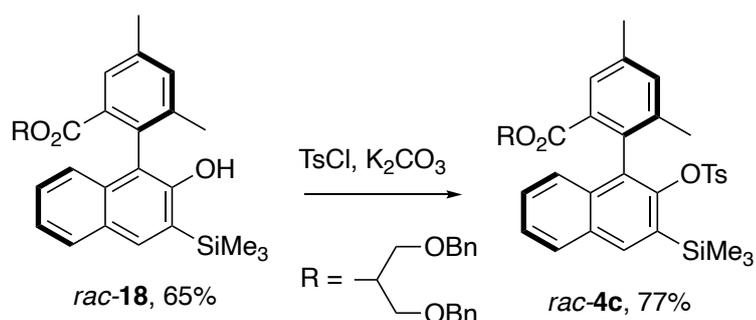


To a solution of *ortho*-bromonaphthol *rac*-**3a** (190 mg, 0.304 mmol) in THF (3.0 mL) was added hexamethyldisilazane (0.13 mL, 0.62 mmol) at room temperature and the resulting mixture was stirred 2 h at 60 °C. After evaporating the solvent and HMDS under reduced pressure, the residue was dissolved in THF (3.0 mL) and the resulting solution was cooled down to -100 °C. *n*-BuLi (2.5 M in hexanes, 0.24 mL, 0.60 mmol) was slowly added at -100 °C and the temperature was allowed to warm to -65 °C over 30 min. Then, 5 mL of a cold

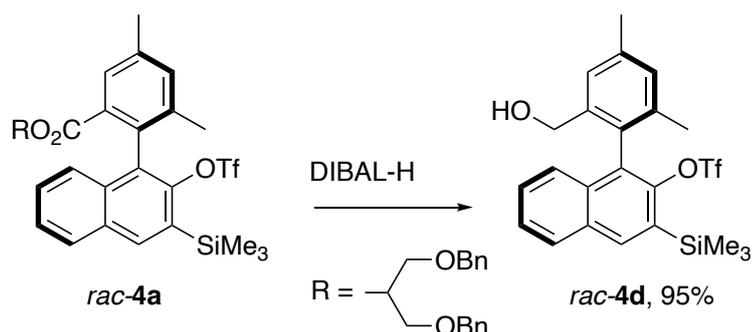
saturated aqueous solution of NaHCO₃ were added to the reaction mixture that was allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic extracts were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluted with petroleum ether/EtOAc = 20:1 to afford desired *ortho*-trimethylsilylnaphthol (**18**, 121 mg, 65%) as a white solid. **Mp** 94–96 °C (amorphous); **HRMS** (ESI+) *m/z* calcd for C₃₉H₄₆NO₅Si⁺ [M+NH₄]⁺ 636.3140, found 636.3137; **¹H NMR** (400 MHz, CDCl₃) δ 7.83 (s, 1H), 7.74–7.69 (m, 2H), 7.37 (s, 1H), 7.31–7.12 (m, 12H), 6.99–6.97 (m, 1H), 5.01 (p, *J* = 5.6 Hz, 1H), 4.93 (s, 1H), 4.36–4.23 (m, 2H), 4.19–4.05 (m, 2H), 3.16–3.03 (m, 2H), 2.93 (dd, *J* = 10.3, 5.7 Hz, 1H), 2.61 (dd, *J* = 10.3, 5.8 Hz, 1H), 2.46 (s, 3H), 1.89 (s, 3H), 0.36 (s, 9H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 167.5 (C), 154.2 (C), 140.1 (C), 138.8 (C), 138.2 (C), 135.7 (CH), 135.1 (CH), 134.2 (C), 134.1 (C), 130.2 (C), 129.2 (CH), 128.8 (C), 128.4 (C), 128.3 (2CH), 128.3 (2CH), 128.2 (CH), 127.6 (2CH), 127.6 (2CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 126.9 (CH), 123.9 (CH), 123.1 (CH), 118.1 (C), 73.0 (CH₂), 72.7 (CH₂), 71.7 (CH), 68.5 (CH₂), 68.1 (CH₂), 21.2 (CH₃), 19.9 (CH₃), -0.7 (3CH₃)



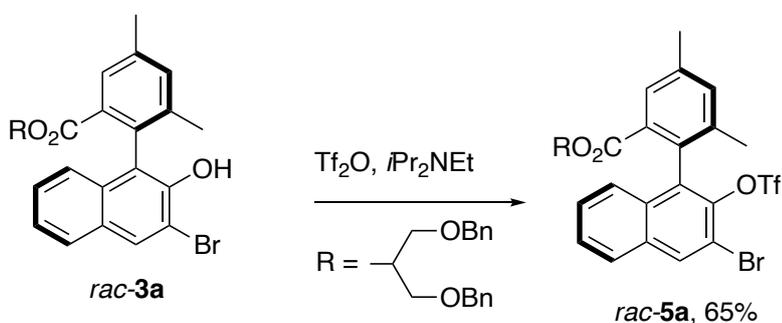
To a stirred solution of *rac-18* (74 mg, 0.12 mmol) in dry MeCN (1.0 mL) at 23 °C was added K₂CO₃ (32 mg, 0.23 mmol). After 5 min, 4-nitrobenzenesulfonyl chloride (53 mg, 0.24 mmol) was added. The reaction mixture was stirred for 24 h at 23 °C and diethyl ether (5 mL) and water (5 mL) were added. The organic phase was separated and was successively washed with water and brine and dried over anhydrous MgSO₄. Filtration and concentration of the filtrate under vacuum afforded the crude product that was purified by silica gel chromatography eluted with petroleum ether/EtOAc = 10:1 to afford *rac-4b* (34 mg, 35%) as a colorless oil. **HRMS** (ESI+) *m/z* calcd for C₄₅H₄₉N₂O₉SSi⁺ (M+NH₄)⁺ 821.2923, found 821.2913; **¹H NMR** (400 MHz, CDCl₃) δ 8.03 (s, 1H), 7.94–7.88 (m, 2H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.65–7.55 (m, 2H), 7.41 (ddd, *J* = 8.1, 6.9, 1.0 Hz, 2H), 7.36–7.20 (m, 10H), 7.11 (d, *J* = 4.0 Hz, 1H), 7.02 (d, *J* = 8.1 Hz, 1H), 6.93 (s, 1H), 5.03 (p, *J* = 5.2 Hz, 1H), 4.39 (s, 2H), 4.33 (s, 2H), 3.38 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.25 (dd, *J* = 10.4, 5.1 Hz, 1H), 3.19 (dd, *J* = 10.3, 4.9 Hz, 1H), 2.95 (dd, *J* = 10.4, 5.4 Hz, 1H), 2.13 (s, 3H), 1.81 (s, 3H), 0.57 (s, 9H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 166.2 (C), 149.5 (C), 149.4 (C), 143.6 (C), 139.0 (C), 138.5 (C), 138.1 (C), 138.1 (C), 137.5 (CH), 134.6 (CH), 134.1 (C), 133.9 (C), 132.4 (C), 131.8 (C), 131.7 (C), 129.5 (C), 128.9 (CH), 128.5 (2CH), 128.5 (2CH), 128.5 (CH), 127.9 (2CH), 127.8 (CH), 127.8 (CH), 127.8 (2CH), 127.7 (2CH), 127.5 (CH), 126.3 (CH), 125.8 (CH), 123.6 (2CH), 73.2 (CH₂), 73.2 (CH₂), 71.7 (CH), 68.5 (CH₂), 68.3 (CH₂), 20.8 (CH₃), 20.2 (CH₃), 0.4 (3CH₃)



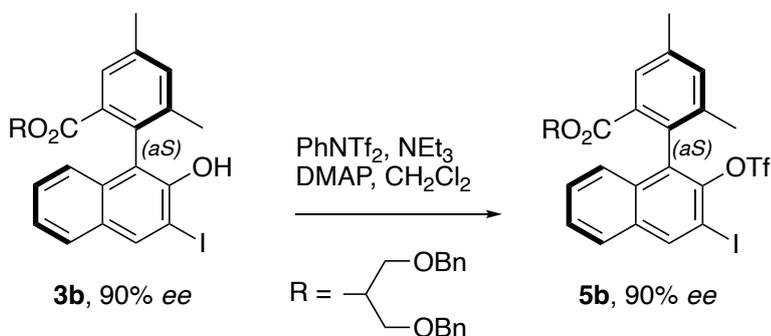
Following the same protocol as above with tosyl chloride (46 mg, 0,24 mmol) instead of 4-nitrobenzenesulfonyl chloride afforded *rac-4c* (71 mg, 77%) as a colorless oil. **HRMS** (ESI+) *m/z* calcd for $\text{C}_{46}\text{H}_{52}\text{NO}_7\text{SSi}^+$ $[\text{M}+\text{NH}_4]^+$ 790.3228, found 790.3225; **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 8.01 (s, 1H), 7.80 (d, $J = 8.1$ Hz, 1H), 7.39–7.34 (m, 1H), 7.33–7.17 (m, 14H), 7.11–7.08 (m, 1H), 6.97–6.90 (m, 3H), 5.00 (p, $J = 5.4$ Hz, 1H), 4.41–4.32 (m, 2H), 4.26 (s, 2H), 3.32 (dd, $J = 10.3, 5.6$ Hz, 1H), 3.18 (dd, $J = 10.3, 5.1$ Hz, 1H), 3.11 (dd, $J = 10.3, 5.4$ Hz, 1H), 2.88 (dd, $J = 10.3, 5.5$ Hz, 1H), 2.34 (s, 3H), 2.23 (s, 3H), 1.81 (s, 3H), 0.54 (s, 9H); **$^{13}\text{C}\{^1\text{H}\}$ NMR** (101 MHz, CDCl_3) δ 166.5 (C), 149.3 (C), 143.0 (C), 138.8 (C), 138.3 (C), 138.3 (C), 137.6 (C), 137.2 (CH), 135.6 (C), 134.4 (CH), 134.3 (C), 134.2 (C), 134.1 (C), 132.0 (C), 131.5 (C), 130.1 (C), 129.0 (2CH), 128.4 (2CH), 128.4 (2CH), 128.3 (CH), 127.7 (2CH), 127.6 (2CH), 127.6 (2CH), 127.6 (CH), 127.1 (CH), 126.6 (2CH), 125.9 (CH), 125.5 (CH), 73.1 (CH₂), 73.0 (CH₂), 71.4 (CH), 68.4 (CH₂), 68.3 (CH₂), 21.8 (CH₃), 21.1 (CH₃), 20.3 (CH₃), 0.5 (3CH₃).



To a solution of *rac-4a* (75 mg, 1.0 mmol) in dichloromethane (2.0 mL) at 0 °C was slowly added a solution of DIBAL-H (1M in hexane, 4 mL, 4 mmol) and the reaction mixture was warmed to 23 °C and maintained at that temperature for 2 h. Then, aqueous 1N HCl (4 mL) was added under vigorous stirring and the layers were decanted and separated. The aqueous layer was extracted twice with EtOAc. The combined organic layers were washed successively with water and brine and dried over anhydrous MgSO_4 . Filtration and concentration of the filtrate under vacuum afforded the crude product that was purified by silica gel chromatography eluted with petroleum ether/EtOAc = 10:1 to afford *rac-4d* (46 mg, 95%) as a colorless oil. **HRMS** (ESI+) *m/z* calcd for $\text{C}_{23}\text{H}_{29}\text{NO}_4\text{F}_3\text{SSi}^+$ $[\text{M}+\text{NH}_4]^+$ 500.1533, found 500.1530; **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 8.12 (s, 1H), 7.92 (d, $J = 8.1$ Hz, 1H), 7.54 (t, $J = 7.5$ Hz, 1H), 7.41 (t, $J = 7.5$ Hz, 1H), 7.39 (s, 1H), 7.25 (d, $J = 9.7$ Hz, 1H), 7.11 (s, 1H), 4.24 (d, $J = 13.2$ Hz, 1H), 4.15 (d, $J = 13.3$ Hz, 1H), 2.44 (s, 3H), 1.89 (s, 3H), 0.51 (s, 9H), **OH** resonance not detected; **$^{13}\text{C}\{^1\text{H}\}$ NMR** (101 MHz, CDCl_3) δ 148.3 (C), 141.0 (C), 139.0 (C), 138.4 (CH), 137.6 (C), 134.2 (C), 132.9 (C), 132.4 (C), 130.3 (CH), 129.8 (C), 128.5 (CH), 128.1 (CH), 128.1 (C), 127.2 (CH), 126.4 (CH), 126.3 (CH), 118.2 (q, $^1J_{\text{C-F}} = 320.9$ Hz, CF₃), 63.0 (CH₂), 21.4 (CH₃), 19.9 (CH₃), 0.4 (3CH₃); **$^{19}\text{F NMR}$** (376 MHz, CDCl_3) δ -73.9.

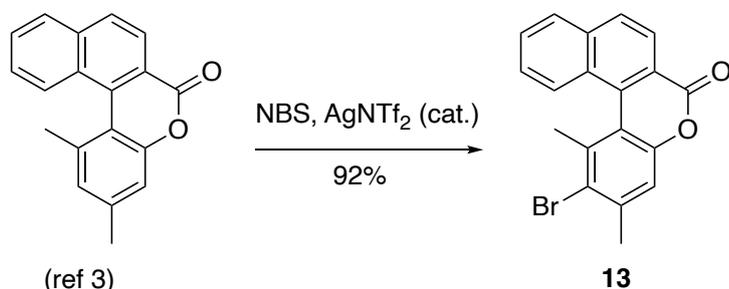


To a solution of *rac-3a* (189 mg, 0.302 mmol) in THF (5.0 mL) at 23 °C was added in order di(isopropyl)ethyl amine (0.10 mL, 0.60 mmol) and Tf₂O (0.10 mL, 0.60 mmol) and the reaction was stirred 12 h at 23 °C. After addition of water (10 mL), the layers were decanted, and the aqueous layer was extracted three times with EtOAc. The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1) to afford *rac-5a* (148 mg, 65%) as a colorless oil. **HRMS** (ESI+) *m/z* calcd for C₃₇H₃₆NBrF₃O₇S⁺ [M+NH₄]⁺ 774.1342, found 774.1342; **¹H NMR** (400 MHz, CDCl₃) δ 8.09 (s, 1H), 7.90 (s, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.39–7.20 (m, 11H), 7.17–7.13 (m, 2H), 5.07 (p, *J* = 5.3 Hz, 1H), 4.4.1 (s, 2H), 4.22 (s, 2H), 3.34 (dd, *J* = 10.4, 5.6 Hz, 1H), 3.28 (dd, *J* = 10.4, 5.1 Hz, 1H), 3.21 (dd, *J* = 10.5, 4.9 Hz, 1H), 2.98 (dd, *J* = 10.4, 5.5 Hz, 1H), 2.48 (s, 3H), 1.91 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 166.1 (C), 141.2 (C), 139.2 (C), 139.0 (C), 138.2 (C), 138.1 (C), 135.4 (CH), 134.1 (C), 133.1 (CH), 133.0 (C), 132.3 (C), 131.6 (C), 130.0 (C), 129.9 (CH), 129.7 (CH), 128.4 (2CH), 128.4 (2CH), 127.8 (CH), 127.7 (CH), 127.7 (2CH), 127.6 (CH), 127.6 (2CH), 127.3 (CH), 126.5 (CH), 123.6 (CH), 118.3 (q, ¹*J*_{C-F} = 322.3 Hz, CF₃), 113.6 (C), 73.1 (CH₂), 73.0 (CH₂), 71.9 (CH), 68.3 (CH₂), 68.3 (CH₂), 21.2 (CH₃), 20.1 (CH₃); **¹⁹F NMR** (376 MHz, CDCl₃) δ -72.6.

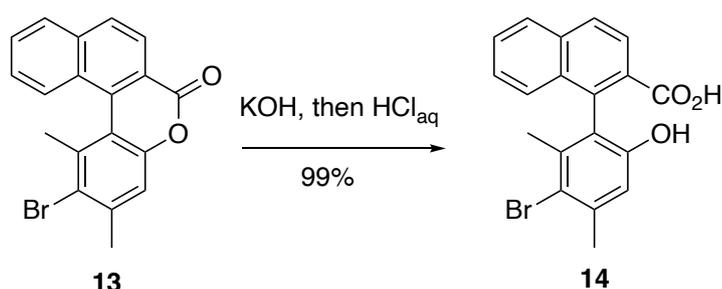


To a stirred solution of **3b** (726 mg, 1.08 mmol, 90 % *ee*) in dichloromethane (10 mL) at 0 °C was added in order *N*-phenyl-bis(trifluoromethanesulfonimide) (785 mg, 2.20 mmol), triethylamine (0.30 mL, 2.2 mmol) and 4-(dimethylamino)pyridine (68 mg, 0.56 mmol). The reaction mixture was allowed to slowly warm to room temperature. After 13 h, volatiles were removed by rotary evaporation under vacuum and the residue was dissolved in EtOAc and washed three time with water and once with brine. The organic phase was dried over anhydrous Na₂SO₄, filtered and concentrated. The crude material was filtered on a short pad of silica gel eluted with petroleum ether/ethyl acetate = 40:1 to afford **5b** (867 mg, quant., 90% *ee*) as a colorless oil. **HRMS** (ESI+) *m/z* calcd for C₃₇H₃₆NF₃I O₇S⁺ [M+NH₄]⁺ 822.1204, found 822.1199; **¹H NMR** (400 MHz, CDCl₃) δ 8.35 (s, 1H), 7.87 (s, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.46–7.42 (m, 1H), 7.35–7.13 (m, 13H), 5.06 (p, *J* = 5.3 Hz, 1H), 4.40 (s, 2H), 4.20 (s, 2H), 3.33 (dd, *J* = 10.4, 5.6 Hz, 1H), 3.26 (dd, *J* = 10.4, 5.1 Hz, 1H), 3.19 (dd, *J* = 10.5, 4.9 Hz, 1H), 2.95 (dd, *J* = 10.5, 5.5 Hz, 1H), 2.45 (s, 3H), 1.89 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 166.0 (C), 143.7 (C), 140.7 (CH), 139.2 (C), 139.0 (C), 138.3 (C), 138.2 (C), 135.3 (CH), 133.7 (C), 133.4 (C), 133.1 (C), 131.8 (C), 130.3 (C), 129.8 (C), 128.4 (2CH), 128.4

(2CH), 127.8 (CH), 127.7 (2CH), 127.6 (CH), 127.6 (CH), 127.4 (2CH), 127.1 (CH), 126.6 (CH), 118.4 (q, $^1J_{C-F} = 321.6$ Hz, CF₃), 116.8 (C), 86.2 (C), 73.2 (CH₂), 73.1 (CH), 71.8 (CH₂), 68.4 (C), 68.3 (C), 21.3 (CH₃), 20.2 (CH₃); **^{19}F NMR** (376 MHz, CDCl₃) δ -72.0; **HPLC** Chiralpak IE, heptane/ethanol = 90:10, 1 mL/min, 220 nm, $t_{\text{major}} = 6.95$ min, $t_{\text{minor}} = 6.33$ min, 90% ee; **Specific rotation** $[\alpha]_{\text{D}}^{25} = 18.4$ ($c = 1.0$, CHCl₃).



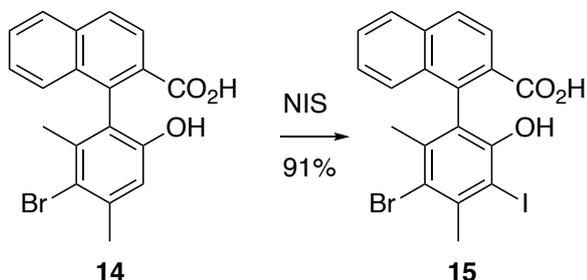
To a solution of 1,3-dimethyl-6H-benzo[b]naphtho[1,2-d]pyran-6-one³ (500 mg, 1.82 mmol) and *N*-bromosuccinimide (340 mg, 1.91 mmol) in dichloromethane (20 mL) was added silver bis(trifluoromethanesulfonyl)imide (35 mg, 0.091 mmol) under an inert atmosphere (glovebox). The reaction mixture was stirred at room temperature (23–25 °C) for 24 h, leading to a dark red suspension. Then, the mixture was diluted in EtOAc and washed three times with water and once with brine. The organic phase was dried over anhydrous Na₂SO₄, filtered and concentrated. The crude product was purified by flash column chromatography on silica gel eluted with petroleum ether/CHCl₃ = 1:1 to afford the desired brominated lactone (**13**, 592 mg, 92%) as a light yellow solid. **Mp** 186–187 °C (CHCl₃); **HRMS** (ESI+) m/z calcd for C₁₉H₁₄O₂Br⁺ [M+H]⁺ 353.0172, found 353.0166; **^1H NMR** (400 MHz, CDCl₃) δ 8.28 (d, $J = 8.5$ Hz, 1H), 8.00 (d, $J = 9.0$ Hz, 1H), 7.97 (d, $J = 8.3$ Hz, 1H), 7.92 (d, $J = 8.5$ Hz, 1H), 7.69 (ddd, $J = 8.5, 7.5, 1.2$ Hz, 1H), 7.60 (ddd, $J = 8.8, 7.7, 1.4$ Hz, 2H), 7.26 (s, 1H), 2.58 (s, 3H), 2.32 (s, 3H); **$^{13}\text{C}\{^1\text{H}\}$ NMR** (101 MHz, CDCl₃) δ 161.5 (C), 150.5 (C), 140.7 (C), 136.5 (C), 136.4 (C), 135.1 (C), 129.5 (CH), 129.1 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 126.5 (CH), 125.4 (C), 124.1 (CH), 121.9 (C), 117.8 (C), 116.3 (CH), 27.1 (CH₃), 24.4 (CH₃).



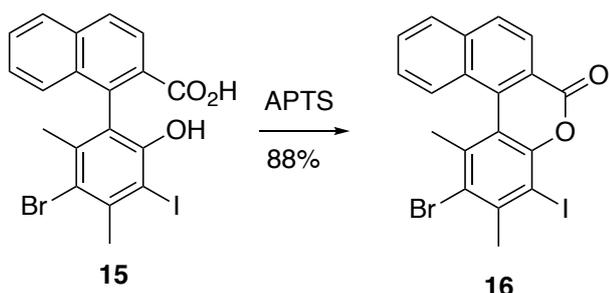
Solid 1,3-dimethyl-2-bromo-6H-benzo[b]naphtho[1,2-d]pyran-6-one (**13**, 562 mg, 1.59 mmol) was added to a 30% KOH ethanolic solution (30 mL). The mixture was heated at reflux until no starting material can be detected by TLC analysis (1 hour). Then, the solution was cooled down to 0 °C and concentrated hydrochloric acid was slowly added until pH = 1. The yellow precipitate that formed upon acidification was filtered off, triturated with water and dried under vacuum to give the desired biaryl **14** (585 mg, 99%) requiring no additional purification. **Mp** 192–193 °C (amorphous); **HRMS** (ESI+) m/z calcd for C₁₉H₁₆O₃Br⁺ [M+H]⁺ 371.0277, found 371.0273; **^1H NMR** (400 MHz, (CD₃)₂CO) δ 8.07 (d, $J = 8.7$ Hz, 1H), 8.04

(3) Bringmann, G.; Hartung, T.; Gobel, L.; Schupp, O.; Peters, K.; von Schnering, H. G. Synthesis and Structure of Benzonaphthopyrans; Helically Distorted, Bridged Biaryls with Different Steric Hindrance at the Axis. *Liebigs Ann. Chem.* **1992**, 769–775.

(d, $J = 9.0$ Hz, 1H), 8.02 (d, $J = 8.5$ Hz, 1H), 7.61 (ddd, $J = 8.5, 7.3, 1.7$ Hz, 1H), 7.50–7.41 (m, 2H), 6.85 (s, 1H), 2.43 (d, $J = 0.3$ Hz, 3H), 1.91 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, $(\text{CD}_3)_2\text{CO}$) δ 168.6 (C), 154.5 (C), 138.5 (C), 138.2 (C), 138.0 (C), 136.1 (C), 133.4 (C), 130.2 (C), 129.0 (CH), 128.7 (CH), 128.4 (CH), 127.7 (CH), 127.4 (CH), 127.1 (CH), 126.2 (C), 117.9 (C), 116.3 (CH), 24.2 (CH_3), 21.5 (CH_3).



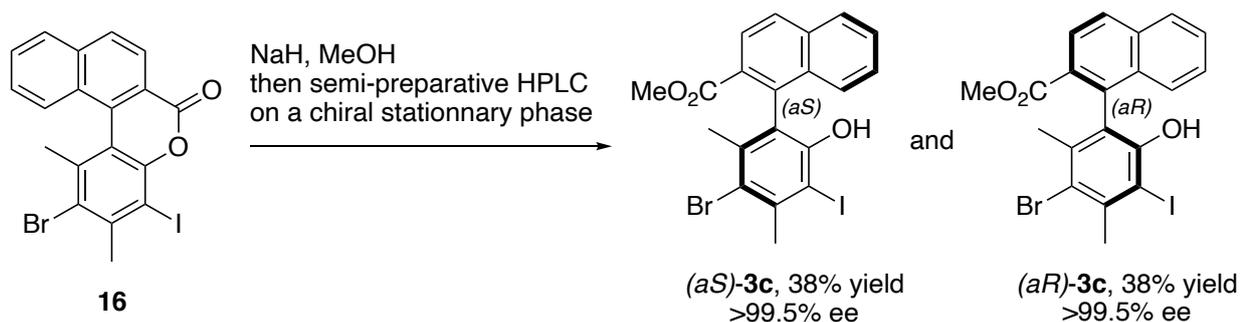
The 2-naphthalenecarboxylic acid **14** (156 mg, 0.42 mmol) was dissolved in dichloromethane (10 mL) and the solution was cooled down to 0 °C with an ice bath. A solution of *N*-iodosuccinimide (99 mg, 0.44 mmol) in dichloromethane (10 mL) was added dropwise at 0 °C, leading to a red solution. When the starting material is no longer detectable by TLC analysis, 10 mL of saturated $\text{Na}_2\text{S}_2\text{O}_3$ aqueous solution were added under vigorous stirring and the layers were decanted and separated. The organic layer was washed successively with water and brine, dried over anhydrous Na_2SO_4 , filtered and concentrated to afford the crude product. This material was purified by flash column chromatography on silica gel eluted with petroleum ether/EtOAc = 2:1 to afford the desired iodinated product **15** (190 mg, 91%) as a yellow solid. **Mp** 204–205 °C (amorphous); **HRMS** (ESI+) m/z calcd for $\text{C}_{19}\text{H}_{15}\text{O}_3\text{BrI}^+$ $[\text{M}+\text{H}]^+$ 496.9244, found 496.9246; ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$) δ 8.12–8.02 (m, 3H), 7.64 (ddd, $J = 8.5, 6.9, 1.3$ Hz, 1H), 7.50 (ddd, $J = 8.8, 7.2, 1.4$ Hz, 1H), 7.37 (ddd, $J = 8.5, 1.2, 0.6$ Hz, 1H), 2.85 (s, 3H), 1.90 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, $(\text{CD}_3)_2\text{CO}$) δ 168.2 (C), 153.7 (C), 140.7 (C), 138.1 (C), 137.0 (C), 136.3 (C), 133.1 (C), 130.3 (C), 129.5 (CH), 129.2 (CH), 128.8 (CH), 128.2 (CH), 127.2 (CH), 127.0 (CH), 125.7 (C), 117.5 (C), 90.7 (C), 31.4 (CH_3), 22.0 (CH_3).



The iodinated phenol **15** (62 mg, 0.13 mmol) was dissolved in toluene (5 mL) and *para*-toluenesulfonic acid (4.3 mg, 0.025 mmol) was added. The mixture was heated at reflux. When the starting material is no longer detectable by TLC analysis, 5 mL of saturated NaHCO_3 aqueous solution were added under vigorous stirring and the layers were decanted and separated. The aqueous layer was extracted with dichloromethane (15 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 , filtered and concentrated. The resulting crude product was purified by flash column chromatography on silica gel eluted with petroleum ether/ CHCl_3 = 1:1 to afford the iodinated lactone **16** (55 mg, 88%) as a white solid. **Mp** 176–177 °C (CHCl_3); **HRMS** (ESI+) m/z calcd for $\text{C}_{19}\text{H}_{13}\text{O}_2\text{BrI}^+$ $[\text{M}+\text{H}]^+$ 478.9138, found 478.9137; ^1H NMR (400 MHz, CDCl_3) δ 8.27 (d, $J = 8.5$ Hz, 1H), 8.02 (d, $J = 8.5$ Hz, 1H), 7.97 (d, $J = 8.2$ Hz, 1H), 7.86 (d, $J = 8.5$ Hz, 1H), 7.69 (ddd, $J = 9.0, 8.0, 1.3$ Hz, 1H),

7.60 (ddd, $J = 8.7, 8.0, 1.4$ Hz, 2H), 2.94 (s, 3H), 2.28 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 161.0 (C), 149.9 (C), 143.3 (C), 136.5 (C), 136.5 (C), 134.7 (C), 130.1 (CH), 129.2 (CH), 128.6 (CH), 128.6 (CH), 128.4 (CH), 126.8 (CH), 124.1 (C), 124.0 (CH), 121.1 (C), 118.2 (C), 88.5 (C), 31.2 (CH_3), 27.4 (CH_3).

The organocatalytic atroposelective opening of the above lactone was attempted under the conditions described above for the synthesis of **3b** (90% ee). The expected ester was obtained in 67% yield but only 73% ee. It was decided to prepare the corresponding racemic methyl ester **3c** and resolve it by HPLC techniques.



To a suspension of NaH (60% dispersion in oil, 92 mg, 2.3 mmol) in anhydrous Et_2O (20 mL) was added anhydrous methanol (94 mg, 2.94 mmol) at 0 °C and the mixture was stirred 30 min at this temperature. Then, a solution of lactone **16** (613 mg, 1.28 mmol) in Et_2O (20 mL) was added dropwise, and the mixture was stirred at room temperature until the starting material is no longer detectable by TLC analysis (30 min). The mixture was then hydrolyzed with 50 mL of aqueous NH_4Cl solution and extracted with Et_2O three times. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash column chromatography on silica gel eluted with pentane/ $\text{EtOAc} = 8:1$ affords the corresponding biaryl (**3c**, 539 mg, 88% yield) as a white solid. The two atropisomers of **3c** were separated by semi-preparative chiral HPLC (Chiralpak IG column, heptane/ethanol = 90:10, 1 mL/min, 254 nm) to provide highly enantio-enriched samples (>99.5% ee). **Mp** 68–70 °C (amorphous); **HRMS** (ESI+) m/z calcd for $\text{C}_{20}\text{H}_{17}\text{O}_3\text{BrI}^+$ $[\text{M}+\text{H}]^+$ 512.9382, found 512.9383; ^1H NMR (400 MHz, CDCl_3) δ 8.07 (d, $J = 8.7$ Hz, 1H), 7.96 (d, $J = 8.6$ Hz, 1H), 7.93 (d, $J = 8.1$ Hz, 1H), 7.59 (ddd, $J = 8.4, 6.8, 1.4$ Hz, 1H), 7.44 (ddd, $J = 8.8, 7.3, 1.2$ Hz, 1H), 7.39 (d, $J = 8.6$ Hz, 1H), 5.19 (s, 1H), 3.74 (s, 3H), 2.86 (s, 3H), 1.94 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 167.4 (C), 151.1 (C), 140.3 (C), 138.2 (C), 136.9 (C), 135.4 (C), 132.0 (C), 128.9 (C), 128.4 (CH), 128.3 (C), 128.1 (CH), 127.6 (CH), 126.6 (CH), 126.0 (CH), 123.7 (CH), 118.1 (C), 90.0 (C), 52.4 (CH_3), 31.3 (CH_3), 21.8 (CH_3). **Specific rotation:** for the first eluted atropisomer (*aS*)-**3c** $[\alpha]_{\text{D}}^{25} = +4.3$ ($c = 1.0$, CHCl_3), for the second eluted atropisomer (*aR*)-**3c** $[\alpha]_{\text{D}}^{25} = -4.3$ ($c = 1.0$, CHCl_3).

In order to determine the absolute configuration of the first and second eluted atropisomers from the HPLC resolution, both atropisomers were submitted to vibrational circular dichroism (Figures S1) and electronic circular dichroism spectroscopies (Figure S2), and the experimental spectra were compared with the simulated spectra for the (*aS*)-**3c**. It was found that the first eluted atropisomer is (*aS*)-configured and that the second eluted is (*aR*)-configured. Full details are available at the end of this document. Products **5c**, **5d**, **6k**, **6l**, and **8** all derived from the second eluted enantiomer of **3c** having an (*aR*) absolute configuration, which is consistent with the (*aS*) absolute configuration in **6k** ascertained by X-ray crystallography (see below, CCDC 2019279, note that the priority order in the Cahn–Ingold–Prelog convention is inverted in this case)

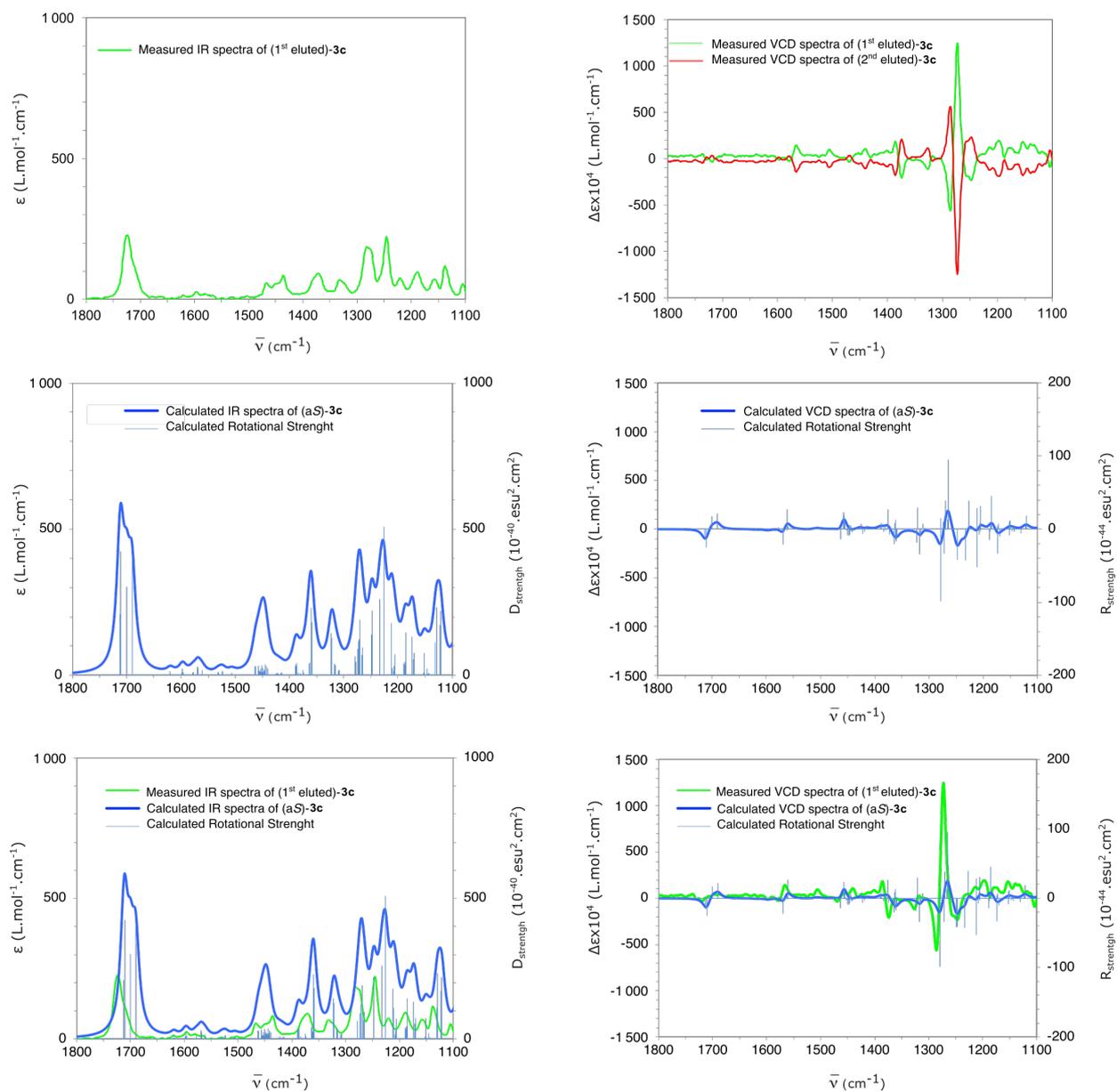


Figure S1. IR and VCD spectra measured in dichloromethane and calculated for (aS)-**3c** using SMD(CD₂Cl₂)/B3LYP/6-311+G(d,p)-MWB46 level.

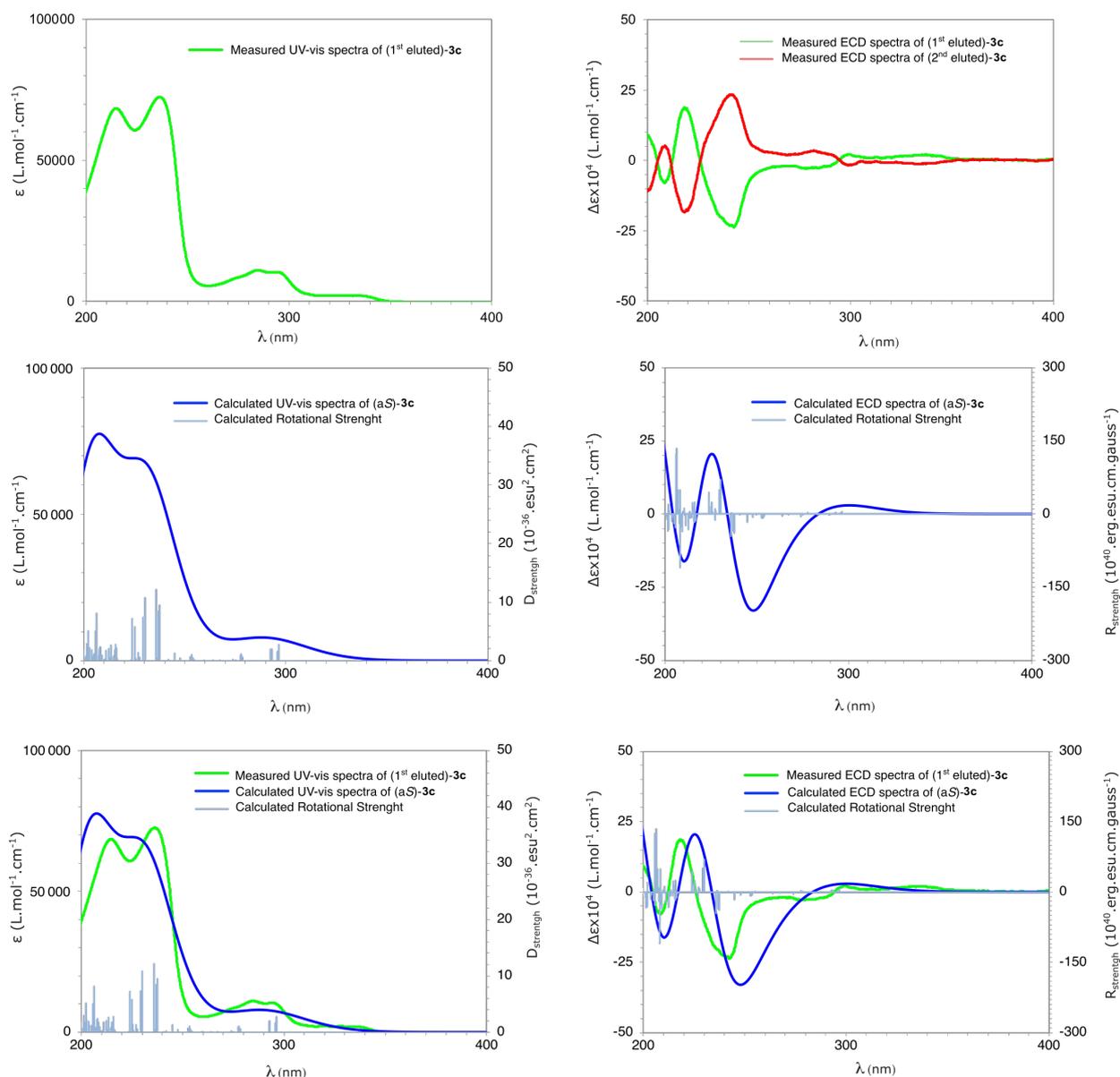
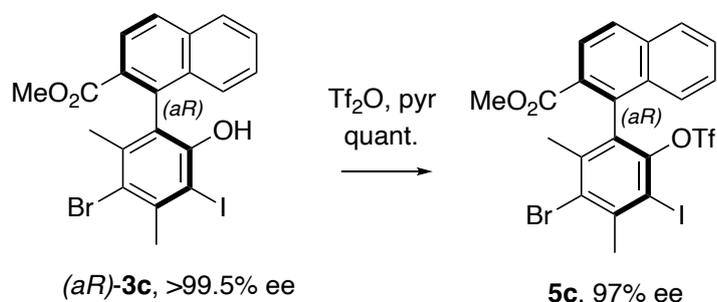
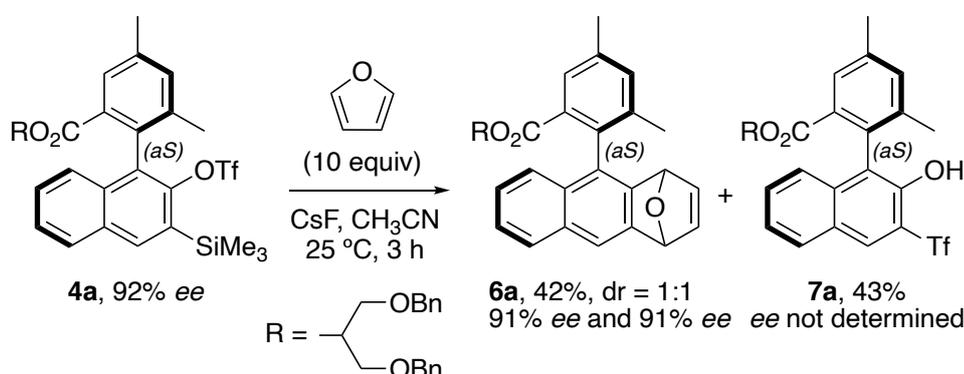


Figure S2. UV-vis and ECD spectra measured in acetonitrile and calculated for (*aS*)-**3c** using SMD(CH₃CN)/B3LYP/6-311+G(d,p)-MWB46 level.



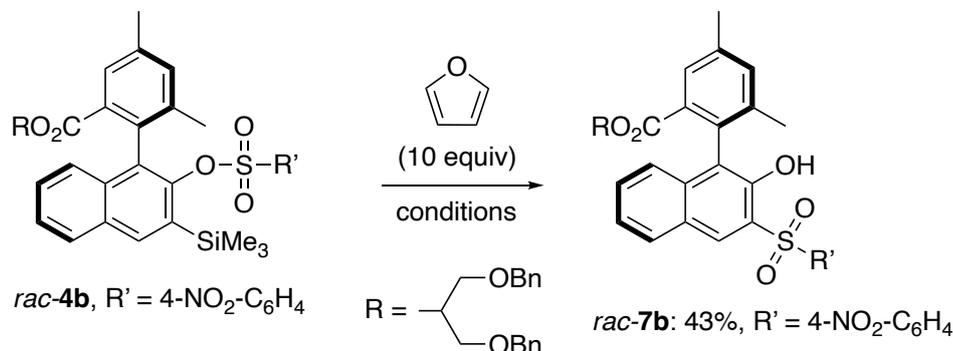
To a solution of (*aR*)-**3c** (120 mg, 0.23 mmol, >99.5% ee, (*aR*)-configured) in anhydrous dichloromethane (5 mL) was added pyridine (56 mg, 0.7 mmol) at 0 °C. To the resulting mixture was added Tf₂O (197 mg, 0.7 mmol) at this temperature and the reaction was monitored by TLC until the starting material is no longer detectable by TLC (1 h) whereupon a saturated aqueous NH₄Cl solution was added. The resulting mixture was extracted three times with EtOAc. The combined organic layers were dried over anhydrous Na₂SO₄, filtered,

After concentration, the residue was purified by flash column chromatography (pentane/EtOAc = 100:1) to afford the desired product (100 mg, 99%) as a colorless oil. **HRMS** (ESI+) m/z calcd for $C_{26}H_{30}O_4BrSiF_3$ $[M+H]^+$ 730.9792, found 730.9788; **1H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.7 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 8.7 Hz, 1H), 7.47 (ddd, J = 8.5, 6.9, 1.2 Hz, 1H), 7.39 (ddd, J = 8.9, 7.0, 1.4 Hz, 1H), 7.22 (dd, J = 8.5, 0.7 Hz, 1H), 4.60 (d, J = 13.1 Hz, 1H), 4.49 (d, J = 13.1 Hz, 1H), 2.99 (s, 3H), 2.02 (s, 3H), 0.89 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H); **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 148.1 (C), 143.9 (C), 141.2 (C), 138.0 (C), 133.0 (C), 131.9 (C), 131.6 (C), 129.8 (CH), 129.1 (C), 128.4 (CH), 127.4 (C), 126.8 (CH), 126.0 (CH), 125.6 (CH), 125.2 (CH), 118.1 (q, $^1J_{C-F}$ = 322.1 Hz, CF_3), 94.5 (C), 63.4 (CH_2), 32.5 (CH_3), 26.0 (3 CH_3), 22.9 (CH_3), 18.5 (C), -5.31 (CH_3), -5.34 (CH_3); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -71.84; **HPLC** Lux-Amylose-1 column, heptane/isopropanol = 99.9:0.1, 1 mL/min, 254 nm, retention time: t_{minor} = 4.01 min, t_{major} = 4.52 min, 94% ee; **Specific rotation** $[\alpha]_D^{25}$ = -14.32 (c = 1.0, $CHCl_3$).

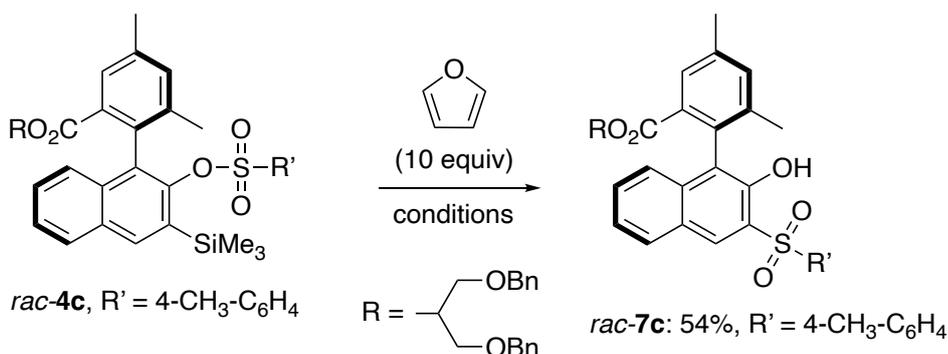


This procedure corresponds to Scheme 3a. The optimized procedure for the synthesis of **6a** is described below. A 10 mL round-bottom flask was charged at room temperature in this order with CsF (23 mg, 0.15 mmol), acetonitrile (1.0 mL), furan (39 μ L, 0.54 mmol) and the silylated aryne precursor **4a** (40 mg, 0.053 mmol, 92% ee). The reaction mixture was stirred at 25 °C for 3 h and poured in a separating funnel containing water (10 mL) and ethyl acetate (10 mL). The layers were separated, the aqueous layer was extracted twice with ethyl acetate and the combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4 , filtrated, and concentrated. The residue was purified by flash column chromatography on silica gel eluted with petroleum ether/ethyl acetate = 200:1 to afford in order the two diastereomers of **6a** (dr = 1:1 as determined by the 1H NMR analysis of the crude material, 13 mg, 42%, 91% ee for each diastereomer) as a colorless oil and the thia-Fries product **7a** (15.5 mg, 43%, 88% ee) as a colorless oil. Analytical samples of the two diastereomers of **6a** could be obtained by flash chromatography (pure fractions) facilitating the analyses. For **6a** (1st eluted diastereomer during the flash chromatography): colorless oil, **HRMS** (ESI+) m/z calcd for $C_{40}H_{40}NO_5$ $[M+NH_4]^+$ 614.2901, found 614.2901; **1H NMR** (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.0 Hz, 1H), 7.63 (s, 1H), 7.45 (s, 1H), 7.36–7.19 (m, 10H), 7.11–7.12 (m, 4H), 6.74 (dd, J = 5.6, 1.8 Hz, 1H), 6.67 (dd, J = 5.6, 1.8 Hz, 1H), 5.75–5.73 (m, 1H), 5.18–5.16 (m, 1H), 4.89 (p, J = 5.8 Hz, 1H), 4.30–4.15 (m, 4H), 3.08 (dd, J = 10.4, 4.8 Hz, 1H), 2.83 (dd, J = 10.3, 5.3 Hz, 1H), 2.73 (dd, J = 10.5, 6.1 Hz, 1H), 2.68 (dd, J = 10.2, 6.0 Hz, 1H), 2.46 (s, 3H), 1.95 (s, 3H); **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 167.6 (C), 143.5 (C), 142.4 (C), 141.8 (CH), 141.0 (CH), 138.2 (C), 138.2 (C), 138.2 (C), 137.8 (C), 134.6 (CH), 133.8 (C), 132.7 (C), 132.0 (C), 131.3 (C), 129.7 (C), 128.5 (CH), 128.5 (2CH), 128.4 (2CH), 128.4 (CH), 127.8 (CH), 127.7 (2CH), 127.7 (CH), 127.6 (2CH), 126.3 (CH), 125.9 (CH), 125.9 (CH), 118.0 (CH), 82.2 (CH), 81.2 (CH), 73.0 (CH_2), 73.0 (CH_2), 71.3 (CH), 68.3 (CH_2), 67.8 (CH_2), 21.2 (CH_3), 20.1 (CH_3); **HPLC** Chiralpak IE, heptane/ethanol = 80:20, 1 mL/min, 220 nm, t_{major} = 7.69 min, t_{minor} = 8.48 min, 91% ee; **Specific rotation**

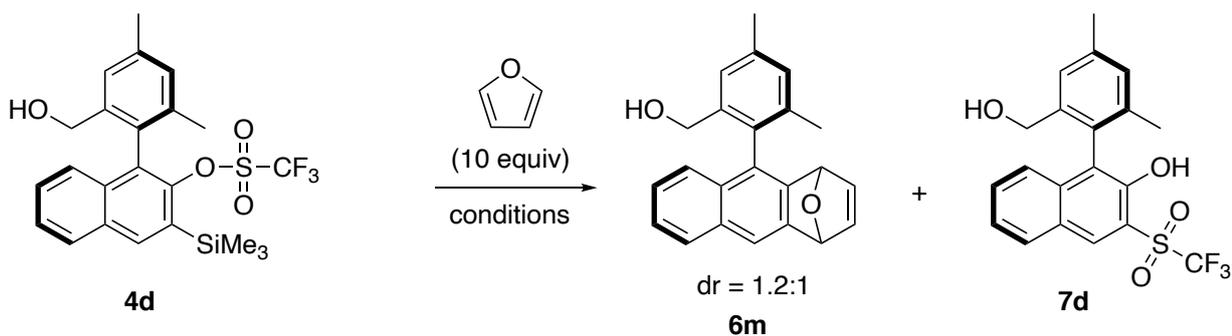
$[\alpha]_{\text{D}}^{25} = 5.2$ ($c = 1.0$, CHCl_3). For **6a** (2nd eluted diastereomer during the flash chromatography): colorless oil, **HRMS** (ESI+) m/z calcd for $\text{C}_{40}\text{H}_{40}\text{NO}_5^+$ $[\text{M}+\text{NH}_4]^+$ 614.2901, found 614.2904; **¹H NMR** (400 MHz, CDCl_3) δ 7.68 (s, 1H), 7.63 (d, $J = 8$ Hz, 1H), 7.41 (s, 1H), 7.36–7.07 (m, 14H), 6.95 (dd, $J = 5.6, 1.8$ Hz, 1H), 6.78 (dd, $J = 5.6, 1.8$ Hz, 1H), 5.68 (m, 1H), 5.37–5.28 (m, 1H), 5.04–4.98 (m, 1H), 4.28 (d, $J = 11.6$, 1H), 4.36 (d, $J = 11.6$, 1H), 4.14 (d, $J = 12.1$ Hz, 1H), 4.11 (d, $J = 12.1$ Hz, 1H), 3.10 (dd, $J = 7.8, 6$ Hz, 1H), 3.08 (dd, $J = 7.8, 6$ Hz, 1H), 2.93 (dd, $J = 10.4, 5.6$ Hz, 1H), 2.68 (dd, $J = 10.5, 6.1$ Hz, 1H), 2.43 (s, 3H), 1.71 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl_3) δ 167.6 (C), 143.4 (C), 143.1 (C), 142.4 (CH), 141.1 (CH), 138.5 (C), 138.4 (C), 138.3 (C), 137.8 (C), 134.3 (CH), 133.7 (C), 132.3 (C), 132.0 (C), 131.4 (C), 129.7 (C), 128.7 (CH), 128.4 (2 CH), 128.3 (2CH), 128.3 (CH), 127.6 (2CH), 127.6 (2CH), 127.5 (CH), 127.5 (CH), 126.3 (CH), 125.9 (CH), 125.9 (CH), 117.9 (CH), 82.1 (CH), 81.0 (CH), 73.0 (CH_2), 72.9 (CH_2), 71.7 (CH), 68.5 (CH_2), 68.3 (CH_2), 21.2 (CH_3), 20.4 (CH_3); **HPLC**: Chiralpak IE, heptane/ethanol = 80:20, 1 mL/min, 220 nm; $t_{\text{major}} = 10.58$ min, $t_{\text{minor}} = 9.66$ min, 91% ee; **Specific rotation** $[\alpha]_{\text{D}}^{25} = -5.4$ ($c = 1.0$, CHCl_3). For **7a**: **HRMS** (ESI+) m/z calcd for $\text{C}_{37}\text{H}_{37}\text{F}_3\text{NO}_7\text{S}^+$ $[\text{M}+\text{NH}_4]^+$ 696.2237, found 696.2238; **¹H NMR** (400 MHz, CDCl_3) δ 8.49 (s, 1H), 7.86 (m, 2H), 7.65 (s, 1H), 7.34–7.12 (m, 14H), 5.03 (p, $J = 5.2$ Hz, 1H), 4.38 (m, 2H), 4.26 (m, 2H), 3.30 (dd, $J = 10.5, 4.7$ Hz, 1H), 3.26 (dd, $J = 10.5, 5.7$ Hz, 1H), 3.18 (dd, $J = 10.4, 5.0$ Hz, 1H), 3.03 (dd, $J = 10.4, 5.6$ Hz, 1H), 2.47 (s, 3H), 1.90 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl_3) δ 166.4 (C), 149.0 (C), 138.7 (C), 138.6 (C), 138.3 (C), 138.0 (C), 138.0 (C), 135.3 (CH), 134.9 (CH), 131.7 (C), 131.4 (CH), 130.7 (C), 130.4 (CH), 129.6 (CH), 128.4 (2CH), 128.4 (2CH), 127.7 (2CH), 127.7 (2CH), 127.5 (2CH), 127.4 (C), 125.6 (C), 125.5 (CH), 124.8 (CH), 120.1 (q, $^1J_{\text{CF}} = 323.2$ Hz, CF_3), 115.9 (C), 73.1 (CH_2), 73.0 (CH_2), 71.7 (CH), 68.3 (CH_2), 68.2 (CH_2), 21.2 (CH_3), 19.8 (CH_3); **¹⁹F NMR** (376 MHz, CDCl_3) δ -78.4.



This procedure corresponds to Entry 11 in Table S1. Following the procedure described for the synthesis of **7a** with the silylated aryl precursor **4b** (40 mg, 0.050 mmol) for 24 h at 20 °C, and using petroleum ether/ethyl acetate = 10:1 for the purification, **7b** (15.6 mg, 43%) was obtained as a colorless oil. **¹H NMR** (400 MHz, CDCl_3) δ 8.24–8.19 (m, 2H), 7.81–7.73 (m, 5H), 7.43 (s, 1H), 7.34–7.19 (m, 8H), 7.15–7.09 (m, 4H), 7.02 (d, $J = 8.2$ Hz, 1H), 5.10 (s, 1H), 5.04 (p, $J = 5.5$ Hz, 1H), 4.34–4.21 (m, 2H), 4.21–4.10 (m, 1H), 3.23 (dd, $J = 10.6, 4.4$ Hz, 1H), 3.14 (dd, $J = 10.7, 5.7$ Hz, 1H), 2.99 (dd, $J = 10.3, 5.6$ Hz, 1H), 2.79 (dd, $J = 10.3, 5.8$ Hz, 1H), 2.49 (s, 3H), 1.96 (s, 3H), OH resonance not detected; **¹³C{¹H} NMR** (101 MHz, CDCl_3) δ 167.2 (C), 147.4 (C), 147.0 (C), 145.2 (C), 140.0 (C), 139.3 (C), 138.1 (C), 138.0 (C), 135.4 (CH), 133.8 (C), 133.4 (C), 130.6 (2CH), 130.0 (CH), 129.6 (C), 129.6 (CH), 129.0 (CH), 128.4 (2CH), 128.4 (2CH), 128.2 (C), 127.7 (CH), 127.7 (C), 127.6 (CH), 127.5 (2CH), 127.4 (2CH), 127.4 (CH), 124.2 (CH), 124.2 (CH), 123.5 (2CH), 121.2 (C), 73.2 (CH_2), 73.1 (CH_2), 71.8 (CH), 68.6 (CH_2), 68.0 (CH_2), 21.3 (CH_3), 20.0 (CH_3).

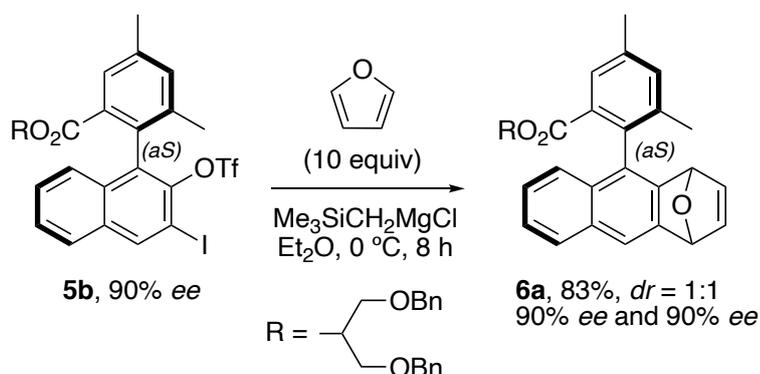


This procedure corresponds to Entry 12 in Table S1. Following the procedure described for the synthesis of **7a** with the silylated aryne precursor **4c** (35 mg, 0.045 mmol) for 72 h at 20 °C, and using petroleum ether/ethyl acetate = 10:1 for the purification, **7c** (17.1 mg, 54%) was obtained as a colorless oil. **HRMS** (ESI+) *m/z* calcd for C₄₃H₄₄O₇NS⁺ [M+NH₄]⁺ 718.2833, found 718.2834; **¹H NMR** (400 MHz, CDCl₃) δ 7.80 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.67 (s, 1H), 7.49 (d, *J* = 9.0 Hz, 1H), 7.43–7.35 (m, 3H), 7.32–7.20 (m, 10H), 7.19–7.13 (m, 3H), 7.05 (m, 2H), 4.99 (p, *J* = 5.4 Hz, 1H), 4.35 (s, 2H), 4.19 (s, 2H), 3.16 (dd, *J* = 10.4, 5.7 Hz, 1H), 3.12–3.05 (m, 2H), 2.83 (dd, *J* = 10.5, 5.7 Hz, 1H), 2.43 (s, 3H), 2.36 (s, 3H), 1.78 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 166.4 (C), 144.5 (C), 144.1 (C), 138.8 (C), 138.3 (C), 138.3 (C), 137.7 (C), 134.6 (CH), 134.1 (C), 133.3 (C), 131.8 (C), 131.8 (C), 131.8 (C), 131.5 (C), 130.4 (C), 129.4 (2CH), 129.1 (CH), 128.9 (CH), 128.4 (2CH), 128.3 (2CH), 128.2 (CH), 127.8 (2CH), 127.7 (2CH), 127.6 (CH), 127.6 (CH), 127.5 (CH), 126.9 (CH), 126.1 (CH), 126.0 (CH), 121.5 (CH), 73.1 (CH₂), 73.0 (CH₂), 71.6 (CH), 68.3 (CH₂), 68.3 (CH₂), 21.8 (CH₃), 21.2 (CH₃), 20.2 (CH₃).

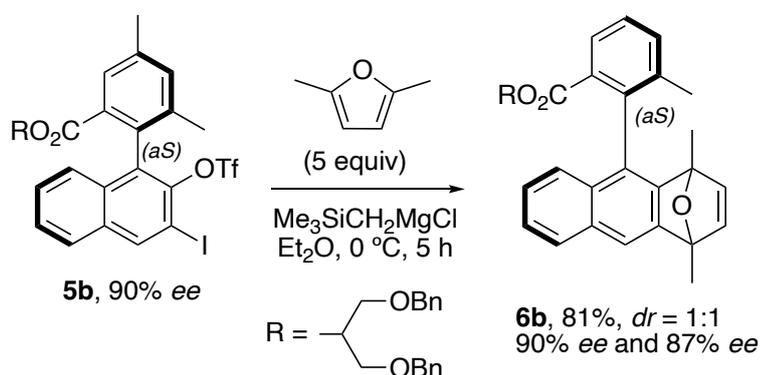


This procedure corresponds to Entry 13 in Table 1. Following the procedure described for the synthesis of **7a** with the silylated aryne precursor **4d** (32 mg, 0.066 mmol) for 12 h at 20 °C, and using petroleum ether/ethyl acetate = 10:1 for the purification, afforded in that order **6m** (8.0 mg, 37%, dr = 1.2:1) and **7d** (9.0 mg, 33%) as colorless oils. For **6m** (1.2:1 mixture of diastereomers): **HRMS** (ESI+) *m/z* calcd for C₂₃H₂₁O₂⁺ [M+H]⁺ 329.1536, found 329.1536; **¹H NMR** (400 MHz, CDCl₃) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.63 (broad s, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.35–7.28 (m, 4H), 7.26 (s, 1H), 7.22–7.10 (m, 4H), 7.04–6.98 (m, 2H), 6.90–6.84 (m, 2H), 5.85 (broad s, 2H), 5.37 (s, 1H), 5.31 (s, 1H), 4.29–4.18 (m, 2H), 4.13–4.01 (m, 2H), 2.45 (s, 6H), 1.95 (s, 3H), 1.76 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 143.7 (C), 143.7 (C), 143.5 (C), 143.5 (C), 142.1 (CH), 141.9 (CH), 141.2 (CH), 140.9 (CH), 139.6 (C), 139.3 (C), 138.0 (C), 137.9 (C), 137.2 (C), 137.2 (C), 132.3 (C), 132.3 (C), 132.2 (C), 132.2 (C), 130.9 (CH), 130.9 (C), 130.3 (CH), 130.0 (CH), 128.5 (CH), 128.5 (CH), 128.4 (C), 128.2 (C), 126.5 (CH), 126.5 (C), 126.4 (CH), 126.2 (CH), 126.2 (CH), 126.1 (CH), 125.3 (CH), 125.2 (CH), 118.3 (CH), 118.3 (CH), 82.2 (CH), 82.2 (CH), 81.0 (C), 81.0 (CH), 63.5 (CH₂), 63.5 (CH₂), 21.3 (CH₃), 21.3 (CH₃), 20.0 (CH₃), 19.9 (CH₃). For **7d**: **HRMS** (ESI+) *m/z* calcd for C₂₀H₂₁F₃O₄NS⁺ [M+NH₄]⁺ 428.1138, found 428.1134; **¹H NMR** (400 MHz, CDCl₃) δ 8.60 (s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.63 (broad s, 1H), 7.57–7.46 (m, 2H), 7.33 (s, 1H), 7.24–

7.16 (m, 2H), 4.2. (s, 2H), 2.45 (s, 3H), 1.85 (s, 3H), OH resonance not detected; $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 148.3 (C), 139.9 (C), 139.3 (C), 138.2 (C), 137.9 (C), 135.4 (CH), 131.9 (CH), 131.1 (CH), 130.4 (CH), 128.3 (C), 127.6 (C), 127.2 (CH), 126.0 (CH), 124.8 (CH), 124.1 (C), 120.19 (q, $^1J_{\text{C-F}} = 327.5$ Hz, CF_3), 116.9 (C), 63.9 (CH_2), 21.5 (CH_3), 19.7 (CH_3); ^{19}F NMR (376 MHz, CDCl_3) δ -78.0.

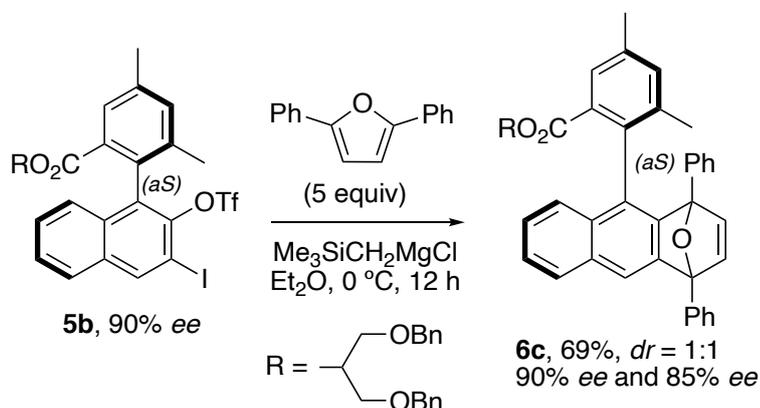


Representative optimized procedure for the synthesis of **6a** (corresponds to Scheme 3b): a round-bottom 25 mL flask was charged with the iodinated aryne precursor (aS)-**5b** (81 mg, 0.10 mmol, 90% *ee*), diethyl ether (2.0 mL) and furan (73 μL , 1.0 mmol), and the reaction mixture was placed at 0 °C. A solution of (trimethylsilylmethyl)magnesium chloride (1 M, Et_2O solution, 1.0 mL) was then added at 0 °C, and the resulting mixture was maintained at that temperature for 8 hours. Water (10 mL) and ethyl acetate (10 mL) were added and the layers were separated. The aqueous layer was extracted twice with EtOAc and the combined organic extract were washed with brine (10 mL), dried by Na_2SO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluted with petroleum ether/ethyl acetate = 200:1 to afford **6a** (*dr* = 1:1 as determined by the ^1H NMR analysis of the crude material, 50 mg, 83%, 90% *ee* for each diastereomer) as a colorless oil. The characterization data for the two diastereomers of **6a** are described above.



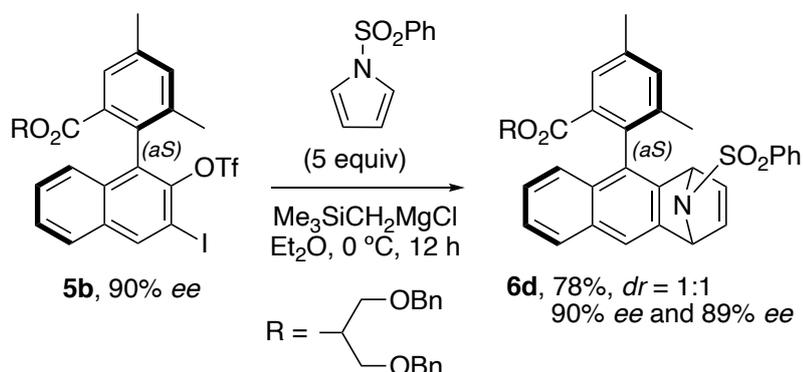
Following the representative optimized procedure for the synthesis of **6a** with **5b** (81 mg, 0.10 mmol, 90% *ee*) and 2,5-dimethylfuran (54 μL , 0.50 mmol) for 5 hours and using petroleum ether/ethyl acetate = 40:1 for the purification afforded the product **6b** (51 mg, 81%, *dr* = 1:1, 90% *ee* and 87% *ee*) as a colorless oil. For **6b** (1:1 mixture of diastereomers): **HRMS** (ESI+) *m/z* calcd for $\text{C}_{42}\text{H}_{44}\text{NO}_5^+$ $[\text{M}+\text{NH}_4]^+$ 642.3214, found 642.3214; **^1H NMR** (400 MHz, CDCl_3) δ 7.70 (broad s, 1H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.61 (d, *J* = 2.0 Hz, 1H), 7.54 (broad s, 1H), 7.34–7.04 (m, 30H), 6.69 (d, *J* = 2.8 Hz, 1H), 6.62 (d, *J* = 2.8 Hz, 1H), 6.52 (d, *J* = 2.8 Hz, 1H), 6.33 (d, *J* = 2.8 Hz, 1H), 4.99 (p, *J* = 5.6 Hz, 1H), 4.85–4.79 (m, 1H),

4.39–3.96 (m, 8H), 3.27 (dd, $J = 10.8, 7.6$ Hz, 1H), 3.06–2.99 (m, 2H), 2.88 (dd, $J = 10.8, 6.4$ Hz, 1H), 2.81 (dd, $J = 10.4, 6.4$ Hz, 1H), 2.63 (dd, $J = 10.0, 7.6$ Hz, 1H), 2.47 (dd, $J = 10.4, 6.4$ Hz, 1H), 2.41 (s, 3H), 2.41 (s, 3H), 2.34 (dd, $J = 10.0, 7.2$ Hz, 1H), 1.91 (s, 3H), 1.89 (s, 3H), 1.86 (s, 3H), 1.71 (s, 3H), 1.21 (s, 3H), 1.05 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3 , 1:1 mixture of diastereomers) δ 167.8 (C), 167.3 (C), 148.6 (C), 148.4 (C), 146.1 (CH), 146.0 (CH), 145.4 (CH), 145.0 (C), 144.7 (CH), 144.5 (C), 138.9 (C), 138.4 (C), 138.3 (C), 138.3 (C), 138.2 (C), 138.1 (C), 137.8 (C), 137.7 (C), 134.4 (CH), 134.0 (C), 134.0 (CH), 133.7 (C), 133.2 (C), 132.7 (C), 131.7 (C), 131.7 (C), 131.6 (C), 131.6 (C), 129.5 (C), 129.2 (C), 128.8 (CH), 128.5 (2CH), 128.5 (CH), 128.3 (2CH), 128.3 (2CH), 128.3 (2CH), 128.1 (CH), 128.1 (CH), 128.1 (CH), 127.7 (CH), 127.7 (2CH), 127.6 (2CH), 127.6 (2CH), 127.5 (2CH), 127.5 (CH), 127.5 (CH), 126.1 (CH), 126.1 (CH), 126.1 (CH), 125.9 (CH), 125.8 (CH), 125.7 (CH), 116.0 (CH), 115.6 (CH), 89.4 (C), 89.4 (C), 87.4 (C), 87.4 (C), 73.0 (CH_2), 73.0 (CH_2), 72.9 (CH_2), 72.9 (CH_2), 71.5 (CH), 71.4 (CH), 68.9 (CH_2), 68.6 (CH_2), 68.2 (CH_2), 67.3 (CH_2), 21.2 (CH_3), 21.2 (CH_3), 20.6 (CH_3), 20.2 (CH_3), 16.5 (CH_3), 15.7 (CH_3), 15.6 (CH_3), 15.4 (CH_3); **HPLC**: Chiralpak IE, heptane/ethanol = 95:5, 1 mL/min, 220 nm; t_{major} (dia 1) = 12.25 min, t_{minor} (dia 1) = 13.60 min; t_{major} (dia 2) = 15.71 min, t_{minor} (dia 2) = 17.98 min.

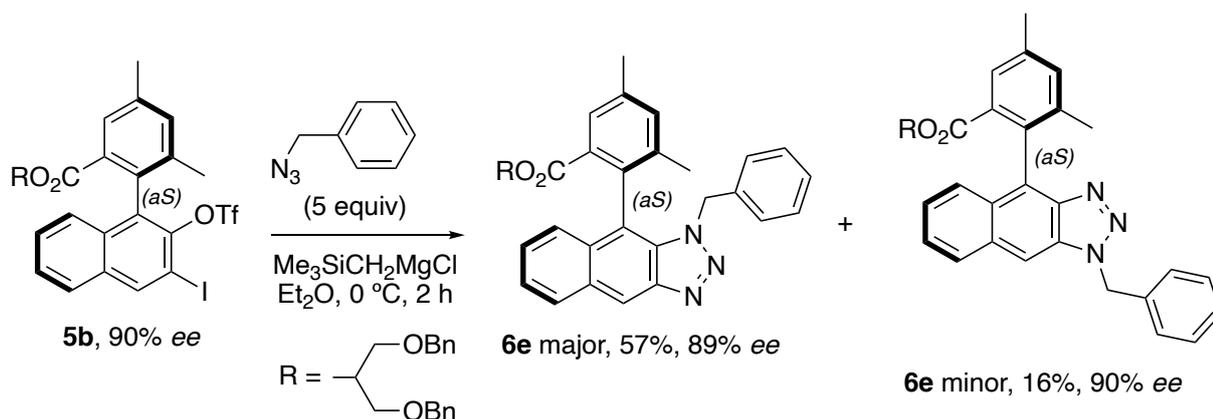


Following the representative optimized procedure for the synthesis of **6a** with **5b** (75 mg, 0.093 mmol, 90% *ee*) and 1,3-diphenylisobenzofuran (127 mg, 0.47 mmol) for 12 hours and using petroleum ether/ethyl acetate = 40:1 for the purification afforded the product **6c** (51 mg, 69%, *dr* = 1:1, 90% *ee* and 85% *ee*) as a colorless oil. For **6c** (1:1 mixture of diastereomers): **HRMS** (ESI+) m/z calcd for $\text{C}_{56}\text{H}_{50}\text{NO}_5^+$ $[\text{M}+\text{NH}_4]^+$ 816.3684, found 816.3684; ^1H NMR (400 MHz, CDCl_3) δ 8.12–8.06 (m, 1H), 8.02–7.95 (m, 1H), 7.76–7.63 (m, 8H), 7.63–7.42 (m, 8H), 7.40–7.02 (m, 40H), 7.00–6.93 (m, 3H), 6.69 (s, 1H), 4.84 (p, $J = 5.2$ Hz, 1H), 4.66–4.56 (m, 1H), 4.42–3.95 (m, 8H), 3.14–3.01 (m, 2H), 2.87 (dd, $J = 10.4, 4.8$ Hz, 1H), 2.79 (dd, $J = 10.4, 6.8$ Hz, 1H), 2.56–2.44 (m, 1H), 2.44 (s, 3H), 2.40 (s, 3H), 2.37–2.30 (m, 1H), 1.92–1.78 (m, 2H), 1.67 (s, 3H), 1.40 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 167.5 (C), 165.6 (C), 150.4 (C), 149.9 (C), 149.0 (C), 148.8 (C), 146.0 (C), 146.0 (C), 143.3 (C), 142.6 (C), 138.5 (C), 138.4 (C), 138.4 (C), 138.3 (C), 138.3 (C), 138.2 (C), 137.6 (C), 137.4 (C), 135.7 (C), 135.5 (C), 135.5 (C), 135.5 (C), 134.4 (CH), 134.3 (C), 134.2 (CH), 133.5 (C), 132.4 (C), 132.4 (C), 132.3 (C), 132.2 (C), 131.8 (C), 131.7 (C), 131.4 (C), 130.8 (C), 129.9 (CH), 128.9 (2CH), 128.8 (2CH), 128.7 (CH), 128.4 (2CH), 128.4 (CH), 128.3 (2CH), 128.3 (2CH), 128.2 (2CH), 128.2 (2CH), 127.6 (CH), 127.6 (2CH), 127.5 (2CH), 127.5 (CH), 127.5 (2CH), 127.5 (CH), 127.4 (2CH), 127.4 (CH), 127.4 (2CH), 127.2 (2CH), 126.9 (CH), 126.8 (2CH), 126.7 (2CH), 126.6 (CH), 126.5 (2CH), 126.4 (CH), 126.3 (CH), 126.2 (2CH), 126.2 (CH), 126.2 (CH), 126.2 (2CH), 126.0 (2CH), 125.8 (CH), 121.8 (CH), 121.0 (CH), 120.4 (CH), 120.1 (CH), 117.9 (CH), 117.6 (CH), 90.7 (C), 90.5 (C), 88.8 (C), 88.7 (C), 72.9 (CH_2), 72.9 (CH_2), 72.8 (CH_2), 72.7 (CH_2), 70.9 (CH), 70.7 (CH), 68.6 (CH_2), 68.4 (CH_2), 68.0 (CH_2), 66.6 (CH_2), 21.1 (CH_3), 21.0 (CH_3), 20.5 (CH_3), 20.2 (CH_3), 2

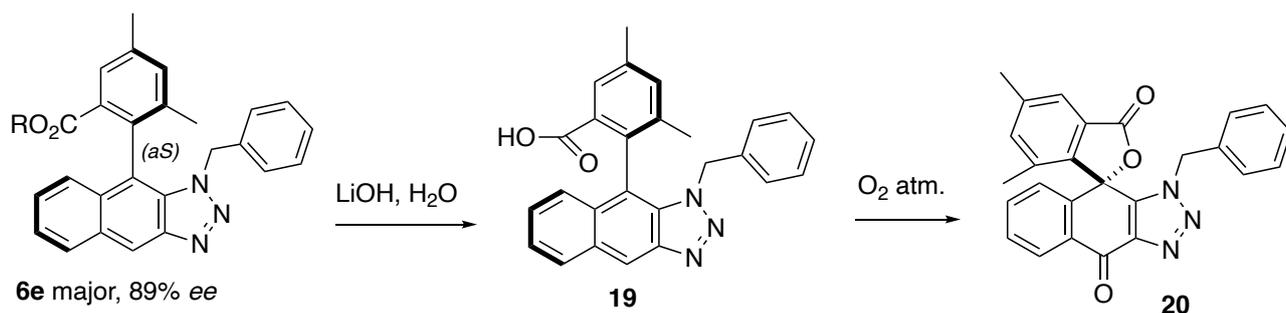
aromatic CH resonances could not be detected (overlap with other signals); **HPLC**: Chiralpak IE, heptane/ethanol = 80:20, 1 mL/min, 220 nm, $t_{\text{major}}(\text{dia1}) = 5.51$ min, $t_{\text{minor}}(\text{dia1}) = 5.95$ min, $t_{\text{major}}(\text{dia2}) = 6.47$ min, $t_{\text{minor}}(\text{dia2}) = 6.97$ min.



Following the representative optimized procedure for the synthesis of **6a** with **5b** (81 mg, 0.10 mmol, 90% *ee*) and 1-(phenylsulfonyl)-1*H*-pyrrole (104 mg, 0.50 mmol) for 3 hours and using petroleum ether/ethyl acetate = 10:1 for the purification afforded the product **6d** (58 mg, 78%, *dr* = 1:1, 90% *ee* and 89% *ee*) as a light purple oil. For **6d** (1:1 mixture of diastereomers): **HRMS** (ESI+) *m/z* calcd for $\text{C}_{46}\text{H}_{45}\text{N}_2\text{O}_6\text{S}^+$ $[\text{M}+\text{NH}_4]^+$ 753.2993, found 753.2994; **¹H NMR** (400 MHz, CDCl_3) δ 7.76–7.52 (m, 8H), 7.50–7.02 (m, 36H), 6.42 (dd, *J* = 6.4, 2.0 Hz, 1H), 6.25 (dd, *J* = 6.4, 2.0 Hz, 1H), 6.22 (dd, *J* = 6.4, 2.0 Hz, 1H), 6.12 (dd, *J* = 6.4, 2.0 Hz, 1H), 5.54 (s, 1H), 5.49 (s, 1H), 5.10 (s, 1H), 4.96 (p, *J* = 5.2 Hz, 1H), 4.92 (s, 1H), 5.78 (p, *J* = 5.2 Hz, 1H), 4.25 (dd, *J* = 22.4, 12.4 Hz, 2H), 4.20–4.04 (m, 6H), 3.17 (dd, *J* = 10.4, 4.4 Hz, 1H), 3.09 (dd, *J* = 10.4, 4.4 Hz, 1H), 2.96 (dd, *J* = 10.4, 4.8 Hz, 1H), 2.79 (dd, *J* = 10.4, 6.8 Hz, 1H), 2.72–2.54 (m, 4H), 2.42 (s, 6H), 1.90 (s, 3H), 1.67 (s, 3H); **¹³C NMR** (101 MHz, CDCl_3) δ 167.5 (C), 167.3 (C), 142.0 (C), 141.8 (C), 141.1 (C), 140.8 (C), 140.6 (CH), 140.0 (C), 139.8 (CH), 139.6 (C), 139.2 (CH), 139.0 (CH), 138.7 (C), 138.6 (C), 138.5 (C), 138.1 (C), 138.0 (C), 138.0 (C), 138.0 (C), 137.9 (C), 134.9 (CH), 134.3 (CH), 133.2 (C), 133.1 (C), 132.8 (CH), 132.8 (CH), 132.5 (C), 132.4 (C), 131.7 (C), 131.6 (C), 131.1 (C), 131.0 (C), 130.3 (C), 123.1 (C), 129.2 (2CH), 129.1 (2CH), 129.1 (CH), 128.6 (CH), 128.4 (CH), 128.4 (2CH), 128.4 (2CH), 128.3 (CH), 128.3 (2CH), 128.3 (2CH), 128.1 (2CH), 128.1 (2CH), 128.0 (CH), 127.7 (CH), 127.7 (CH), 127.7 (2CH), 127.6 (CH), 127.6 (2CH), 127.5 (2CH), 127.4 (2CH), 126.6 (CH), 126.5 (CH), 126.2 (CH), 126.2 (CH), 126.1 (CH), 125.9 (CH), 118.5 (CH), 118.4 (CH), 73.0 (CH_2), 72.9 (CH_2), 72.9 (CH_2), 71.7 (CH_2), 71.2 (CH), 71.2 (CH), 68.7 (CH_2), 68.2 (CH_2), 68.0 (CH_2), 68.0 (CH), 67.7 (CH_2), 67.7 (CH), 66.6 (CH), 66.6 (CH), 21.2 (CH_3), 21.2 (CH_3), 20.3 (CH_3), 20.2 (CH_3). **HPLC**: Chiralpak ID, heptane/ethanol = 60:40, 1 mL/min, 254 nm, $t_{\text{major}} \text{ dia1} = 10.03$ min, $t_{\text{minor}} \text{ dia1} = 12.4$ min; $t_{\text{major}} \text{ dia2} = 14.21$ min, $t_{\text{minor}} \text{ dia2} = 8.81$ min.



Following the representative optimized procedure for the synthesis of **6a** with **5b** (77 mg, 0.096 mmol, 90% ee) and benzyl azide (64 mg, 0.48 mmol) for 2 hours and using petroleum ether/ethyl acetate = 10:1 to 5:1 for the purification afforded in this order the two regioisomers **6e** minor (10 mg, 16%, 90% ee) and **6e** major (36 mg, 57%, 89% ee) as colorless oils. For **6e** minor: **HRMS** (ESI+) m/z calcd for $C_{43}H_{40}N_3O_4^+$ $[M+H]^+$ 662.3013, found 662.3013; **1H NMR** (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.83 (d, J = 8.6 Hz, 1H), 7.69 (s, 1H), 7.53 (d, J = 8.7 Hz, 1H), 7.42–7.19 (m, 14 H), 7.15–7.09 (m, 4H), 5.89 (d, J = 15.6 Hz, 1H), 5.78 (d, J = 15.6 Hz, 1H), 4.81 (p, J = 5.4 Hz, 1H), 4.16 (broad s, 2H), 4.09 (broad s, 2 H), 2.99 (dd, J = 10.6, 4.7 Hz, 1H), 2.88 (dd, J = 10.6, 5.5 Hz, 1H), 2.80 (dd, J = 10.3, 5.4 Hz, 1H), 2.63 (dd, J = 10.3, 5.4 Hz, 1H), 2.50 (s, 3H), 1.83 (s, 3H); **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 166.5 (C), 144.2 (C), 138.5 (C), 138.2 (C), 138.1 (C), 138.1 (C), 135.1 (C), 135.1 (CH), 133.0 (C), 132.5 (C), 131.7 (C), 131.1 (C), 130.2 (C), 129.3 (CH), 129.0 (2CH), 128.7 (C), 128.4 (CH), 128.3 (2CH), 128.3 (CH), 128.2 (2CH), 127.6 (2CH), 127.4 (CH), 127.4 (CH), 127.4 (2CH), 126.3 (CH), 126.2 (CH), 124.6 (CH), 104.4 (CH), 72.9 (CH₂), 72.8 (CH₂), 71.2 (CH), 68.2 (CH₂), 67.8 (CH₂), 52.1 (CH₂), 21.1 (CH₃), 20.3 (CH₃); **HPLC** Chiralpak IA, heptane/ethanol = 80:20, 1 mL/min, 254 nm, t_{major} = 7.56 min, t_{minor} = 18.13 min; **Specific rotation** $[\alpha]_D^{25}$ = -51.3 (c = 1.0, $CHCl_3$). For **6e** major: **HRMS** (ESI+) m/z calcd for $C_{43}H_{40}N_3O_4^+$ $[M+H]^+$ 662.3013, found 662.3013; **1H NMR** (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.74 (s, 1H), 7.27–6.97 (m, 17H), 6.52 (s, 1H), 6.50 (s, 1H), 5.57 (d, J = 16.1 Hz, 1H), 5.04 (d, J = 16.1 Hz, 1H), 4.78–4.74 (m, 1H), 4.12 (d, J = 12 Hz, 1H), 4.11 (d, J = 12 Hz, 1H), 3.92 (broad s, 2H), 2.85 (dd, J = 10.5, 4.3 Hz, 1H), 2.54 (dd, J = 10.3, 5.1 Hz, 1H), 2.49 (dd, J = 10.5, 6.2 Hz, 1H), 2.37 (s, 3H), 2.37 (dd, J = 10.5, 6.2 Hz, 1H), 1.09 (s, 3H); **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 166.6 (C), 145.3 (C), 139.9 (C), 138.6 (C), 137.8 (C), 136.2 (C), 135.0 (CH), 132.7 (C), 131.3 (C), 131.2 (C), 130.6 (C), 129.9 (C), 129.4 (CH), 128.9 (C), 128.9 (CH), 128.2 (2CH), 128.2 (2CH), 128.0 (2CH), 127.7 (CH), 127.6 (2CH), 127.6 (CH), 127.5 (CH), 127.4 (2CH), 126.6 (2CH), 126.5 (CH), 124.9 (CH), 124.4 (CH), 118.4 (C), 117.0 (CH), 72.8 (CH₂), 72.7 (CH₂), 71.5 (CH), 67.9 (CH₂), 67.7 (CH₂), 52.5 (CH₂), 21.1 (CH₃), 19.6 (CH₃); **HPLC**: Chiralpak ID, heptane/ethanol = 80:20, 1 mL/min, 220 nm, t_{major} = 17.36 min, t_{minor} = 15.52 min; **Specific rotation** $[\alpha]_D^{25}$ = -21.6 (c = 1.0, $CHCl_3$).



To a THF solution (3 mL) of the major regioisomer of **6e** (89% ee, 30 mg, 0.045 mmol) was added a solution of LiOH (22 mg in 1 mL). The reaction was stirred vigorously and heated at 60 °C for 4 days. To the cooled reaction mixture was added 1N HCl (10 mL) and the aqueous layer was extracted twice with EtOAc. The combined organic phases were washed with brine and dried over anhydrous Na_2SO_4 , and solvents were evaporated in vacuum. The resulting crude material was purified by flash chromatography to give the pure carboxylic acid (**19**, 16 mg, 87%) as a white solid. **1H NMR** (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.84 (s, 1H), 7.35 (dd, J = 7.2, 7.2 Hz, 1H), 7.26–7.20 (m, 1H), 7.15 (s, 1H), 7.12 (d, J = 6.0 Hz, 1H), 7.26 (dd, J = 7.2, 7.2 Hz, 1H), 7.01–6.91 (m, 2H), 6.49 (d, J = 7.6 Hz, 2H), 5.58 (d, J = 16.0 Hz, 1 H), 5.21 (d, J = 16.0 Hz, 1 H), 4.96 (broad s, 1H), 2.48 (s, 3H), 1.21 (s, 3H); **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$) δ 170.5 (C), 145.3 (C), 140.2 (C), 138.7

(C), 136.2 (C), 135.6 (CH), 132.3 (C), 131.6 (C), 131.3 (C), 130.9 (C), 129.8 (C), 129.7 (CH), 129.4 (CH), 128.2 (2CH), 127.8 (CH), 126.7 (CH), 126.5 (2CH), 124.8 (CH), 124.5 (CH), 118.3 (C), 117.2 (CH), 52.6 (CH₂), 21.2 (CH₃), 19.7 (CH₃). Recrystallization of this material from chloroform/hexane 3:1 (very slow evaporation in air) afforded a mixture of crystalline solids, including some colorless prisms suitable for single-crystal X-ray diffraction analyses, which revealed the existence of, at least, two polymorphs of **20**, an aerobic oxidation product (Figure S3, Table S2), confirming the regioselectivity in **6e**. Some resolution of the enantiomers seemingly occurred during crystallization. CCDC 1997613 contains the supplementary crystallographic information for one polymorph of **20**. It can be obtained free of charge from the Cambridge Crystallographic Data Centre.

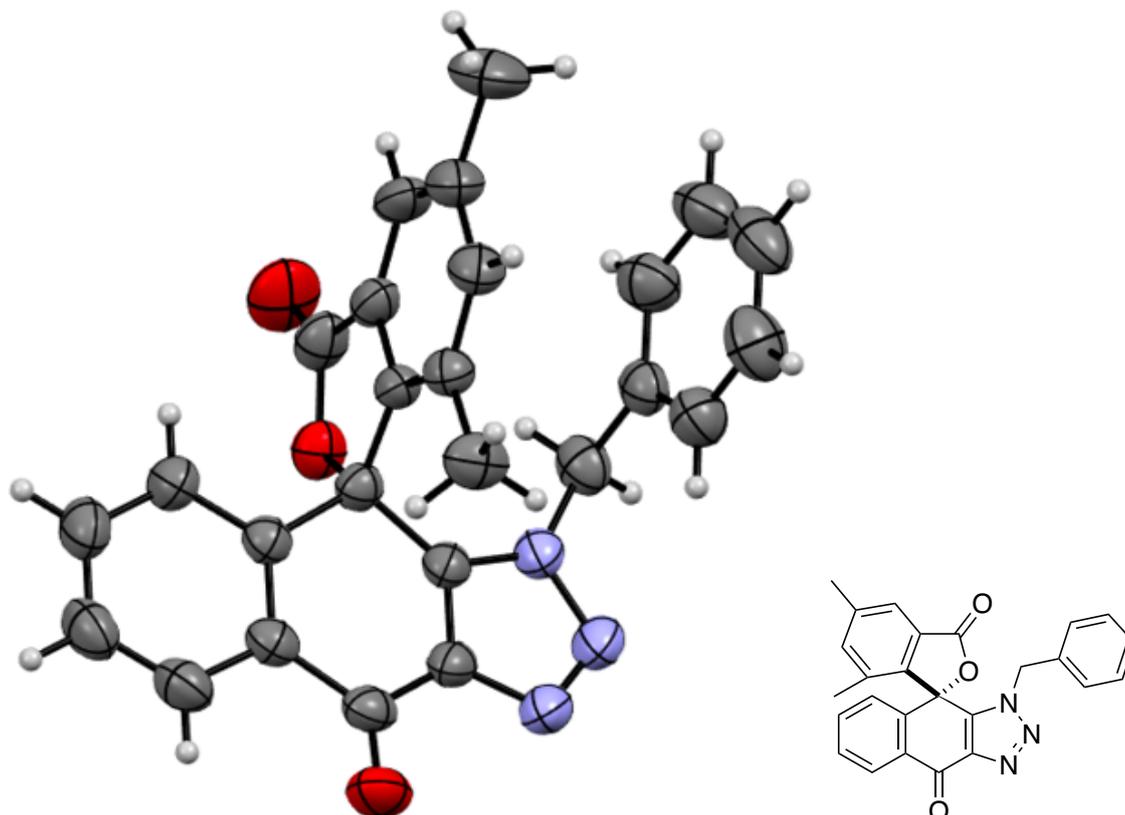
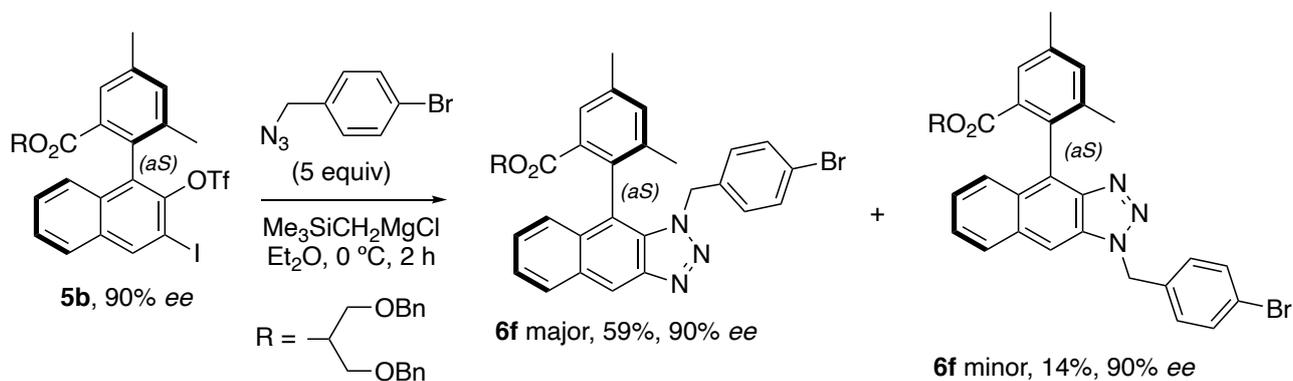


Figure S3. ORTEP representation of **20** obtained by single-crystal X-ray diffraction analysis. The ellipsoids are drawn at the 50% probability level and H atoms are represented as fixed-size spheres of 0.15 Å radius

Table S2. Crystal data and structure refinement for CCDC 1997613

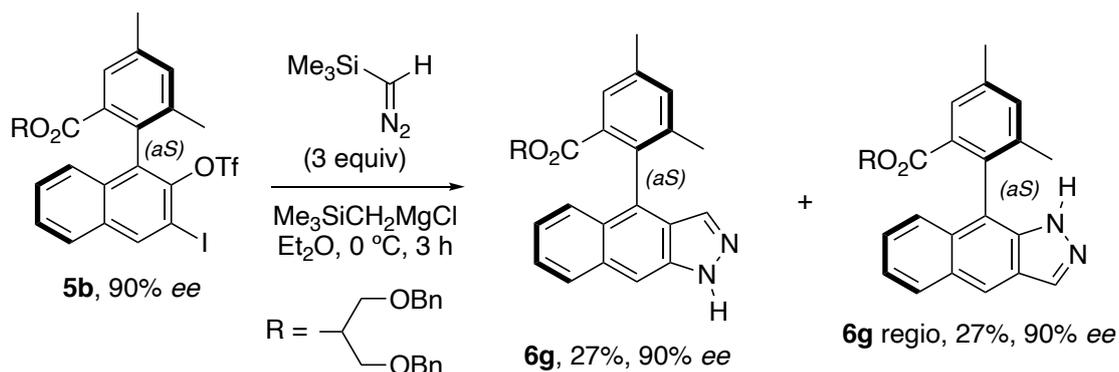
Empirical formula	C ₂₆ H ₁₉ N ₃ O ₃
Formula weight	421.44
Temperature/K	293
Crystal system	monoclinic
Space group	P2 ₁ /c
a/Å	11.34720(10)
b/Å	12.24780(10)
c/Å	15.79970(10)
α/°	90
β/°	106.2480(10)
γ/°	90

Volume/Å ³	2108.11(3)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.328
μ/mm^{-1}	0.717
F(000)	880.0
Crystal size/mm ³	0.38 × 0.16 × 0.1
Radiation	CuK α (λ = 1.54184)
2 θ range for data collection/°	8.116 to 141.856
Index ranges	-13 ≤ h ≤ 13, -15 ≤ k ≤ 14, -19 ≤ l ≤ 19
Reflections collected	59899
Independent reflections	4060 [R_{int} = 0.0271, R_{sigma} = 0.0085]
Data/restraints/parameters	4060/0/291
Goodness-of-fit on F ²	1.031
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0382, wR_2 = 0.1053
Final R indexes [all data]	R_1 = 0.0405, wR_2 = 0.1079
Largest diff. peak/hole / e Å ⁻³	0.16/-0.15

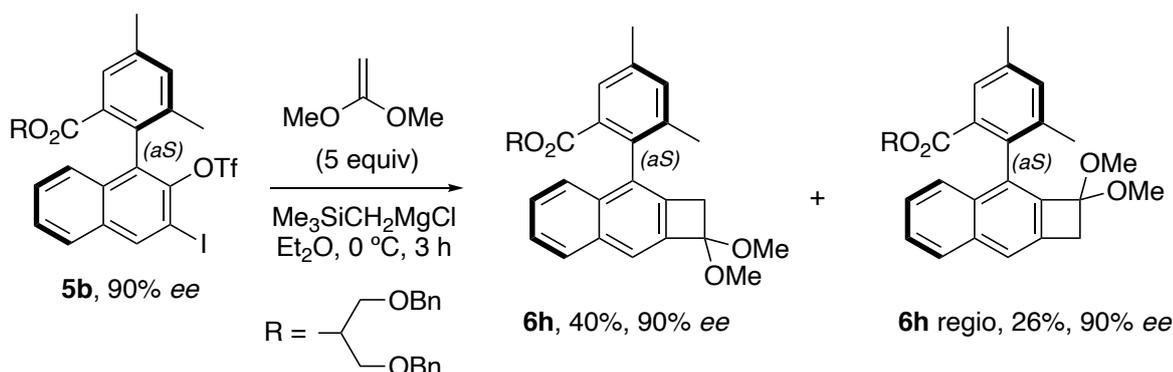


Following the representative optimized procedure for the synthesis of **6a** with **5b** (77 mg, 0.096 mmol, 90% ee) and 4-bromobenzyl azide (102 mg, 0.48 mmol) for 2 hours and using petroleum ether/ethyl acetate = 10:1 to 5:1 for the purification afforded, in this order, the two regioisomers **6f major** (42 mg, 59%, 89% ee) and **6f minor** (10 mg, 14%, 90% ee) as colorless oils. The regioselectivity in **6f** was attributed as in **6e** on the basis of the analogy of the chemical transformations and the NMR spectra of the products. For **6f major**: **HRMS** (ESI+) m/z calcd for $\text{C}_{43}\text{H}_{39}\text{BrN}_3\text{O}_4^+$ [$\text{M}+\text{H}$]⁺ 742.2108, found 742.2104; **¹H NMR** (400 MHz, CDCl_3) δ 8.54 (s, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.74 (s, 1H), 7.30–7.08 (m, 13H), 7.02–6.97 (m, 3H), 6.39 (s, 1H), 6.37 (s, 1H), 5.46 (d, J = 16.2 Hz, 1H), 5.00 (d, J = 16.2 Hz, 1H), 4.77 (p, J = 5.5 Hz, 1H), 4.15 (d, J = 12.1 Hz, 1H), 4.08 (d, J = 12.0 Hz, 1H), 3.93 (s, 2H), 2.89 (dd, J = 10.5, 4.2 Hz, 1H), 2.57 (dd, J = 10.3, 5.0 Hz, 1H), 2.51 (dd, J = 10.5, 6.3 Hz, 1H), 2.45–2.41 (m, 4H), 1.16 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl_3) δ 166.5 (C), 144.1 (C), 140.0 (C), 138.7 (C), 137.7 (C), 137.7 (C), 135.2 (C), 135.0 (CH), 132.7 (C), 131.3 (C), 131.2 (C), 131.1 (2CH), 130.6 (C), 129.4 (C), 129.4 (CH), 129.0 (CH), 128.3 (2CH), 128.2 (2CH), 128.2 (2CH), 127.6 (2CH), 127.5 (CH), 127.4 (CH), 127.3 (2CH), 126.7 (CH), 125.0 (CH), 124.4 (CH), 121.6 (C), 118.1 (C), 117.1 (CH), 72.9 (CH₂), 72.7 (CH₂), 71.5 (CH), 68.0 (CH₂), 67.7 (CH₂), 51.9 (CH₂), 21.1 (CH₃), 19.7 (CH₃); **HPLC** Chiralpak IA, heptane/ethanol = 80:20, 1 mL/min, 220 nm, t_{major} = 8.61 min, t_{minor} = 16.65 min; **Specific rotation** $[\alpha]_{\text{D}}^{25}$ = 99.3 (c = 1.0, CHCl_3). For **6f minor**: **HRMS** (ESI+) m/z calcd for $\text{C}_{43}\text{H}_{39}\text{BrN}_3\text{O}_4^+$ [$\text{M}+\text{H}$]⁺ 742.2108, found 742.2107; **¹H NMR** (400 MHz, CDCl_3) δ 7.89 (s, 1H), 7.85 (d, J = 8.6 Hz, 1H), 7.66 (s, 1H), 7.54 (d, J = 8.7 Hz, 1H), 7.49–7.38 (m, 4H), 7.34–7.25 (m, 5H), 7.24–7.06 (m, 8H), 5.82 (d, J = 15.8 Hz, 1H), 5.69 (d, J = 15.8 Hz, 1H), 4.81 (p, J = 5.4 Hz, 1H), 4.17 (s, 2H), 4.11

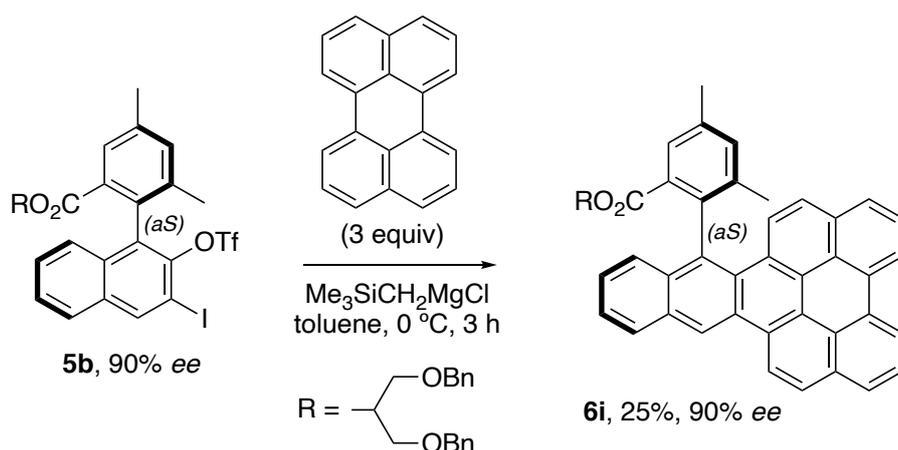
(s, 2H), 3.03 (dd, $J = 10.6, 5.5$ Hz, 1H), 2.92 (dd, $J = 10.6, 5.5$ Hz, 1H), 2.83 (dd, $J = 10.3, 5.4$ Hz, 1H), 2.68 (dd, $J = 10.3, 5.4$ Hz, 1H), 2.50 (m, 3H), 1.82 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 166.6 (C), 144.3 (C), 138.6 (C), 138.4 (C), 138.2 (C), 138.2 (C), 135.2 (CH), 134.3 (C), 133.2 (C), 132.6 (C), 132.3 (2CH), 131.8 (C), 131.1 (C), 130.6 (C), 129.6 (CH), 129.5 (CH), 129.4 (2CH), 128.9 (C), 128.4 (CH), 128.4 (2CH), 128.4 (2CH), 128.3 (CH), 128.3 (CH), 127.6 (CH), 127.5 (2CH), 126.5 (2CH), 124.9 (CH), 122.6 (C), 104.3 (CH), 73.00 (CH₂), 73.00 (CH₂), 71.4 (CH), 68.3 (CH₂), 67.9 (CH₂), 51.5 (CH₂), 21.3 (CH₃), 20.5 (CH₃); **HPLC**: Chiralpak IB, heptane/ethanol = 80:20, 1 mL/min, 230 nm, $t_{\text{major}} = 6.88$ min, $t_{\text{minor}} = 8.10$ min; **Specific rotation** $[\alpha]_{\text{D}}^{25} = 53.4$ ($c = 1.0, \text{CHCl}_3$).



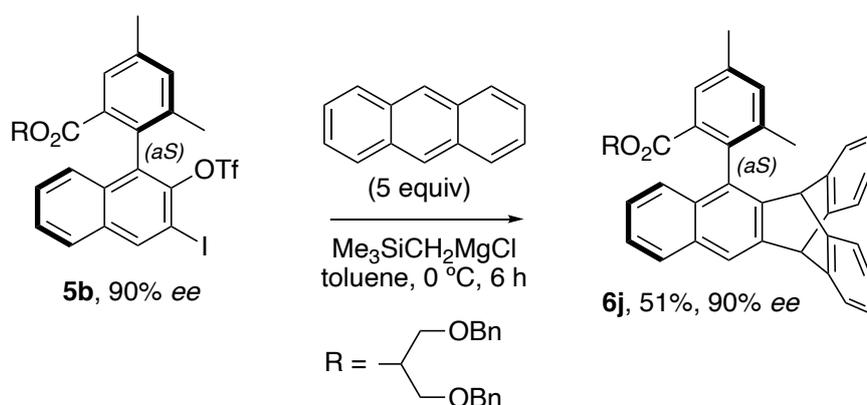
Following the representative optimized procedure for the synthesis of **6a** with **5b** (100 mg, 0.124 mmol, 90% *ee*) and trimethylsilyldiazomethane (2.0M in Et_2O , 0.19 mL, 0.38 mmol) for 3 hours and using petroleum ether/ethyl acetate = 3:1 for the purification afforded, in this order, the two regioisomers **6g** (19 mg, 27%, 90% *ee*) and **6g regio** (19 mg, 27%, 90% *ee*) as colorless oils. For **6g**: **HRMS** (ESI+) m/z calcd for $\text{C}_{37}\text{H}_{35}\text{N}_2\text{O}_4^+$ $[\text{M}+\text{H}]^+$ 571.2591, found 571.2591; ^1H NMR (400 MHz, CDCl_3) δ 9.71 (brs, 1H), 7.86 (d, $J = 8.5$ Hz, 1H), 7.77 (s, 1H), 7.74 (s, 1H), 7.72 (s, 1H), 7.44 (d, $J = 8.8$ Hz, 1H), 7.39–7.23 (m, 7H), 7.36 (s, 1H), 7.19–7.04 (m, 5H), 4.78 (p, $J = 5.3$ Hz, 1H), 4.14 (dd, $J = 16.8, 12.4$ Hz, 2H), 4.06 (dd, $J = 16.8, 12.4$ Hz, 2H), 2.77 (dd, $J = 10.4, 5.1$ Hz, 2H), 2.64 (dd, $J = 10.3, 5.6$ Hz, 1H), 2.56 (dd, $J = 10.4, 5.7$ Hz, 1H), 2.48 (s, 3H), 1.79 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 167.0 (C), 138.3 (C), 138.2 (C), 138.1 (C), 137.9 (C), 135.3 (C), 134.6 (CH), 134.0 (C), 133.1 (C), 132.2 (C), 131.1 (C), 128.9 (CH), 128.4 (CH), 128.3 (2CH), 128.2 (2CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.5 (CH), 127.4 (2CH), 127.4 (2CH), 127.2 (C), 126.3 (CH), 125.7 (CH), 123.6 (CH), 103.8 (CH), 72.8 (CH₂), 72.8 (CH₂), 71.3 (CH), 67.9 (CH₂), 67.8 (CH₂), 21.1 (CH₃), 20.00 (CH₃); **HPLC** Chiralpak IG, heptane/ethanol = 80:20, 1 mL/min, 230 nm, $t_{\text{major}} = 11.21$ min, $t_{\text{minor}} = 9.61$ min; **Specific rotation** $[\alpha]_{\text{D}}^{25} = -32.3$ ($c = 1.0, \text{CHCl}_3$). For **6g regio**: **HRMS** (ESI+) m/z calcd for $\text{C}_{37}\text{H}_{35}\text{N}_2\text{O}_4^+$ $[\text{M}+\text{H}]^+$ 571.2591, found 571.2592; ^1H NMR (400 MHz, CDCl_3) δ 9.47 (s, 1H), 8.15 (s, 2H), 7.88 (d, $J = 8.1$ Hz, 1H), 7.71 (s, 1H), 7.35 (s, 1H), 7.27 (d, $J = 8.9$ Hz, 1H), 7.26–7.16 (m, 8H), 7.07 (d, $J = 7.7$ Hz, 2H), 7.02 (d, $J = 7.7$ Hz, 2H), 4.75 (p, $J = 5.4$ Hz, 1H), 4.09 (s, 2H), 4.00 (d, $J = 12.2$ Hz, 1H), 3.96 (d, $J = 12.2$ Hz, 1H), 2.79 (dd, $J = 10.4, 4.7$ Hz, 1H), 2.61–2.51 (m, 2H), 2.43 (s, 3H), 2.42 (dd, $J = 10.4, 4.7$ Hz, 1H), 1.74 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 167.2 (C), 139.1 (C), 138.6 (C), 138.2 (C), 138.1 (C), 137.9 (C), 135.7 (CH), 135.0 (CH), 133.1 (C), 131.7 (C), 130.9 (C), 129.5 (CH), 129.4 (C), 129.4 (CH), 128.4 (2CH), 128.4 (2CH), 127.6 (2CH), 127.6 (CH), 127.6 (CH), 127.6 (2CH), 126.2 (CH), 124.7 (CH), 123.8 (C), 123.4 (CH), 118.9 (CH), 116.5 (C), 73.0 (CH₂), 73.0 (CH₂), 71.5 (CH), 68.1 (CH₂), 67.9 (CH₂), 21.3 (CH₃), 19.9 (CH₃); **HPLC** Chiralpak IH, heptane/ethanol = 80:20, 1 mL/min, 230 nm, $t_{\text{major}} = 8.15$ min, $t_{\text{minor}} = 5.98$ min; **Specific rotation** $[\alpha]_{\text{D}}^{25} = -8.4$ ($c = 1.0, \text{CHCl}_3$).



Following the representative optimized procedure for the synthesis of **6a** with **5b** (82 mg, 0.10 mmol, 90% *ee*) and 1,1-dimethoxyethene (50 μL , 0.53 mmol) for 3 hours and using petroleum ether/ethyl acetate = 20:1 to 10:1 for the purification afforded, in this order, **6h** (25 mg, 40%, 90% *ee*) and **6h regio** (16 mg, 26%, 90% *ee*) as colorless oils. For **6h**: **HRMS** (ESI+) *m/z* calcd for $\text{C}_{40}\text{H}_{44}\text{O}_6\text{N}^+$ $[\text{M}+\text{NH}_4]^+$ 634.3163, found 634.3165; **^1H NMR** (400 MHz, CDCl_3) δ 7.81 (d, $J = 8.1$ Hz, 1H), 7.68 (s, 1H), 7.66 (s, 1H), 7.39–7.17 (m, 12H), 7.12 (m, 2H), 4.98 (p, $J = 5.7$ Hz, 1H), 4.32 (s, 2H), 4.14 (d, $J = 12.1$ Hz, 1H), 4.11 (d, $J = 12.1$ Hz, 1H), 3.48 (s, 3H), 3.42 (s, 3H), 3.29 (d, $J = 14.6$ Hz, 1H), 3.19 (d, $J = 14.6$ Hz, 1H), 3.04 (dd, $J = 10.4, 5.9$ Hz, 1H), 2.97 (m, 1H), 2.93 (m, 1H), 2.58 (dd, $J = 10.4, 6.0$ Hz, 1H), 2.45 (s, 3H), 1.92 (s, 3H); **$^{13}\text{C}\{^1\text{H}\}$ NMR** (101 MHz, CDCl_3) δ 167.7 (C), 142.9 (C), 138.4 (C), 138.3 (C), 138.2 (C), 137.7 (C), 136.9 (C), 134.4 (C), 134.3 (CH), 133.7 (C), 133.2 (C), 133.2 (C), 132.4 (C), 129.2 (CH), 128.7 (CH), 128.4 (2CH), 128.3 (2CH), 127.6 (2CH), 127.6 (2CH), 127.5 (CH), 127.5 (CH), 126.1 (CH), 125.5 (CH), 125.0 (CH), 119.0 (CH), 105.4 (C), 73.0 (CH₂), 72.9 (CH₂), 71.4 (CH), 68.3 (CH₂), 68.2 (CH₂), 51.4 (CH₃), 51.3 (CH₃), 42.5 (CH₂), 21.2 (CH₃), 20.3 (CH₃); **HPLC**: (S,S)-Whelk-O1, heptane/ethanol = 95:5, 1 mL/min, 254 nm, $t_{\text{major}} = 10.87$ min, $t_{\text{minor}} = 11.98$ min; **Specific rotation** $[\alpha]_{\text{D}}^{25} = 3.8$ ($c = 1.0$, CHCl_3). For **6h regio**: **HRMS** (ESI+) *m/z* calcd for $\text{C}_{40}\text{H}_{44}\text{O}_6\text{N}^+$ $[\text{M}+\text{NH}_4]^+$ 634.3163, found 634.3165; **^1H NMR** (400 MHz, CDCl_3) δ 7.77–7.73 (m, 2H), 7.49 (s, 1H), 7.40–7.12 (m, 14H), 4.95 (p, $J = 6.0$ Hz, 1H), 4.32 (s, 2H), 4.15 (d, $J = 12.1$ Hz, 1H), 4.10 (d, $J = 12.2$ Hz, 1H), 3.41 (d, $J = 15.2$ Hz, 1H), 3.30 (d, $J = 15.2$ Hz, 1H), 3.07 (dd, $J = 5.1, 1.9$ Hz, 1H), 3.05 (dd, $J = 5.1, 2.2$ Hz, 1H), 3.00 (s, 3H), 2.99 (s, 3H), 2.80 (dd, $J = 10.2, 6.3$ Hz, 1H), 2.62 (dd, $J = 10.5, 6.1$ Hz, 1H), 2.42 (s, 3H), 1.97 (s, 3H); **$^{13}\text{C}\{^1\text{H}\}$ NMR** (101 MHz, CDCl_3) δ 167.2 (C), 142.7 (C), 138.8 (C), 138.4 (C), 138.4 (C), 138.1 (C), 137.6 (C), 135.3 (C), 134.7 (C), 134.5 (CH), 132.8 (C), 132.3 (C), 131.6 (C), 129.0 (CH), 128.4 (2CH), 128.3 (2CH), 128.2 (CH), 127.6 (CH), 127.6 (2CH), 127.6 (2CH), 127.5 (CH), 126.8 (CH), 125.6 (CH), 125.2 (CH), 121.1 (CH), 106.3 (C), 73.0 (CH₂), 73.0 (CH₂), 71.4 (CH), 68.5 (CH₂), 67.9 (CH₂), 51.1 (CH₃), 51.0 (CH₃), 42.5 (CH₂), 21.2 (CH₃), 20.5 (CH₃); **HPLC** (S,S)-Whelk-O1, heptane/ethanol = 95:5, 1 mL/min, 254 nm, $t_{\text{major}} = 13.65$ min, $t_{\text{minor}} = 15.08$ min; **Specific rotation** $[\alpha]_{\text{D}}^{25} = -59.5$ ($c = 1.0$, CHCl_3).

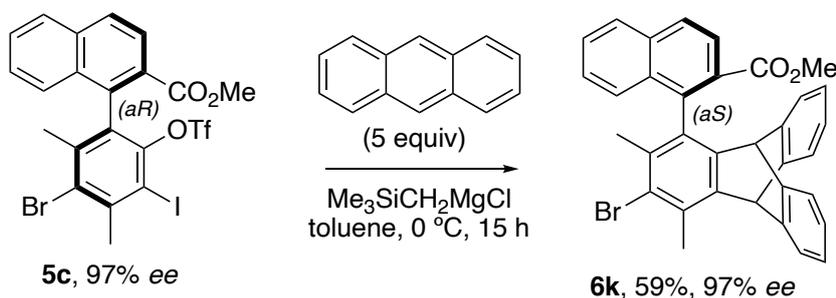


Following the representative optimized procedure for the synthesis of **6a** with **5b** (81 mg, 0.10 mmol, 90% *ee*) and perylene (76 mg, 0.30 mmol), using toluene (2.0 mL) in place of diethyl ether to solubilize all substrates prior the addition of the Grignard reagent, for 3 hours and using petroleum ether/ethyl acetate = 40:1 for the purification afforded the product **6i** (20 mg, 25%, 90% *ee*) as a yellow oil. **HRMS** (ESI+) *m/z* calcd for $\text{C}_{56}\text{H}_{46}\text{O}_4\text{N}^+$ $[\text{M}+\text{NH}_4]^+$ 796.3421, found 796.3421; **¹H NMR** (400 MHz, CDCl_3) δ 9.58 (s, 1H), 9.12 (d, *J* = 9.2 Hz, 1H), 8.76 (dd, *J* = 11.2, 7.6 Hz, 2H), 8.26–8.17 (m, 3H), 8.10 (d, *J* = 7.6 Hz, 1H), 8.01 (s, 1H), 7.91–7.84 (m, 2H), 7.83–7.76 (m, 1H), 7.60–7.52 (m, 2H), 7.46–7.35 (m, 3H), 7.21–7.12 (m, 3H), 7.04–6.87 (m, 5H), 6.68–6.61 (m, 2H), 4.75 (p, *J* = 5.6 Hz, 1H), 3.84 (d, *J* = 12.4 Hz, 1H), 3.79 (d, *J* = 12.4 Hz, 1H), 3.63 (broad s, 2H), 2.81 (dd, *J* = 10.8, 4.4 Hz, 1H), 2.62 (s, 3H), 2.48 (dd, *J* = 10.4, 6.4 Hz, 1H), 2.36–2.28 (m, 2H), 1.55 (s, 3H); **¹³C NMR** (101 MHz, CDCl_3) δ 167.4 (C), 139.9 (C), 138.1 (C), 138.1 (C), 137.9 (C), 137.9 (C), 136.0 (C), 135.9 (CH), 133.1 (C), 132.7 (C), 132.5 (C), 131.3 (C), 131.3 (C), 131.2 (C), 131.2 (C), 131.2 (C), 131.1 (C), 131.1 (C), 131.1 (C), 129.9 (CH), 128.5 (CH), 128.2 (2CH), 128.1 (CH), 128.0 (2CH), 127.4 (CH), 127.4 (C), 127.3 (2CH), 127.2 (CH), 127.2 (CH), 127.1 (2CH), 126.9 (CH), 126.8 (CH), 126.6 (CH), 126.4 (CH), 126.4 (CH), 126.3 (C), 126.3 (CH), 125.8 (CH), 125.8 (CH), 125.5 (C), 124.3 (C), 122.9 (CH), 122.5 (CH), 120.8 (CH), 120.4 (CH), 72.7 (CH₂), 72.7 (CH₂), 71.6 (CH), 68.4 (CH₂), 67.6 (CH₂), 21.4 (CH₃), 20.2 (CH₃); **HPLC**: Chiralpak IF, heptane/ethanol = 80:20, 1 mL/min, 230 nm, *t*_{major} = 8.99 min, *t*_{minor} = 11.12 min; **Specific rotation** $[\alpha]_{\text{D}}^{25} = 69.4$ (*c* = 1.0, CHCl_3).



Following the representative optimized procedure for the synthesis of **6a** with **5b** (80 mg, 0.10 mmol, 90% *ee*) and anthracene (89 mg, 0.50 mmol) for 6 hours and using petroleum ether/ethyl acetate = 40:1 for the purification afforded the product **6j** (36 mg, 51%, 90% *ee*) as a colorless oil. **HRMS** (ESI+) *m/z* calcd for $\text{C}_{50}\text{H}_{46}\text{O}_4\text{N}^+$ $[\text{M}+\text{NH}_4]^+$ 724.3421, found 724.3422; **¹H NMR** (400 MHz, CDCl_3) δ 7.81 (broad s, 1H), 7.62–7.57 (m, 2H), 7.39–7.34 (m, 3H), 7.31–7.19 (m, 7H), 7.19–7.02 (m, 8H), 6.99–6.85 (m, 4H), 5.46 (s, 1H), 4.88 (s,

1H), 4.62–4.53 (m, 1H), 4.00 (d, $J = 12.2$ Hz, 1H), 3.98 (d, $J = 12.2$ Hz, 1H), 3.96 (d, $J = 12.0$ Hz, 1H), 3.84 (d, $J = 12.0$ Hz, 1H), 2.78 (dd, $J = 10.6, 4.0$ Hz, 1H), 2.53 (s, 3H), 2.01 (dd, $J = 10.6, 6.9$ Hz, 1H), 1.79 (dd, $J = 10.1, 5.3$ Hz, 1H), 1.74 (dd, $J = 10.1, 7.8$ Hz, 1H), 1.63 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 167.5 (C), 145.0 (C), 144.7 (C), 144.5 (C), 144.4 (C), 141.7 (C), 138.8 (C), 138.8 (C), 138.4 (C), 138.4 (C), 137.8 (C), 134.7 (C), 134.6 (CH), 132.7 (C), 132.6 (C), 131.4 (C), 131.2 (C), 129.2 (CH), 128.3 (2CH), 128.3 (2CH), 127.6 (CH), 127.5 (CH), 127.5 (2CH), 127.5 (2CH), 127.2 (CH), 126.1 (CH), 125.8 (CH), 125.7 (CH), 125.6 (CH), 125.6 (CH), 125.5 (CH), 125.5 (CH), 124.6 (CH), 123.9 (CH), 123.7 (CH), 123.6 (CH), 121.0 (CH), 72.8 (CH_2), 72.6 (CH_2), 70.7 (CH), 68.7 (CH_2), 66.8 (CH_2), 54.2 (CH), 51.1 (CH), 21.3 (CH_3), 20.4 (CH_3); **HPLC** Chiralpak IF, heptane/ethanol = 80:20, 1 mL/min, 254 nm, $t_{\text{major}} = 5.50$ min, $t_{\text{minor}} = 7.49$ min; **Specific rotation** $[\alpha]_{\text{D}}^{25} = 21.5$ ($c = 1.0$, CHCl_3).



A round bottom flask containing the arylene precursor **5c** (64 mg, 0.1 mmol, 97.5% *ee*) was charged with 3 mL of anhydrous toluene. The toluene was evaporated by rotary evaporation and the step was repeated twice to remove all of moisture. Then the flask was charged with 0.5 mL of Et_2O and anthracene (89 mg, 0.5 mmol) under an argon atmosphere. The suspension was cooled down to 0 °C and trimethylsilylmagnesium chloride (1 M in Et_2O , 1.0 mmol) was added slowly at this temperature. After stirring overnight at 0 °C, the reaction mixture was quenched with water. The mixture was extracted three times with EtOAc and the combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (pentane/ $\text{EtOAc} = 20:1$) to afford **6k** (32 mg, 59%) as a white solid; **Mp** 271–273 °C (CDCl_3); HRMS (ESI+) m/z calcd for $\text{C}_{34}\text{H}_{26}\text{O}_2\text{Br}^+$ $[\text{M}+\text{H}]^+$ 547.1096, found 547.1094; ^1H NMR (300 MHz, CDCl_3) δ 8.11 (d, $J = 8.7$ Hz, 1H), 8.06 (d, $J = 8.8$ Hz, 1H), 8.01 (d, $J = 8.3$ Hz, 1H), 7.60 (ddd, $J = 8.5, 7.0, 1.2$ Hz, 1H), 7.40–7.36 (m, 2H), 7.25 (ddd, $J = 9.5, 7.2, 1.3$ Hz, 1H), 7.07 (dd, $J = 8.7, 0.8$ Hz, 1H), 7.03–6.88 (m, 4H), 6.78 (ddd, 8.4, 6.8, 1.2 Hz, 1H), 6.49 (d, 7.3 Hz, 1H), 5.77 (s, 1H), 4.55 (s, 1H), 3.10 (s, 3H), 2.75 (s, 3H), 1.89 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ 168.0 (C), 145.3 (C), 145.1 (C), 145.1 (C), 145.0 (C), 142.9 (C), 142.5 (C), 139.1 (C), 135.1 (C), 133.3 (C), 132.9 (C), 132.3 (C), 131.4 (C), 128.8 (C), 128.3 (CH), 128.1 (CH), 128.1 (CH), 127.7 (CH), 127.1 (CH), 125.9 (CH), 125.1 (2CH), 125.1 (2CH), 124.9 (C), 123.9 (2CH), 123.6 (CH), 123.5 (CH), 52.0 (CH), 51.8 (CH_3), 51.8 (CH), 21.7 (CH_3), 20.0 (CH_3); **HPLC** (S,S)-Whelk-O1 column, heptane/isopropanol = 95:5, 1 mL/min, 220 nm, retention time: $t_{\text{minor}} = 9.97$ min, $t_{\text{major}} = 11.67$ min, 97.5% *ee*; **Specific rotation** $[\alpha]_{\text{D}}^{25} = -22.9$ ($c = 1.0$, CHCl_3). Recrystallization of **6k** (97.5% *ee*) from *d*-chloroform (slow evaporation in air) afforded crystalline needles suitable for single-crystal X-ray diffraction analysis, which confirmed both the structure and the absolute configuration in **6k** (Figure S4, Table S3). CCDC 2019279 contains the supplementary crystallographic information for this compound. It can be obtained free of charge from the Cambridge Crystallographic Data Centre.

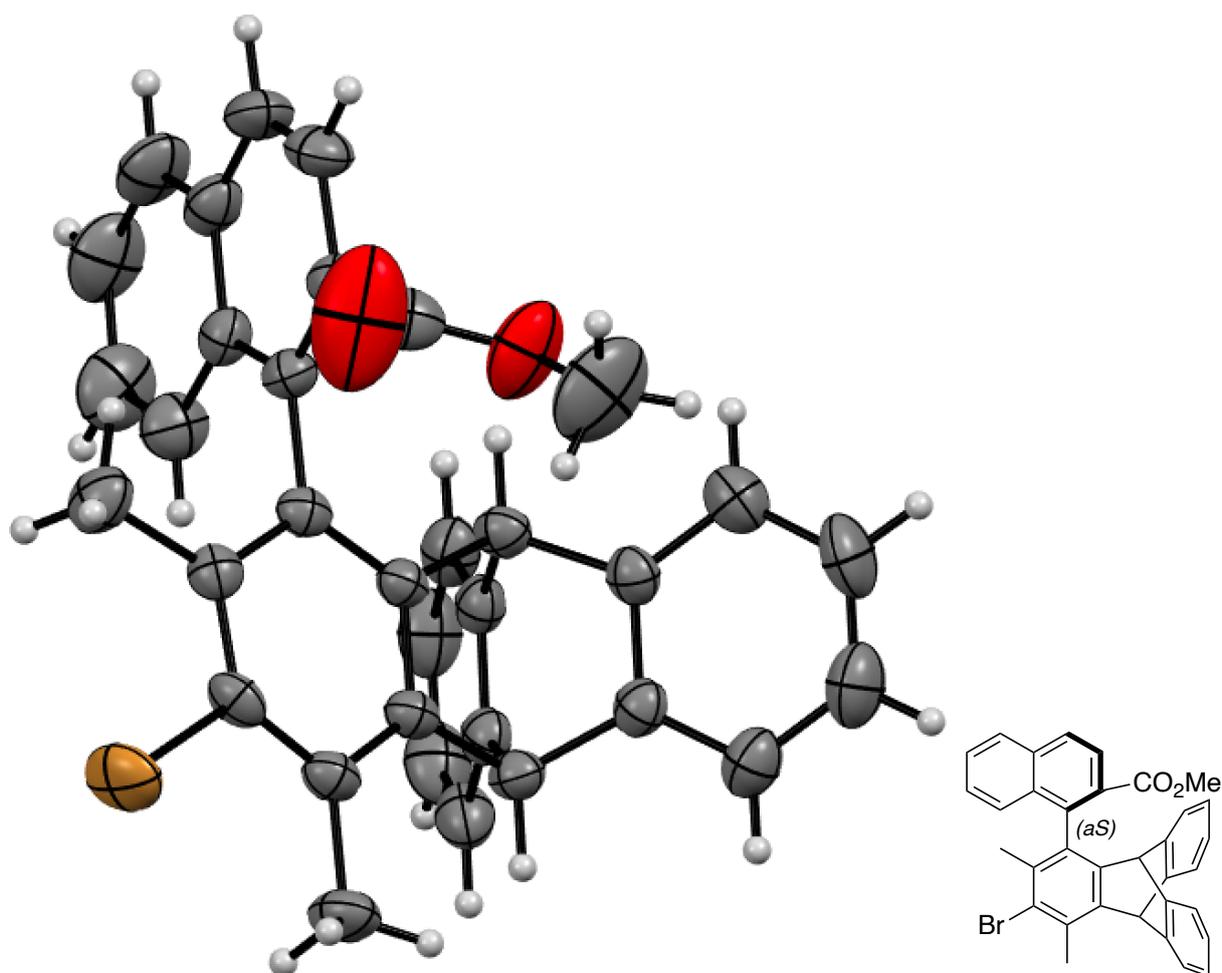
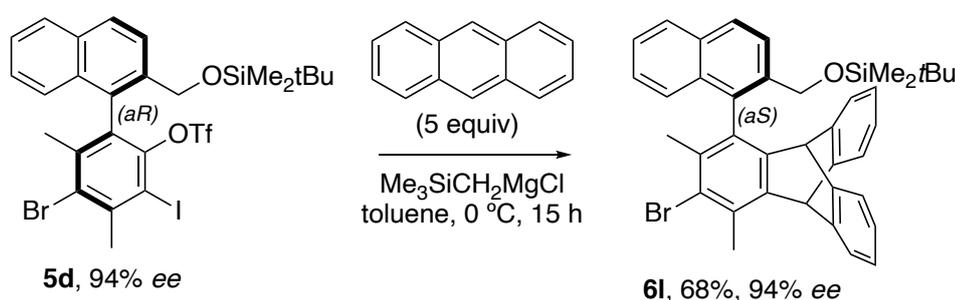


Figure S4. ORTEP representation of **6k** obtained by single-crystal X-ray diffraction analysis. The ellipsoids are drawn at the 50% probability level and H atoms are represented as fixed-size spheres of 0.15 Å radius. These measurements allowed the unambiguous determination of the absolute configuration in **6k** to be (*aS*) as depicted.

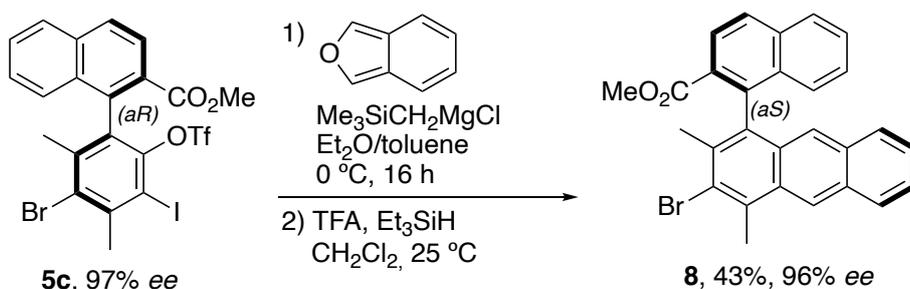
Table S3. Crystal data and structure refinement for CCDC 2019279

Empirical formula	C ₃₄ H ₂₅ BrO ₂
Formula weight	545.45
Temperature/K	295
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
<i>a</i> /Å	9.19570(10)
<i>b</i> /Å	15.9140(2)
<i>c</i> /Å	17.6662(2)
α /°	90
β /°	90
γ /°	90
Volume/Å ³	2585.28(6)
<i>Z</i>	4
ρ_{calc} /cm ³	1.401
μ /mm ⁻¹	2.395
<i>F</i> (000)	1120.0
Crystal size/mm ³	0.14 × 0.03 × 0.01

Radiation	CuK α (λ = 1.54184)
2 θ range for data collection/ $^\circ$	7.476 to 142.026
Index ranges	-10 \leq h \leq 11, -19 \leq k \leq 19, -21 \leq l \leq 21
Reflections collected	28374
Independent reflections	4945 [R_{int} = 0.0456, R_{sigma} = 0.0307]
Data/restraints/parameters	4945/0/338
Goodness-of-fit on F^2	1.043
Final R indexes [$ I > 2\sigma(I)$]	R_1 = 0.0379, wR_2 = 0.0971
Final R indexes [all data]	R_1 = 0.0438, wR_2 = 0.1014
Largest diff. peak/hole / e \AA^{-3}	0.35/-0.36
Flack parameter	-0.02(2)



A round bottom flask containing the arylene precursor **5d** (92 mg, 0.13 mmol, 94% ee) was charged with 3 mL of anhydrous toluene. The toluene was evaporated by rotary evaporation and the step was repeated twice to remove all moisture. Then the flask was charged with 0.5 mL of Et₂O and anthracene (112 mg, 0.63 mmol) under an argon atmosphere. The suspension was cooled down to 0 °C and trimethylsilylmagnesium chloride (1 M in Et₂O, 1.3 mmol) was added slowly at this temperature. After stirring overnight at 0 °C, the mixture was quenched with water. The mixture was extracted three times with EtOAc and the combined organic layer was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (pentane/EtOAc = 100:1) to afford the **6l** (54 mg, 68%) as a colorless oil; **HRMS** (ESI+) m/z calcd for C₃₉H₄₃NOSiBr⁺ [M+NH₄]⁺ 650.2279, found 650.2280; **¹H NMR** (400 MHz, CDCl₃) δ 8.06 (d, J = 8.6 Hz, 1H), 7.98 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 8.6 Hz, 1H), 7.49 (ddd, J = 8.8, 7.0, 1.0 Hz, 1H), 7.41 (dd, J = 7.8 Hz, 1H), 7.20 (ddd, J = 8.9, 7.1, 1.1 Hz, 1H), 7.05 (dd, J = 7.2 Hz, 1H), 7.02–6.92 (m, 3H), 6.9 (d, J = 8.6 Hz, 1H), 6.81 (ddd, 8.2, 6.9, 1.2 Hz, 1H), 6.53 (d, 7.2 Hz, 1H), 5.80 (s, 1H), 4.60 (s, 1H), 4.24 (dd, J = 14.0, 2.6 Hz, 2H), 2.78 (s, 3H), 1.91 (s, 3H), 0.89 (s, 9H), -0.09 (s, 3H), -0.12 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 145.2 (C), 145.1 (C), 145.1 (C), 145.1 (C), 143.3 (C), 143.1 (C), 137.3 (C), 133.5 (C), 133.3 (C), 133.0 (C), 132.2 (C), 132.0 (C), 131.9 (C), 128.2 (CH), 128.1 (CH), 126.3 (CH), 126.0 (CH), 125.8 (CH), 125.5 (C), 125.5 (CH), 125.3 (CH), 125.2 (2CH), 124.8 (CH), 124.2 (CH), 123.8 (CH), 123.7 (CH), 123.5 (CH), 63.2 (CH₂), 51.9 (CH), 51.7 (CH), 26.1 (3CH₃), 21.5 (CH₃), 20.0 (CH₃), 18.5 (C), -5.3 (CH₃), -5.3 (CH₃); **HPLC** Lux-Cellulose-2 column, heptane/isopropanol = 99.5:0.5, 1 mL/min, 254 nm, retention time: t_{minor} = 5.07 min, t_{major} = 5.57 min, 95.5% ee; **Specific rotation** $[\alpha]_{\text{D}}^{25}$ = -20.2 (c = 1.0, CHCl₃).



Prior to the synthesis of **8**, we prepared isobenzofuran by a retro-Diels–Alder cycloaddition of 1,4-dihydro-1,4-epoxynaphthalene (itself obtained from the Diels–Alder cycloaddition between benzyne and furan) promoted by 3,6-di(pyridin-2-yl)-1,2,4,5-tetrazine as described by Peña, Moresco and co-workers,⁴ except we performed the reaction in toluene instead of dichloromethane. After concentration in vacuum at 20 degrees, the crude material was purified by standard silica gel chromatography eluted with 2:8 ethyl acetate/cyclohexane without any special precaution to afford pure isobenzofuran, as described by Peters and Herges.⁵ We confirm that solid isobenzofuran can be stored without detectable degradation at -18 °C for several weeks, previously reported as up to 8 months at -15 °C by Peters and Herges.

A round bottom flask containing the arylene precursor **5c** (46 mg, 0.072 mmol, 97.5% *ee*) was charged with 3 mL of anhydrous toluene. The toluene was evaporated by rotary evaporation and this step was repeated twice to remove all moisture. Then the flask was charged with 0.3 mL of Et₂O and freshly prepared isobenzofuran (84 mg, 0.72 mmol) diluted in anhydrous toluene (1 mL) under an argon atmosphere. The suspension was cooled down to 0 °C and trimethylsilylmagnesium chloride (1 M in Et₂O, 0.72 mmol) was added slowly at this temperature. After stirring 15 h at 0 °C, the reaction mixture was quenched with water. The aqueous layer was extracted three times with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (pentane/EtOAc = 20:1) to afford the two diastereomers of the intermediate cycloadduct (colorless oil, 30 mg). This material was directly diluted in anhydrous dichloromethane (2 mL), and Et₃SiH (42 mg, 0.36 mmol) and TFA (41 mg, 0.36 mmol) were subsequently added to the solution, resulting in an immediate yellow coloration of the solution. The mixture was stirred at 25 °C until starting material is no longer detectable by TLC analysis (1 hour). The reaction was quenched with a saturated NaHCO₃ aqueous solution at this temperature and extracted with dichloromethane two times. After concentration under reduced pressure, flash column chromatography on silica gel (pentane/EtOAc = 20:1) afforded the desired anthracene atropisomer **8** (15 mg, 43% after two steps) as a colorless oil. **HRMS** (ESI+) *m/z* calcd for C₂₈H₂₂O₂Br⁺ [M+H]⁺ 471.0782, found 471.0783; **¹H NMR** (400 MHz, CDCl₃) δ 8.66 (s, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 8.01–7.98 (m, 2H), 7.55 (ddd, *J* = 8.7, 6.8, 1.7 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.44 (s, 1H), 7.36 (ddd, *J* = 8.8, 6.9, 1.2 Hz, 1H), 7.29 (ddd, *J* = 9.0, 7.0, 1.2 Hz, 1H), 7.28–7.22 (m, 2H), 3.47 (s, 3H), 3.12 (s, 3H), 2.16 (s, 3H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ 167.4 (C), 140.4 (C), 135.4 (C), 134.3 (C), 133.5 (C), 133.2 (C), 132.8 (C), 131.5 (C), 131.5 (C), 130.8 (C), 130.5 (C), 128.5 (C), 128.4 (CH), 128.4 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 127.7 (CH), 127.4 (C), 127.3 (CH), 126.3 (CH), 125.7 (CH), 125.5 (CH), 125.5 (CH), 123.5 (CH), 52.1 (CH₃), 22.8 (CH₃), 20.7 (CH₃); **HPLC** (S,S)-Whelk-O1 column, heptane/ethanol = 95:5, 1 mL/min, 254 nm, retention time: *t*_{major} = 8.66 min, *t*_{minor} = 9.74 min, 96.5% *ee*; **Specific rotation** [α]_D²⁵ = -34.7 (c = 1.0, CHCl₃).

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Computational studies

The density functional theory (DFT) calculations reported in this section were performed with the Gaussian16 suite.⁶ All geometries were fully optimized using the B3LYP hybrid density functional⁷ with either the 6-311+G(d,p) or 6-311++G(d,p) or 6-31G(d) or 6-31+G(d,p) basis set in the gas phase or using the IEFPCM solvation model for acetonitrile or diethylether or chloroform.⁸ Dispersion effects were accounted for using Grimme's D3 dispersion model.⁹ The second derivatives were analytically calculated in order to determine if a minimum (zero negative eigenvalue) or a transition state (one negative eigenvalue) existed for the resulting geometry. The connection between the transition states and the corresponding minima was performed manually by steepest descend optimization. All energies are relative free Gibbs energies expressed in kJ/mol as computed at 298 K. The Cartesian coordinates, number of negative eigenvalues, absolute free Gibbs energies expressed in Hartrees (1 Ha = 2625.5 kJ.mol⁻¹) of all stationary points are reported at the end of this section.

Aryne atropisomers 2a (R = Me) and 2c: geometries and configurational stabilities

Exploration of the potential energy surface for both aryne atropisomers **2a** (R = Me) and **2c** was first performed at the B3LYP/6-31+G(d) level of theory in the gas phase. Four possible transitions states corresponding to the enantiomerization could be located in each case due to rotations around both the biaryl stereogenic axes and the ester C(sp²)–C(sp²) bonds as illustrated in Figure S5. At this level of theory, the influence of the conformation of the ester group was found negligible, and as expected, the less energy demanding transition states were identified with the C(sp²) atom of the ester group overhanging the naphthyl unit in **TS-enant-2a-conf1** and the methyl group in **TS-enant-2c-conf1**.

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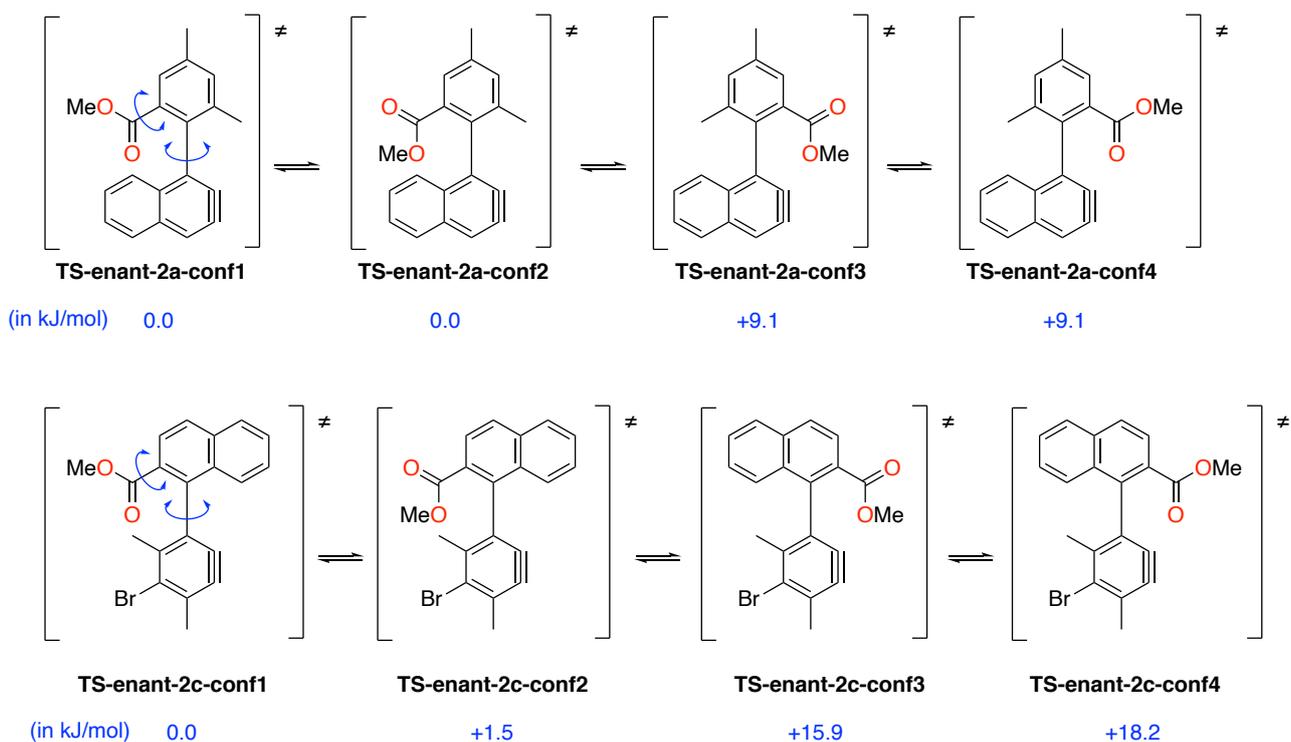


Figure S5. The four possible transitions states for the enantiomerization of aryne atropisomer **2a** (top) and **2c** (bottom). Relative free Gibbs energies calculated at 298 K using B3LYP/6-31+G(d) in the gas phase expressed in kJ/mol.

For both aryne atropisomers **2a** and **2c**, the geometries and relative free Gibbs energies of the kinetically favored enantiomerization transition states identified above were recomputed at the B3LYP-D3/6-311++G(d,p) level of theory including a solvation model for diethylether (Figure S6). The barriers to enantiomerization of the corresponding virtual biaryl derivatives having two C(sp²)-H bonds in place of the aryne triple bond were also computed for comparison. The optimized geometries of aryne atropisomers **2a** and **2c** are depicted in Figure S7.

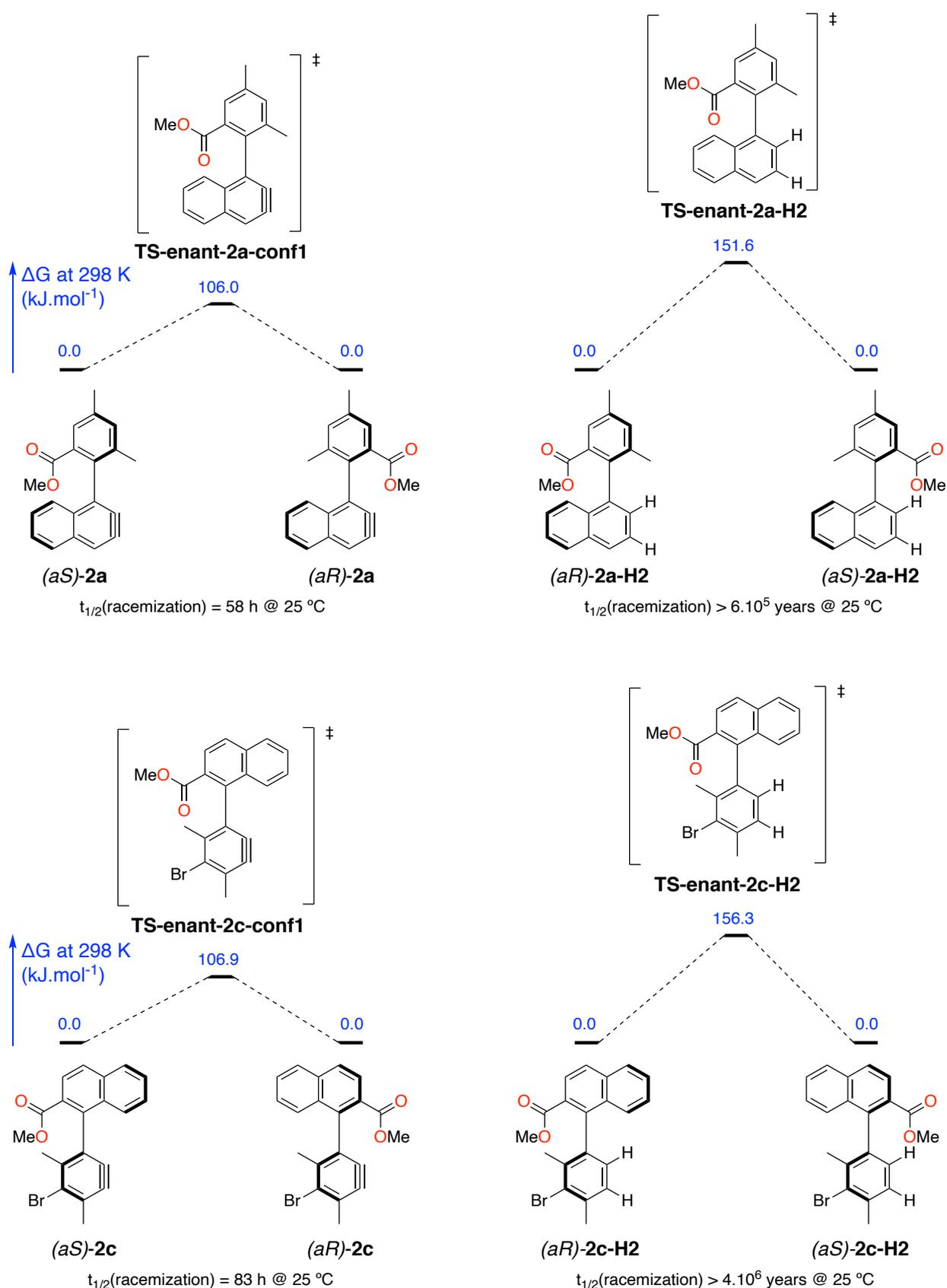


Figure S6. Computed enantiomerization energy profiles for the aryne atropisomer **2a** (top) and **2c** (bottom) and comparison with those of the corresponding virtual biaryl derivatives having two C(sp²)–H bonds in place of the aryne triple bond. Relative free Gibbs energies calculated at 298 K using B3LYP-D3/6-311++G(d,p) in diethylether (iefpcm) expressed in kJ/mol.

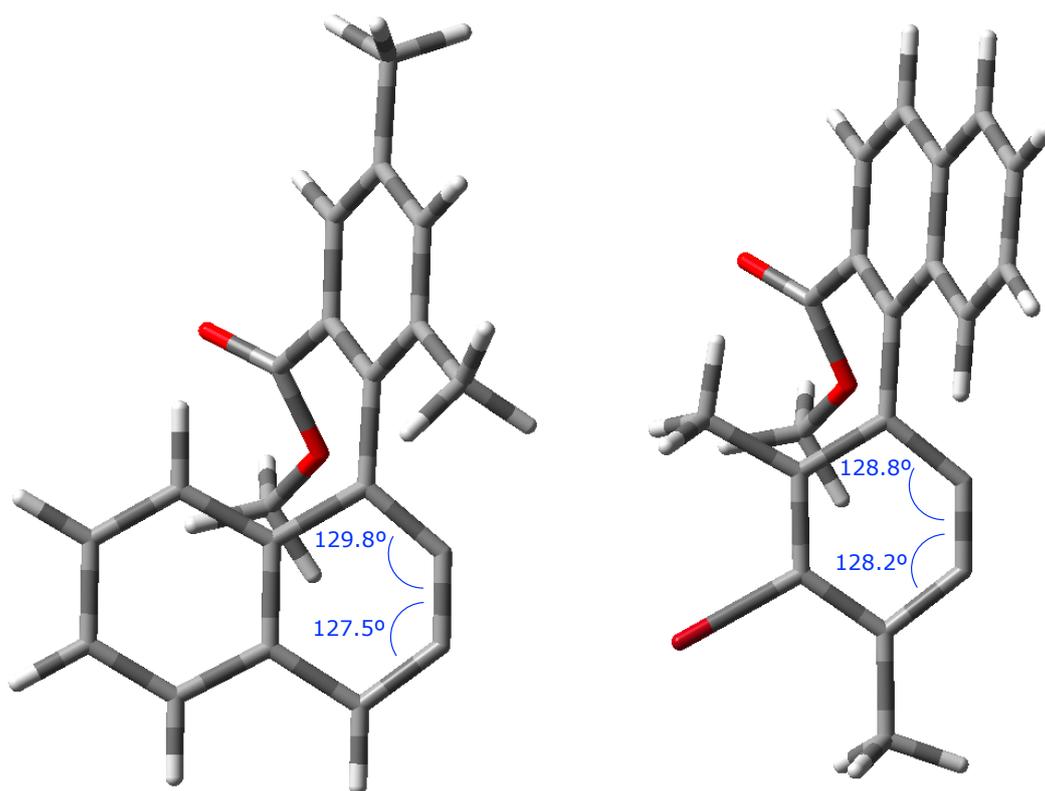


Figure S7. Optimized geometries of aryne atropisomers **2a** (R = Me, left) and **2c** (right) obtained by DFT calculations [B3LYP-D3/6-311++G(d,p) in diethylether (iefpcm)].

7,8-[5]helicynes: geometry and configurational stability

For comparison, the barriers to enantiomerization 7,8-[5]helicyne, [5]helicene,¹⁰ 1,14-dimethyl-7,8-[5]helicyne and 1,14-dimethyl-[5]helicene¹¹ were also computed (Figure S8).

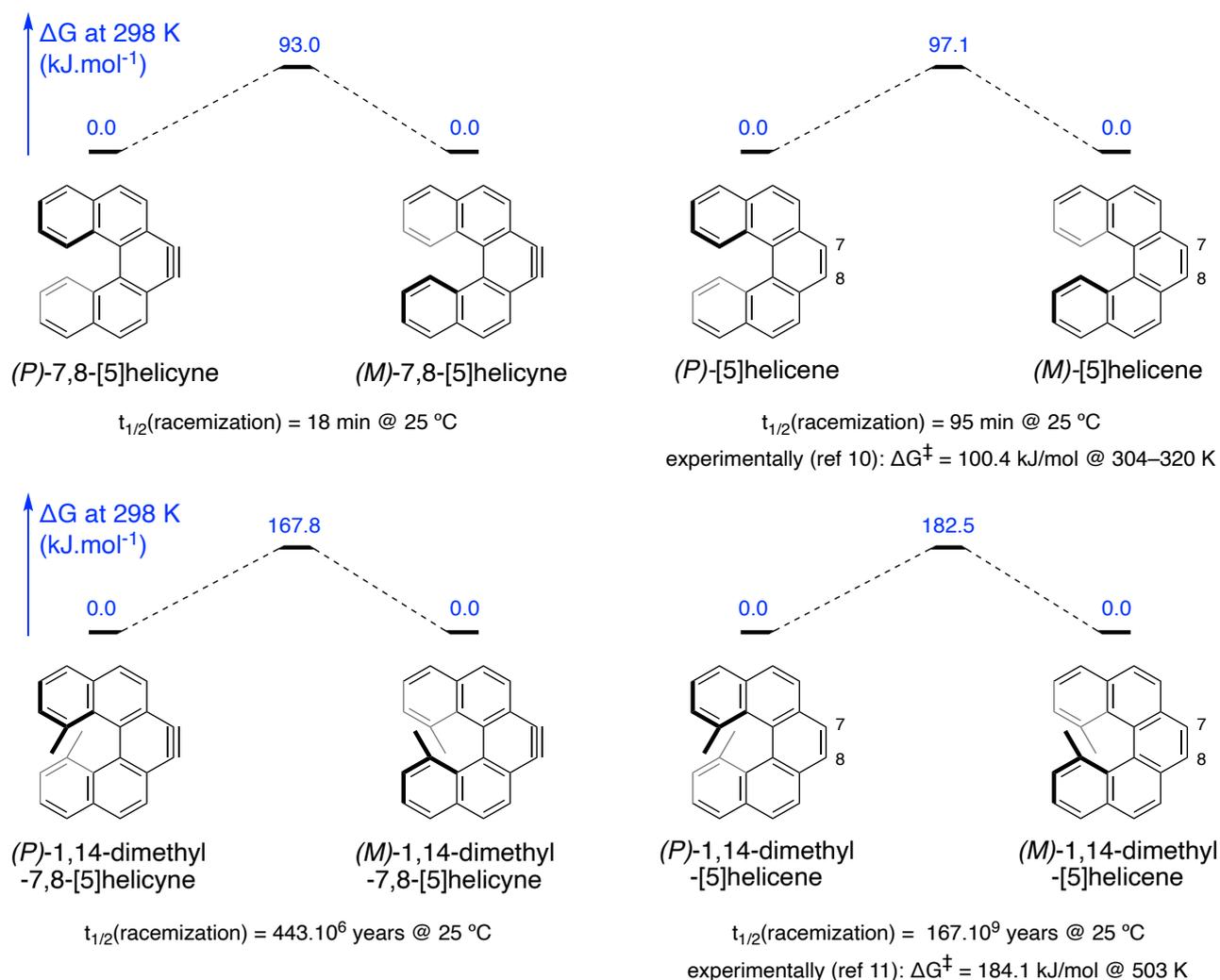


Figure S8. Computed enantiomerization energy profiles for 7,8-[5]helicyne, [5]helicene, 1,14-dimethyl-7,8-[5]helicyne and 1,14-dimethyl-[5]helicene. Relative free Gibbs energies calculated at 298 K using B3LYP/6-311++G(d,p) in diethylether (iefpcm) expressed in kJ/mol .

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1,2-Elimination vs thia-Fries rearrangement

The experimental investigations reported in the present study revealed a propensity of the Kobayashi-type precursors (e.g. **4a**) of the aryne atropisomers to undergo a thia-Fries rearrangement instead of the expected 1,2-elimination. A simplistic modeling of both transformations using DFT methods with a H atom or a 2,6-dimethylphenyl substituent vicinal to the sulfonate leaving group provided some clues on the physical reasons at the origin of this tendency. As can be seen from Figure S9, the introduction of a 2,6-dimethylphenyl substituent next to sulfonate group resulted in an increase of the barrier to the 1,2-elimination [with $\Delta(\Delta G^\ddagger) = +2.8$ kJ/mol] and a decreased of the barrier to the thia-Fries rearrangement [with $\Delta(\Delta G^\ddagger) = -8.6$ kJ/mol], both effects favoring kinetically the thia-Fries rearrangement over the 1,2-elimination. The principal physical effect at the origin of these variations is seemingly the van der Waals repulsion (steric effect) from the hindered 2,6-dimethylphenyl substituent that induces modifications in the conformational preferences of the reactive species.

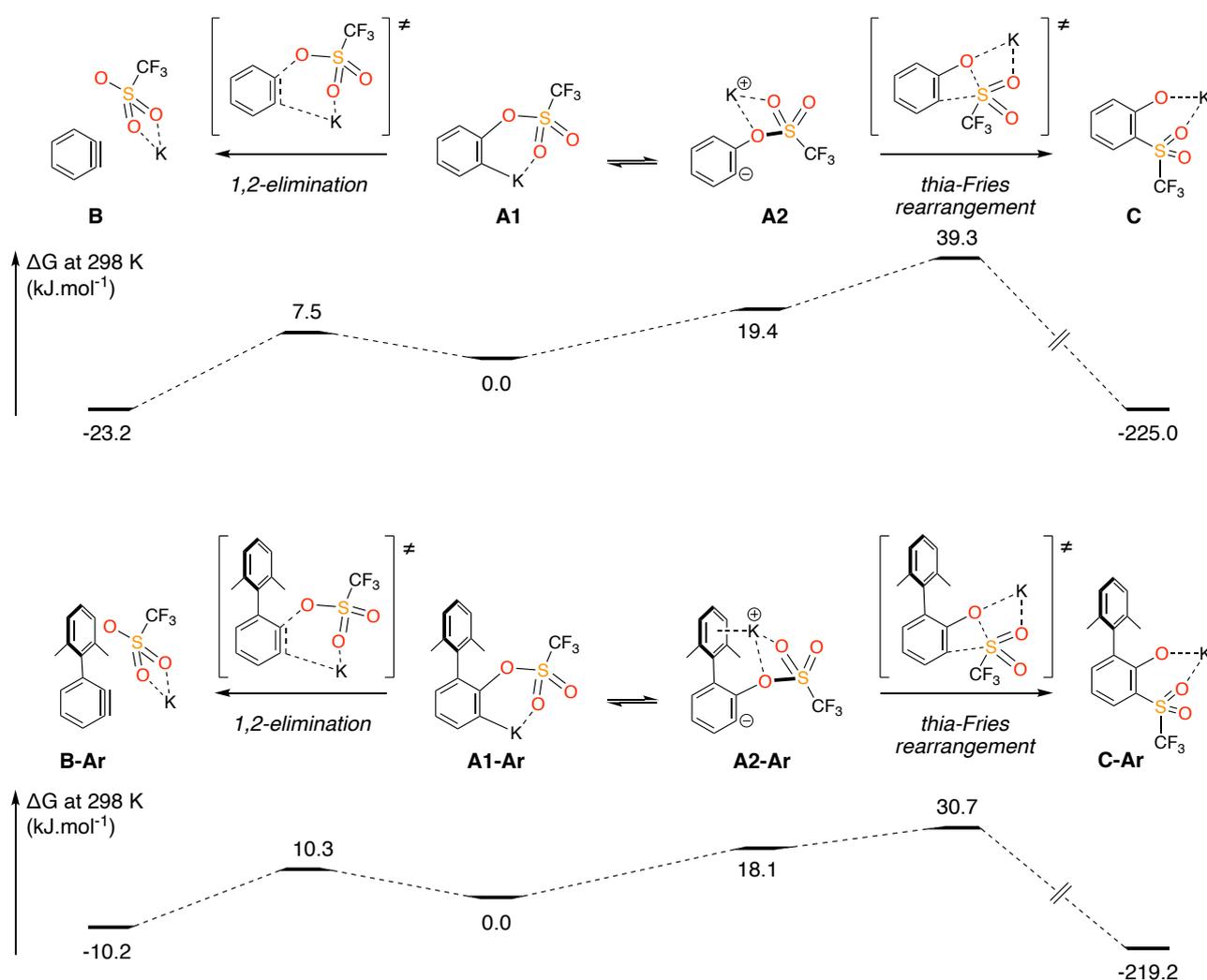


Figure S9. Model energy profiles of the 1,2-elimination and the thia-Fries rearrangement of the two virtual (2-triflate)aryl potassium reactive species **A1** and **A1-Ar**. Free Gibbs energies were calculated at 298 K using B3LYP-D3/6-311+G(d,p) in acetonitrile and are expressed in $\text{kJ}\cdot\text{mol}^{-1}$.

Cartesian coordinates, number of negative eigenvalues and absolute free Gibbs energies at 298 K in Hartrees for all stationary points

A1						TS(A1-B)					
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)			Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z				X	Y	Z
1	6	0	1.312823	-0.813837	-0.288052	1	6	0	1.787269	-0.473322	-0.293852
2	6	0	1.658572	-2.157274	-0.362259	2	6	0	2.147668	-1.795939	-0.325865
3	6	0	2.999614	-2.467415	-0.130915	3	6	0	3.533710	-1.940188	-0.160923
4	6	0	3.891772	-1.434893	0.174747	4	6	0	4.344228	-0.806840	0.007375
5	6	0	3.439568	-0.110656	0.244370	5	6	0	3.794340	0.481344	0.014756
6	6	0	2.096792	0.276249	0.005227	6	6	0	2.395316	0.668665	-0.151782
7	1	0	3.335539	-3.497036	-0.182779	7	1	0	3.967871	-2.933564	-0.164930
8	1	0	4.936759	-1.667328	0.361048	8	1	0	5.414576	-0.936977	0.133894
9	1	0	4.177143	0.652777	0.494027	9	1	0	4.457520	1.332886	0.149049
10	8	0	-0.131314	-0.593716	-0.626762	10	8	0	-0.082240	-0.408531	-0.621713
11	16	0	-1.035524	0.244432	0.370674	11	16	0	-1.036278	-0.336259	0.559669
12	8	0	-0.817037	-0.108673	1.765029	12	8	0	-0.995388	-1.501154	1.445096
13	8	0	-1.129592	1.649893	-0.013544	13	8	0	-1.050564	0.988190	1.202890
14	6	0	-2.672773	-0.542648	-0.153599	14	6	0	-2.688220	-0.445068	-0.348689
15	9	0	-2.872905	-0.373666	-1.459025	15	9	0	-2.811081	0.566976	-1.214079
16	9	0	-3.656093	0.052369	0.524644	16	9	0	-3.689103	-0.376720	0.537557
17	9	0	-2.664851	-1.842881	0.131811	17	9	0	-2.782176	-1.599767	-1.015219
18	1	0	0.926092	-2.922806	-0.591994	18	1	0	1.472836	-2.629860	-0.457004
19	19	0	1.379096	3.101257	-0.248572	19	19	0	0.523607	2.972280	-0.107702
0 negative eigenvalue						1 negative eigenvalue					
Sum of electronic and thermal Free Energies=						Sum of electronic and thermal Free Energies=					
-1792.646047						-1792.643187					

B						A2					
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)			Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z				X	Y	Z
1	6	0	2.485334	0.016887	-0.371184	1	6	0	1.496429	-0.074339	-0.115076
2	6	0	2.469668	-1.348152	-0.158644	2	6	0	2.321901	0.405205	0.896013
3	6	0	3.776211	-1.786599	0.150319	3	6	0	3.641051	-0.046455	0.880723
4	6	0	4.874772	-0.909926	0.216832	4	6	0	4.039835	-0.932064	-0.127301
5	6	0	4.756571	0.476167	-0.019498	5	6	0	3.125246	-1.351840	-1.101190
6	6	0	3.442609	0.811649	-0.319121	6	6	0	1.769435	-0.931515	-1.143352
7	1	0	3.932548	-2.842551	0.345693	7	1	0	1.964267	1.094716	1.652670
8	1	0	5.852897	-1.311965	0.460298	8	1	0	4.340293	0.288251	1.638725
9	1	0	5.602405	1.148815	0.035391	9	1	0	5.065629	-1.290646	-0.148911
10	8	0	-0.735125	0.377965	-1.080252	10	1	0	3.494968	-2.040155	-1.861932
11	16	0	-1.157463	-0.491408	0.045649	11	8	0	0.106129	0.546452	-0.067389
12	8	0	-0.871646	-1.926028	-0.126661	12	16	0	-1.070833	-0.055479	0.808147
13	8	0	-0.836097	0.073435	1.375107	13	8	0	-0.596035	-0.868996	1.913537
14	6	0	-3.038736	-0.392562	-0.026442	14	8	0	-2.013852	1.034911	1.022716
15	9	0	-3.447937	0.879591	0.112549	15	6	0	-1.936267	-1.235056	-0.400163

16	9	0	-3.593473	-1.120908	0.955566
17	9	0	-3.497628	-0.854016	-1.200723
18	1	0	1.612158	-2.005469	-0.203677
19	19	0	0.174480	2.806524	0.086646

0 negative eigenvalue					
Sum of electronic and thermal Free Energies=			-1792.654901		

16	9	0	-2.035086	-0.666922	-1.599980
17	9	0	-3.162241	-1.478834	0.072641
18	9	0	-1.270936	-2.379846	-0.495858
19	19	0	-0.328062	3.308597	-0.646893

0 negative eigenvalue					
Sum of electronic and thermal Free Energies=			-1792.638667		

TS(A2-C)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	1.443059	0.527433	0.149605
2	6	0	2.386467	1.538040	0.007478
3	6	0	3.710006	1.126924	-0.189895
4	6	0	4.016276	-0.235516	-0.226246
5	6	0	2.999475	-1.193659	-0.070309
6	6	0	1.656289	-0.833093	0.120743
7	1	0	2.118751	2.588351	0.044230
8	1	0	4.490856	1.869904	-0.309737
9	1	0	5.045444	-0.549763	-0.375768
10	1	0	3.284373	-2.245146	-0.106324
11	8	0	0.089159	0.925212	0.332847
12	16	0	-0.934672	-0.311432	0.791214
13	8	0	-0.682819	-0.905888	2.101274
14	8	0	-2.205600	0.429417	0.654162
15	6	0	-1.186131	-1.678765	-0.552305
16	9	0	-0.741393	-1.245077	-1.728546
17	9	0	-2.504178	-1.903530	-0.652301
18	9	0	-0.598269	-2.811981	-0.213448
19	19	0	-1.744667	3.045619	-0.458098

1 negative eigenvalue					
Sum of electronic and thermal Free Energies=			-1792.631083		

C

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	1.612438	-1.054057	0.209545
2	6	0	2.153159	-2.370367	0.038859
3	6	0	1.353664	-3.473925	-0.182209
4	6	0	-0.047811	-3.366319	-0.256956
5	6	0	-0.634739	-2.119987	-0.112365
6	6	0	0.176090	-0.995378	0.099530
7	1	0	3.231929	-2.467243	0.100014
8	1	0	1.817300	-4.448472	-0.298426
9	1	0	-0.664145	-4.239940	-0.426129
10	1	0	-1.711182	-2.038024	-0.166925
11	8	0	2.332252	-0.025909	0.442967
12	16	0	-0.491850	0.629070	0.317852
13	8	0	-0.518902	1.056710	1.724826
14	8	0	0.038175	1.584268	-0.674632
15	6	0	-2.339848	0.504560	-0.163370
16	9	0	-2.495248	0.013807	-1.395537
17	9	0	-2.825693	1.747149	-0.126888
18	9	0	-3.023298	-0.250416	0.702124
19	19	0	2.728628	2.413999	-0.350261

0 negative eigenvalue					
Sum of electronic and thermal Free Energies=			-1792.731740		

A1-Ar

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-0.747640	1.253956	0.131230
2	6	0	0.513651	1.838731	0.003441
3	6	0	0.502518	3.213144	-0.264213
4	6	0	-0.712572	3.887414	-0.401929
5	6	0	-1.922911	3.194640	-0.278013
6	6	0	-1.997247	1.808935	0.004804
7	1	0	1.445096	3.739764	-0.367165
8	1	0	-0.708568	4.954204	-0.609729
9	1	0	-2.842302	3.766539	-0.405370
10	8	0	-0.668882	-0.198632	0.514476

TS(A1-Ar-B-Ar)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	0.542738	1.695730	-0.019745
2	6	0	-0.824275	1.851706	-0.020750
3	6	0	-1.132399	3.216020	0.160905
4	6	0	-0.123631	4.177121	0.308122
5	6	0	1.229319	3.816655	0.277132
6	6	0	1.589773	2.457185	0.094627
7	1	0	-2.176613	3.508443	0.179990
8	1	0	-0.404642	5.217250	0.442827
9	1	0	1.985570	4.589940	0.389153
10	8	0	0.919717	-0.141774	-0.388118

11	16	0	-1.128336	-1.304618	-0.518783
12	8	0	-2.456166	-1.817784	-0.192818
13	8	0	-0.810377	-0.958464	-1.895649
14	6	0	0.095392	-2.640541	0.024366
15	9	0	1.329645	-2.293443	-0.320341
16	9	0	-0.232942	-3.780953	-0.588782
17	9	0	0.030681	-2.816317	1.343426
18	19	0	-4.425170	0.266119	0.551634
19	6	0	1.792539	1.079409	0.134554
20	6	0	2.260446	0.709288	1.410218
21	6	0	2.519293	0.735324	-1.021484
22	6	0	3.464299	0.005856	1.513822
23	6	0	3.718935	0.029297	-0.881943
24	6	0	4.192341	-0.332872	0.375897
25	1	0	3.831269	-0.278126	2.494829
26	1	0	4.280396	-0.243932	-1.769485
27	1	0	5.123835	-0.880760	0.469423
28	6	0	1.472949	1.053992	2.651397
29	1	0	1.228510	2.119246	2.684822
30	1	0	0.524605	0.509155	2.671745
31	1	0	2.031630	0.799888	3.554040
32	6	0	2.006108	1.093974	-2.396631
33	1	0	0.989362	0.719172	-2.539121
34	1	0	1.972387	2.177305	-2.541023
35	1	0	2.643728	0.667328	-3.173388

0 negative eigenvalue
Sum of electronic and thermal Free Energies= -2102.306466

11	16	0	1.199866	-1.131211	0.729097
12	8	0	2.643553	-1.363931	0.907388
13	8	0	0.402068	-0.928628	1.938670
14	6	0	0.548027	-2.726267	-0.040822
15	9	0	-0.768644	-2.649697	-0.238703
16	9	0	0.801724	-3.755864	0.779767
17	9	0	1.150520	-2.956713	-1.214198
18	19	0	3.960291	0.809632	-0.677739
19	6	0	-1.870638	0.808032	-0.194925
20	6	0	-2.104398	0.268003	-1.473600
21	6	0	-2.626220	0.388722	0.915870
22	6	0	-3.108303	-0.692347	-1.625969
23	6	0	-3.618178	-0.579326	0.726801
24	6	0	-3.861342	-1.115973	-0.534338
25	1	0	-3.295879	-1.113051	-2.608383
26	1	0	-4.200190	-0.915614	1.578578
27	1	0	-4.634362	-1.865459	-0.665739
28	6	0	-1.283178	0.705202	-2.661559
29	1	0	-1.281369	1.793821	-2.766478
30	1	0	-0.242198	0.393137	-2.541922
31	1	0	-1.669003	0.271528	-3.585835
32	6	0	-2.362188	0.946326	2.294163
33	1	0	-1.308273	0.830148	2.556502
34	1	0	-2.598840	2.012463	2.348346
35	1	0	-2.963340	0.428161	3.043690

1 negative eigenvalue
Sum of electronic and thermal Free Energies= -2102.302558

B-Ar

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	1.718608	1.351623	-0.171044
2	6	0	2.302790	0.106410	-0.106870
3	6	0	3.662022	0.271314	-0.485838
4	6	0	4.215452	1.511657	-0.845830
5	6	0	3.461101	2.701498	-0.854434
6	6	0	2.131864	2.488533	-0.478514
7	1	0	4.294589	-0.610605	-0.485878
8	1	0	5.264109	1.551965	-1.123025
9	1	0	3.897352	3.654270	-1.128614
10	8	0	-0.915352	0.728265	0.475892
11	16	0	-1.700543	0.549852	-0.771446
12	8	0	-2.425490	1.773915	-1.181687
13	8	0	-1.025950	-0.183370	-1.853140
14	6	0	-3.071326	-0.624172	-0.227813
15	9	0	-2.558685	-1.790975	0.194269
16	9	0	-3.912184	-0.879857	-1.244135
17	9	0	-3.783615	-0.091028	0.779301
18	19	0	-1.055887	3.380713	1.277504

A2-Ar

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	0.200080	1.481163	-0.317156
2	6	0	-1.171450	1.611941	-0.083511
3	6	0	-1.652488	2.926058	-0.107861
4	6	0	-0.773033	3.984083	-0.348631
5	6	0	0.585415	3.733633	-0.577004
6	6	0	1.147137	2.433419	-0.573775
7	1	0	-2.709158	3.106119	0.058321
8	1	0	-1.155111	5.001640	-0.361211
9	1	0	1.225042	4.595955	-0.768124
10	8	0	0.618943	0.023512	-0.327411
11	16	0	1.681453	-0.553595	0.690271
12	8	0	1.794700	0.209399	1.920242
13	8	0	1.426760	-1.992824	0.739864
14	6	0	3.348344	-0.406267	-0.227570
15	9	0	3.152033	-0.442974	-1.543013
16	9	0	4.095922	-1.455301	0.131590
17	9	0	3.983059	0.706479	0.109618
18	19	0	-0.581567	-2.919812	-1.006560

19	6	0	1.714941	-1.195746	0.297479	19	6	0	-2.092255	0.456705	0.134769
20	6	0	1.356231	-1.400785	1.643549	20	6	0	-2.740627	-0.126059	-0.972979
21	6	0	1.524705	-2.206963	-0.663270	21	6	0	-2.314710	-0.035922	1.434770
22	6	0	0.824500	-2.637703	2.018530	22	6	0	-3.607275	-1.205956	-0.762377
23	6	0	0.985595	-3.430363	-0.252135	23	6	0	-3.176894	-1.124754	1.609105
24	6	0	0.641602	-3.649069	1.078885	24	6	0	-3.820605	-1.708344	0.520558
25	1	0	0.549809	-2.805608	3.054623	25	1	0	-4.112878	-1.656198	-1.610473
26	1	0	0.827065	-4.213181	-0.986409	26	1	0	-3.347517	-1.512617	2.607894
27	1	0	0.225511	-4.603616	1.382411	27	1	0	-4.488351	-2.549591	0.670205
28	6	0	1.521512	-0.303466	2.665072	28	6	0	-2.500458	0.398492	-2.369230
29	1	0	2.539138	0.097028	2.664678	29	1	0	-2.824498	1.438903	-2.460264
30	1	0	0.848366	0.527596	2.437515	30	1	0	-1.435707	0.379677	-2.619678
31	1	0	1.294169	-0.664911	3.669438	31	1	0	-3.038923	-0.195387	-3.109714
32	6	0	1.842886	-1.971935	-2.120433	32	6	0	-1.652278	0.610476	2.627735
33	1	0	1.313500	-1.086950	-2.481667	33	1	0	-0.565435	0.629819	2.523808
34	1	0	2.911160	-1.809206	-2.284257	34	1	0	-1.976899	1.649850	2.734666
35	1	0	1.535557	-2.826725	-2.725693	35	1	0	-1.899814	0.079235	3.548495
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0 negative eigenvalue						0 negative eigenvalue					
Sum of electronic and thermal Free Energies=						Sum of electronic and thermal Free Energies=					
-2102.310336						-2102.299564					

TS(A2-Ar-C-Ar)

Center	Atomic	Atomic	Coordinates (Angstroms)			
Number	Number	Type	X	Y	Z	

1	6	0	0.211902	1.105040	0.164644	
2	6	0	-1.105622	1.548519	0.058015	
3	6	0	-1.261967	2.939634	-0.037322	
4	6	0	-0.148099	3.779604	-0.012833	
5	6	0	1.145675	3.241984	0.103733	
6	6	0	1.362502	1.859852	0.192605	
7	1	0	-2.261462	3.352193	-0.124361	
8	1	0	-0.289860	4.854538	-0.082062	
9	1	0	1.986432	3.934868	0.120220	
10	8	0	0.410457	-0.298027	0.244179	
11	16	0	1.964134	-0.734068	0.689046	
12	8	0	2.361882	-0.362316	2.045274	
13	8	0	1.830037	-2.183842	0.434066	
14	6	0	3.353049	-0.295589	-0.583123	
15	9	0	2.808066	-0.007784	-1.762357	
16	9	0	4.127568	-1.380740	-0.724464	
17	9	0	4.109449	0.700202	-0.157482	
18	19	0	-0.861805	-2.778634	-0.534279	
19	6	0	-2.261588	0.604499	0.045267	
20	6	0	-2.901804	0.291966	-1.171702	
21	6	0	-2.678599	-0.002868	1.248227	
22	6	0	-3.960626	-0.624370	-1.166796	
23	6	0	-3.741394	-0.912601	1.217528	
24	6	0	-4.380685	-1.223310	0.018855	
25	1	0	-4.452573	-0.873319	-2.101181	
26	1	0	-4.067043	-1.380981	2.140402	

C-Ar

Center	Atomic	Atomic	Coordinates (Angstroms)			
Number	Number	Type	X	Y	Z	

1	6	0	-0.308621	0.186789	0.147510	
2	6	0	-1.395080	1.041427	-0.261687	
3	6	0	-1.146890	2.307170	-0.763537	
4	6	0	0.153333	2.821483	-0.910894	
5	6	0	1.235161	2.035673	-0.551707	
6	6	0	1.000412	0.748164	-0.050923	
7	1	0	-1.992592	2.923328	-1.053751	
8	1	0	0.311509	3.817505	-1.304471	
9	1	0	2.235442	2.428843	-0.665231	
10	8	0	-0.483205	-0.974878	0.645856	
11	16	0	2.309926	-0.336132	0.446506	
12	8	0	2.486112	-0.400136	1.905284	
13	8	0	2.290085	-1.611039	-0.297085	
14	6	0	3.923854	0.481570	-0.176316	
15	9	0	3.884338	0.709227	-1.491775	
16	9	0	4.910599	-0.378885	0.084915	
17	9	0	4.173634	1.628783	0.462619	
18	19	0	0.169644	-3.433890	0.189742	
19	6	0	-2.790395	0.527922	-0.125419	
20	6	0	-3.316932	-0.326397	-1.112990	
21	6	0	-3.567010	0.891867	0.990300	
22	6	0	-4.627088	-0.796822	-0.978108	
23	6	0	-4.874715	0.404506	1.097325	
24	6	0	-5.404643	-0.433577	0.119534	
25	1	0	-5.038664	-1.452735	-1.738514	
26	1	0	-5.477702	0.681606	1.956025	

27	1	0	-5.200866	-1.932663	0.008443	27	1	0	-6.419265	-0.805397	0.213899
28	6	0	-2.436915	0.908491	-2.470146	28	6	0	-2.479015	-0.727288	-2.303426
29	1	0	-2.600978	1.989363	-2.478798	29	1	0	-2.181961	0.147077	-2.890034
30	1	0	-1.364070	0.752735	-2.616075	30	1	0	-1.557578	-1.220620	-1.982522
31	1	0	-2.967323	0.476140	-3.320364	31	1	0	-3.024612	-1.409313	-2.958254
32	6	0	-1.977940	0.305198	2.549621	32	6	0	-2.997292	1.787616	2.065580
33	1	0	-0.951692	-0.073702	2.536948	33	1	0	-2.049303	1.394135	2.443736
34	1	0	-1.915942	1.382947	2.721149	34	1	0	-2.789380	2.789898	1.679958
35	1	0	-2.498581	-0.150893	3.393388	35	1	0	-3.689514	1.883359	2.904241

1 negative eigenvalue
Sum of electronic and thermal Free Energies= -2102.294761

0 negative eigenvalue
Sum of electronic and thermal Free Energies= -2102.389939

2a

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-3.621002	0.386247	2.041101
2	6	0	-3.921826	-0.271737	0.873230
3	6	0	-2.898613	-0.726332	-0.003230
4	6	0	-1.517120	-0.471634	0.347722
5	6	0	-1.253123	0.197138	1.575082
6	6	0	-2.272794	0.616634	2.396537
7	1	0	-4.285479	-1.600502	-1.482180
8	1	0	-4.416933	0.723408	2.695307
9	1	0	-4.955113	-0.460012	0.601959
10	6	0	-3.251388	-1.422032	-1.215423
11	6	0	-0.428319	-0.881349	-0.527457
12	1	0	-0.225483	0.374965	1.865361
13	1	0	-2.039824	1.124681	3.325363
14	6	0	-0.940962	-1.547904	-1.601121
15	6	0	-2.133452	-1.776141	-1.908570
16	6	0	1.003082	-0.598297	-0.249852
17	6	0	1.874771	-1.670608	0.031621
18	6	0	1.509221	0.715731	-0.209543
19	6	0	3.212187	-1.399686	0.326278
20	6	0	2.849061	0.951951	0.111863
21	6	0	3.723634	-0.099503	0.370303
22	1	0	3.874977	-2.232079	0.543205
23	1	0	3.198893	1.976768	0.151113
24	6	0	1.379058	-3.096957	0.037928
25	1	0	0.493390	-3.206673	0.669129
26	1	0	1.092828	-3.420406	-0.967039
27	1	0	2.151053	-3.774886	0.404998
28	6	0	5.180584	0.148914	0.671741
29	1	0	5.349662	1.175298	1.003071
30	1	0	5.545459	-0.527850	1.448322
31	1	0	5.793117	-0.017375	-0.220642
32	6	0	0.675708	1.931150	-0.470673
33	8	0	0.833106	2.990883	0.100209
34	8	0	-0.248627	1.736971	-1.421579

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Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-4.295810	1.168411	-0.317909
2	6	0	-4.291584	-0.199917	-0.420439
3	6	0	-3.113981	-0.967482	-0.212890
4	6	0	-1.849053	-0.293449	0.074155
5	6	0	-1.937307	1.111821	0.226922
6	6	0	-3.102297	1.822268	0.035587
7	1	0	-4.172545	-2.862938	-0.540968
8	1	0	-5.207895	1.732249	-0.475001
9	1	0	-5.207607	-0.733056	-0.651310
10	6	0	-3.224579	-2.396504	-0.296495
11	6	0	-0.580661	-1.071060	0.211541
12	1	0	-1.092907	1.659317	0.579612
13	1	0	-3.095478	2.896179	0.184307
14	6	0	-1.005131	-2.363077	0.154910
15	6	0	-2.038161	-3.041397	-0.056945
16	6	0	0.879446	-0.734417	0.209028
17	6	0	1.793415	-1.840639	0.187239
18	6	0	1.488749	0.545384	0.086728
19	6	0	3.151915	-1.644388	-0.065229
20	6	0	2.847387	0.690962	-0.213071
21	6	0	3.706070	-0.395171	-0.318903
22	1	0	3.800063	-2.514442	-0.074800
23	1	0	3.243624	1.694117	-0.326378
24	6	0	1.388554	-3.275234	0.429199
25	1	0	0.749268	-3.386498	1.309013
26	1	0	0.862317	-3.707370	-0.427057
27	1	0	2.278249	-3.885703	0.597647
28	6	0	5.158685	-0.225937	-0.676888
29	1	0	5.536992	0.748500	-0.360431
30	1	0	5.774057	-1.002098	-0.216536
31	1	0	5.296740	-0.296873	-1.761181
32	6	0	0.927718	1.883587	0.454831
33	8	0	0.723698	2.233128	1.598023
34	8	0	0.812792	2.698825	-0.603538

35	6	0	-1.174585	2.819364	-1.651355
36	1	0	-0.644231	3.711573	-1.986086
37	1	0	-1.850086	2.459882	-2.423590
38	1	0	-1.722794	3.040662	-0.734421

0 negative eigenvalue					
Sum of electronic and thermal Free Energies=			-922.146215		

35	6	0	0.422816	4.063336	-0.322723
36	1	0	1.154051	4.536726	0.333250
37	1	0	0.391134	4.558586	-1.289600
38	1	0	-0.559150	4.085096	0.151675

1 negative eigenvalue					
Sum of electronic and thermal Free Energies=			-922.105848		

2a-H2

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	3.528826	0.212603	-2.240678
2	6	0	3.869716	-0.284071	-1.005212
3	6	0	2.872025	-0.624338	-0.052789
4	6	0	1.492127	-0.439637	-0.393014
5	6	0	1.176243	0.066701	-1.683447
6	6	0	2.167112	0.386346	-2.582342
7	1	0	4.257479	-1.278561	1.474796
8	1	0	4.300564	0.469483	-2.957519
9	1	0	4.912225	-0.425200	-0.738930
10	6	0	3.210622	-1.142094	1.224466
11	6	0	0.490431	-0.764532	0.574664
12	1	0	0.137526	0.200861	-1.959025
13	1	0	1.904351	0.772367	-3.560797
14	6	0	0.867151	-1.277111	1.797084
15	6	0	2.227122	-1.467157	2.126918
16	6	0	-0.958511	-0.558374	0.270817
17	6	0	-1.768906	-1.678188	-0.007700
18	6	0	-1.534452	0.724834	0.194389
19	6	0	-3.118169	-1.486999	-0.313205
20	6	0	-2.884721	0.882434	-0.137135
21	6	0	-3.701215	-0.218228	-0.376561
22	1	0	-3.732135	-2.357495	-0.525163
23	1	0	-3.286350	1.886553	-0.205066
24	6	0	-1.193370	-3.075877	-0.007486
25	1	0	-0.274984	-3.124954	-0.597939
26	1	0	-0.935559	-3.401503	1.003778
27	1	0	-1.908148	-3.789737	-0.420280
28	6	0	-5.169073	-0.054213	-0.684652
29	1	0	-5.388573	0.948698	-1.056343
30	1	0	-5.500630	-0.778291	-1.433026
31	1	0	-5.773351	-0.213993	0.214645
32	6	0	-0.764445	1.991774	0.398017
33	8	0	-1.004527	3.026221	-0.191992
34	8	0	0.206591	1.880931	1.315325
35	6	0	1.064399	3.027420	1.486961
36	1	0	0.489031	3.887594	1.831609

TS-enant-2a-H2

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-4.248632	1.106800	0.127219
2	6	0	-4.206840	-0.250776	-0.071076
3	6	0	-2.991245	-0.978472	0.044057
4	6	0	-1.746843	-0.277239	0.236200
5	6	0	-1.865841	1.099041	0.557887
6	6	0	-3.065705	1.772395	0.508106
7	1	0	-3.978667	-2.902735	-0.056040
8	1	0	-5.184819	1.648345	0.056298
9	1	0	-5.117862	-0.805285	-0.270458
10	6	0	-3.030206	-2.394955	0.081128
11	6	0	-0.508641	-1.042065	0.221876
12	1	0	-1.021664	1.629337	0.956443
13	1	0	-3.101183	2.817610	0.794132
14	6	0	-0.658313	-2.408236	0.454738
15	6	0	-1.889036	-3.087291	0.387335
16	6	0	0.914586	-0.594560	0.006086
17	6	0	1.856264	-1.556297	-0.475120
18	6	0	1.489311	0.676493	0.319378
19	6	0	3.228837	-1.363661	-0.273149
20	6	0	2.859639	0.818515	0.545633
21	6	0	3.755197	-0.228493	0.330448
22	1	0	3.907547	-2.135544	-0.624503
23	1	0	3.229589	1.796910	0.801322
24	6	0	1.504501	-2.754966	-1.347036
25	1	0	1.597376	-3.710823	-0.823911
26	1	0	0.496960	-2.693553	-1.753946
27	1	0	2.206823	-2.780898	-2.184942
28	6	0	5.220073	-0.094222	0.651356
29	1	0	5.565443	0.934195	0.521235
30	1	0	5.410481	-0.372940	1.693507
31	1	0	5.828435	-0.745905	0.020217
32	6	0	0.854754	2.017073	0.132352
33	8	0	0.940631	2.962443	0.888400
34	8	0	0.299679	2.097376	-1.091788
35	6	0	-0.274262	3.371743	-1.451581
36	1	0	0.493218	4.146581	-1.447624

37	1	0	1.796037	2.728890	2.233764	37	1	0	-0.678006	3.233639	-2.451461
38	1	0	1.556295	3.270749	0.544107	38	1	0	-1.068606	3.638369	-0.753847
39	1	0	0.103539	-1.517037	2.528450	39	1	0	0.217816	-3.000477	0.668341
40	1	0	2.488692	-1.863403	3.101689	40	1	0	-1.910951	-4.160325	0.538516
-----						-----					
0 negative eigenvalue						1 negative eigenvalue					
Sum of electronic and thermal Free Energies=						Sum of electronic and thermal Free Energies=					
-923.462216						-923.404479					
2c						TS-enant-2c-conf1					
-----						-----					
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)			Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z				X	Y	Z
1	6	0	-2.564153	-1.156064	-1.368920	1	6	0	-2.459423	-2.102978	-0.337099
2	6	0	-1.401122	-1.140116	-2.119488	2	6	0	-1.147598	-2.568396	-0.353874
3	6	0	-0.268644	-0.770689	-1.771495	3	6	0	-0.180189	-1.806197	-0.194929
4	6	0	0.138434	-0.258031	-0.553059	4	6	0	0.022703	-0.467984	0.083169
5	6	0	-0.953862	-0.237340	0.358037	5	6	0	-1.299574	0.121706	0.114444
6	6	0	-2.238052	-0.666031	-0.076997	6	6	0	-2.449371	-0.708872	-0.072174
7	35	0	-3.702776	-0.559435	1.183054	7	35	0	-4.224965	0.082502	0.051742
8	6	0	-3.925228	-1.595261	-1.818375	8	6	0	-3.682817	-2.946100	-0.542467
9	1	0	-4.298715	-2.413079	-1.196176	9	1	0	-4.326775	-2.930555	0.341632
10	1	0	-4.647089	-0.777747	-1.738814	10	1	0	-4.282906	-2.576550	-1.378653
11	1	0	-3.887475	-1.930762	-2.854175	11	1	0	-3.390830	-3.975710	-0.746348
12	6	0	-0.741772	0.251464	1.771367	12	6	0	-1.478075	1.603534	0.297695
13	1	0	-1.111086	-0.477928	2.495320	13	1	0	-2.517175	1.899953	0.203928
14	1	0	0.312701	0.428938	1.973774	14	1	0	-1.122847	1.926823	1.274688
15	1	0	-1.285167	1.184527	1.947488	15	1	0	-0.925814	2.141317	-0.472840
16	6	0	1.513769	0.212378	-0.232051	16	6	0	1.422179	0.057439	0.125057
17	6	0	2.554457	-0.759261	-0.070446	17	6	0	2.457768	-0.968760	0.166178
18	6	0	1.808067	1.559243	-0.057115	18	6	0	1.875927	1.370497	-0.056736
19	6	0	2.313727	-2.156866	-0.181878	19	6	0	2.236731	-2.261706	0.717532
20	6	0	3.884657	-0.322781	0.231291	20	6	0	3.778885	-0.691784	-0.308381
21	6	0	3.123975	1.974181	0.277028	21	6	0	3.203003	1.630556	-0.498809
22	6	0	3.335295	-3.065019	-0.031300	22	6	0	3.206638	-3.240832	0.688101
23	1	0	1.311155	-2.507920	-0.386890	23	1	0	1.319728	-2.473200	1.248790
24	6	0	4.916676	-1.285894	0.376446	24	6	0	4.749220	-1.726245	-0.357238
25	6	0	4.137138	1.062888	0.398315	25	6	0	4.111769	0.629347	-0.688663
26	1	0	3.307764	3.030938	0.422936	26	1	0	3.479507	2.658544	-0.697366
27	6	0	4.651295	-2.627901	0.244998	27	6	0	4.466872	-2.986773	0.110496
28	1	0	3.130724	-4.125622	-0.122138	28	1	0	3.003913	-4.204757	1.140213
29	1	0	5.921193	-0.942301	0.599092	29	1	0	5.731490	-1.492319	-0.753240
30	1	0	5.143699	1.390597	0.633601	30	1	0	5.101412	0.845253	-1.074711
31	1	0	5.447058	-3.355032	0.359225	31	1	0	5.217459	-3.767734	0.076046
32	6	0	0.792828	2.654508	-0.149976	32	6	0	1.198374	2.642915	0.345569
33	8	0	0.831736	3.655970	0.535492	33	8	0	0.951960	2.924778	1.496513
34	8	0	-0.146896	2.433625	-1.078198	34	8	0	1.040468	3.494465	-0.681022
35	6	0	-1.211328	3.404811	-1.163144	35	6	0	0.534863	4.808641	-0.347322
36	1	0	-0.812074	4.385338	-1.424732	36	1	0	1.205542	5.303243	0.355841

37	1	0	-1.872951	3.036792	-1.943235
38	1	0	-1.738256	3.467432	-0.209952

0 negative eigenvalue					
Sum of electronic and thermal Free Energies=			-3495.703469		

37	1	0	0.494127	5.349326	-1.289315
38	1	0	-0.459763	4.726807	0.093125

1 negative eigenvalue					
Sum of electronic and thermal Free Energies=			-3495.662749		

2c-H2

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-2.615390	-0.142959	-1.502224
2	6	0	-1.598731	0.292074	-2.357010
3	6	0	-0.288082	0.416330	-1.913752
4	6	0	0.051855	0.112909	-0.596007
5	6	0	-0.934187	-0.329576	0.304535
6	6	0	-2.242495	-0.443657	-0.184918
7	35	0	-3.627278	-1.040315	1.033669
8	6	0	-4.029710	-0.270951	-2.004240
9	1	0	-4.393834	-1.297056	-1.903262
10	1	0	-4.711225	0.365334	-1.432933
11	1	0	-4.090964	0.014717	-3.055182
12	6	0	-0.594182	-0.631228	1.740731
13	1	0	-0.832411	-1.668132	1.992298
14	1	0	0.462192	-0.462308	1.940522
15	1	0	-1.174800	0.004974	2.413758
16	6	0	1.481930	0.261461	-0.181795
17	6	0	2.323627	-0.897446	-0.170385
18	6	0	2.033774	1.499852	0.114733
19	6	0	1.825627	-2.193534	-0.477736
20	6	0	3.709479	-0.762496	0.162486
21	6	0	3.418388	1.627715	0.406312
22	6	0	2.648572	-3.294620	-0.440846
23	1	0	0.782299	-2.307924	-0.742548
24	6	0	4.531945	-1.918649	0.190059
25	6	0	4.230372	0.527187	0.444410
26	1	0	3.812807	2.615814	0.607659
27	6	0	4.014837	-3.158406	-0.101943
28	1	0	2.249423	-4.274925	-0.674916
29	1	0	5.580398	-1.805810	0.444539
30	1	0	5.282501	0.629625	0.686682
31	1	0	4.652771	-4.034530	-0.077496
32	6	0	1.247554	2.771445	0.122548
33	8	0	1.695456	3.839427	-0.242627
34	8	0	0.009266	2.620020	0.612584
35	6	0	-0.842573	3.784272	0.590774
36	1	0	-0.966655	4.140208	-0.432846
37	1	0	-1.793923	3.450692	0.998010
38	1	0	-0.417053	4.579149	1.204612

TS-enant-2c-H2

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-2.468117	-2.083310	-0.328498
2	6	0	-1.244227	-2.661339	-0.666899
3	6	0	-0.075460	-1.926269	-0.638644
4	6	0	-0.018156	-0.558102	-0.279270
5	6	0	-1.285693	0.106403	-0.217916
6	6	0	-2.440250	-0.698816	-0.140781
7	35	0	-4.147597	0.156135	0.224205
8	6	0	-3.716116	-2.917992	-0.245224
9	1	0	-4.169251	-2.846392	0.747327
10	1	0	-4.469361	-2.581362	-0.962805
11	1	0	-3.489179	-3.965643	-0.446959
12	6	0	-1.482547	1.588092	-0.403956
13	1	0	-2.394813	1.759823	-0.974007
14	1	0	-1.572352	2.136658	0.534208
15	1	0	-0.670804	2.011152	-0.989081
16	6	0	1.364231	0.011623	-0.120301
17	6	0	2.468166	-0.921321	0.088463
18	6	0	1.766969	1.358919	-0.229689
19	6	0	2.324085	-2.136174	0.821163
20	6	0	3.797155	-0.577416	-0.322368
21	6	0	3.087844	1.686677	-0.641279
22	6	0	3.379392	-2.996246	1.017693
23	1	0	1.371546	-2.368031	1.276338
24	6	0	4.852533	-1.516989	-0.172668
25	6	0	4.056853	0.733091	-0.787621
26	1	0	3.314905	2.729007	-0.824003
27	6	0	4.650464	-2.711940	0.471452
28	1	0	3.234061	-3.892784	1.609385
29	1	0	5.837823	-1.245858	-0.536510
30	1	0	5.045652	0.993714	-1.147264
31	1	0	5.467963	-3.411511	0.602531
32	6	0	1.037355	2.524485	0.344786
33	8	0	0.568736	2.523549	1.462819
34	8	0	1.078717	3.620038	-0.437258
35	6	0	0.545188	4.832865	0.138525
36	1	0	1.085740	5.089092	1.050530
37	1	0	0.685158	5.598670	-0.620424
38	1	0	-0.514103	4.707924	0.366552

39	1	0	0.483790	0.753701	-2.596038
40	1	0	-1.844010	0.533591	-3.385327

0 negative eigenvalue			Sum of electronic and thermal Free Energies=		
			-3497.020079		

7,8-[5]helicyne

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	3.535054	0.956741	0.687000
2	6	0	2.814993	2.112885	0.686716
3	6	0	1.438029	2.095653	0.339950
4	6	0	0.730255	0.870209	0.065880
5	6	0	1.579970	-0.287618	-0.189777
6	6	0	2.959045	-0.250921	0.191398
7	6	0	0.594579	3.207799	0.156362
8	6	0	-0.730252	0.870205	-0.065962
9	6	0	-1.438022	2.095623	-0.340157
10	6	0	-0.594574	3.207787	-0.156671
11	6	0	-2.814981	2.112818	-0.686947
12	1	0	-3.269958	3.059848	-0.949665
13	6	0	-3.535040	0.956673	-0.687131
14	6	0	-2.959039	-0.250938	-0.191392
15	6	0	-1.579971	-0.287594	0.189809
16	1	0	4.578886	0.955676	0.980834
17	1	0	3.269973	3.059941	0.949334
18	1	0	-4.578866	0.955576	-0.980987
19	6	0	3.779389	-1.387071	-0.023990
20	6	0	1.145686	-1.420039	-0.926846
21	6	0	1.978103	-2.491423	-1.167914
22	6	0	3.299697	-2.497392	-0.679135
23	1	0	4.812296	-1.346765	0.305166
24	1	0	0.143776	-1.438148	-1.329934
25	1	0	1.613101	-3.331245	-1.748285
26	1	0	3.941831	-3.353034	-0.853453
27	6	0	-1.145700	-1.419929	0.927015
28	6	0	-3.779388	-1.387062	0.024111
29	6	0	-3.299708	-2.497308	0.679395
30	6	0	-1.978123	-2.491283	1.168196
31	1	0	-0.143794	-1.437994	1.330118
32	1	0	-4.812289	-1.346795	-0.305069
33	1	0	-3.941846	-3.352928	0.853802
34	1	0	-1.613133	-3.331036	1.748673

0 negative eigenvalue
Sum of electronic and thermal Free Energies= -845.451302

39	1	0	0.831853	-2.434825	-0.921448
40	1	0	-1.206578	-3.710490	-0.937831

1 negative eigenvalue			Sum of electronic and thermal Free Energies=		
			-3496.960536		

TS-enant-7,8-[5]helicyne

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-3.400761	1.161883	0.742804
2	6	0	-2.755326	2.233857	0.222120
3	6	0	-1.448498	2.083810	-0.322308
4	6	0	-0.742024	0.810117	-0.391897
5	6	0	-1.660495	-0.338262	-0.218562
6	6	0	-2.891066	-0.149093	0.501955
7	6	0	-0.614202	3.164986	-0.606775
8	6	0	0.742012	0.810118	-0.391913
9	6	0	1.448484	2.083813	-0.322340
10	6	0	0.614179	3.164987	-0.606788
11	6	0	2.755321	2.233864	0.222065
12	1	0	3.165748	3.233642	0.287426
13	6	0	3.400766	1.161892	0.742740
14	6	0	2.891072	-0.149085	0.501899
15	6	0	1.660491	-0.338259	-0.218600
16	1	0	-4.345254	1.272092	1.263459
17	1	0	-3.165754	3.233634	0.287489
18	1	0	4.345268	1.272103	1.263380
19	6	0	-3.701441	-1.257804	0.841147
20	6	0	-1.514202	-1.617123	-0.802182
21	6	0	-2.351061	-2.680642	-0.514233
22	6	0	-3.421678	-2.523758	0.375777
23	1	0	-4.591471	-1.075533	1.433820
24	1	0	-0.788825	-1.763448	-1.575243
25	1	0	-2.185111	-3.632348	-1.006185
26	1	0	-4.058643	-3.362446	0.631288
27	6	0	1.514199	-1.617121	-0.802223
28	6	0	3.701457	-1.257792	0.841079
29	6	0	3.421696	-2.523746	0.375710
30	6	0	2.351070	-2.680635	-0.514287
31	1	0	0.788815	-1.763452	-1.575278
32	1	0	4.591494	-1.075516	1.433740
33	1	0	4.058670	-3.362431	0.631211
34	1	0	2.185120	-3.632339	-1.006241

1 negative eigenvalue
Sum of electronic and thermal Free Energies= -845.415860

[5]helicene							TS-enant-[5]helicene												
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)			Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)										
			X	Y	Z				X	Y	Z								
1	6	0	3.502330	0.914115	0.697942	1	6	0	-3.420422	1.109022	0.696212								
2	6	0	2.747764	2.044877	0.702043	2	6	0	-2.726247	2.161891	0.207044								
3	6	0	1.364878	2.017188	0.335101	3	6	0	-1.382178	2.007115	-0.265651								
4	6	0	0.722522	0.781359	0.056278	4	6	0	-0.737656	0.729808	-0.334266								
5	6	0	1.585182	-0.368990	-0.189503	5	6	0	-1.672420	-0.412925	-0.198279								
6	6	0	2.961212	-0.307379	0.190478	6	6	0	-2.923834	-0.211543	0.479621								
7	6	0	0.648446	3.240660	0.210648	7	6	0	-0.678683	3.212422	-0.509735								
8	6	0	-0.722523	0.781354	-0.056311	8	6	0	0.737656	0.729808	-0.334266								
9	6	0	-1.364886	2.017173	-0.335165	9	6	0	1.382179	2.007115	-0.265652								
10	6	0	-0.648459	3.240651	-0.210747	10	6	0	0.678686	3.212422	-0.509736								
11	6	0	-2.747775	2.044848	-0.702090	11	6	0	2.726248	2.161891	0.207043								
12	1	0	-3.182052	2.997367	-0.986514	12	1	0	3.129117	3.167194	0.259392								
13	6	0	-3.502343	0.914088	-0.697943	13	6	0	3.420423	1.109020	0.696211								
14	6	0	-2.961217	-0.307391	-0.190453	14	6	0	2.923834	-0.211544	0.479620								
15	6	0	-1.585179	-0.368995	0.189501	15	6	0	1.672420	-0.412926	-0.198279								
16	1	0	4.543188	0.939446	1.002071	16	1	0	-4.387359	1.238747	1.169418								
17	1	0	3.182034	2.997408	0.986439	17	1	0	-3.129114	3.167197	0.259393								
18	1	0	-4.543205	0.939416	-1.002057	18	1	0	4.387360	1.238744	1.169416								
19	6	0	3.802810	-1.425586	-0.027257	19	6	0	-3.758268	-1.307791	0.796872								
20	6	0	1.166430	-1.510941	-0.918140	20	6	0	-1.521991	-1.697658	-0.767513								
21	6	0	2.017226	-2.569075	-1.160098	21	6	0	-2.378273	-2.752434	-0.502572								
22	6	0	3.341032	-2.546715	-0.679780	22	6	0	-3.476812	-2.580217	0.348970								
23	1	0	4.835982	-1.366509	0.298827	23	1	0	-4.665799	-1.111764	1.358124								
24	1	0	0.161550	-1.549250	-1.313253	24	1	0	-0.775056	-1.859595	-1.515515								
25	1	0	1.664261	-3.419530	-1.732482	25	1	0	-2.204584	-3.708255	-0.983915								
26	1	0	3.998969	-3.390271	-0.855025	26	1	0	-4.130844	-3.410845	0.587689								
27	6	0	-1.166412	-1.510935	0.918149	27	6	0	1.521990	-1.697659	-0.767512								
28	6	0	-3.802813	-1.425591	0.027327	28	6	0	3.758268	-1.307793	0.796872								
29	6	0	-3.341022	-2.546705	0.679861	29	6	0	3.476811	-2.580220	0.348971								
30	6	0	-2.017204	-2.569063	1.160147	30	6	0	2.378270	-2.752434	-0.502571								
31	1	0	-0.161523	-1.549240	1.313239	31	1	0	0.775055	-1.859596	-1.515514								
32	1	0	-4.835992	-1.366524	-0.298738	32	1	0	4.665799	-1.111766	1.358124								
33	1	0	-3.998964	-3.390249	0.855151	33	1	0	4.130841	-3.410847	0.587691								
34	1	0	-1.664228	-3.419512	1.732532	34	1	0	2.204580	-3.708256	-0.983913								
35	1	0	-1.171644	4.171873	-0.398967	35	1	0	1.238317	4.138408	-0.579412								
36	1	0	1.171625	4.171890	0.398841	36	1	0	-1.238314	4.138409	-0.579412								
0 negative eigenvalue			Sum of electronic and thermal Free Energies=				-846.763764			1 negative eigenvalue			Sum of electronic and thermal Free Energies=				-846.726760		
1,14-dimethyl-7,8-[5]helicene							TS-1,14-dimethyl-[5]helicene												
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)			Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)										
			X	Y	Z				X	Y	Z								
1	6	0	-3.499619	1.056654	0.688287	1	6	0	3.026707	1.412907	-1.130304								

2	6	0	-2.823873	2.237529	0.635618	2	6	0	2.610267	2.413793	-0.311985
3	6	0	-1.450037	2.242231	0.279546	3	6	0	1.434343	2.226973	0.479467
4	6	0	-0.729656	1.019174	0.010624	4	6	0	0.731071	0.949683	0.513570
5	6	0	-1.560158	-0.140362	-0.305404	5	6	0	1.591370	-0.183676	0.101839
6	6	0	-2.912704	-0.143083	0.178697	6	6	0	2.536823	0.076257	-0.943025
7	6	0	-0.603504	3.353072	0.123944	7	6	0	0.617235	3.263611	0.922869
8	6	0	0.729628	1.019186	-0.010602	8	6	0	-0.731200	0.949616	0.513587
9	6	0	1.449987	2.242252	-0.279543	9	6	0	-1.434593	2.226851	0.479515
10	6	0	0.603438	3.353081	-0.123939	10	6	0	-0.617538	3.263539	0.922886
11	6	0	2.823817	2.237570	-0.635638	11	6	0	-2.610564	2.413557	-0.311892
12	1	0	3.299822	3.175622	-0.893157	12	1	0	-3.052181	3.401385	-0.351227
13	6	0	3.499577	1.056703	-0.688322	13	6	0	-3.026959	1.412636	-1.130192
14	6	0	2.912687	-0.143042	-0.178723	14	6	0	-2.536943	0.076033	-0.942941
15	6	0	1.560154	-0.140338	0.305412	15	6	0	-1.591399	-0.183804	0.101858
16	1	0	-4.528710	1.023246	1.028591	16	1	0	3.805217	1.581556	-1.866020
17	1	0	-3.299897	3.175576	0.893124	17	1	0	3.051782	3.401665	-0.351351
18	1	0	4.528661	1.023309	-1.028649	18	1	0	-3.805522	1.581220	-1.865866
19	6	0	-3.713450	-1.300467	0.055533	19	6	0	3.134200	-0.997804	-1.635446
20	6	0	-1.165381	-1.221825	-1.159203	20	6	0	1.678219	-1.465333	0.709363
21	6	0	-2.005107	-2.322911	-1.275365	21	6	0	2.278819	-2.508963	0.005380
22	6	0	-3.246924	-2.400340	-0.627429	22	6	0	2.929691	-2.297968	-1.214819
23	1	0	-4.715768	-1.287590	0.469802	23	1	0	3.800133	-0.779501	-2.463294
24	1	0	-1.702909	-3.135195	-1.928471	24	1	0	2.314204	-3.491997	0.464550
25	1	0	-3.859230	-3.288888	-0.730856	25	1	0	3.370669	-3.129821	-1.751980
26	6	0	1.165420	-1.221804	1.159231	26	6	0	-1.678000	-1.465494	0.709342
27	6	0	3.713452	-1.300417	-0.055584	27	6	0	-3.134208	-0.998105	-1.635348
28	6	0	3.246958	-2.400296	0.627388	28	6	0	-2.929478	-2.298249	-1.214770
29	6	0	2.005161	-2.322880	1.275365	29	6	0	-2.278486	-2.509197	0.005379
30	1	0	4.715758	-1.287525	-0.469880	30	1	0	-3.800211	-0.779886	-2.463161
31	1	0	3.859277	-3.288838	0.730796	31	1	0	-3.370383	-3.130147	-1.751922
32	1	0	1.702997	-3.135164	1.928485	32	1	0	-2.313707	-3.492249	0.464524
33	6	0	-0.047719	-1.195842	2.064745	33	6	0	-1.506044	-1.641854	2.201120
34	1	0	-0.913503	-1.696743	1.627126	34	1	0	-1.043777	-2.590976	2.470228
35	1	0	-0.349612	-0.179023	2.316123	35	1	0	-0.966268	-0.826485	2.671376
36	1	0	0.195041	-1.715454	2.994611	36	1	0	-2.512010	-1.643565	2.636287
37	6	0	0.047804	-1.195856	-2.064655	37	6	0	1.506444	-1.641741	2.201178
38	1	0	0.913579	-1.696723	-1.626978	38	1	0	0.966774	-0.826389	2.671541
39	1	0	0.349684	-0.179034	-2.316040	39	1	0	1.044161	-2.590856	2.470312
40	1	0	-0.194893	-1.715497	-2.994521	40	1	0	2.512462	-1.643561	2.636214

0 negative eigenvalue

Sum of electronic and thermal Free Energies= -924.032170

1 negative eigenvalue

Sum of electronic and thermal Free Energies= -923.968257

1,14-dimethyl-7,8-[5]helicene

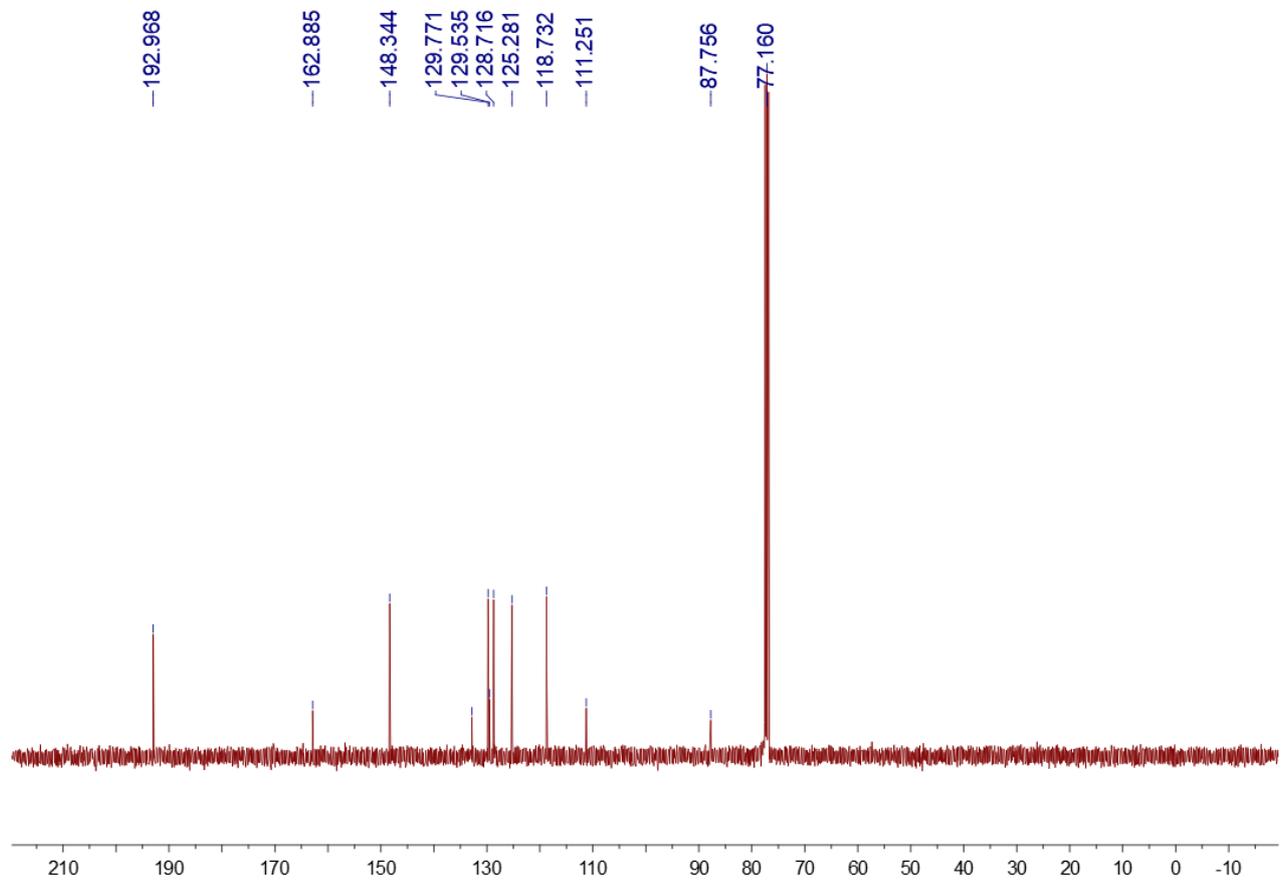
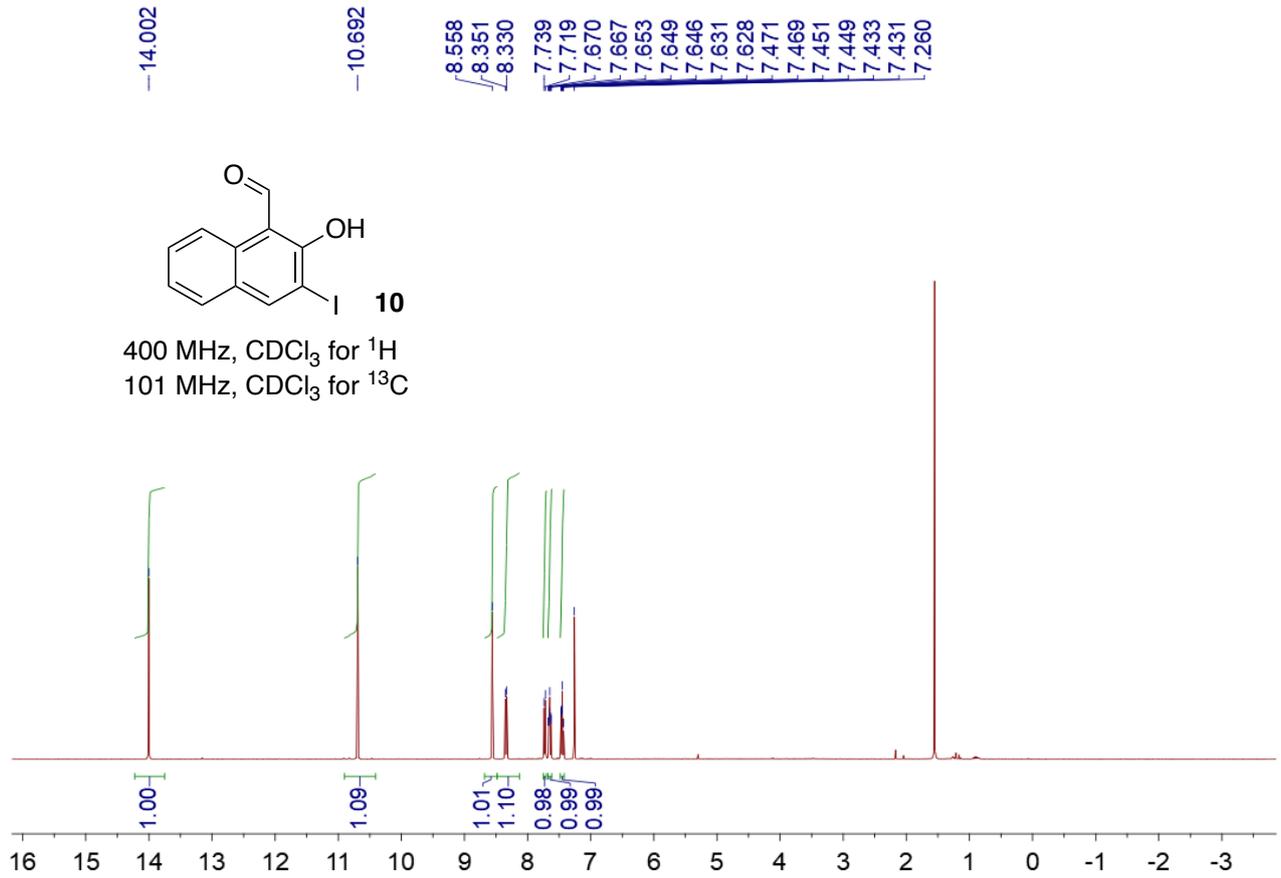
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
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2	6	0	-2.749033	2.173744	0.679302
3	6	0	-1.372959	2.169795	0.288709
4	6	0	-0.721672	0.936268	0.002169

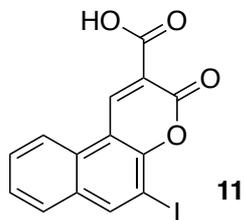
TS-1,14-dimethyl-[5]helicene

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	3.089766	1.334465	-1.098553
2	6	0	2.618766	2.335821	-0.314457
3	6	0	1.375714	2.168918	0.388934
4	6	0	0.730522	0.897707	0.438968

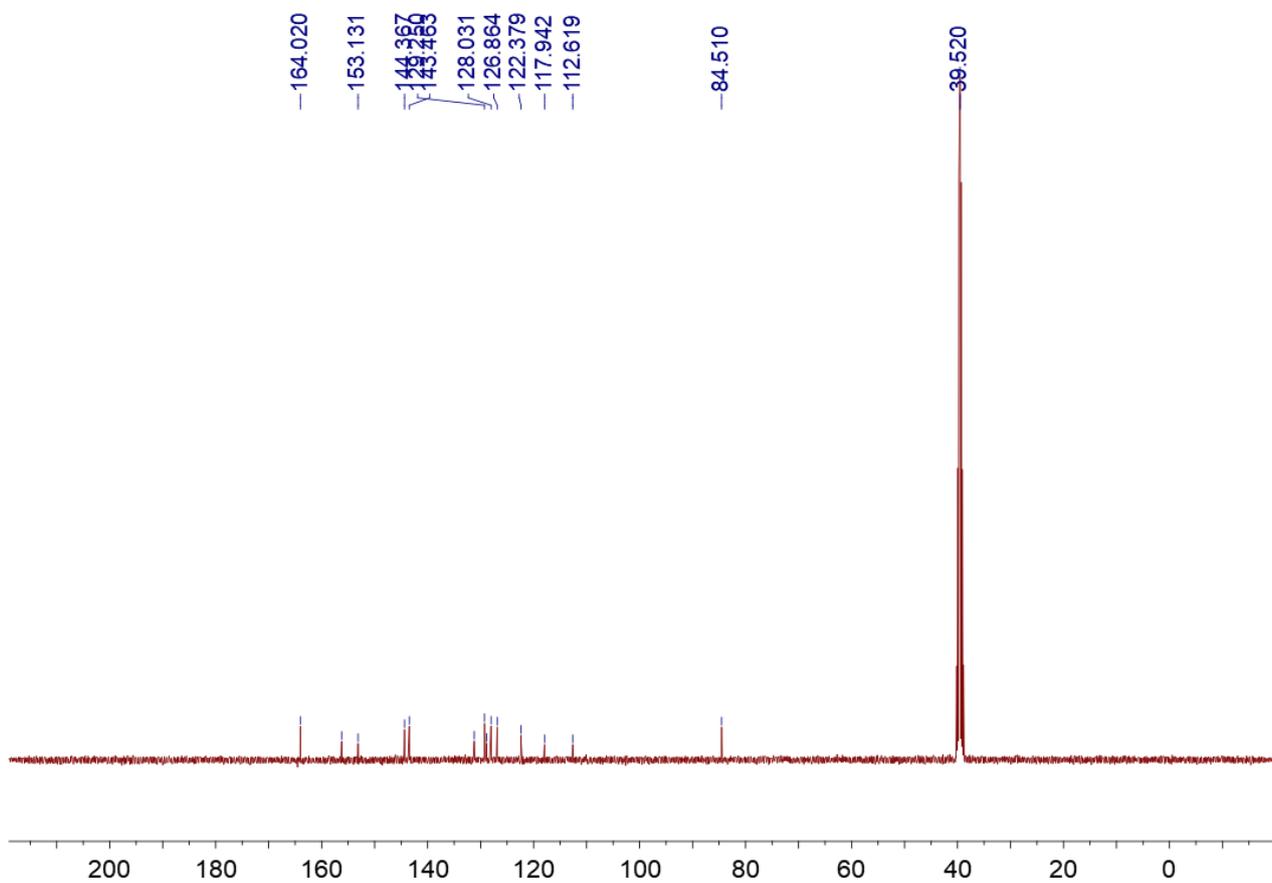
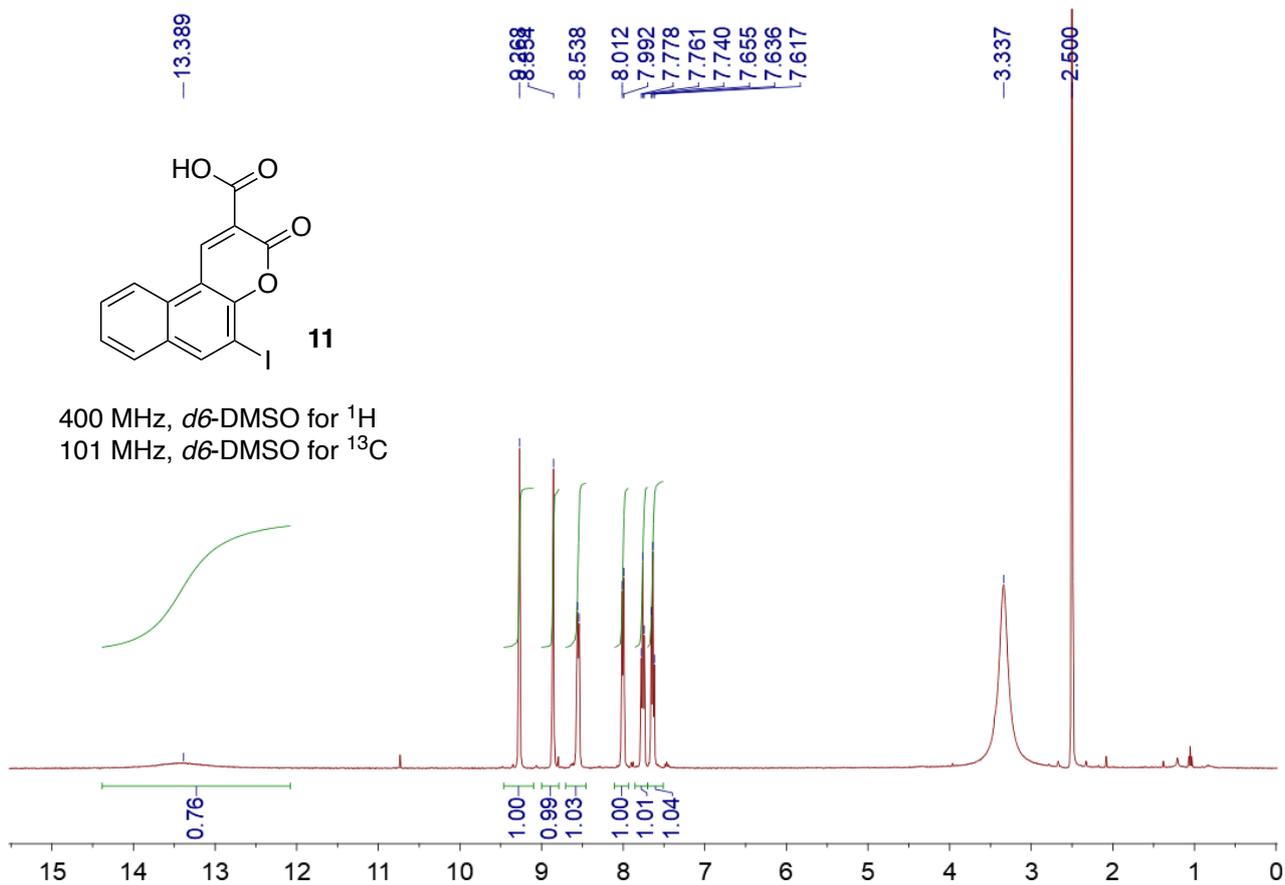
5	6	0	-1.568845	-0.213374	-0.304676	5	6	0	1.605877	-0.244425	0.085594
6	6	0	-2.916514	-0.192149	0.185014	6	6	0	2.588384	-0.001073	-0.927712
7	6	0	-0.655543	3.391122	0.193974	7	6	0	0.682816	3.347746	0.762687
8	6	0	0.721672	0.936269	-0.002169	8	6	0	-0.730285	0.897880	0.438909
9	6	0	1.372959	2.169795	-0.288709	9	6	0	-1.375175	2.169229	0.388693
10	6	0	0.655543	3.391122	-0.193974	10	6	0	-0.682081	3.347906	0.762558
11	6	0	2.749033	2.173744	-0.679301	11	6	0	-2.618024	2.336379	-0.315011
12	1	0	3.199275	3.116603	-0.970974	12	1	0	-3.063068	3.324921	-0.341486
13	6	0	3.461735	1.017911	-0.722499	13	6	0	-3.089062	1.335087	-1.099169
14	6	0	2.916514	-0.192149	-0.185014	14	6	0	-2.588092	-0.000577	-0.928053
15	6	0	1.568845	-0.213374	0.304676	15	6	0	-1.605878	-0.244055	0.085498
16	1	0	-4.485936	1.009426	1.079596	16	1	0	3.912747	1.496763	-1.786026
17	1	0	-3.199275	3.116603	0.970974	17	1	0	3.064061	3.324254	-0.340751
18	1	0	4.485936	1.009426	-1.079596	18	1	0	-3.911809	1.497545	-1.786884
19	6	0	-3.744767	-1.326967	0.050442	19	6	0	3.200532	-1.082662	-1.594176
20	6	0	-1.194243	-1.299248	-1.159674	20	6	0	1.675684	-1.520571	0.708598
21	6	0	-2.059403	-2.380281	-1.287987	21	6	0	2.286873	-2.575616	0.030757
22	6	0	-3.304785	-2.430996	-0.645814	22	6	0	2.971965	-2.379284	-1.173101
23	1	0	-4.745718	-1.295953	0.467470	23	1	0	3.894532	-0.874119	-2.401427
24	1	0	-1.771977	-3.197127	-1.942154	24	1	0	2.309913	-3.552853	0.503178
25	1	0	-3.938858	-3.303196	-0.758446	25	1	0	3.421973	-3.218209	-1.691721
26	6	0	1.194243	-1.299248	1.159674	26	6	0	-1.676280	-1.520012	0.708809
27	6	0	3.744767	-1.326967	-0.050442	27	6	0	-3.200480	-1.082107	-1.594392
28	6	0	3.304785	-2.430996	0.645814	28	6	0	-2.972469	-2.378710	-1.172950
29	6	0	2.059403	-2.380281	1.287987	29	6	0	-2.287704	-2.575007	0.031101
30	1	0	4.745718	-1.295953	-0.467470	30	1	0	-3.894241	-0.873512	-2.401834
31	1	0	3.938858	-3.303196	0.758446	31	1	0	-3.422681	-3.217595	-1.691459
32	1	0	1.771977	-3.197127	1.942154	32	1	0	-2.311202	-3.552119	0.503755
33	6	0	-0.030450	-1.300312	2.049629	33	6	0	-1.498521	-1.670483	2.203141
34	1	0	-0.883359	-1.806749	1.593220	34	1	0	-1.037134	-2.614960	2.489403
35	1	0	-0.350123	-0.290310	2.307229	35	1	0	-0.958799	-0.846341	2.657521
36	1	0	0.205367	-1.827065	2.977306	36	1	0	-2.503986	-1.663345	2.639716
37	6	0	0.030450	-1.300312	-2.049629	37	6	0	1.497519	-1.671423	2.202843
38	1	0	0.883359	-1.806749	-1.593220	38	1	0	0.958576	-0.846863	2.657401
39	1	0	0.350123	-0.290310	-2.307229	39	1	0	1.035090	-2.615505	2.488713
40	1	0	-0.205367	-1.827066	-2.977306	40	1	0	2.502910	-1.665478	-2.639599
41	1	0	-1.181817	4.321298	0.379172	41	1	0	-1.236729	4.273447	0.872475
42	1	0	1.181817	4.321298	-0.379172	42	1	0	1.237656	4.273158	0.872723
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0 negative eigenvalue			Sum of electronic and thermal Free Energies=			1 negative eigenvalue			Sum of electronic and thermal Free Energies=		
			-925.345188						-925.275662		

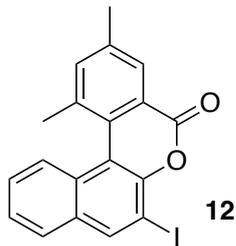
Copies of NMR spectra and HPLC chromatograms, CD spectroscopy



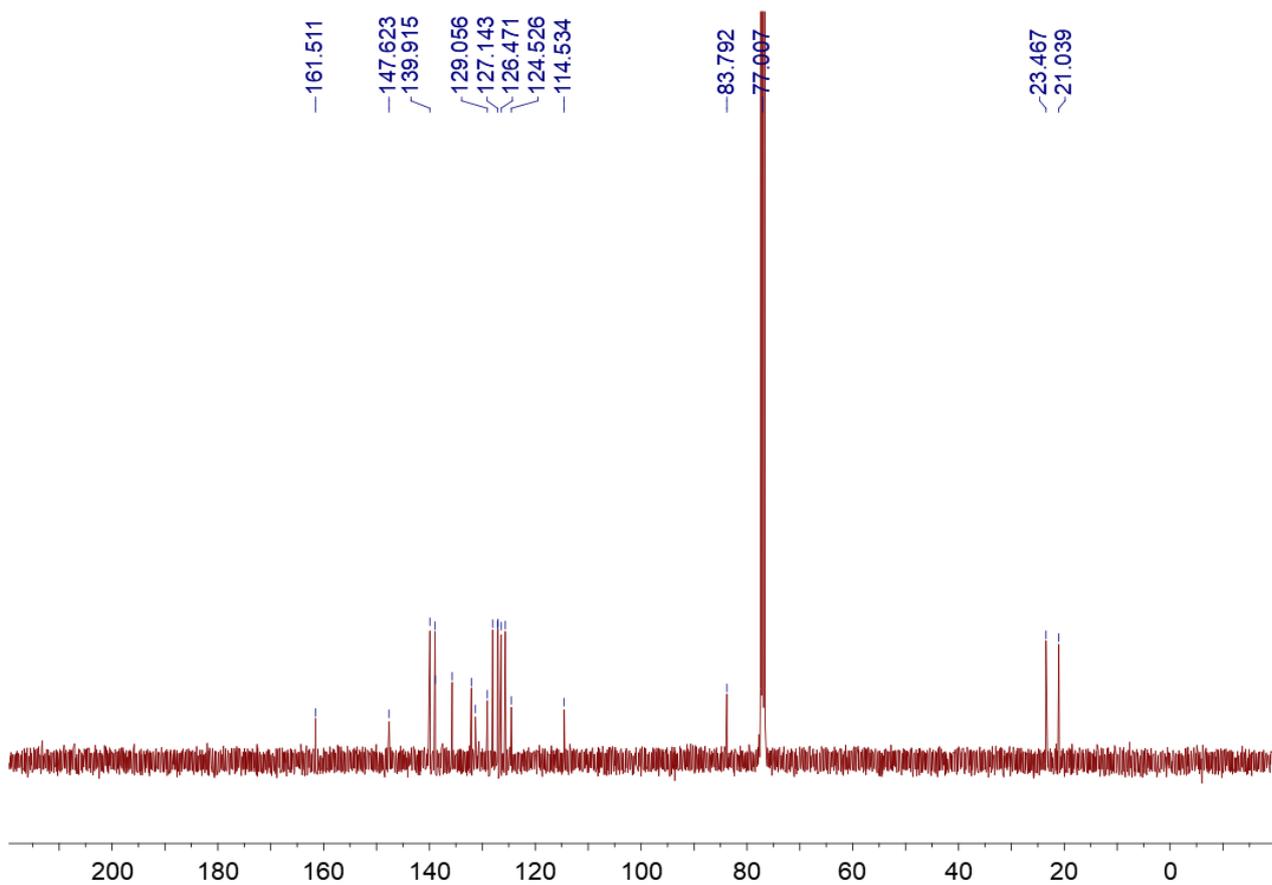
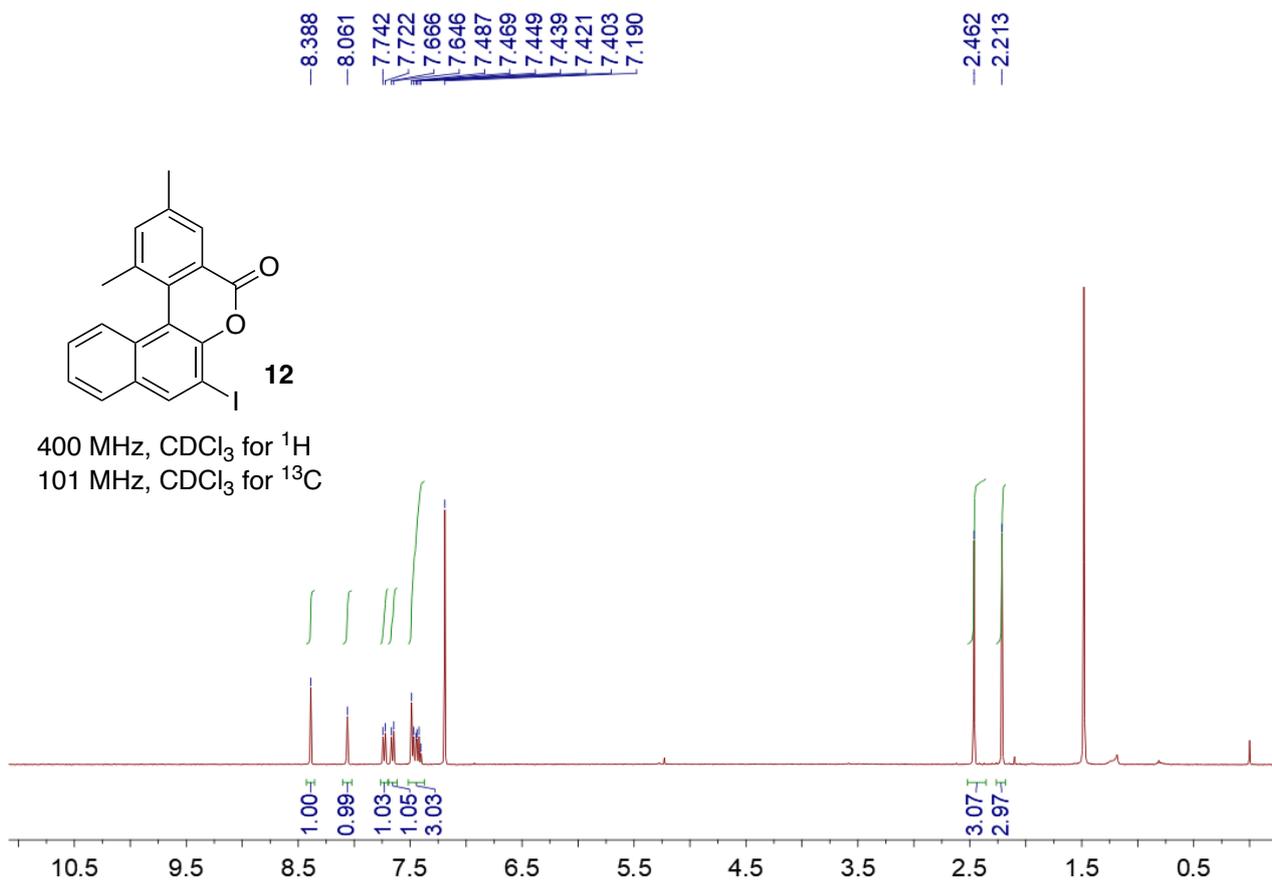


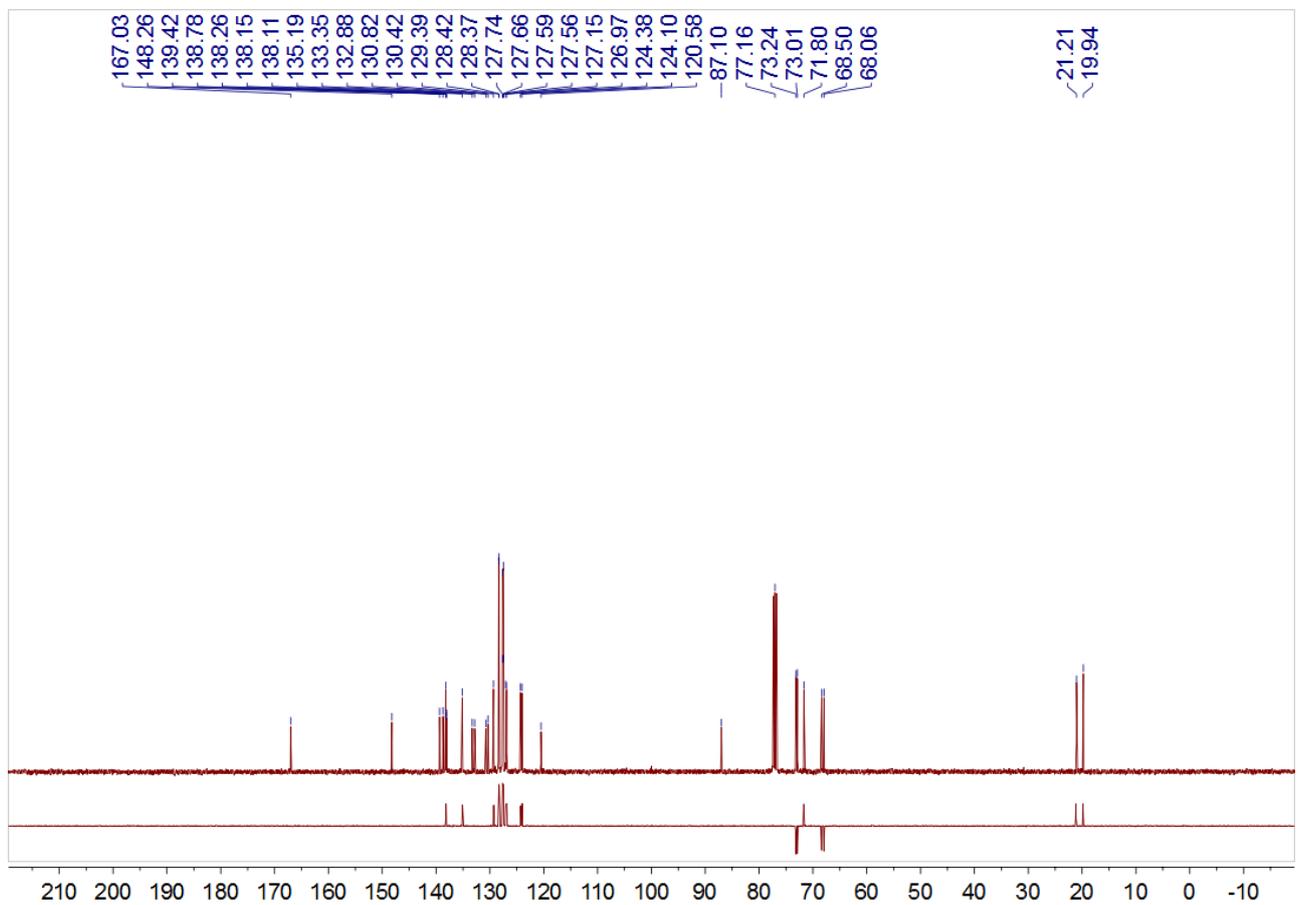
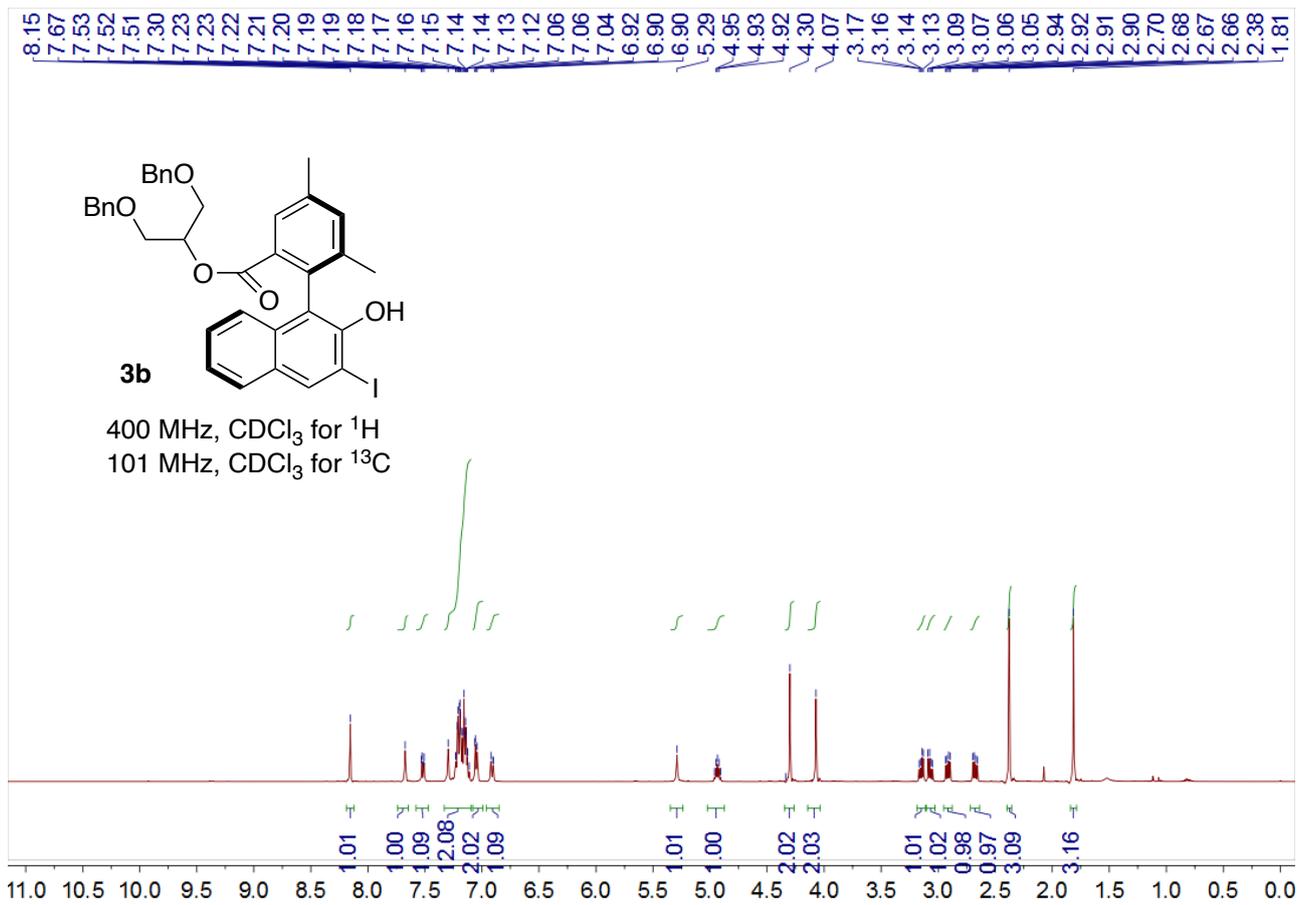
400 MHz, *d*₆-DMSO for ¹H
 101 MHz, *d*₆-DMSO for ¹³C

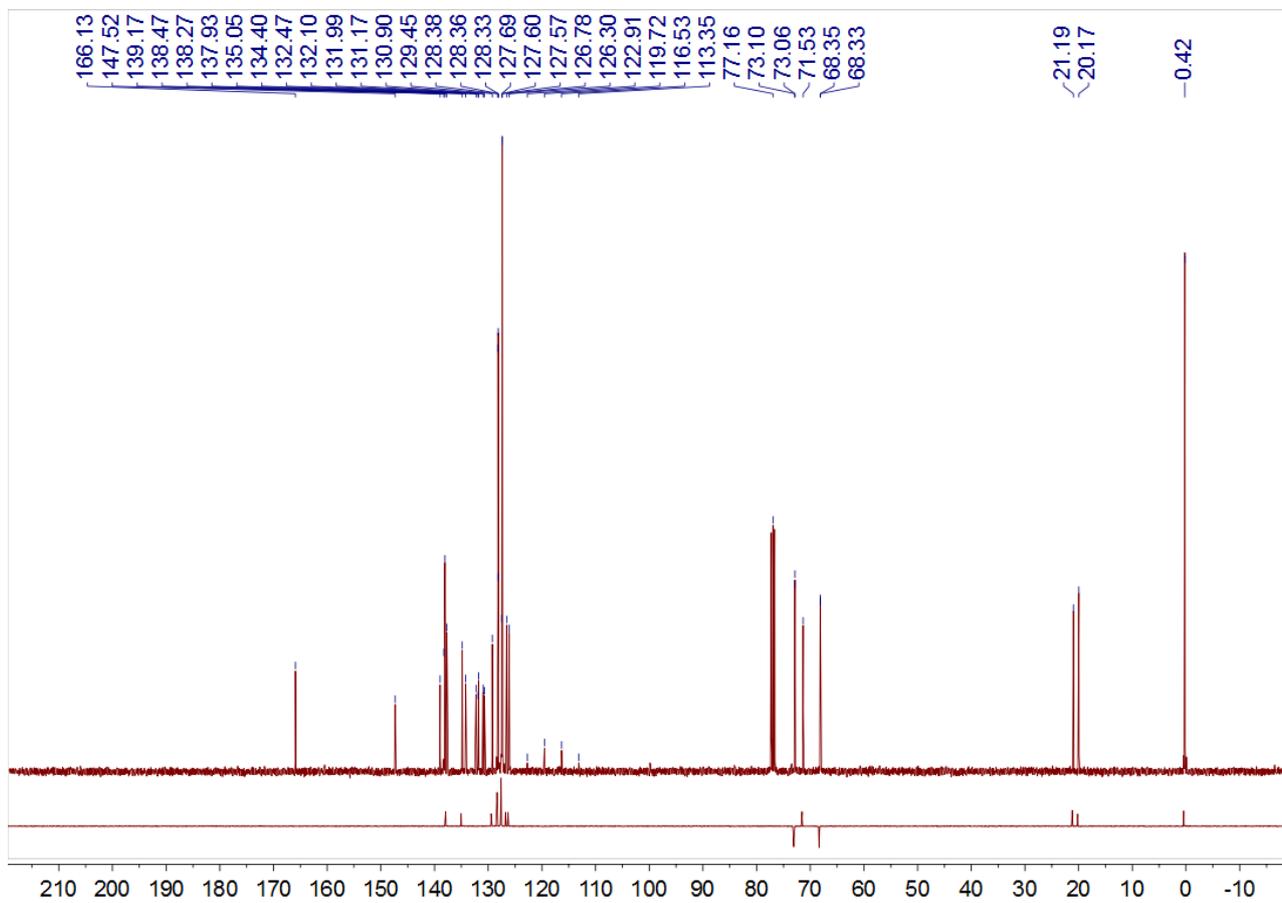
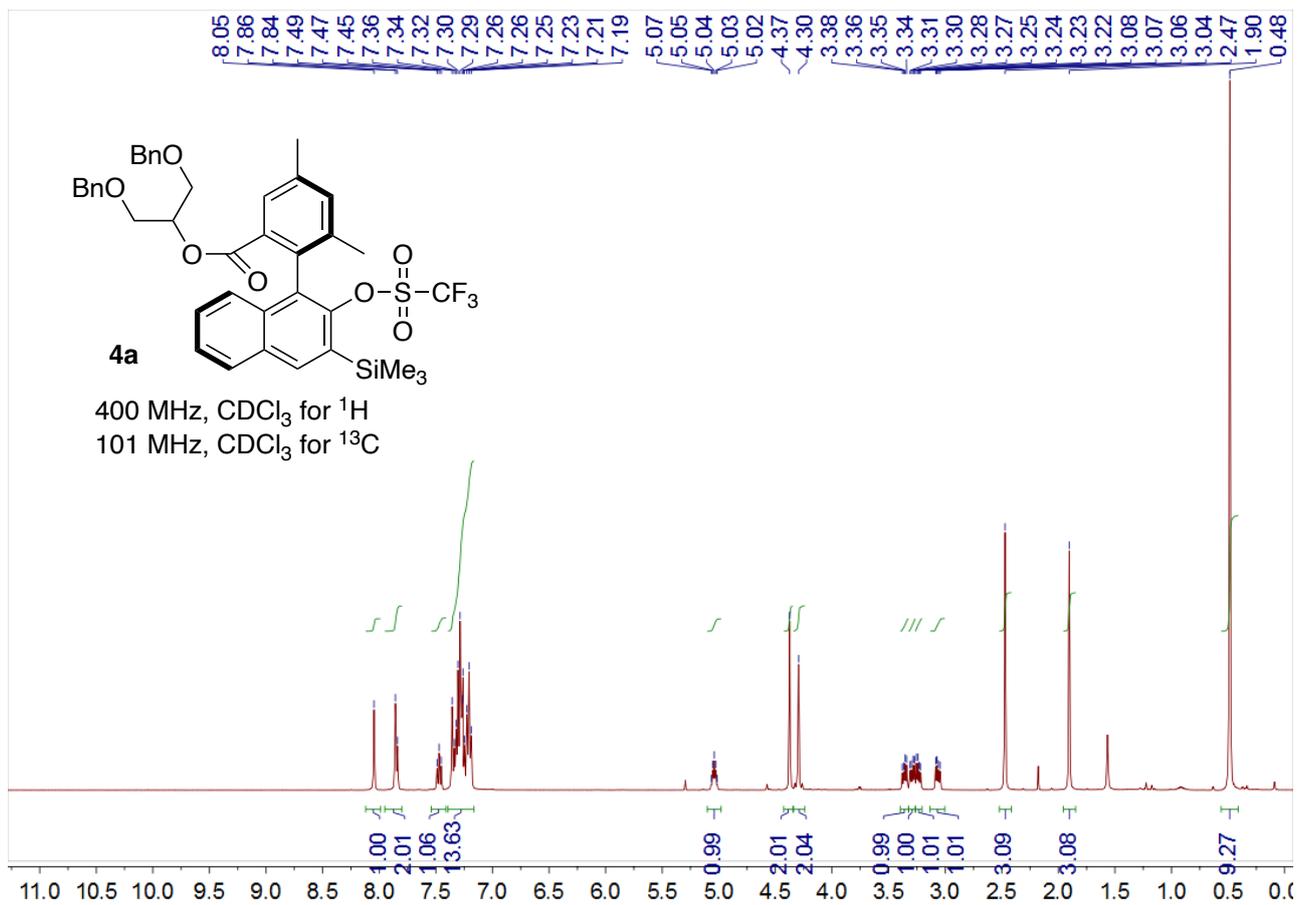


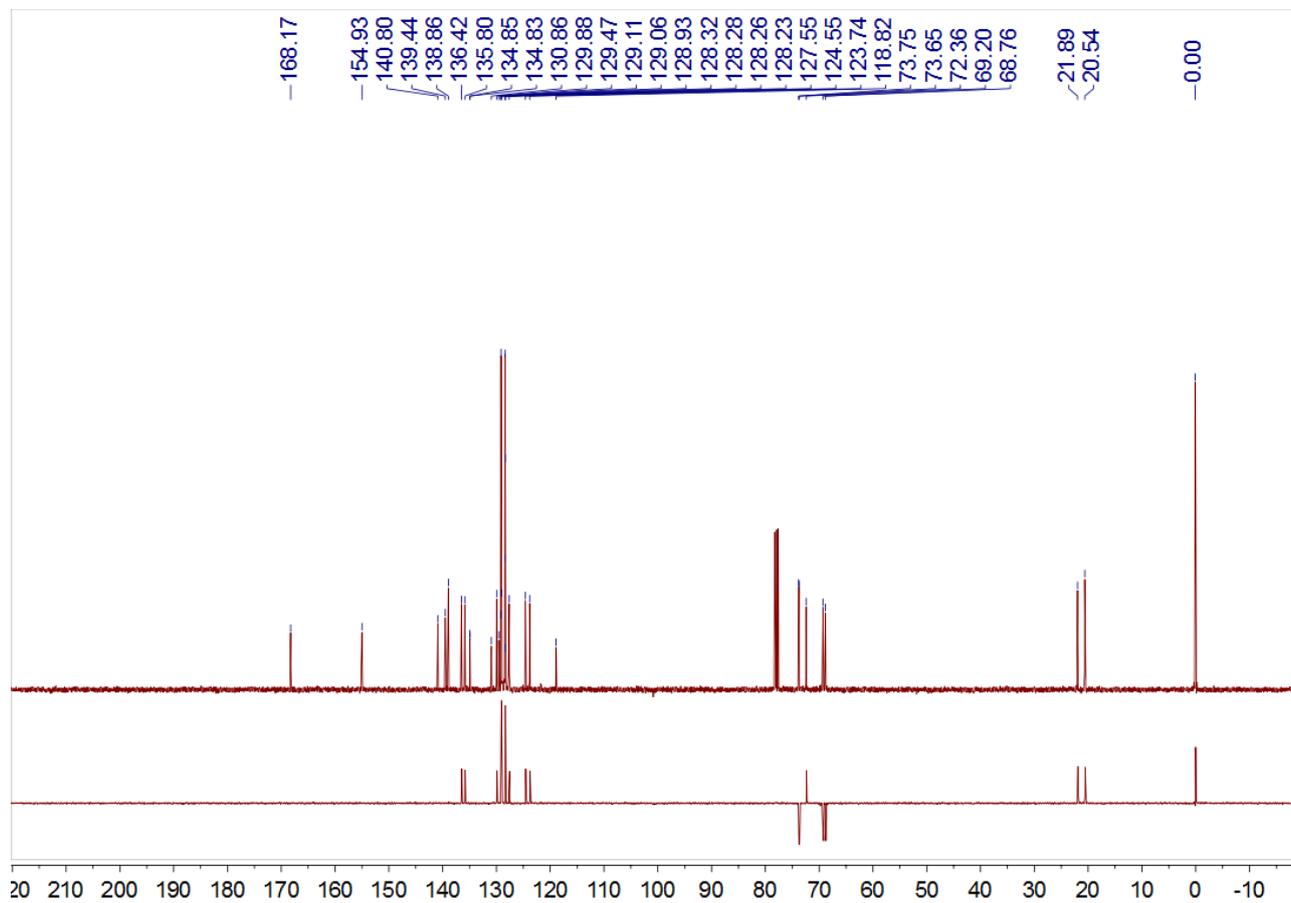
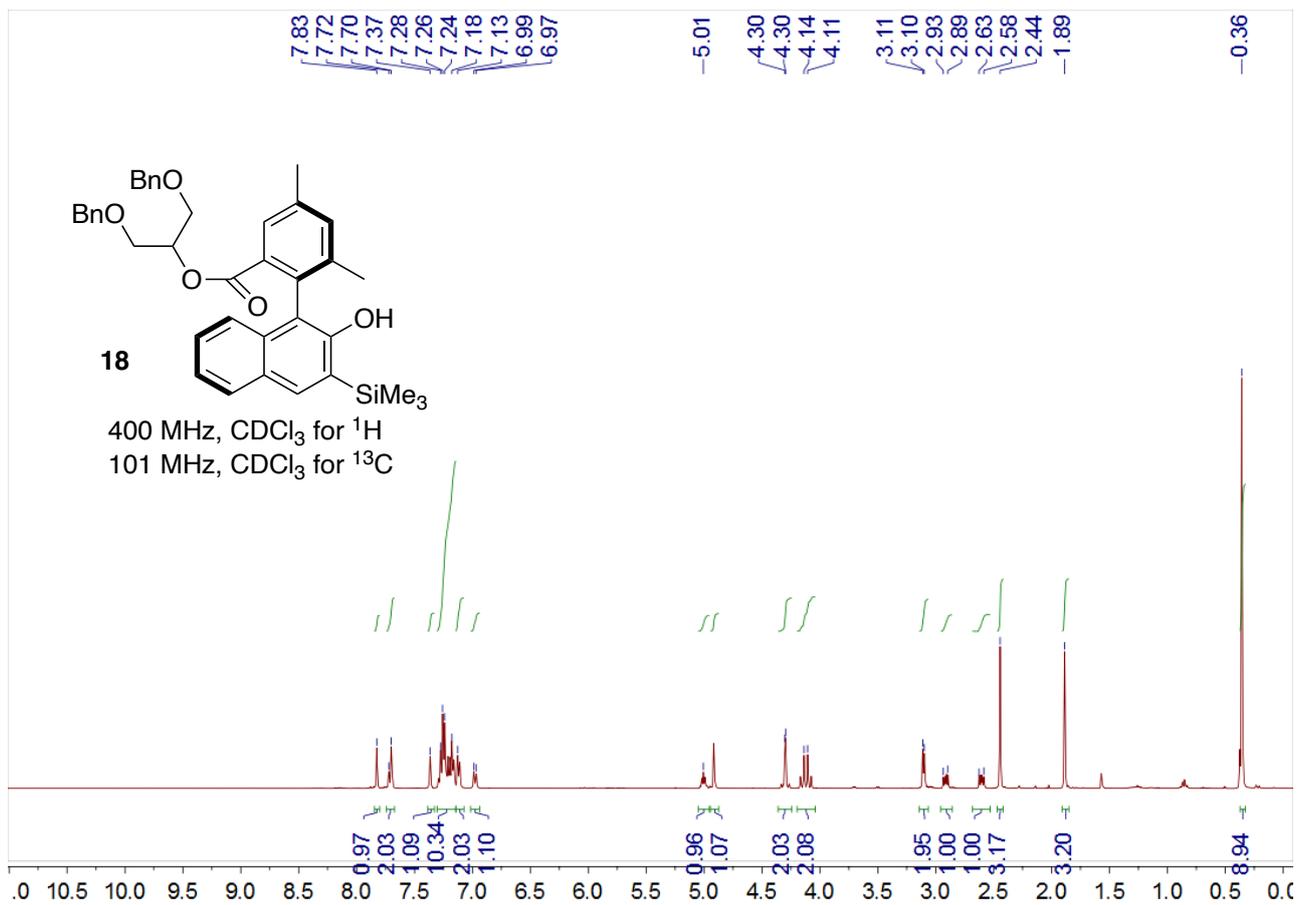


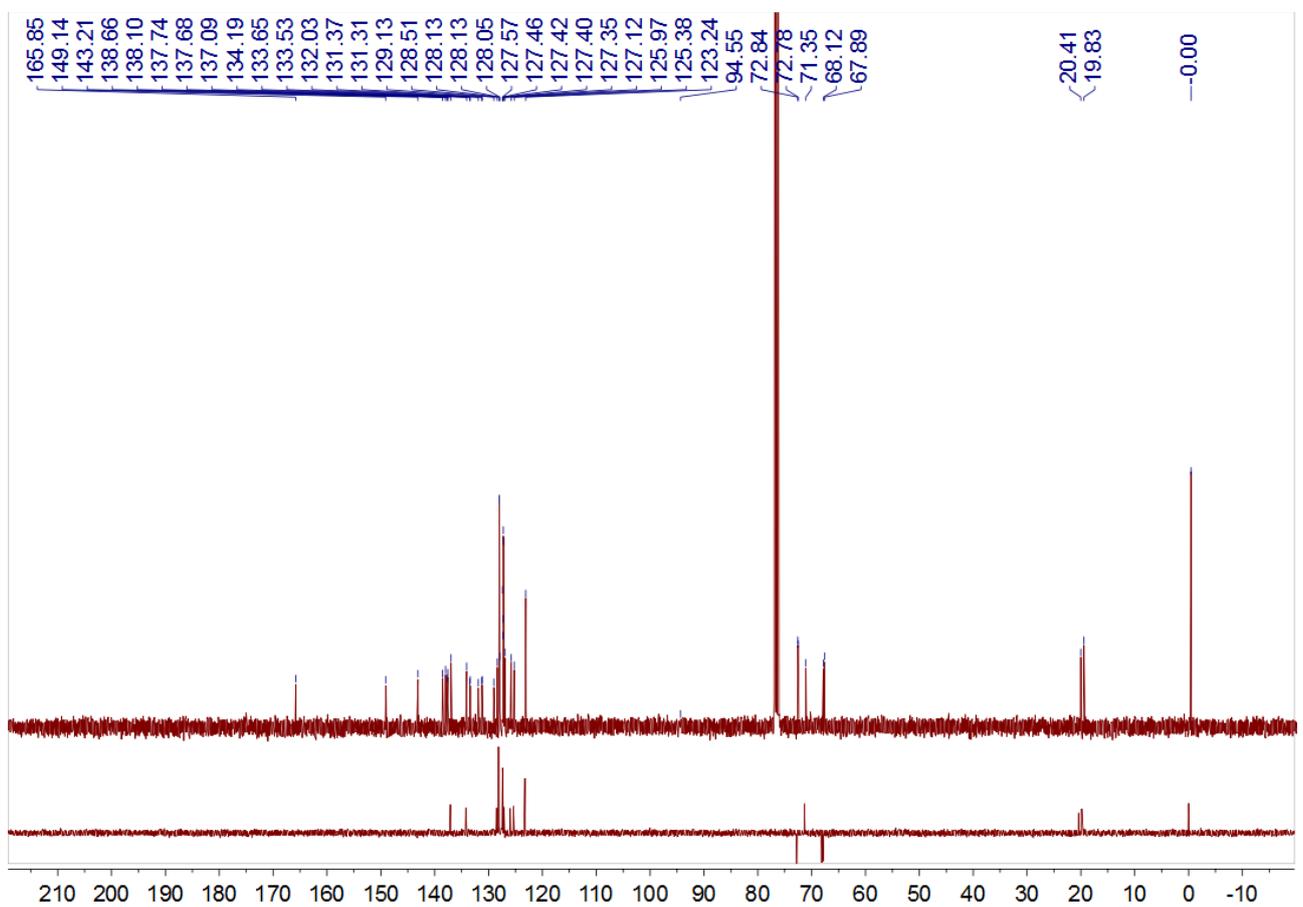
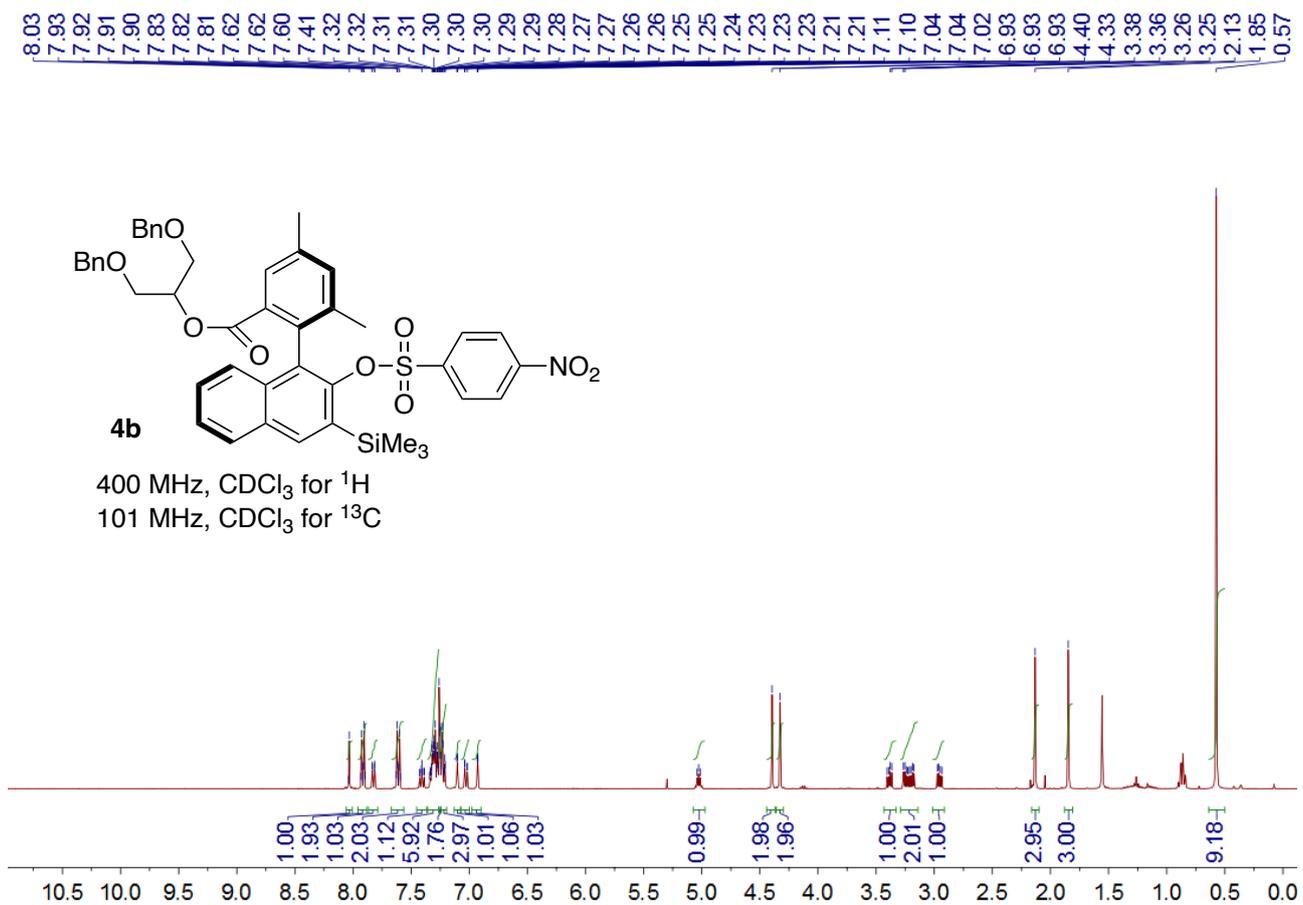
400 MHz, CDCl₃ for ¹H
 101 MHz, CDCl₃ for ¹³C

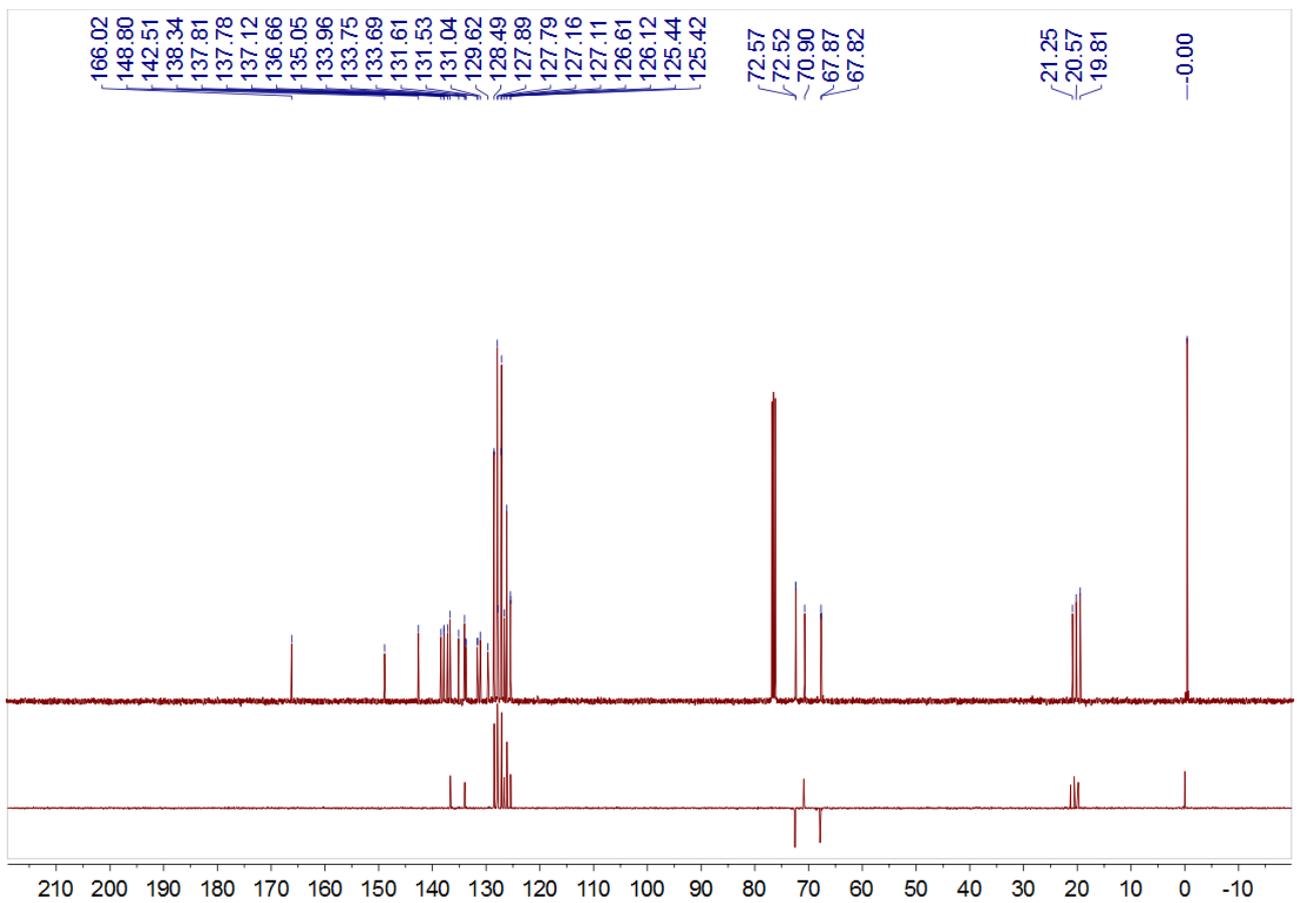
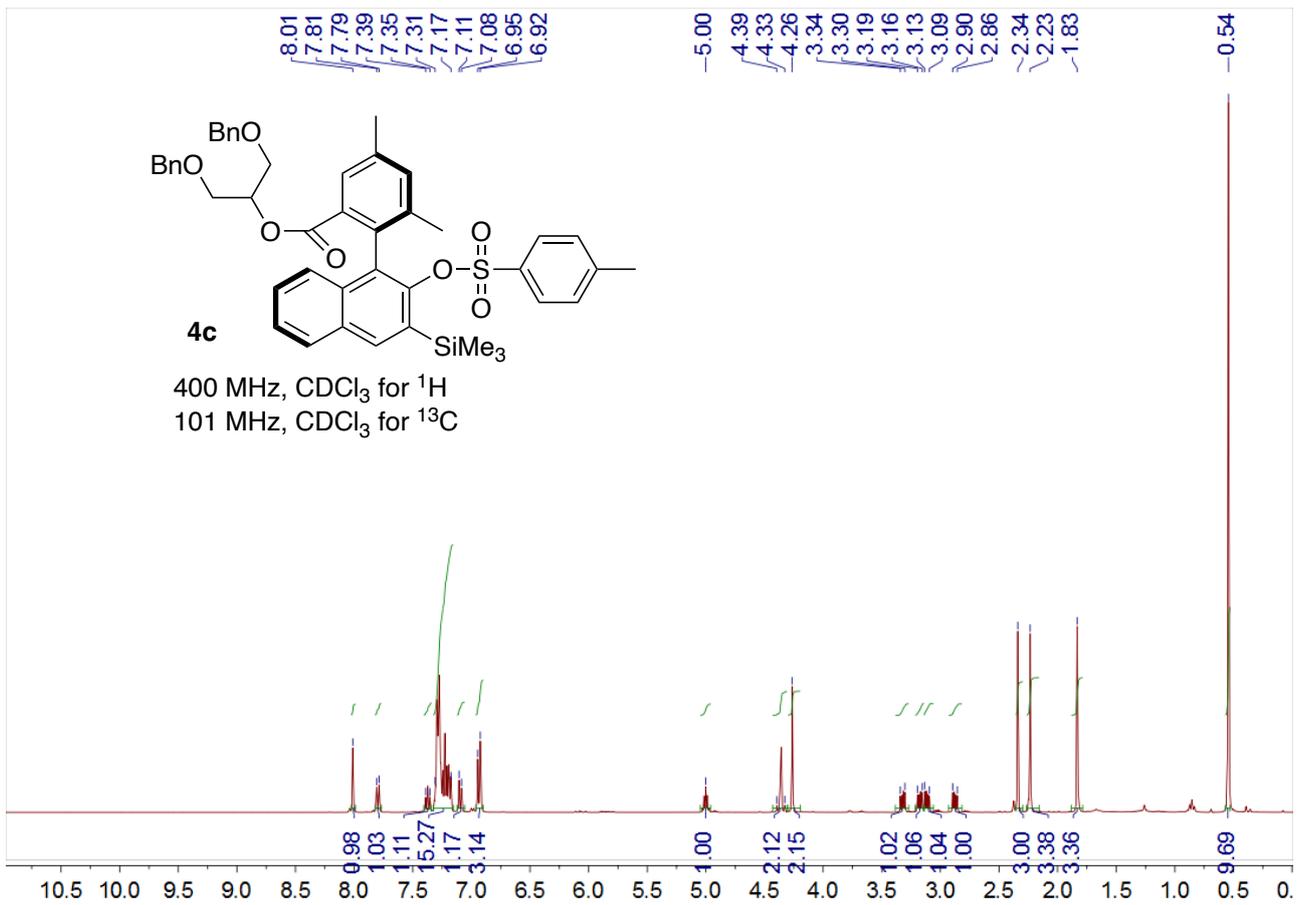


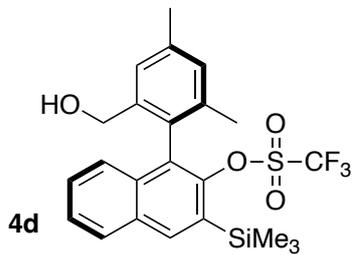




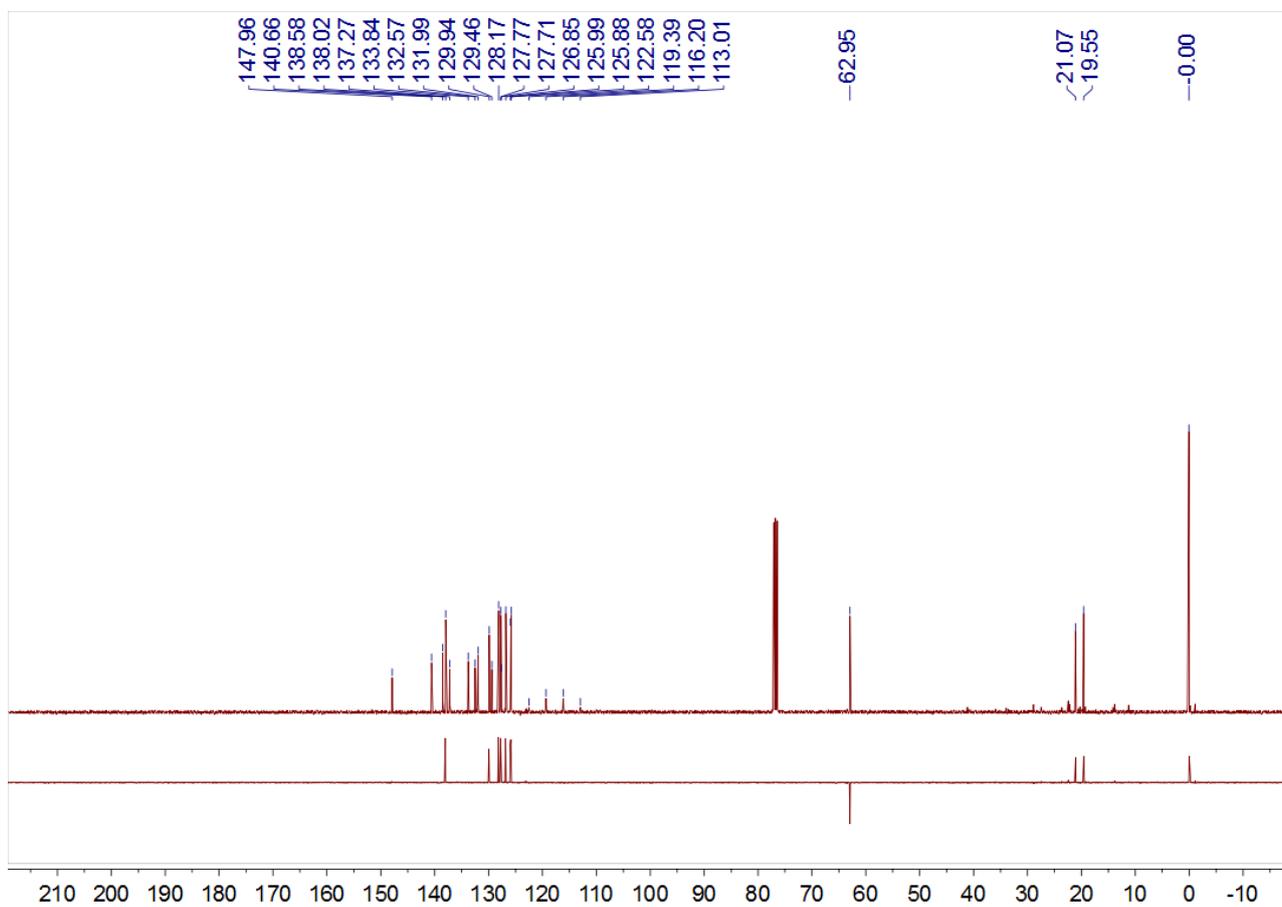
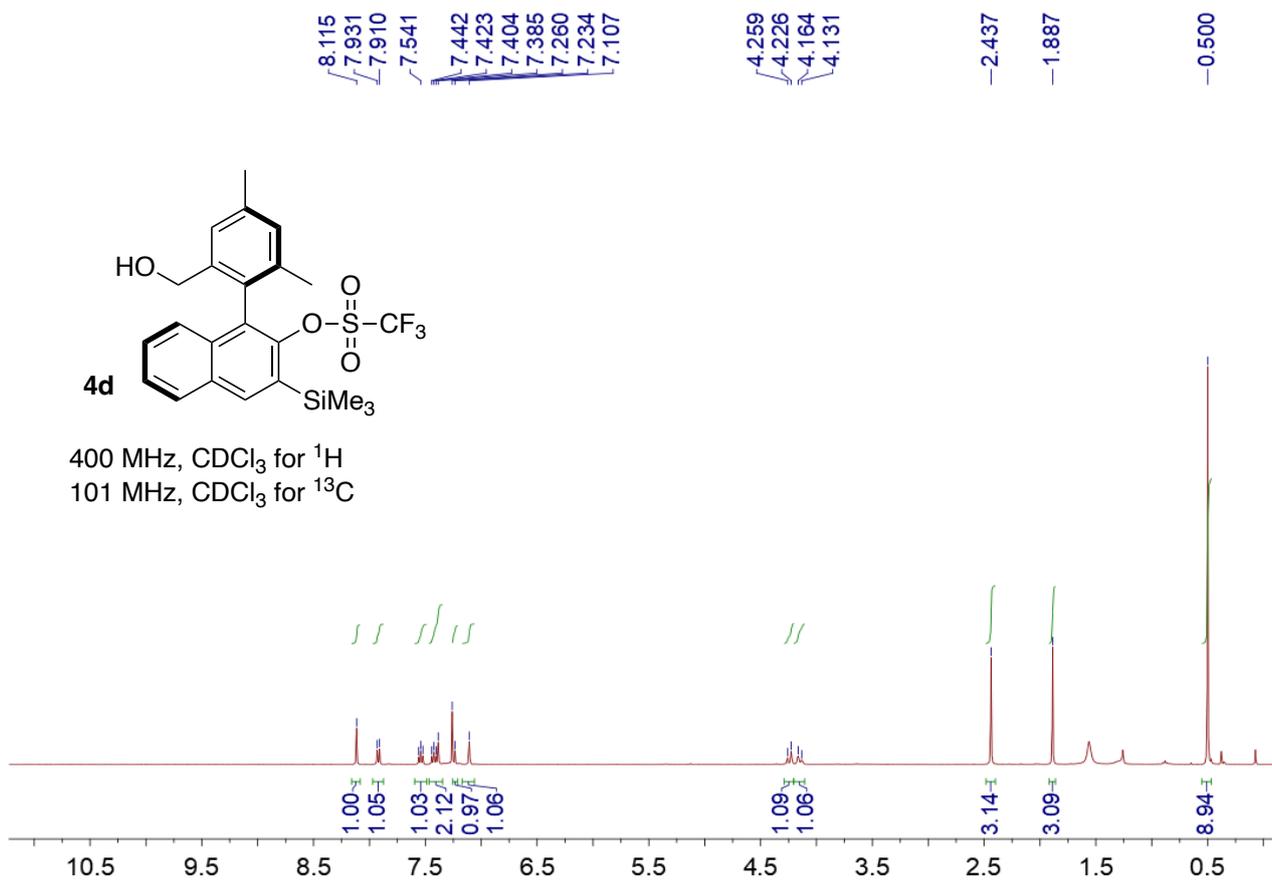


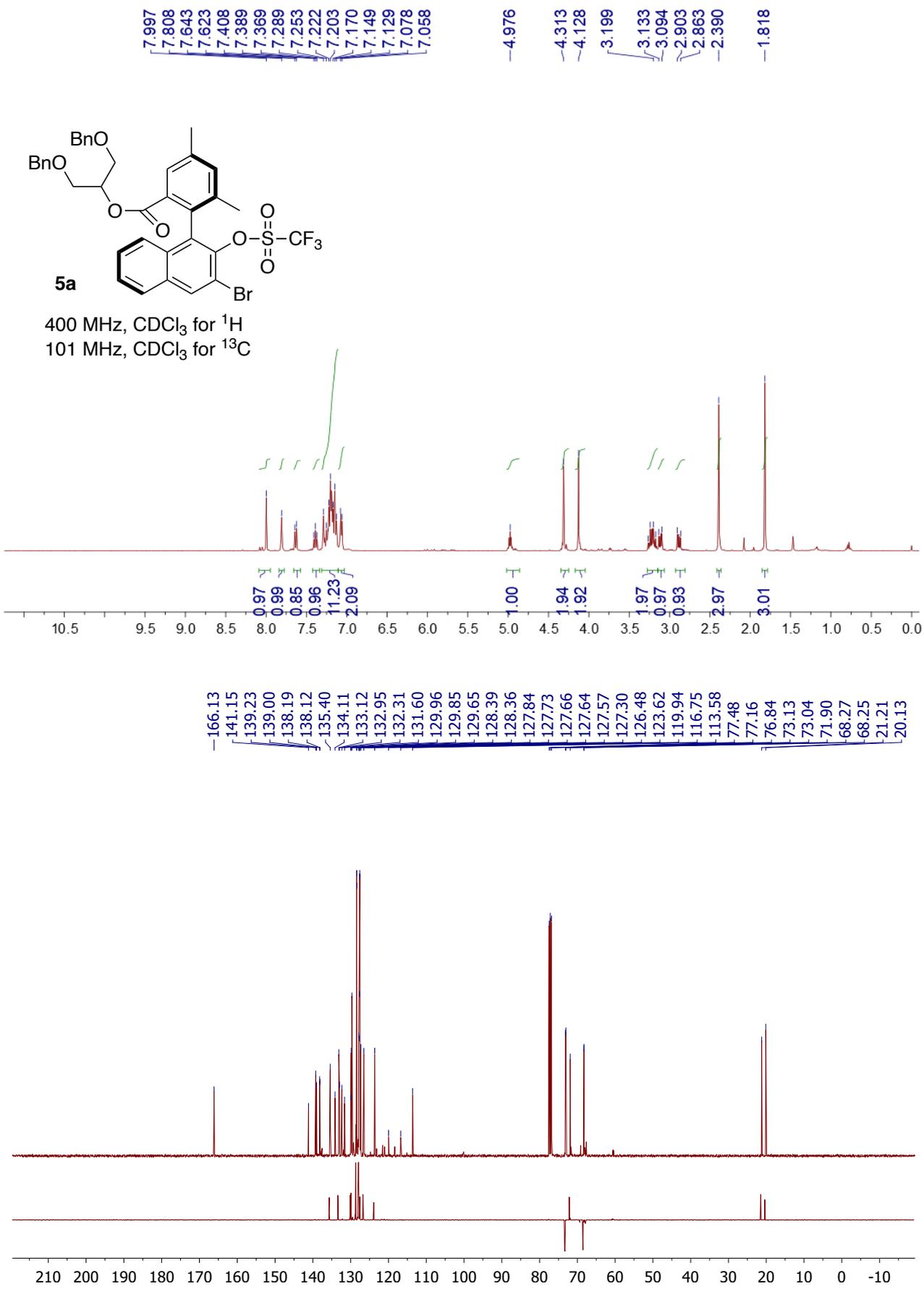


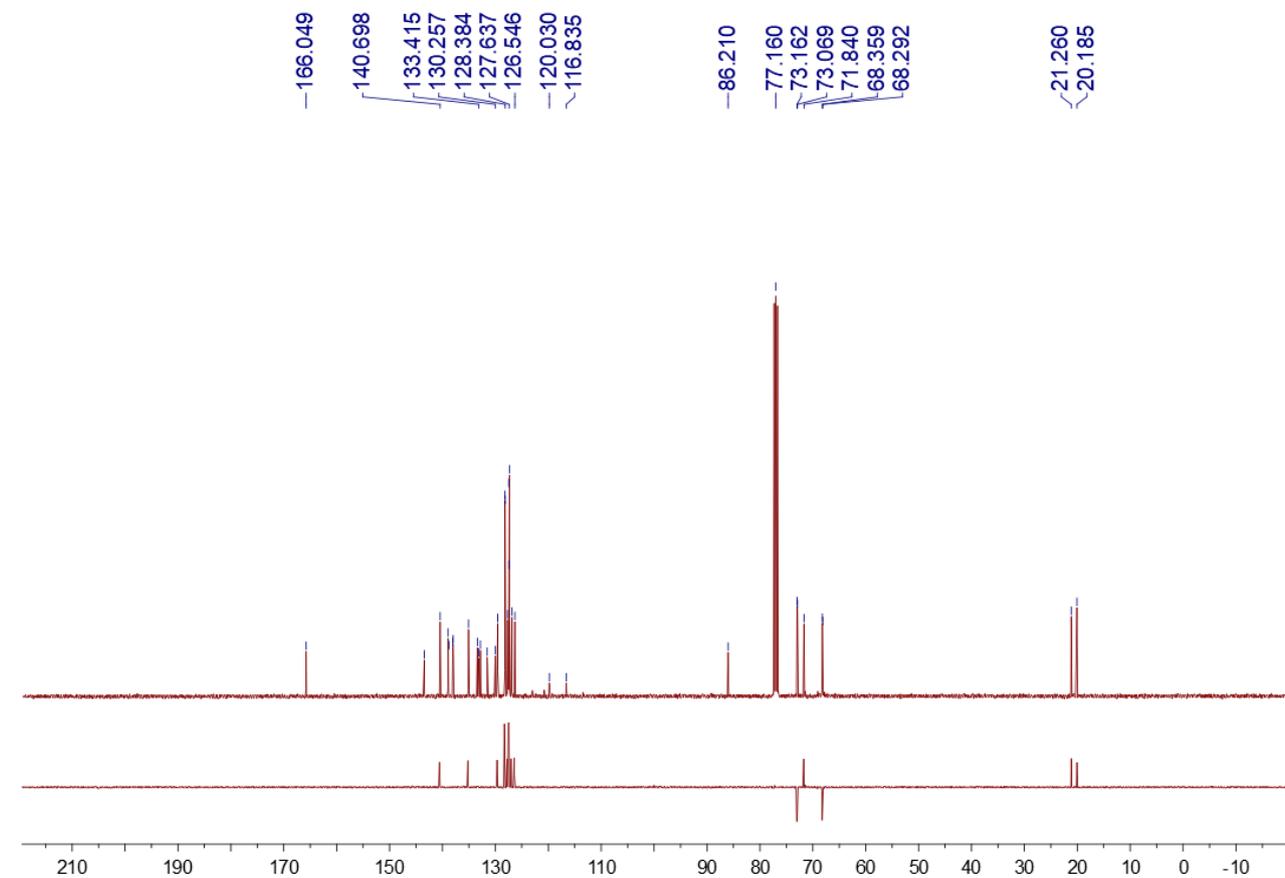
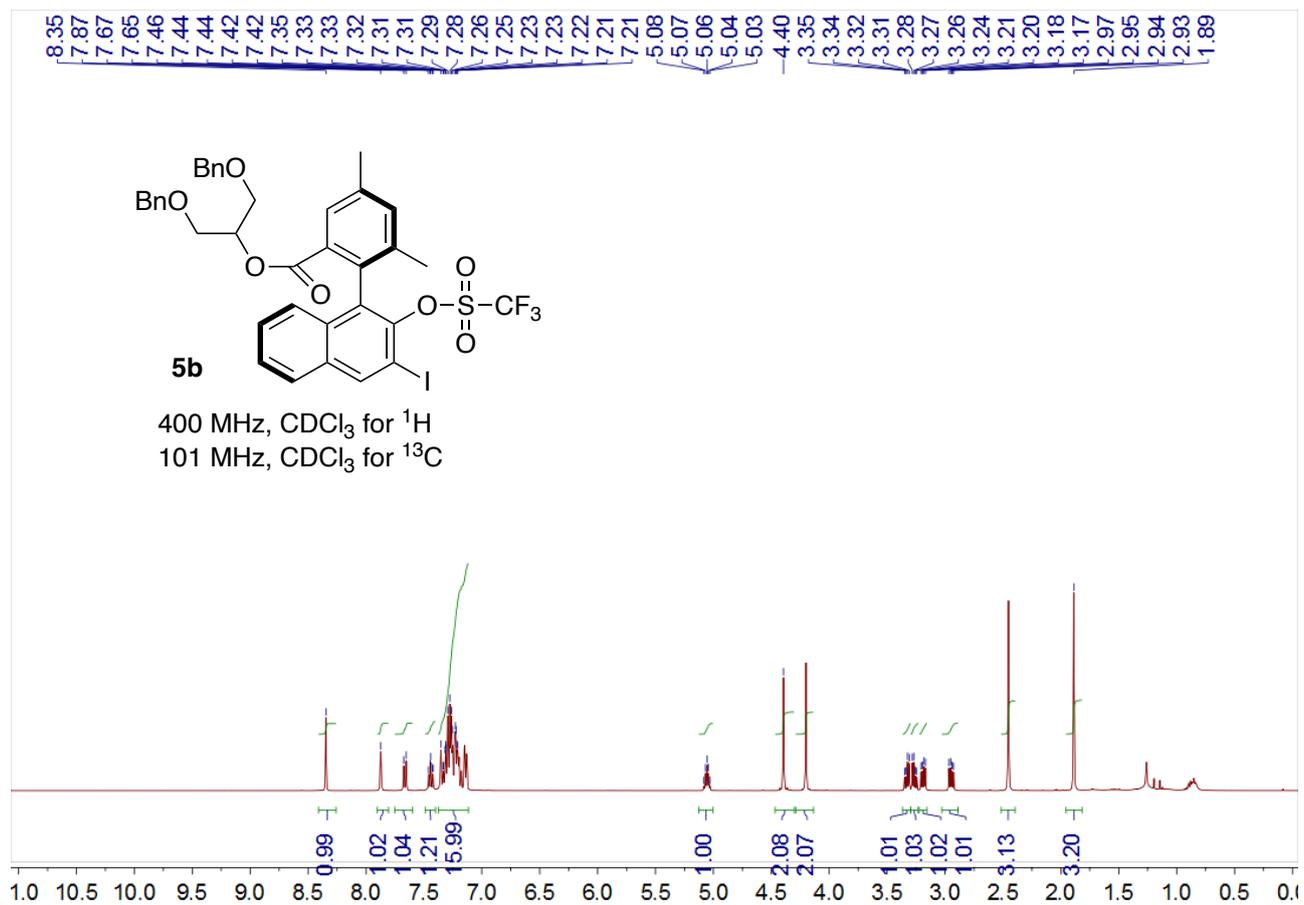


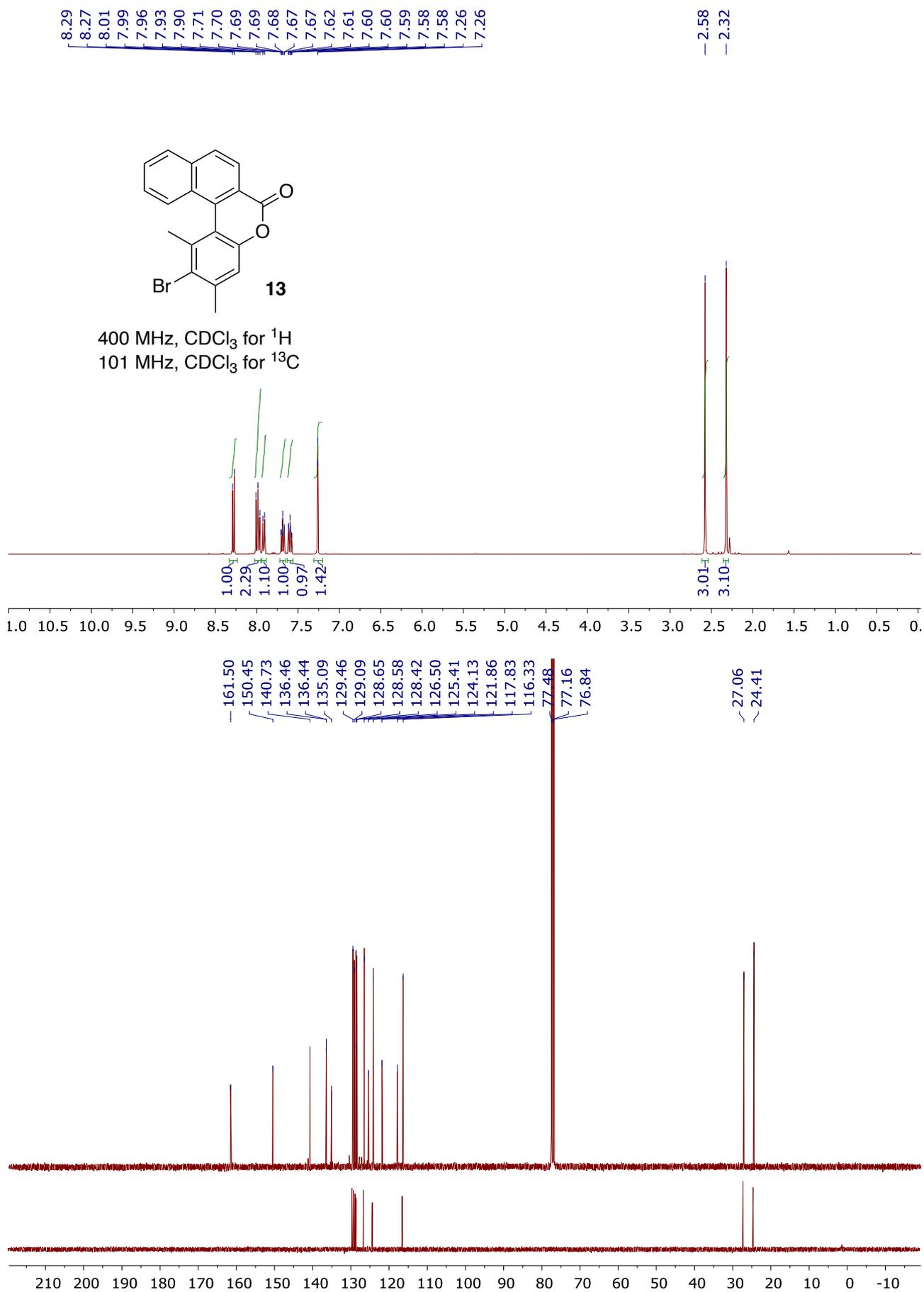


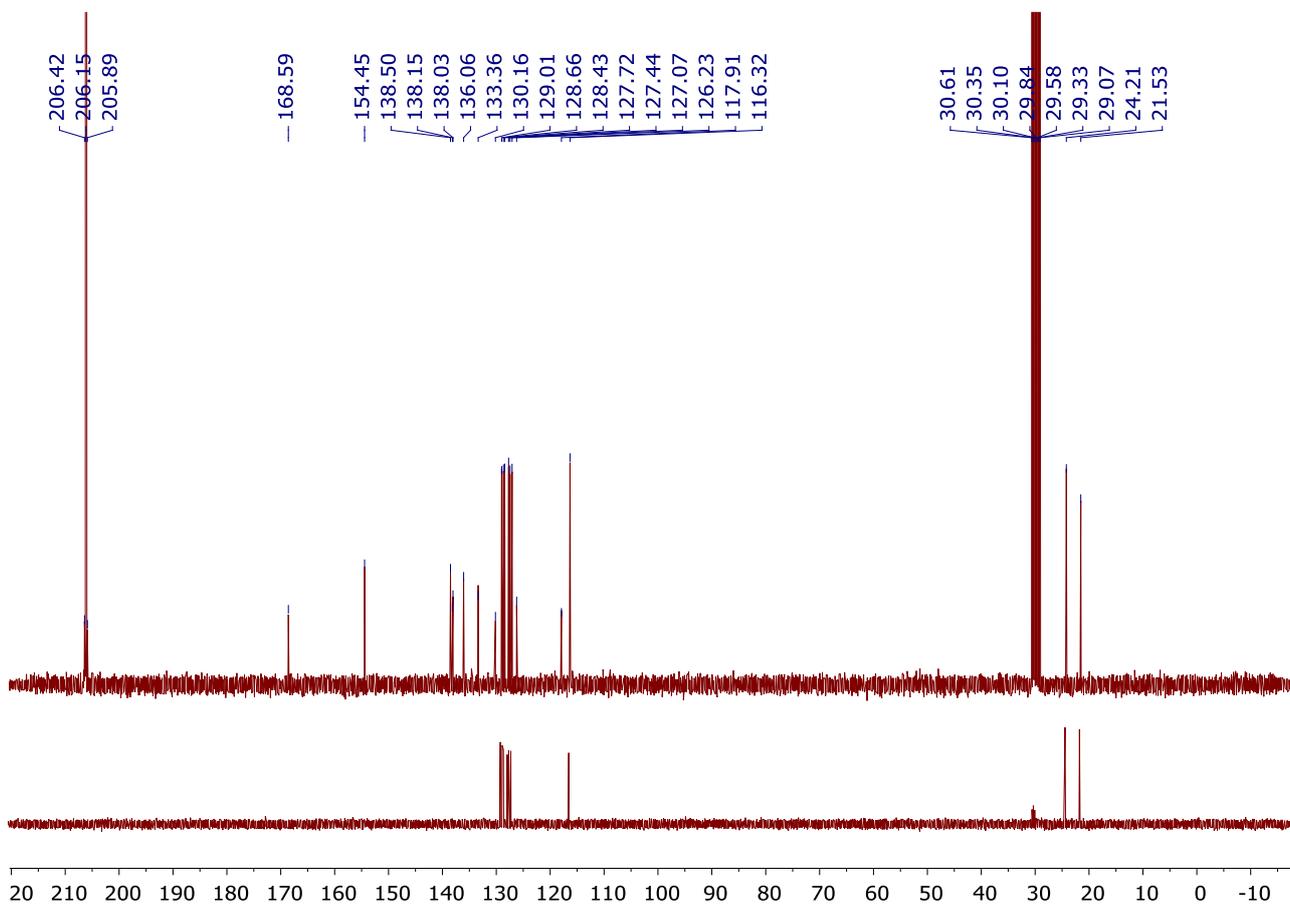
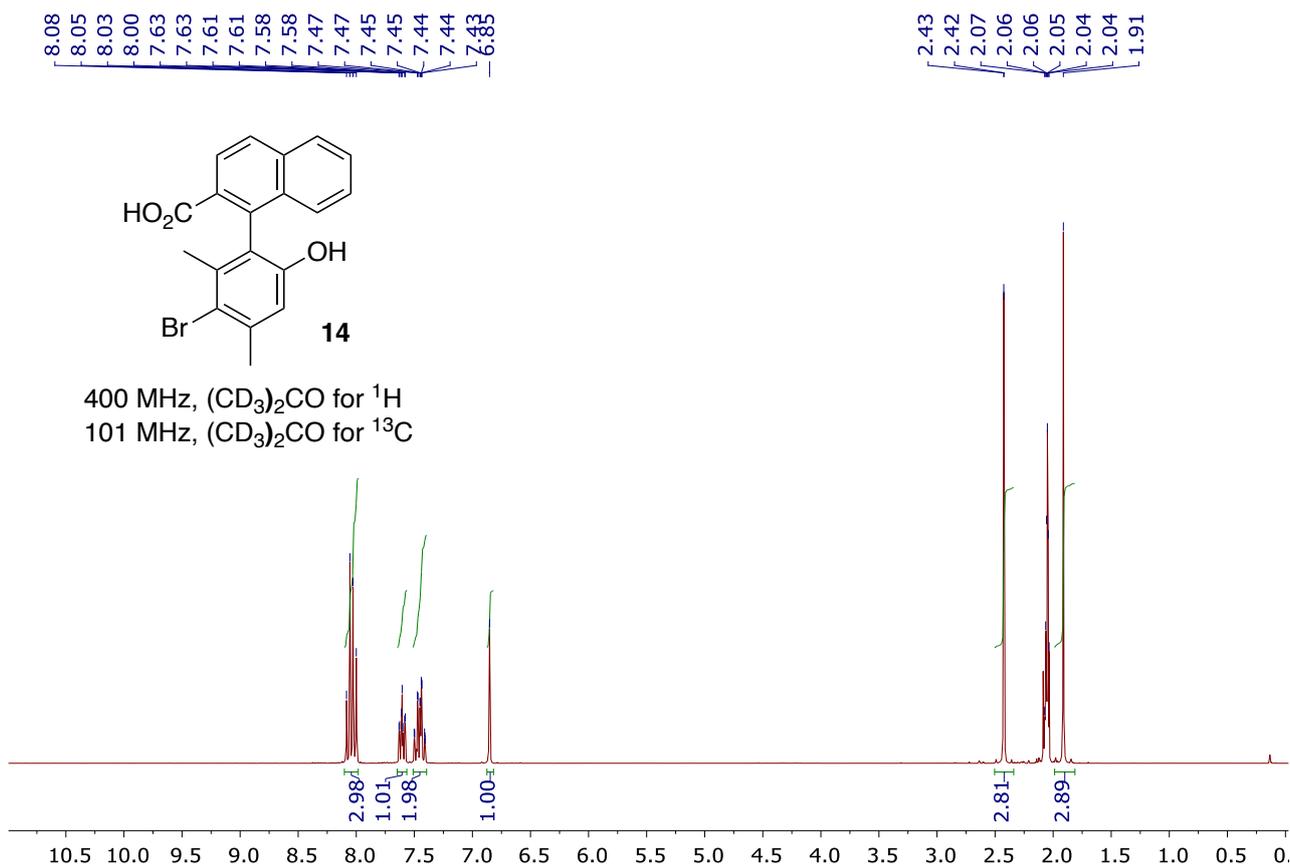
400 MHz, CDCl₃ for ¹H
 101 MHz, CDCl₃ for ¹³C

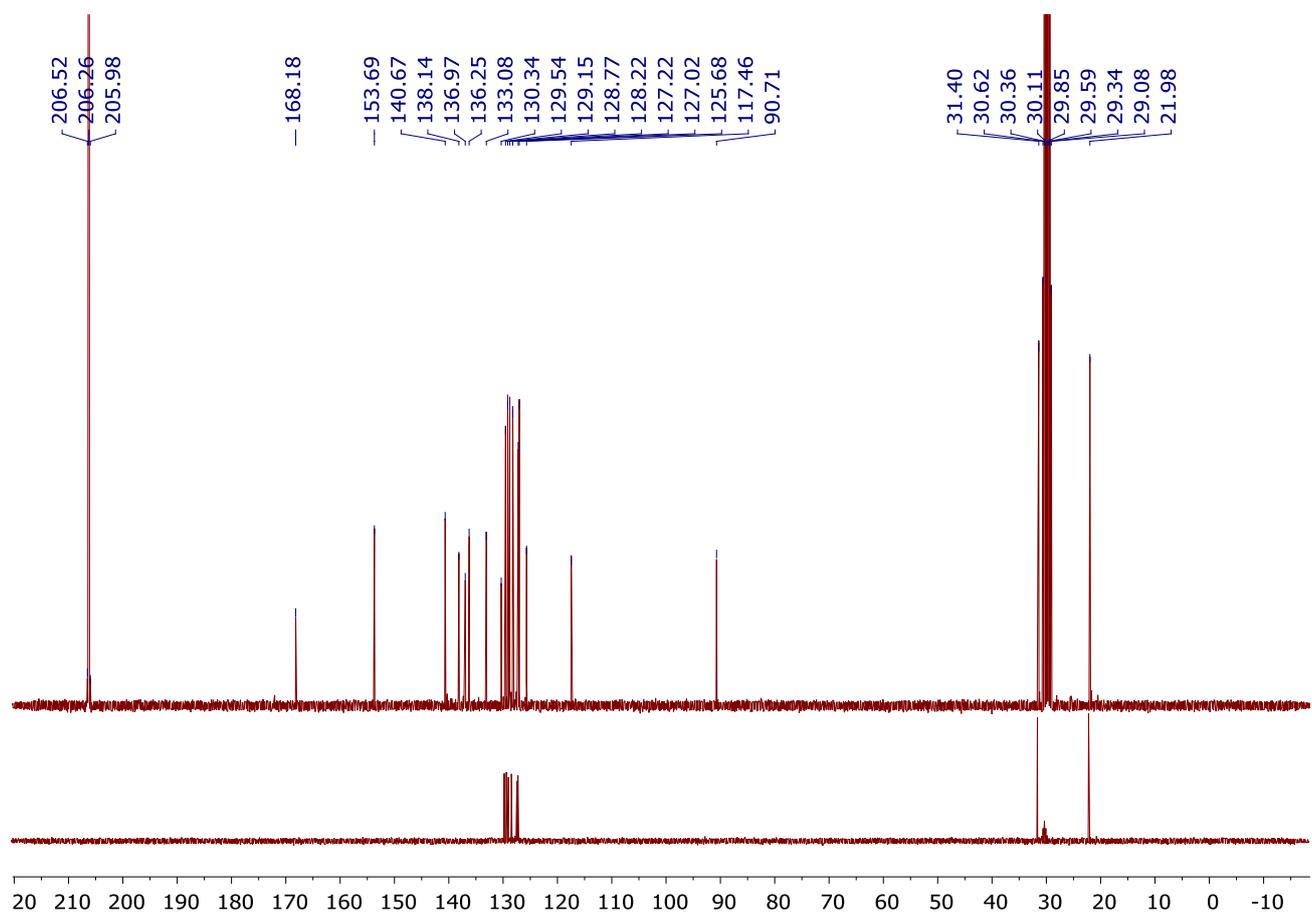
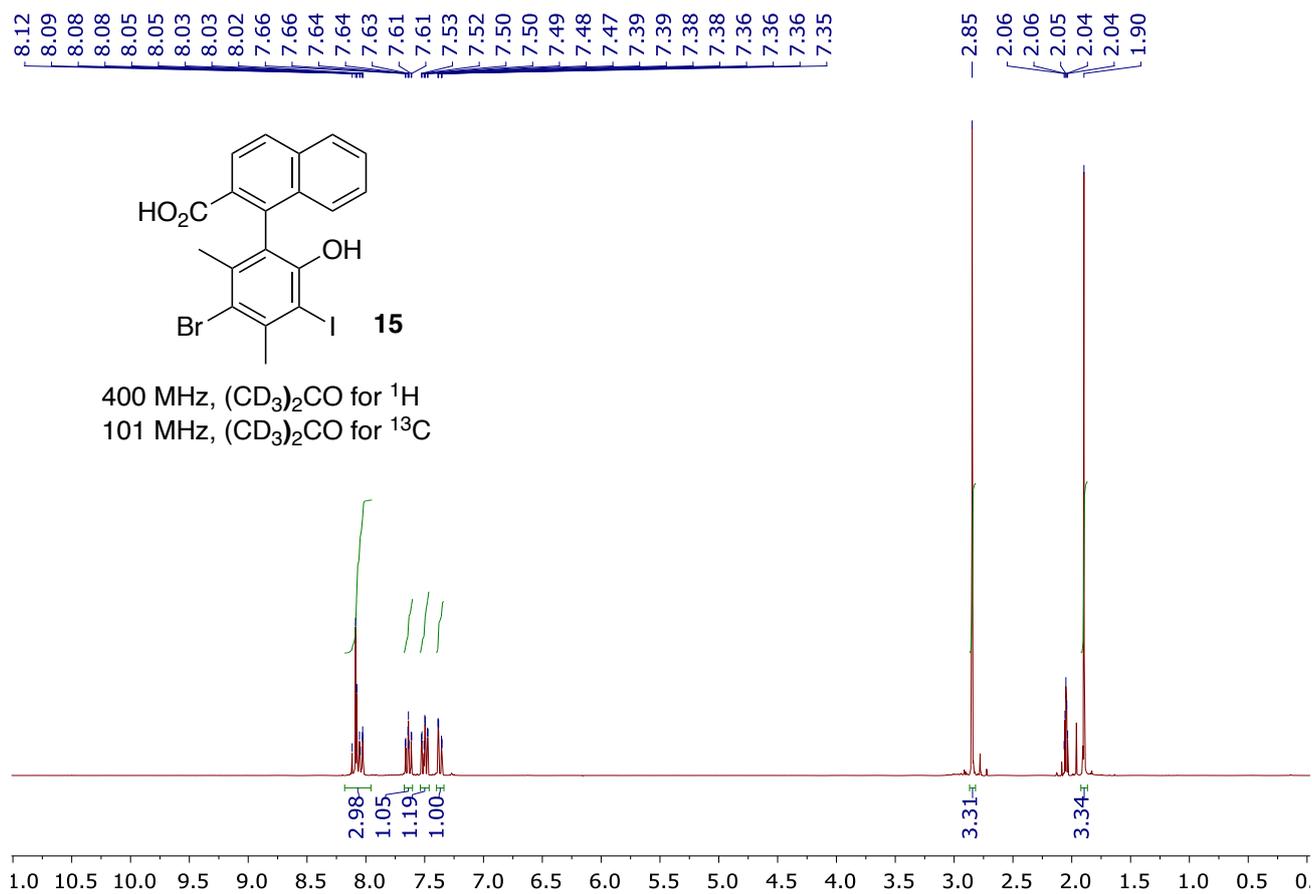


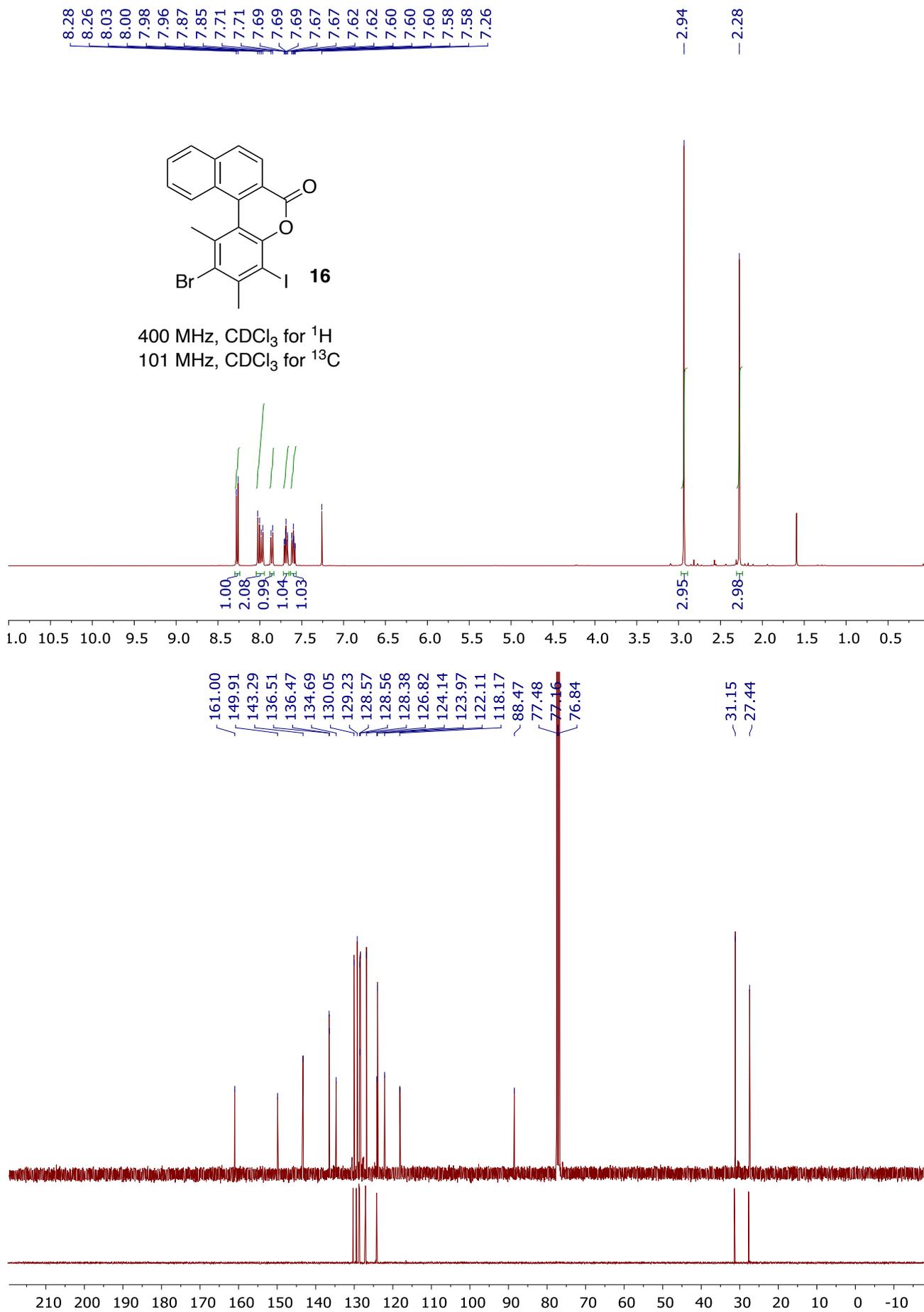


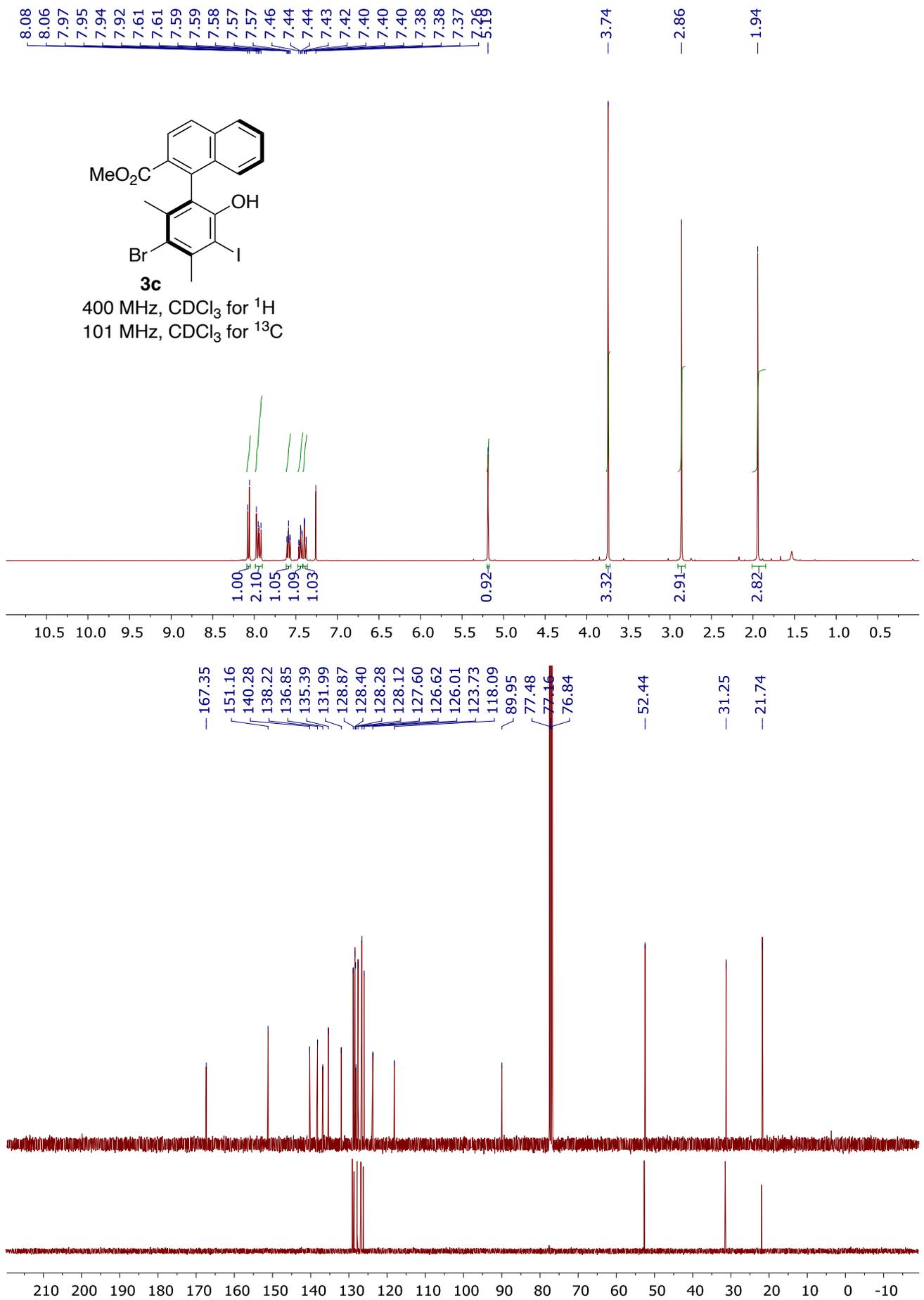


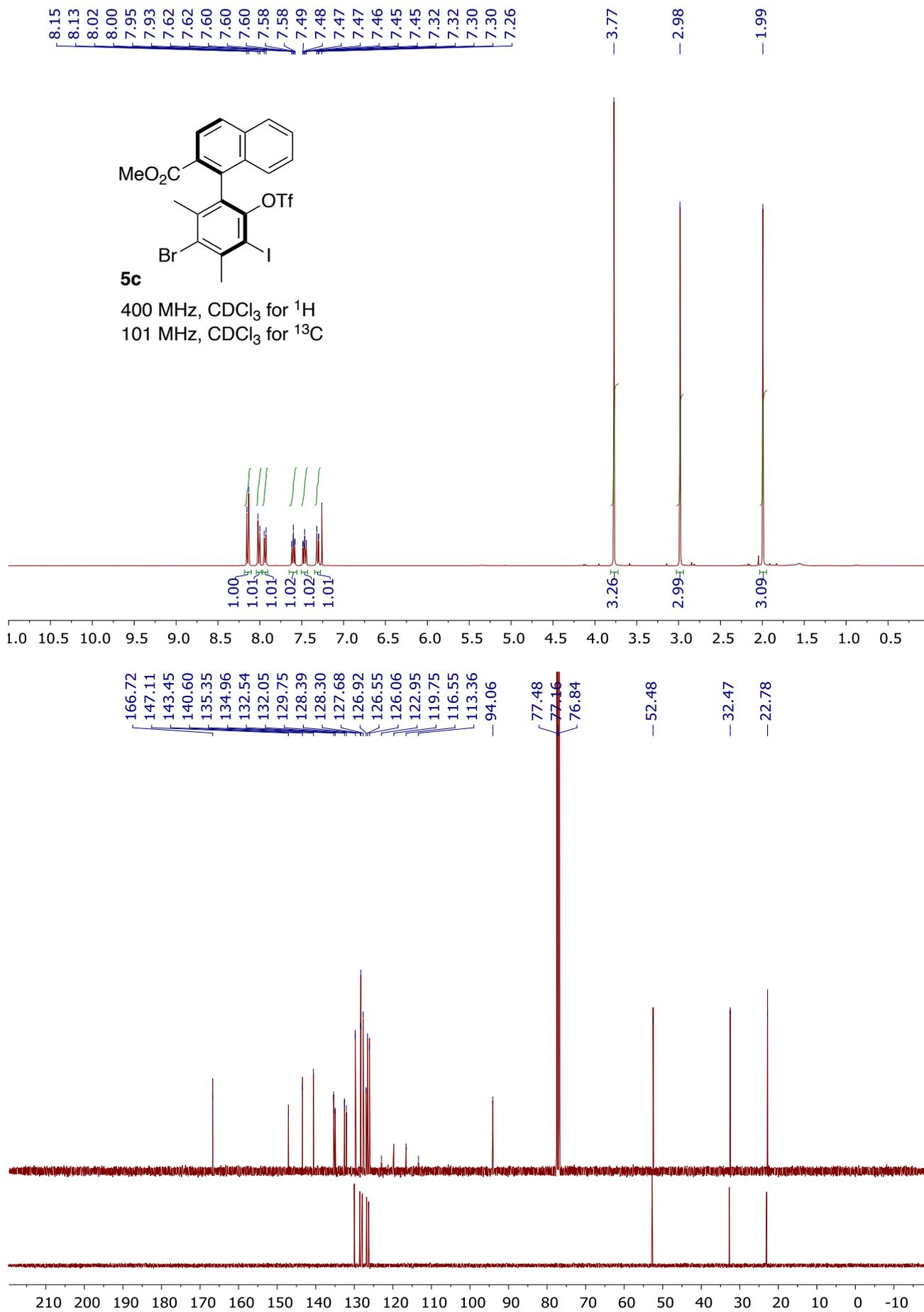


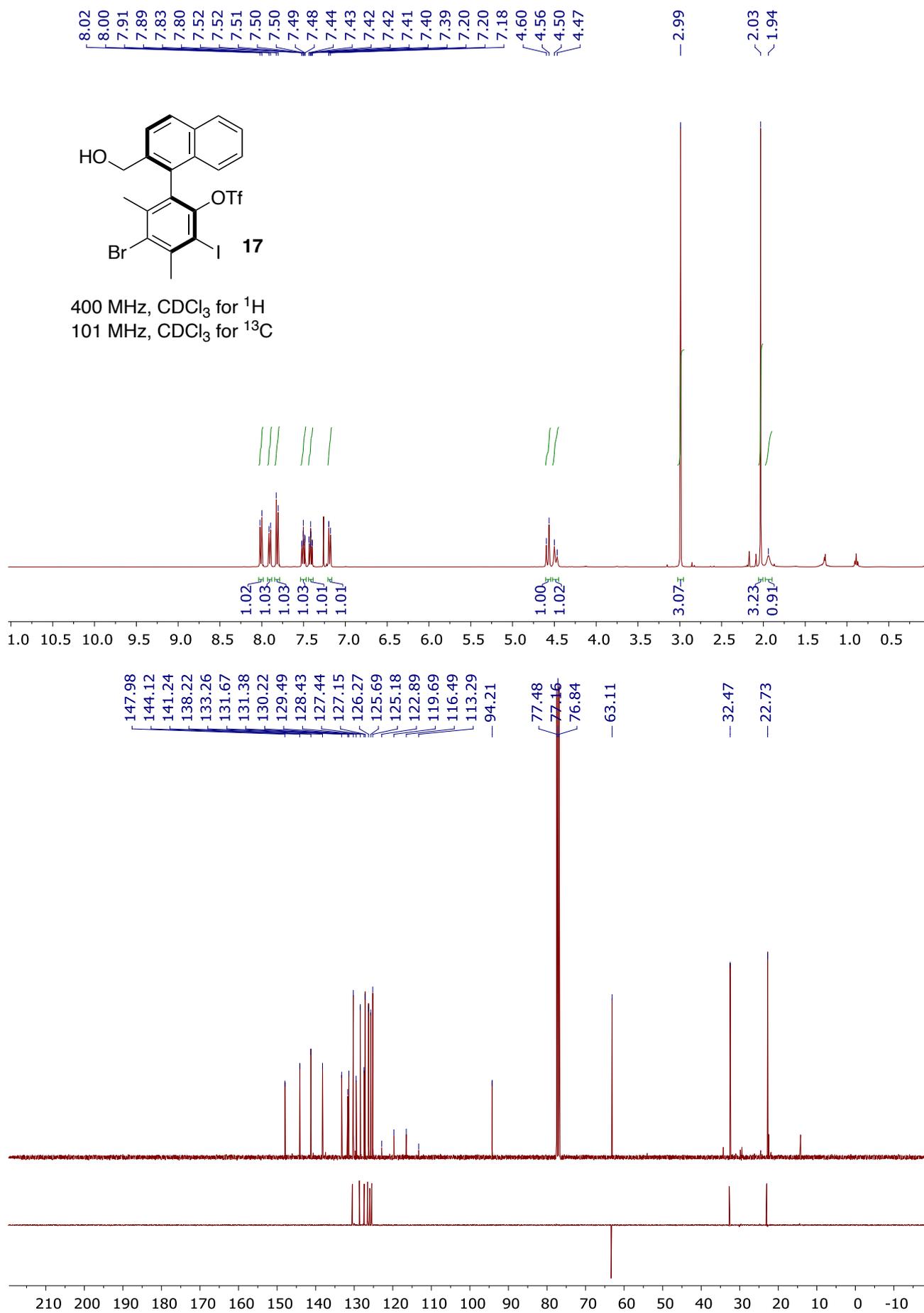


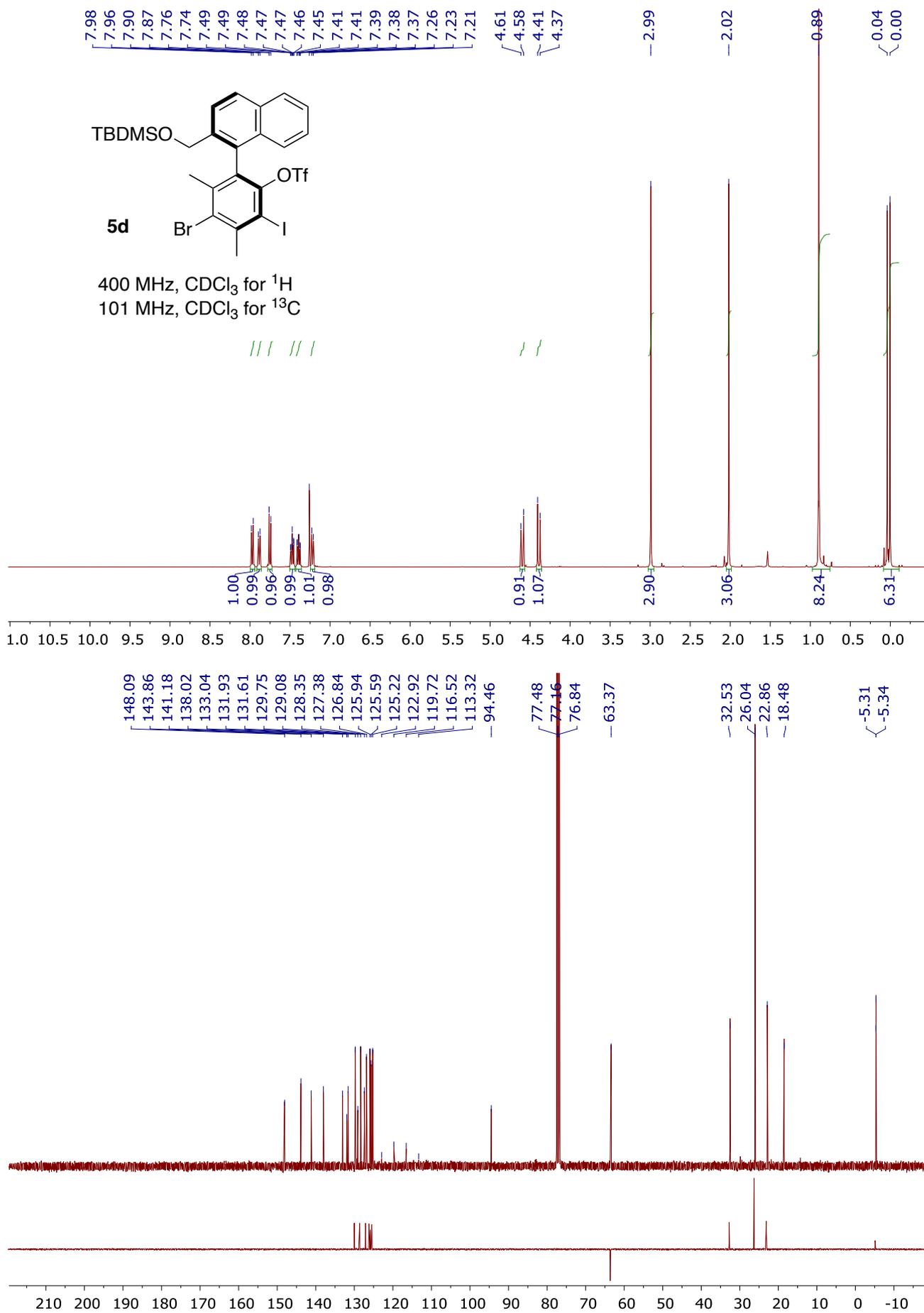


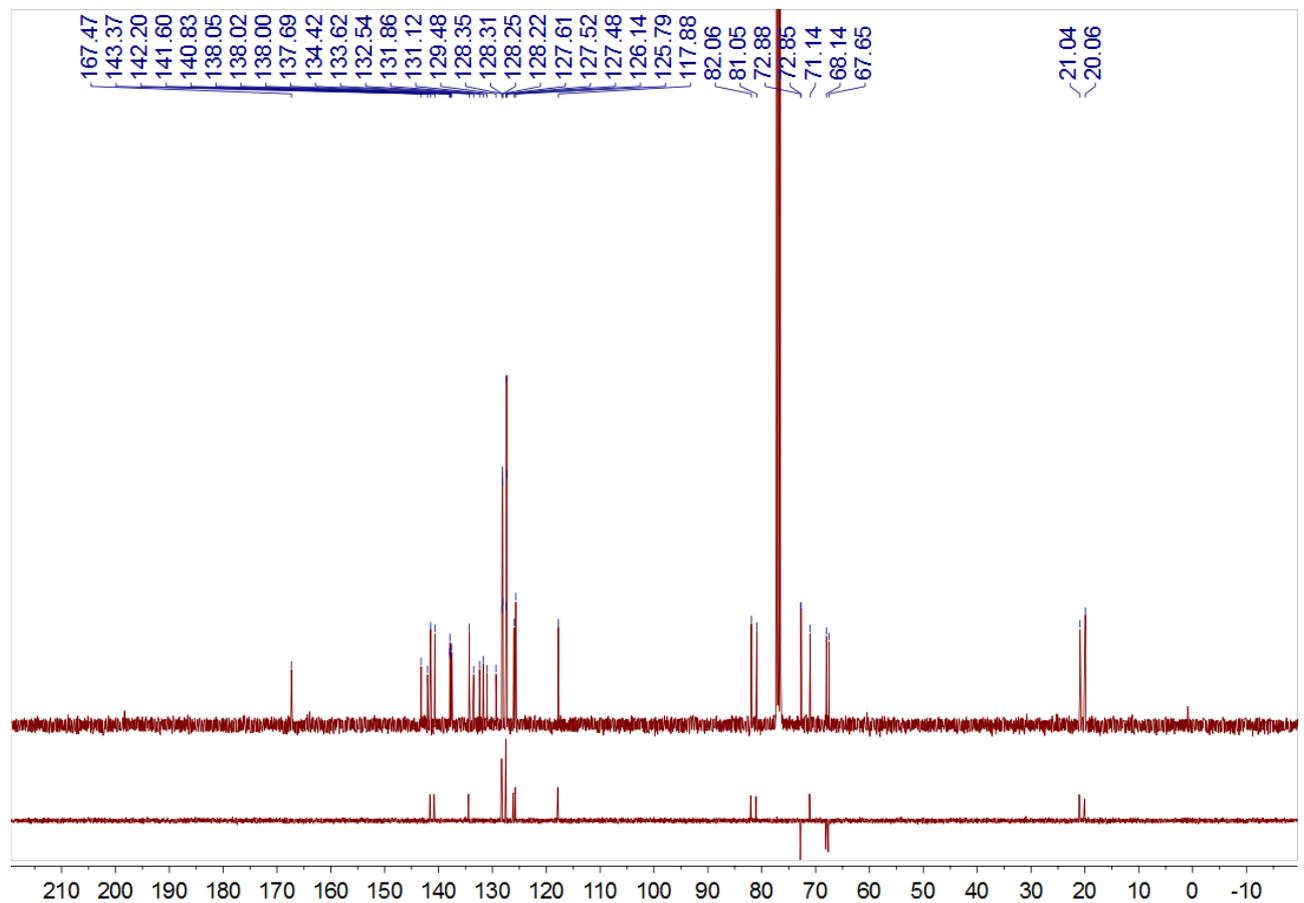
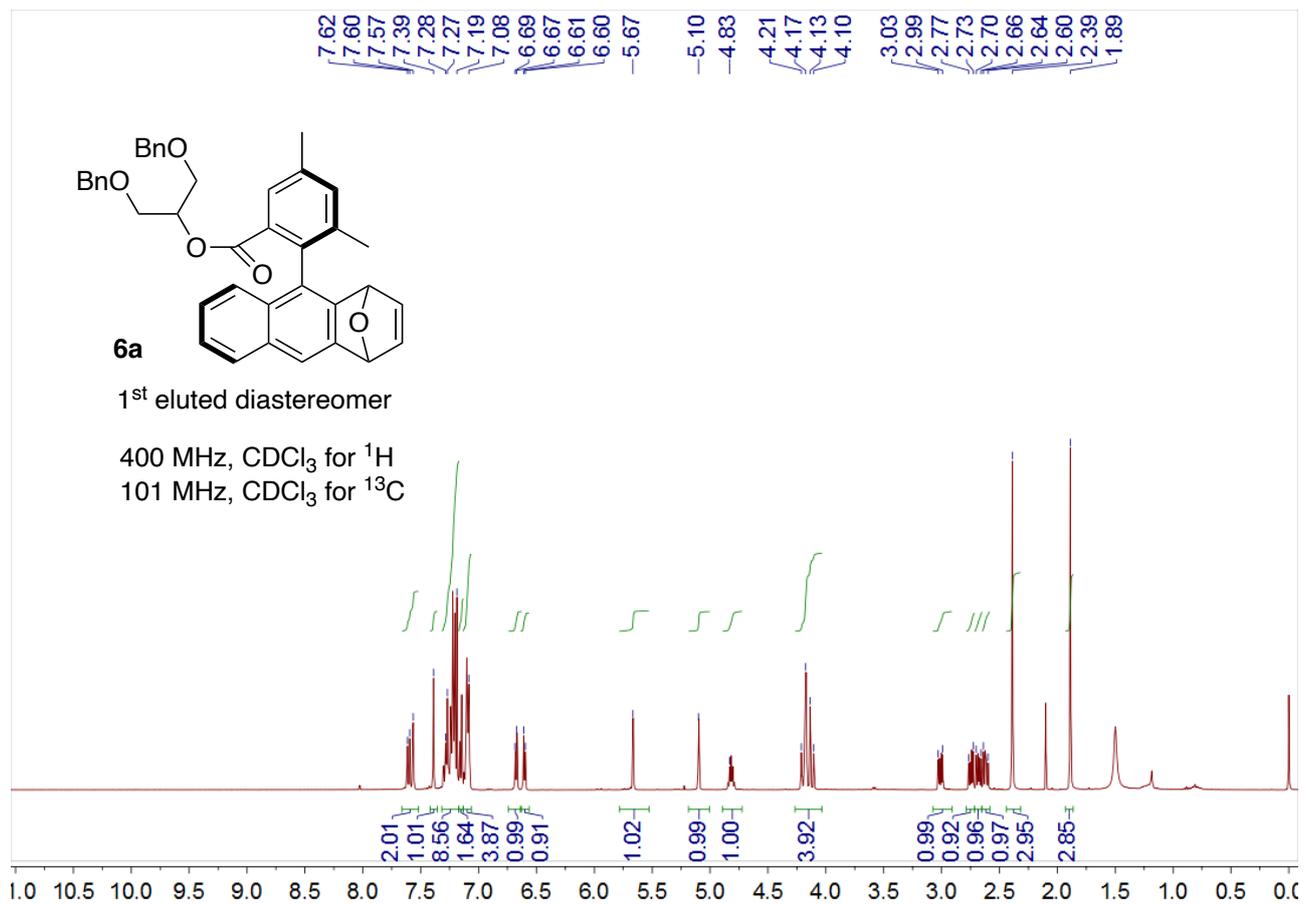


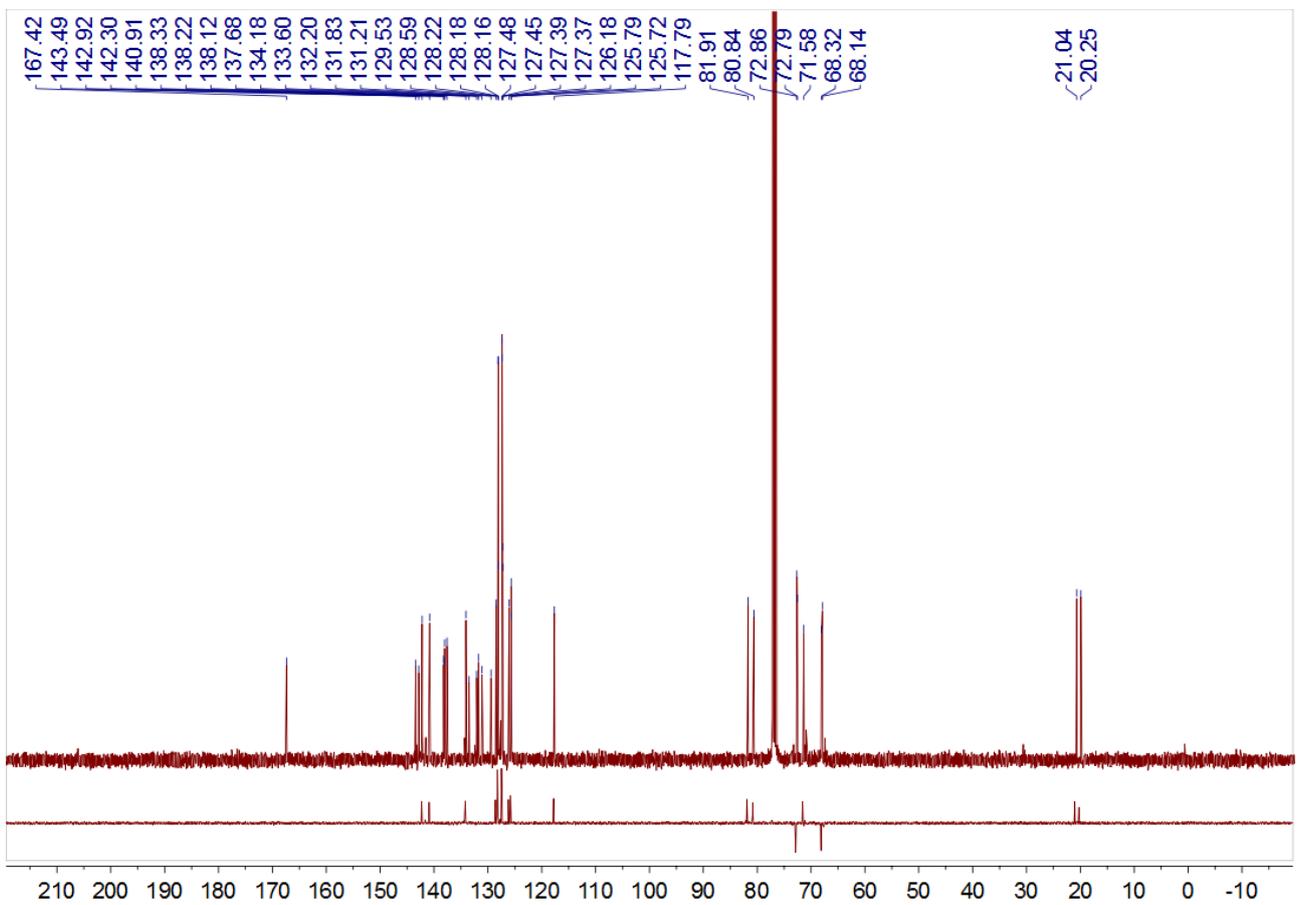
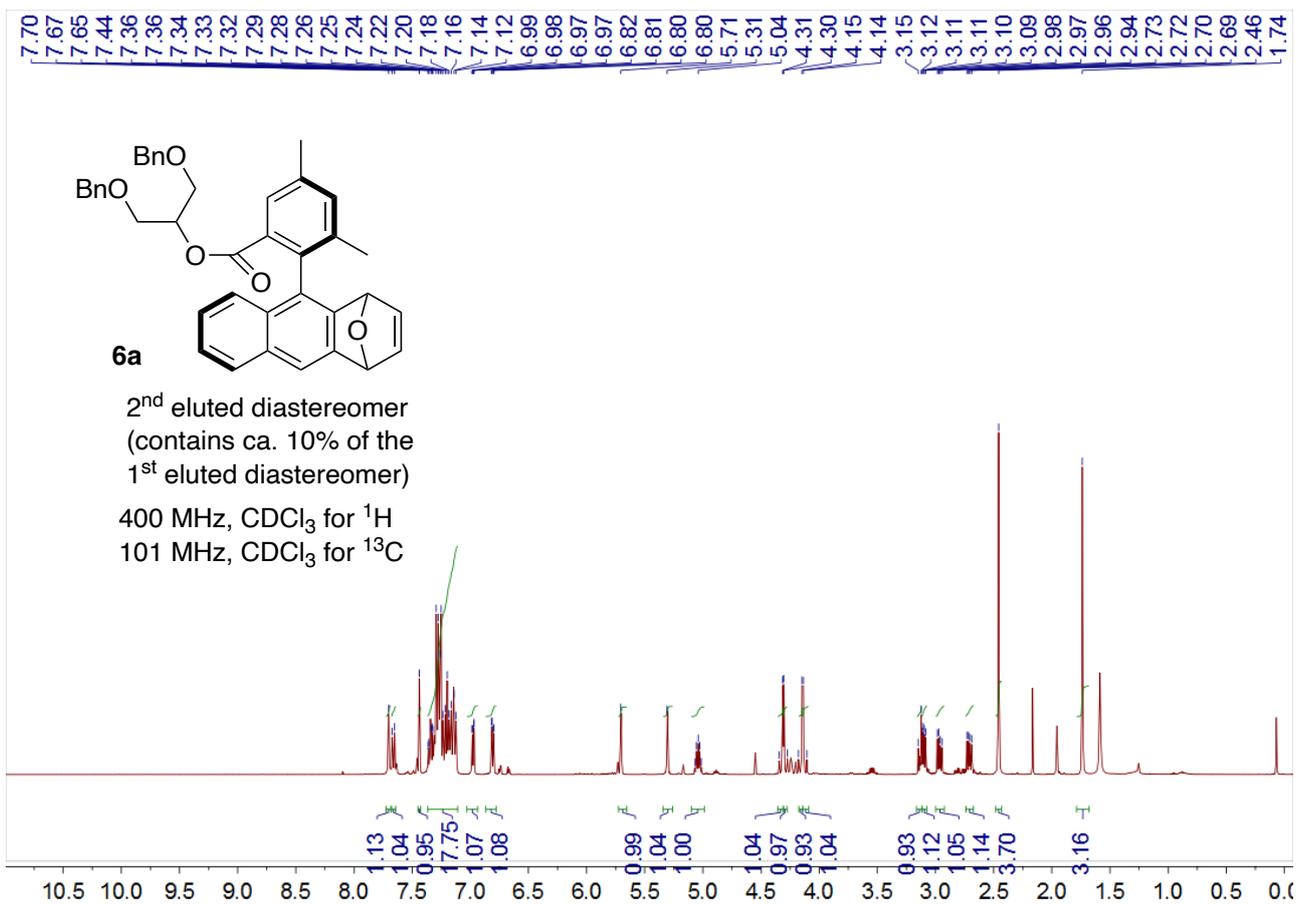


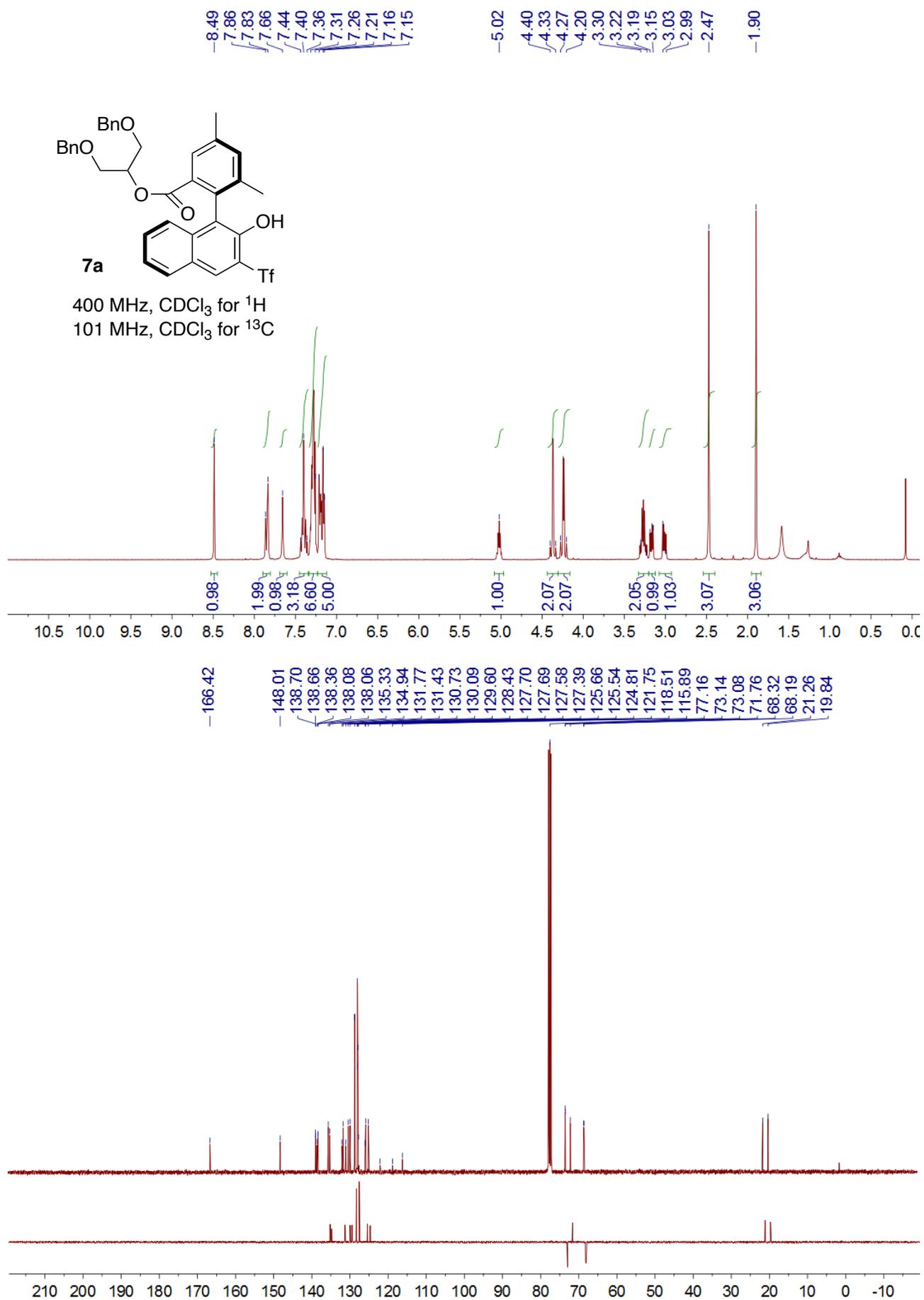


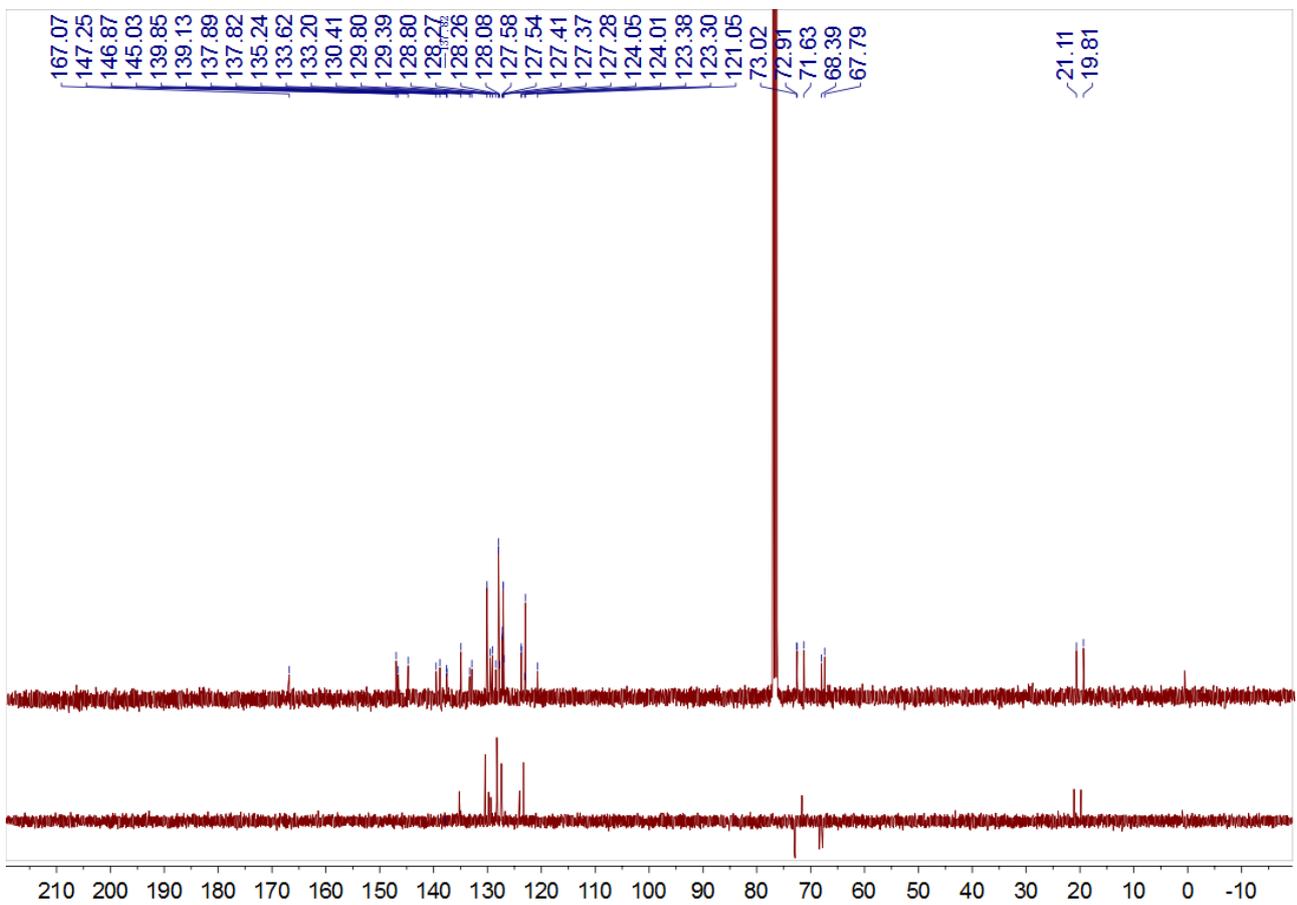
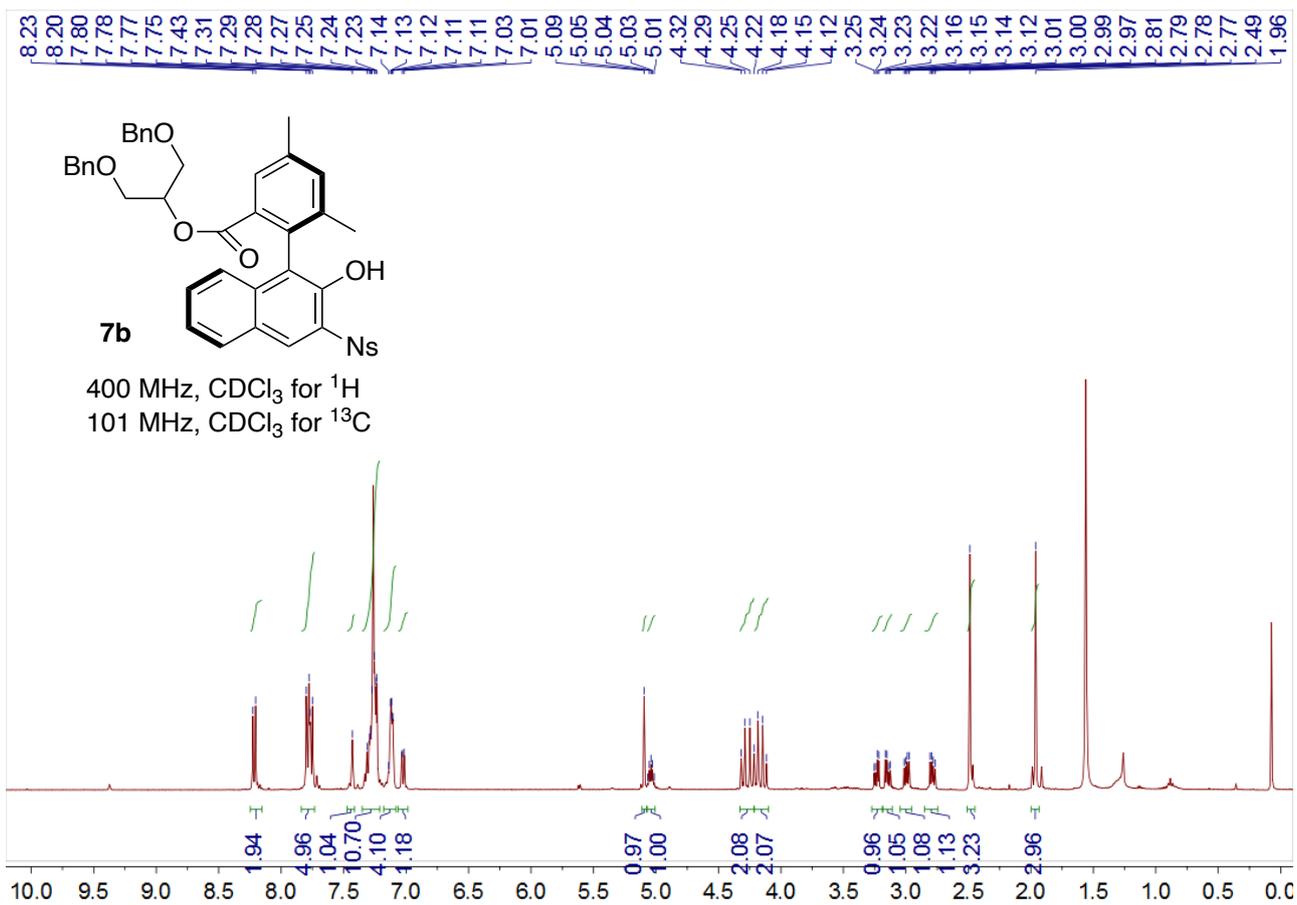


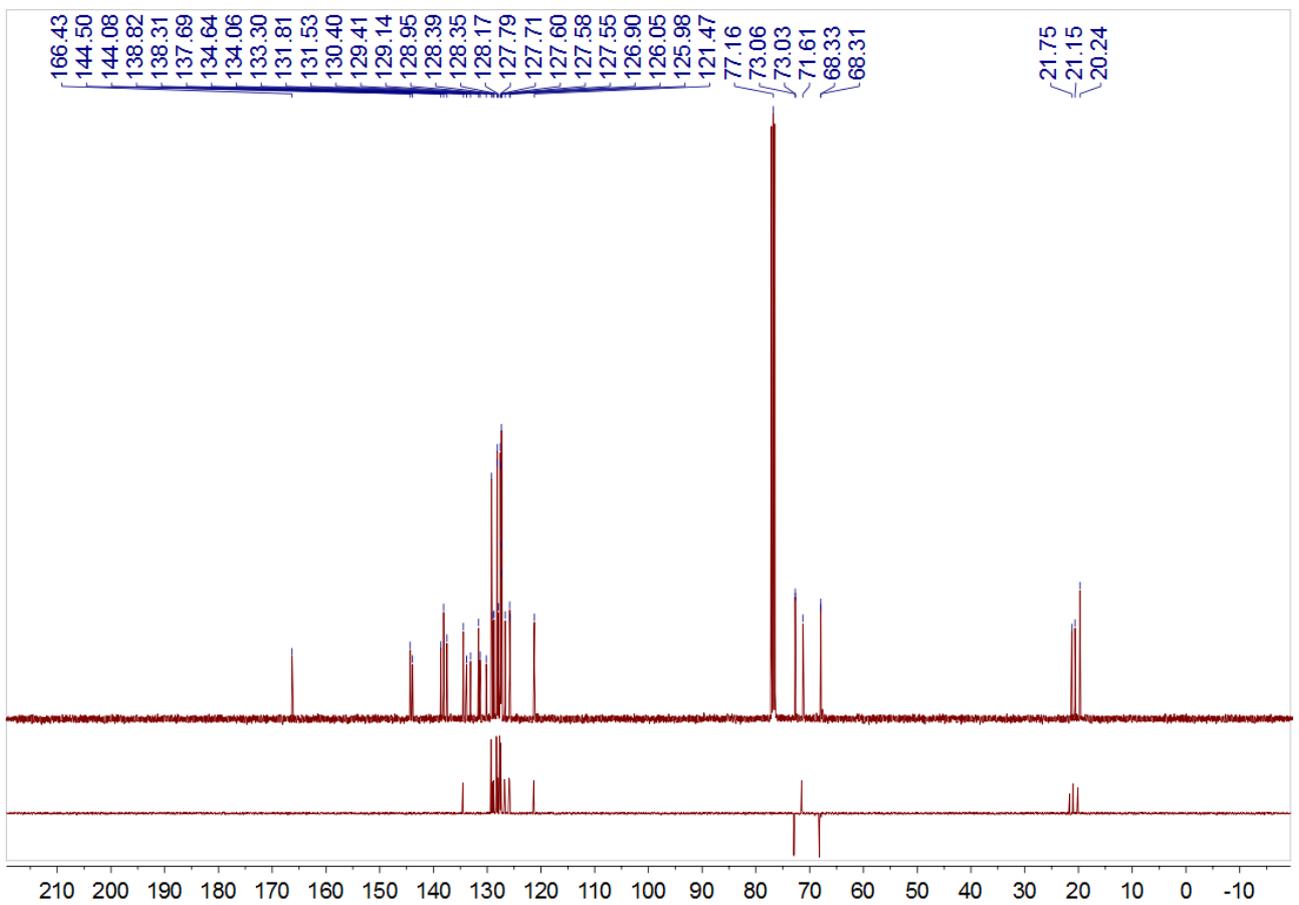
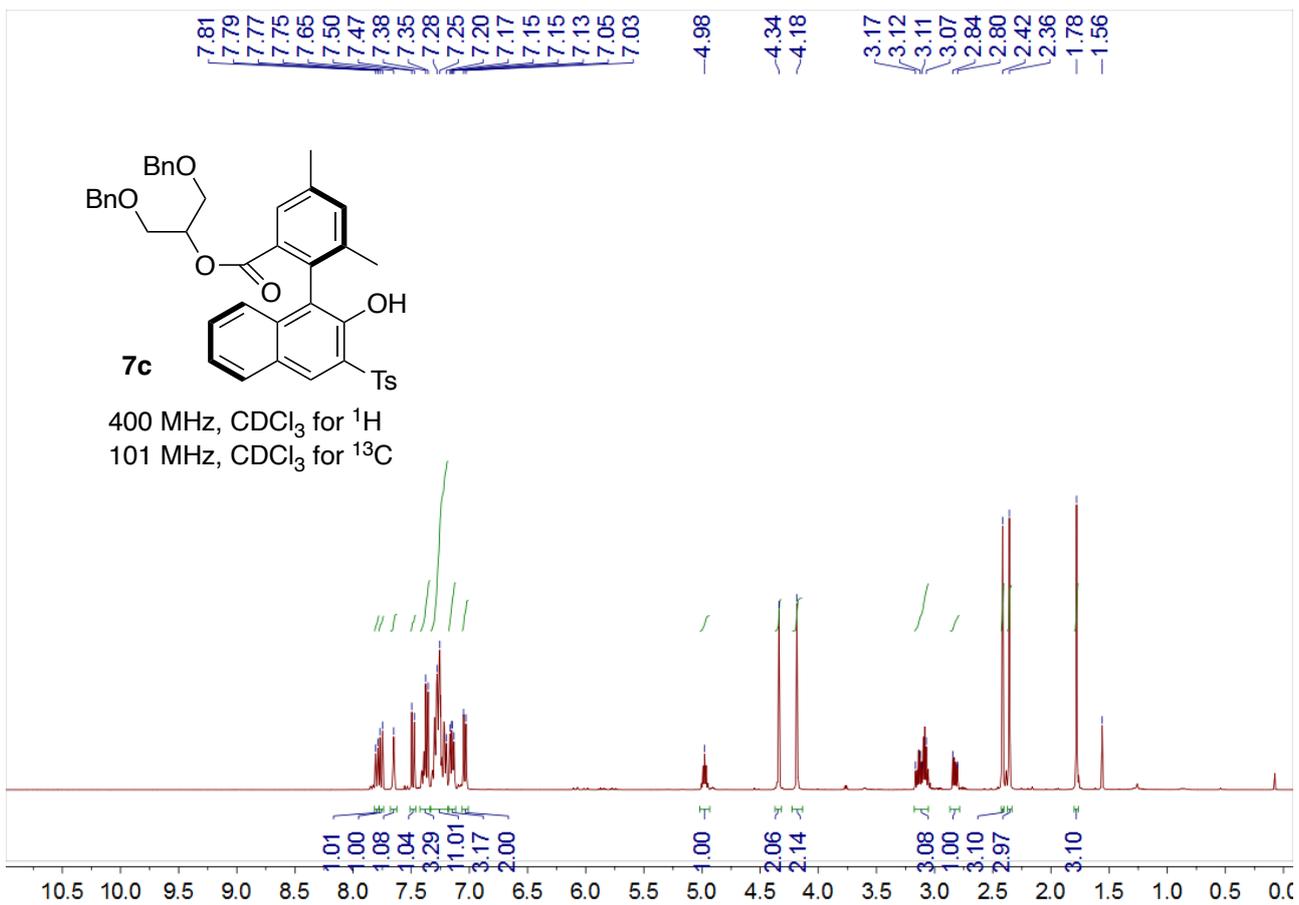


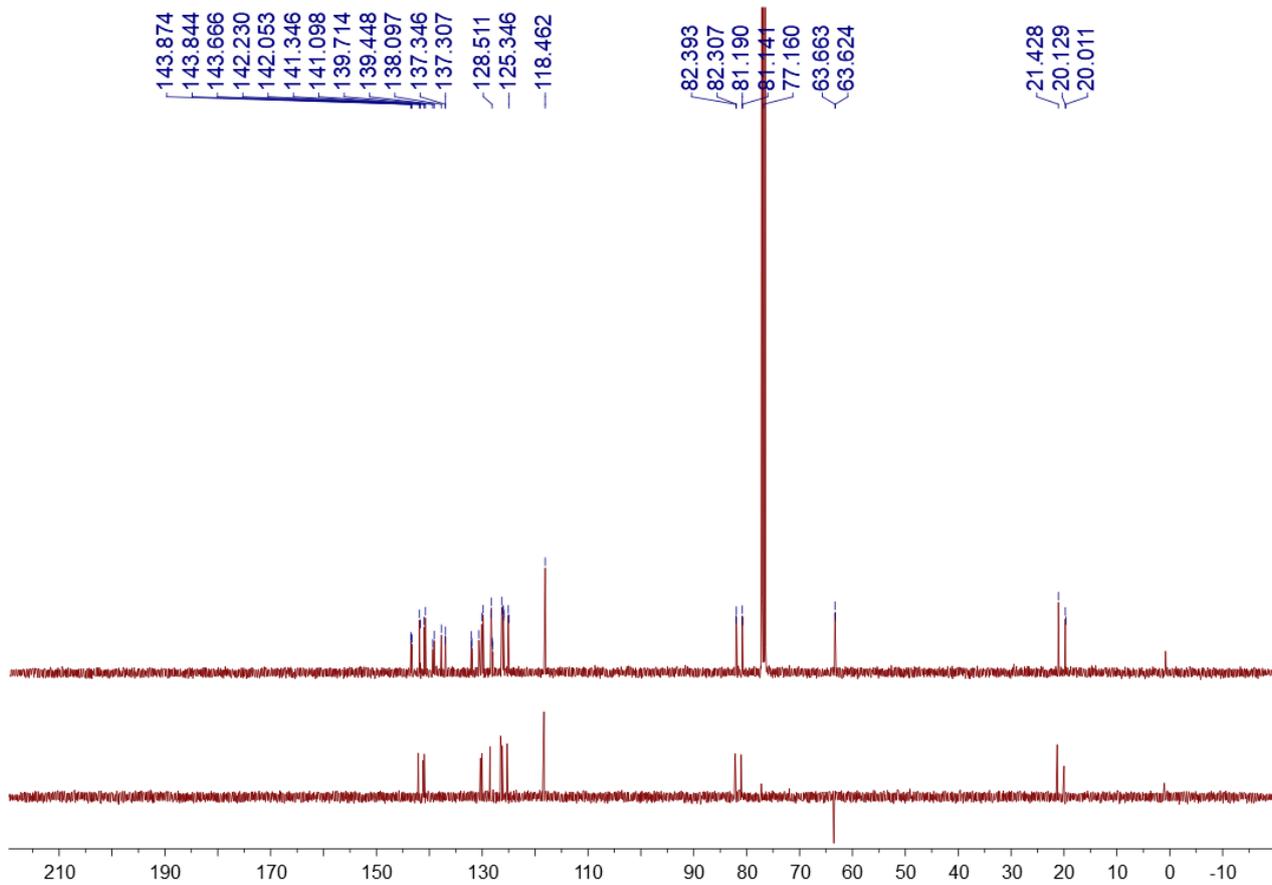
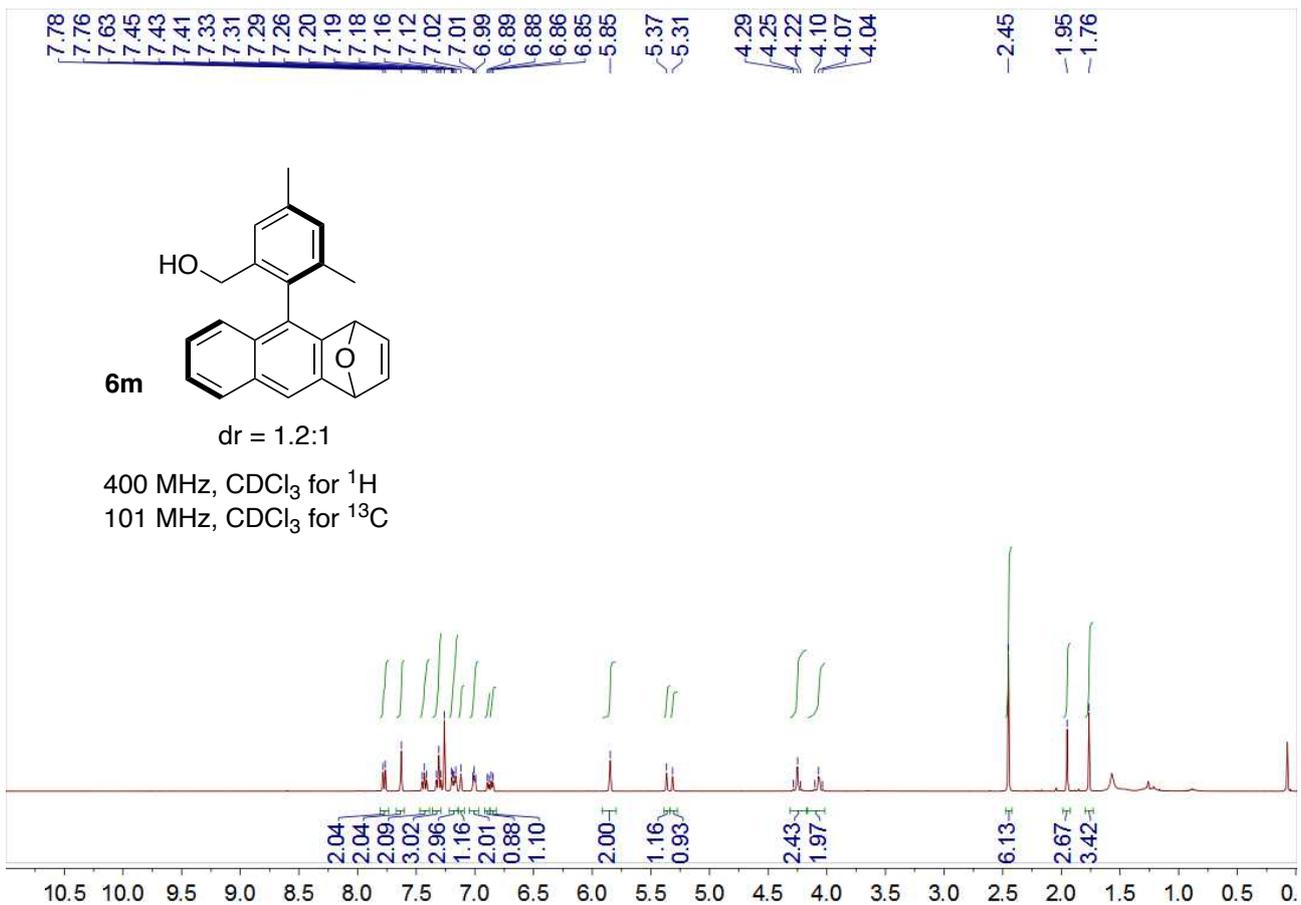


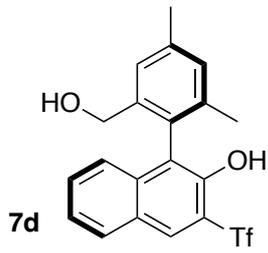




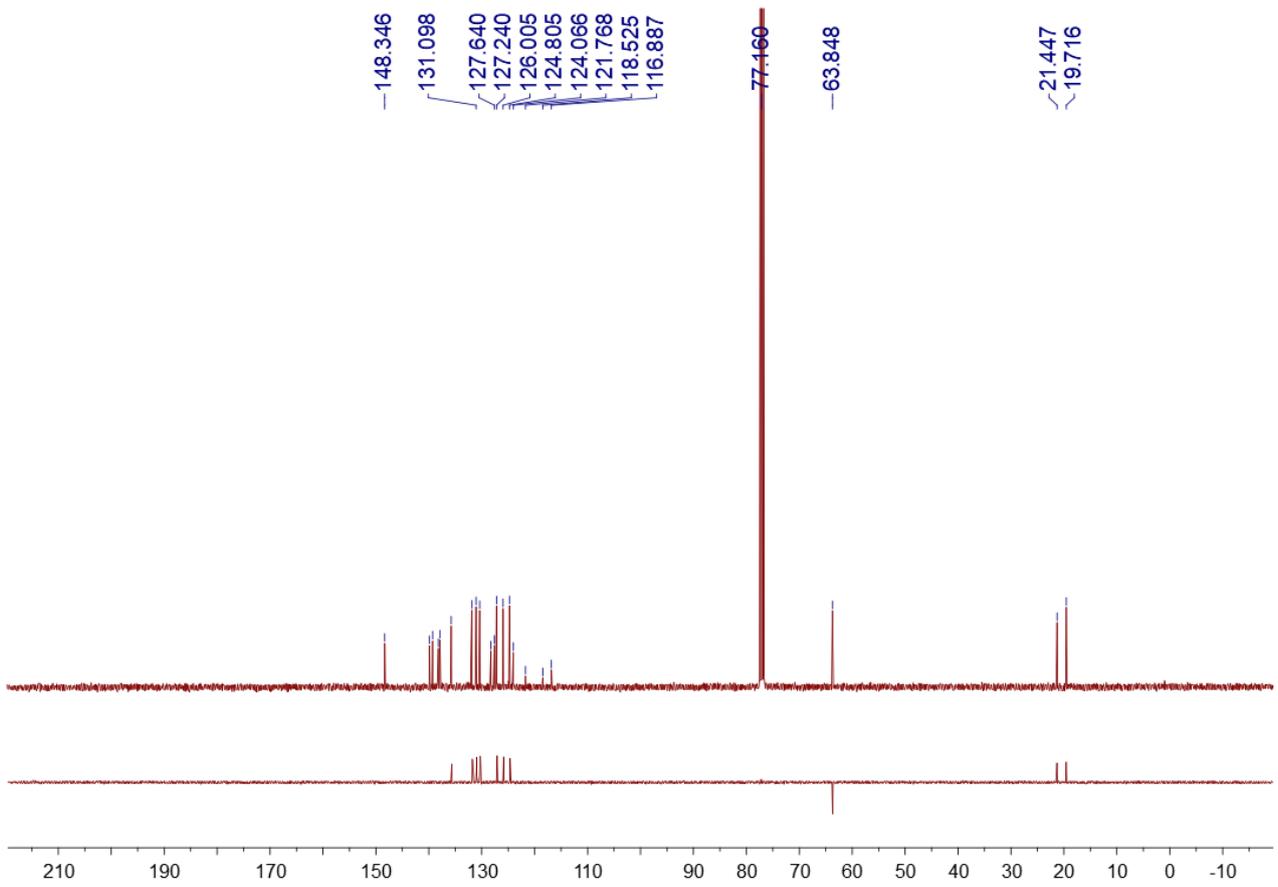
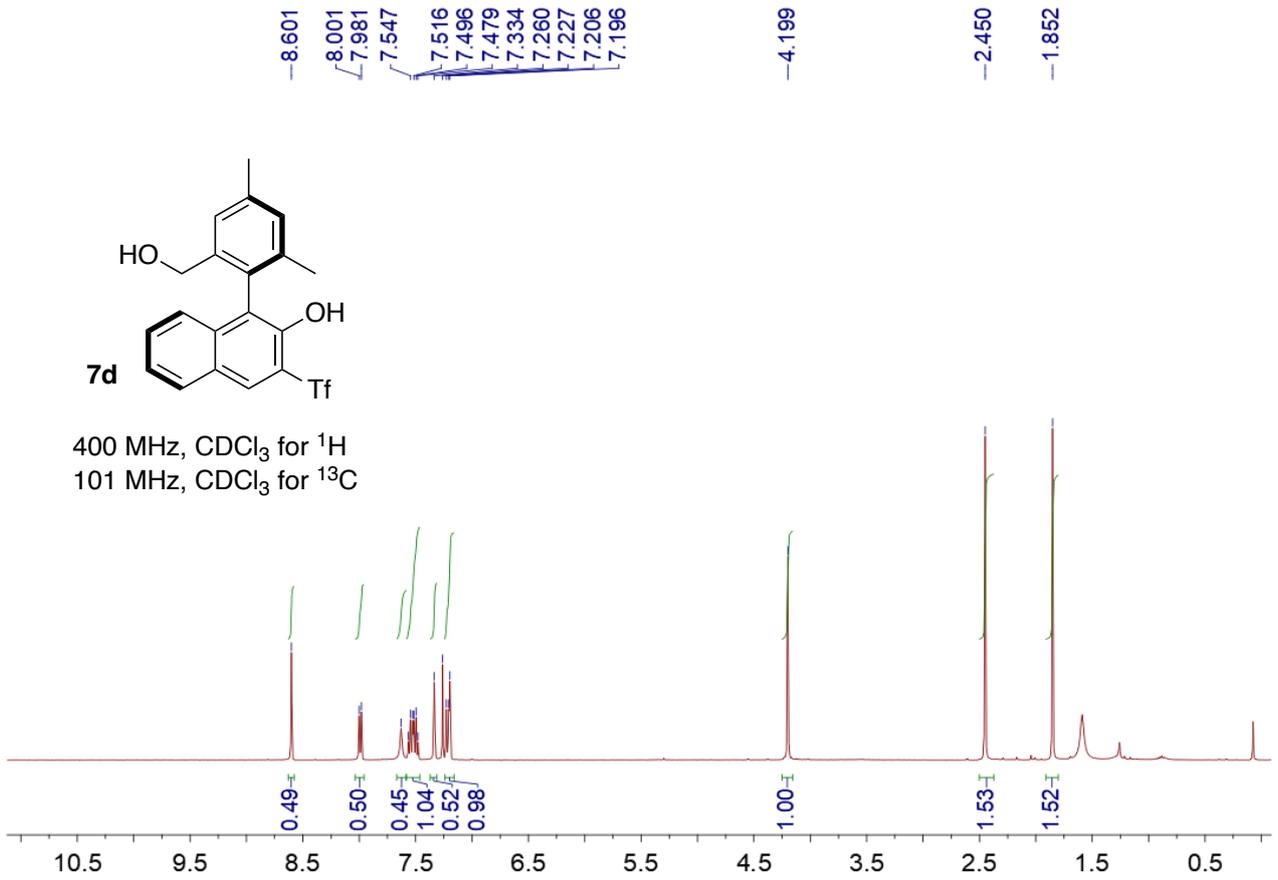


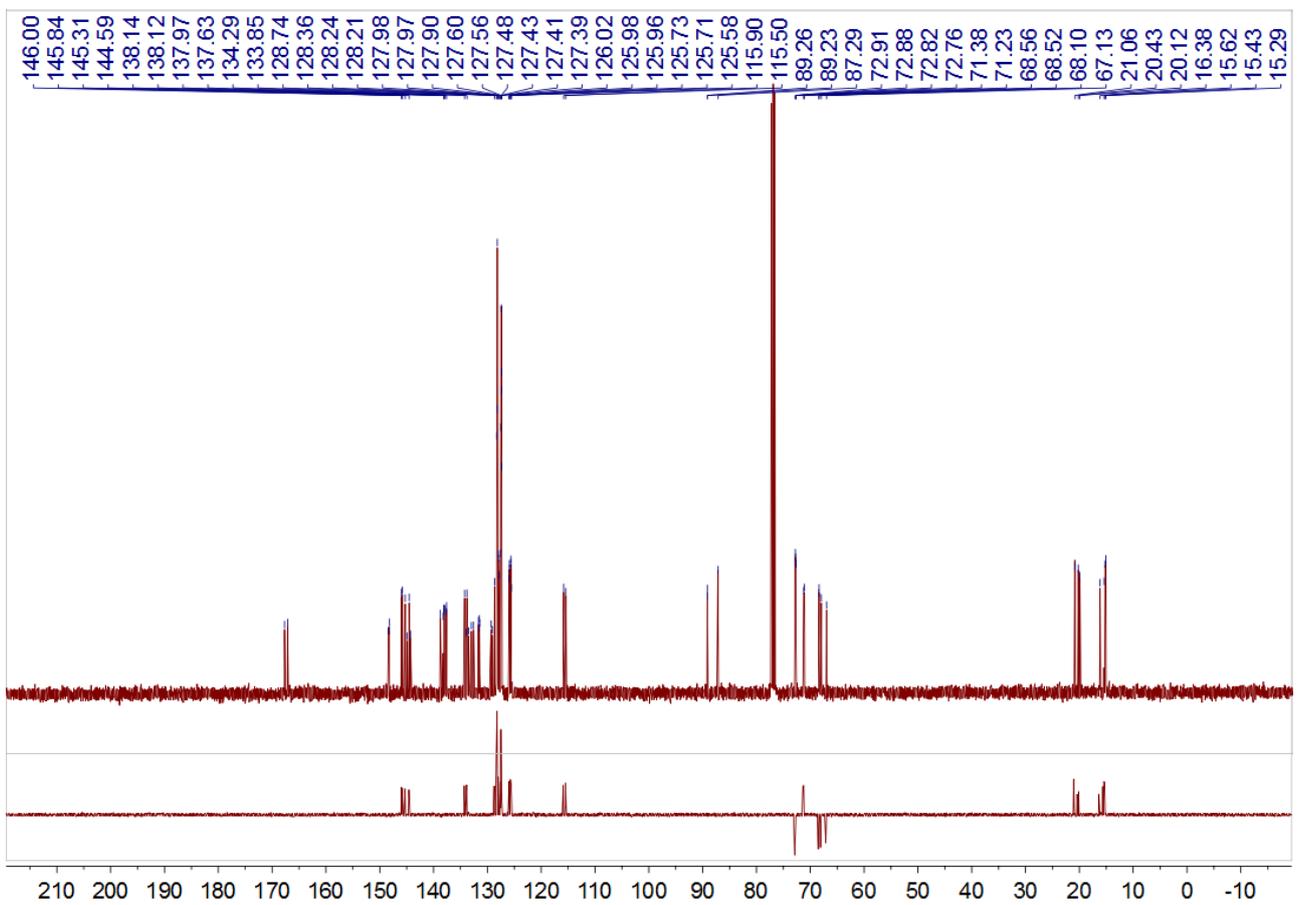
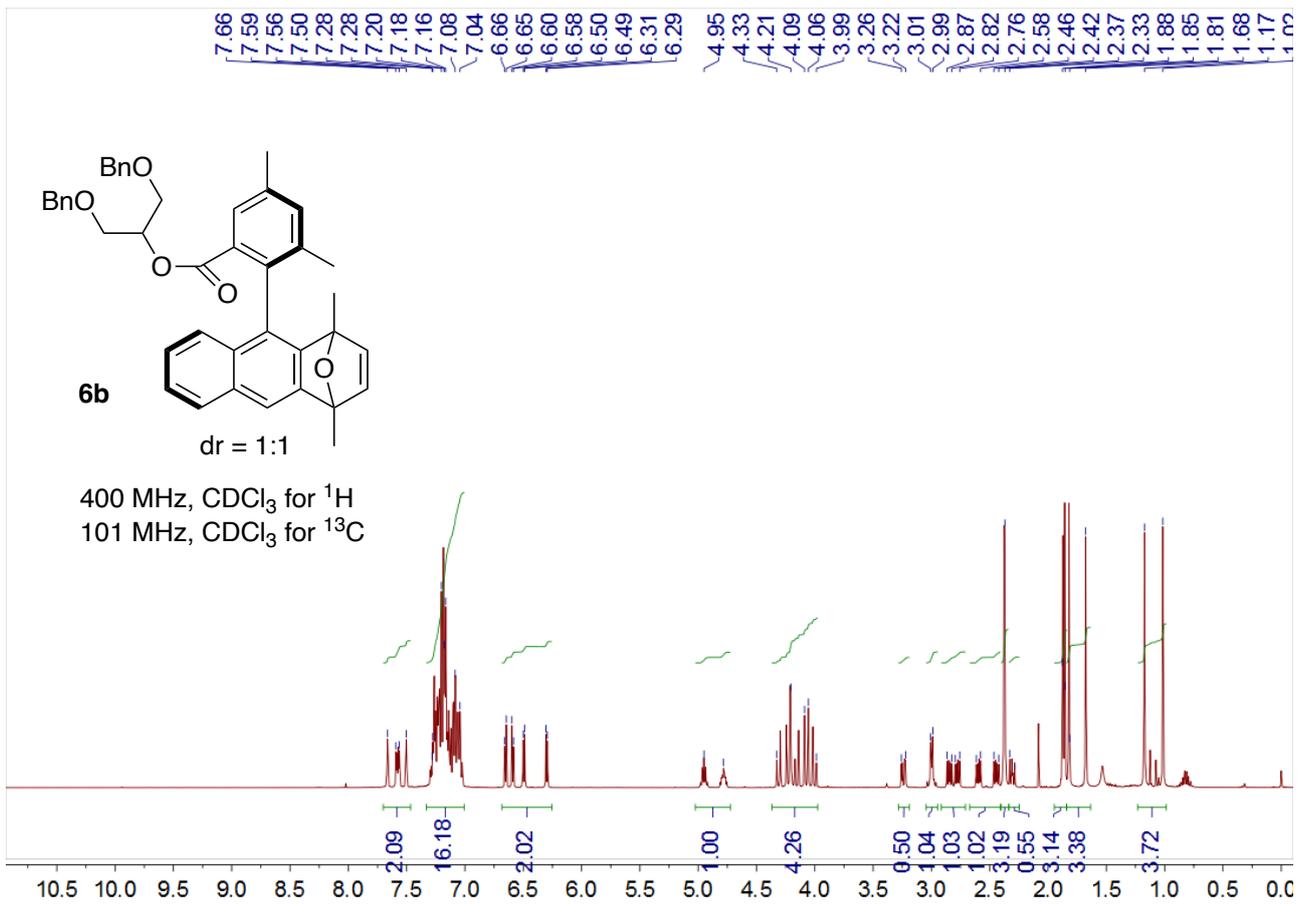


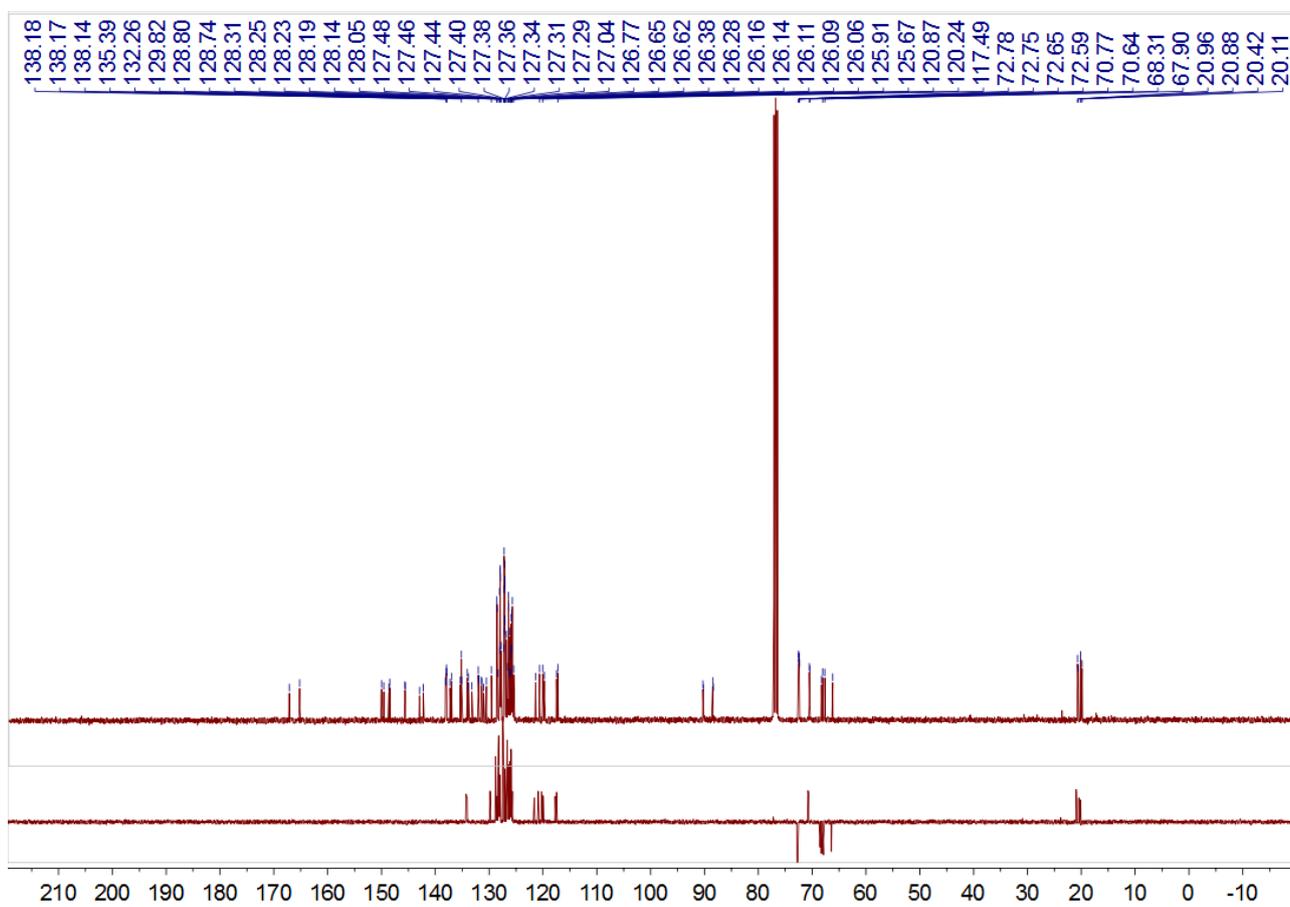
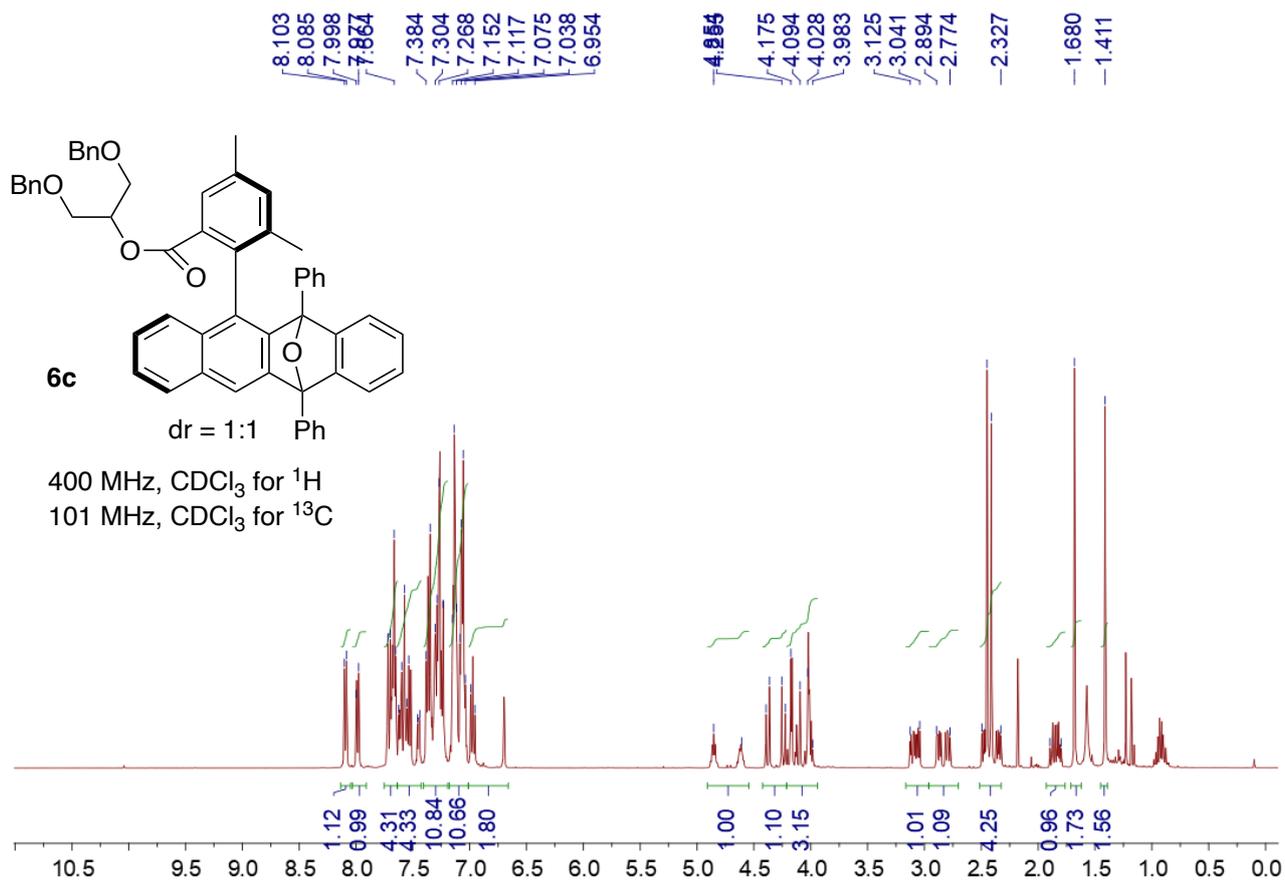


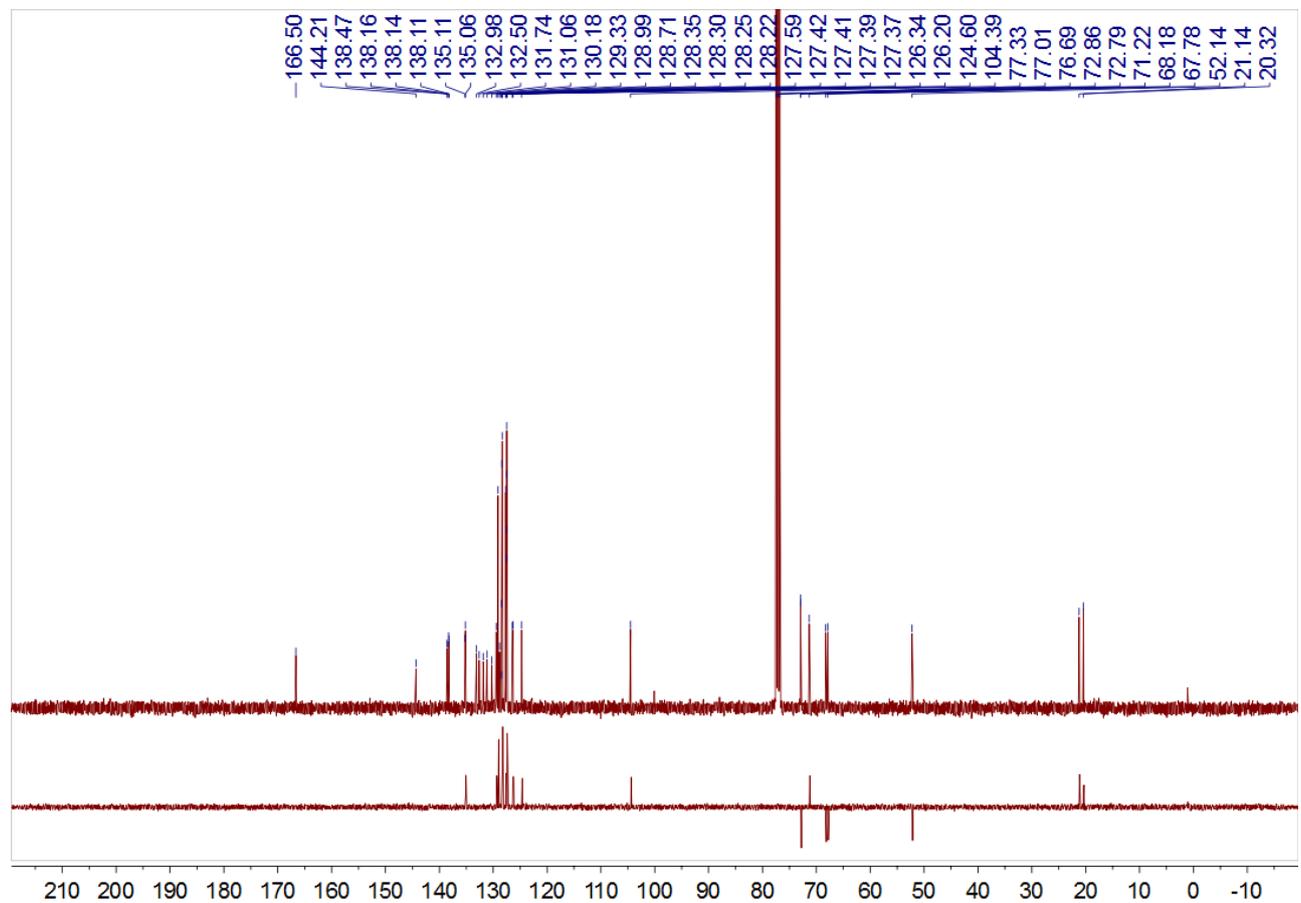
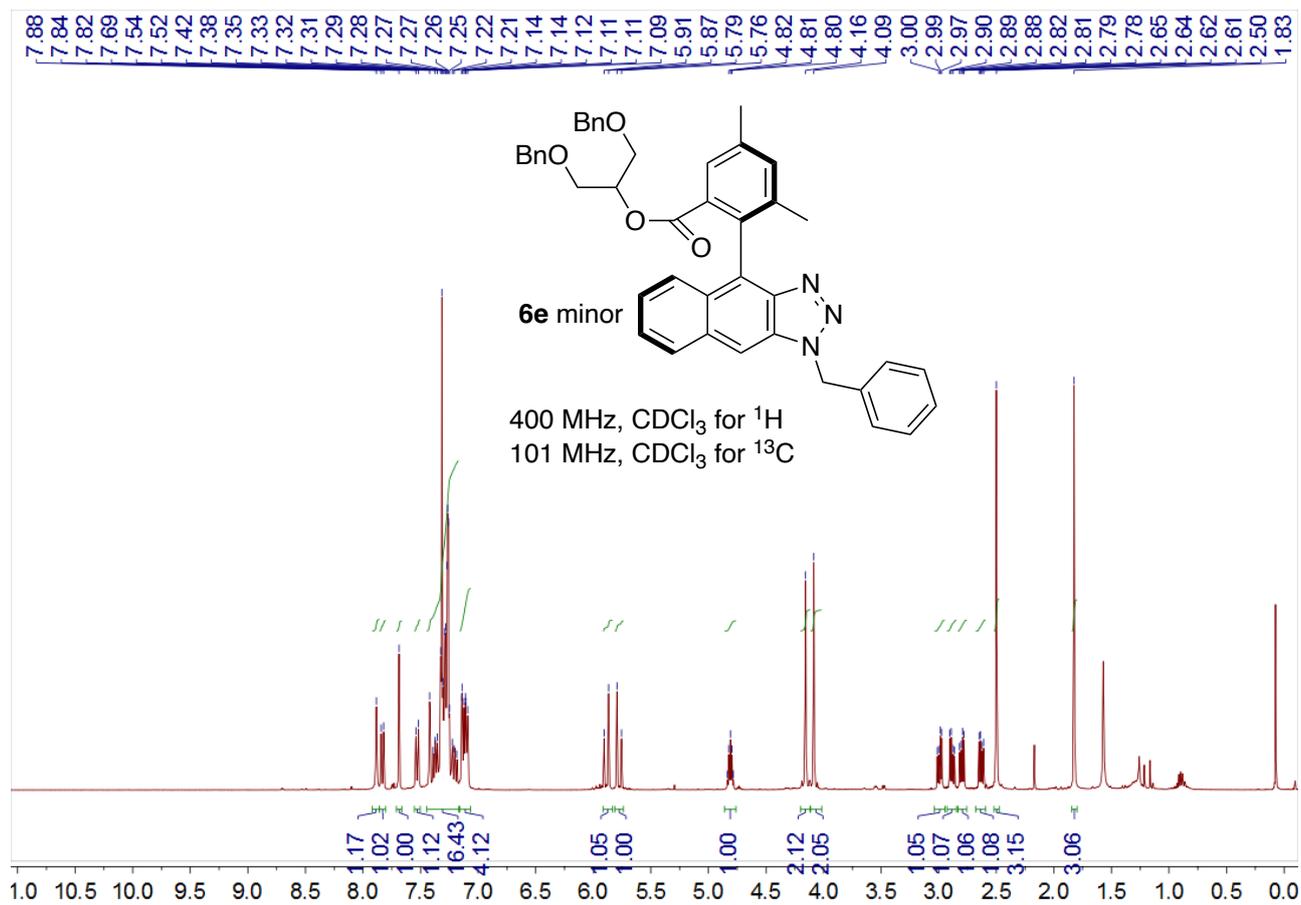


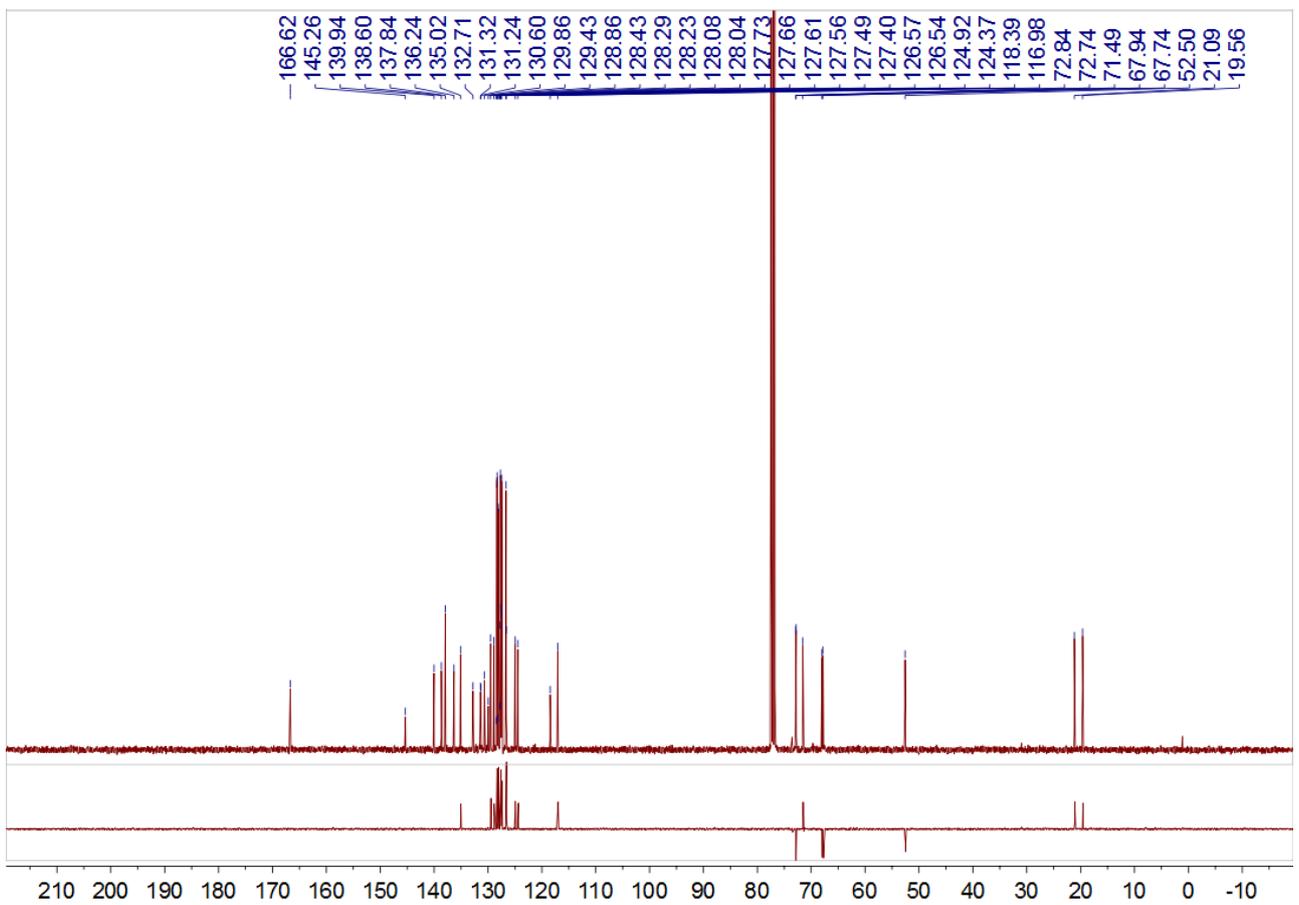
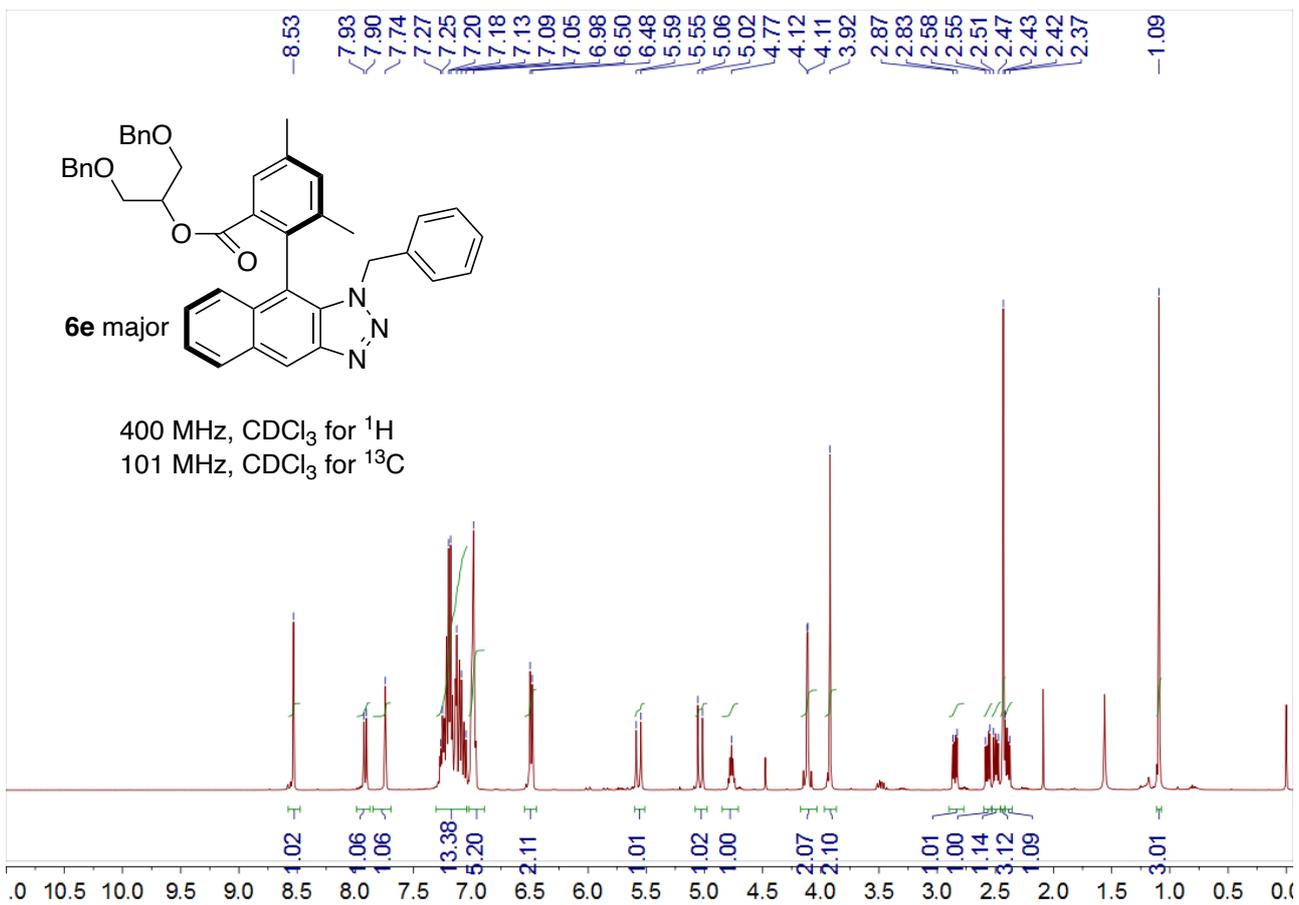
400 MHz, CDCl_3 for ^1H
 101 MHz, CDCl_3 for ^{13}C

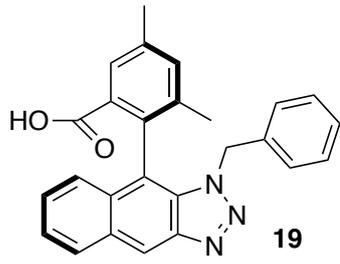




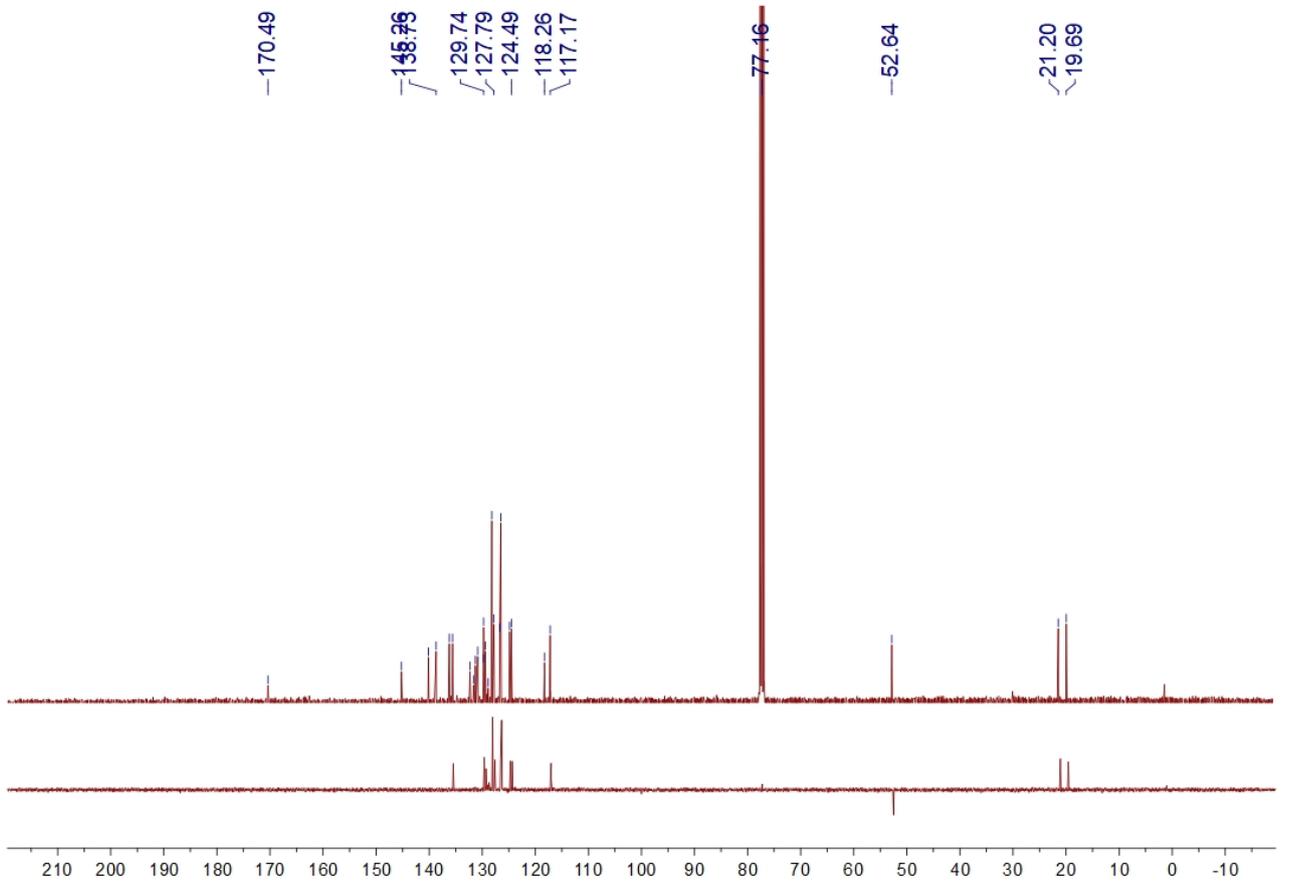
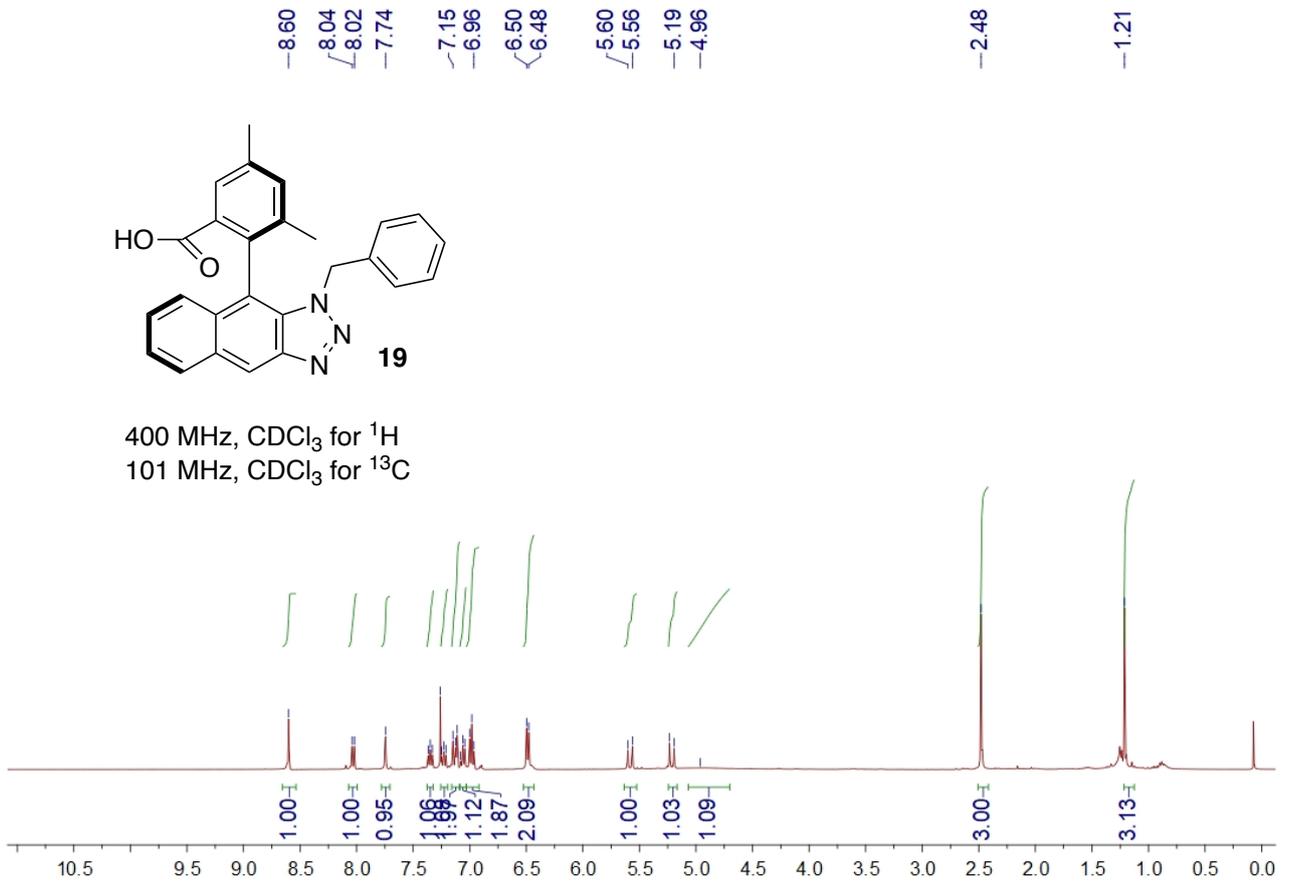


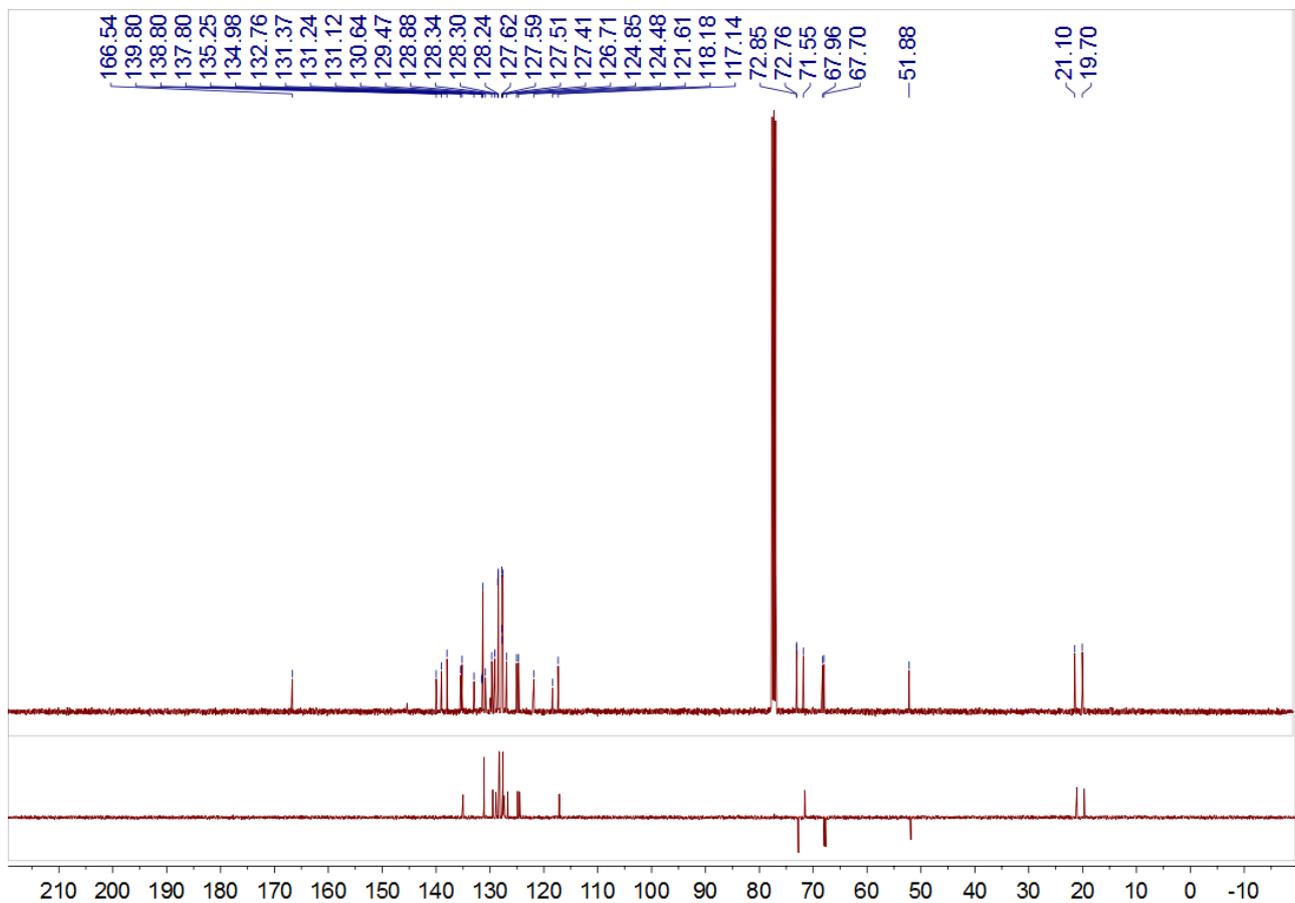
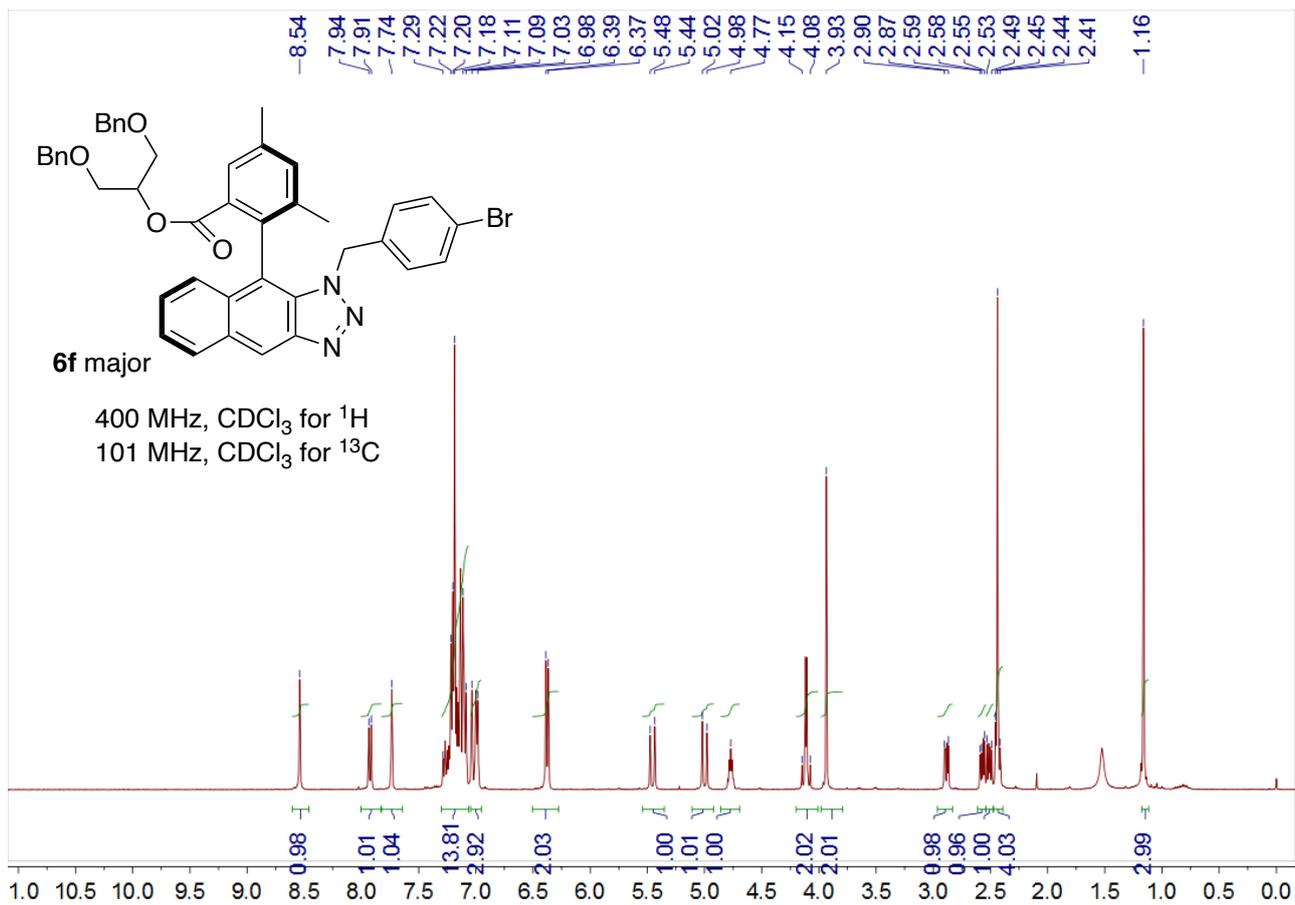


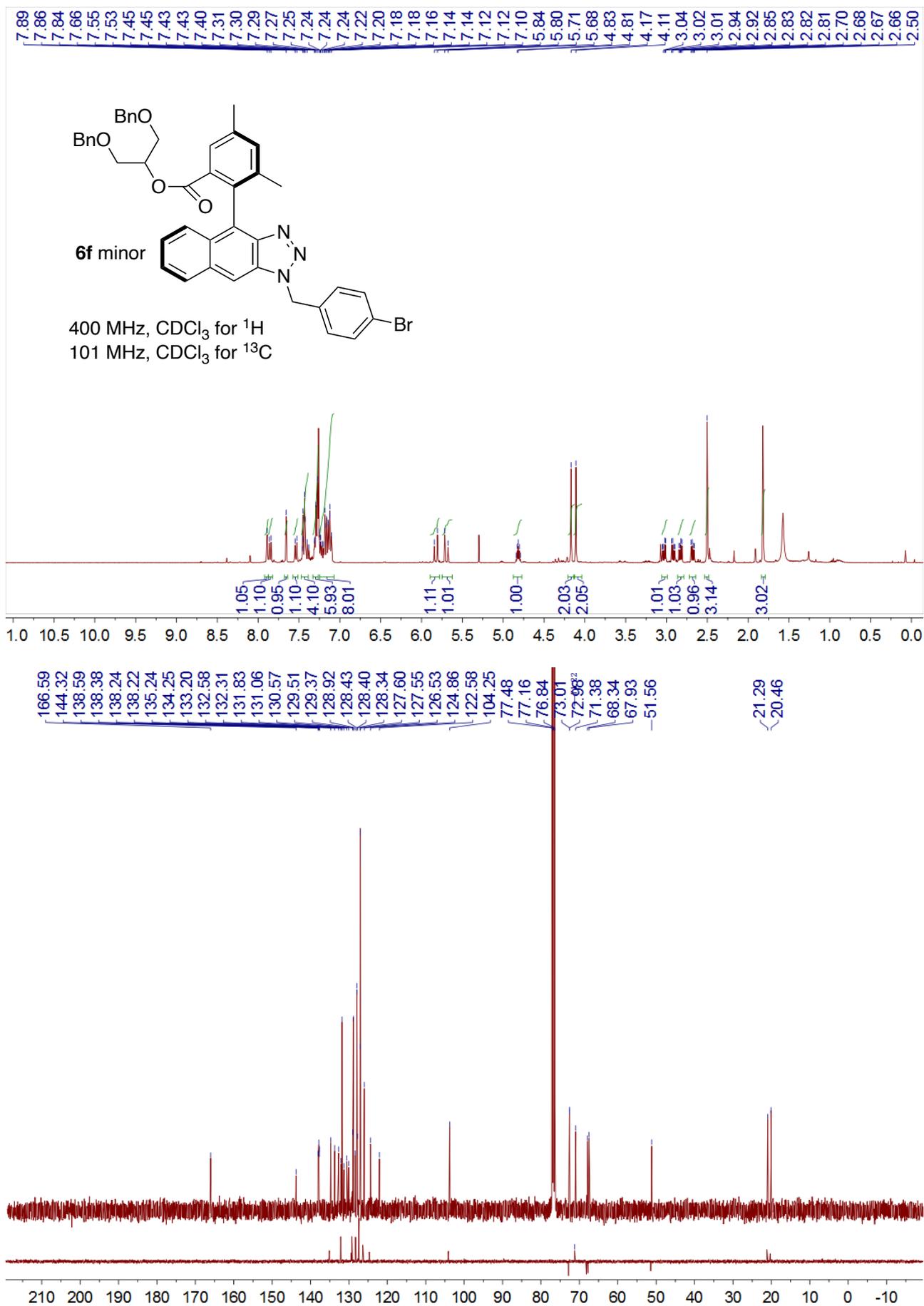


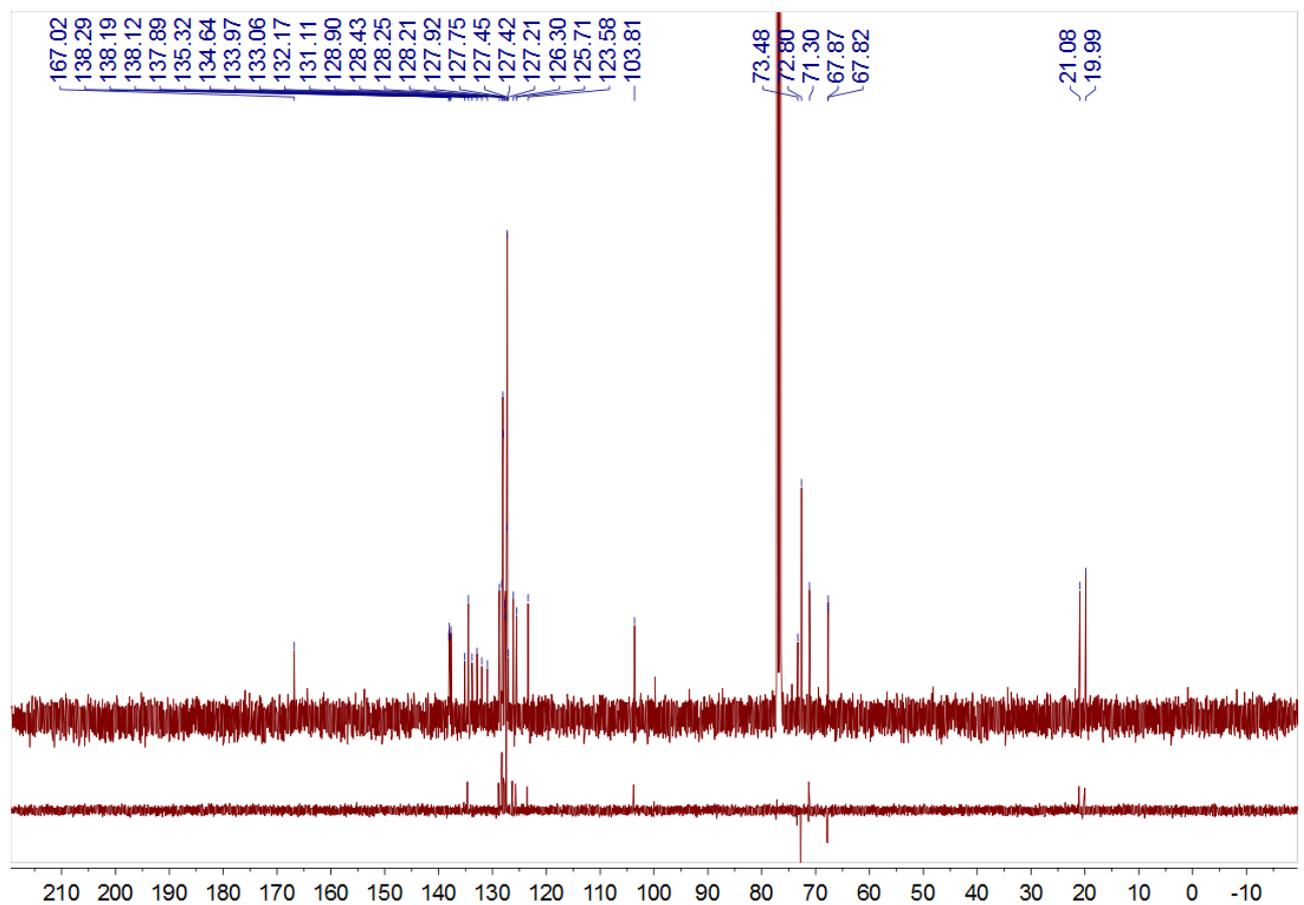
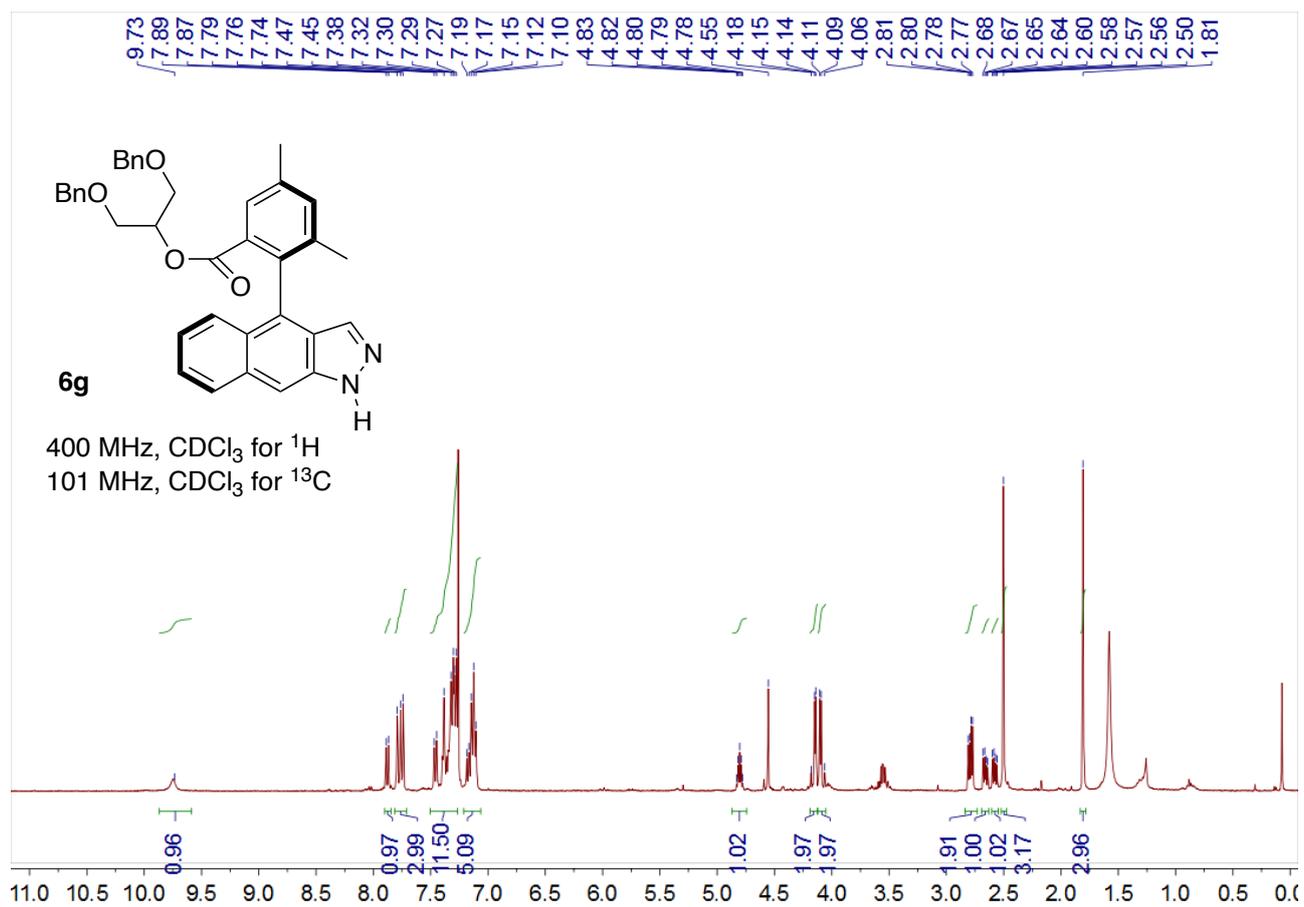


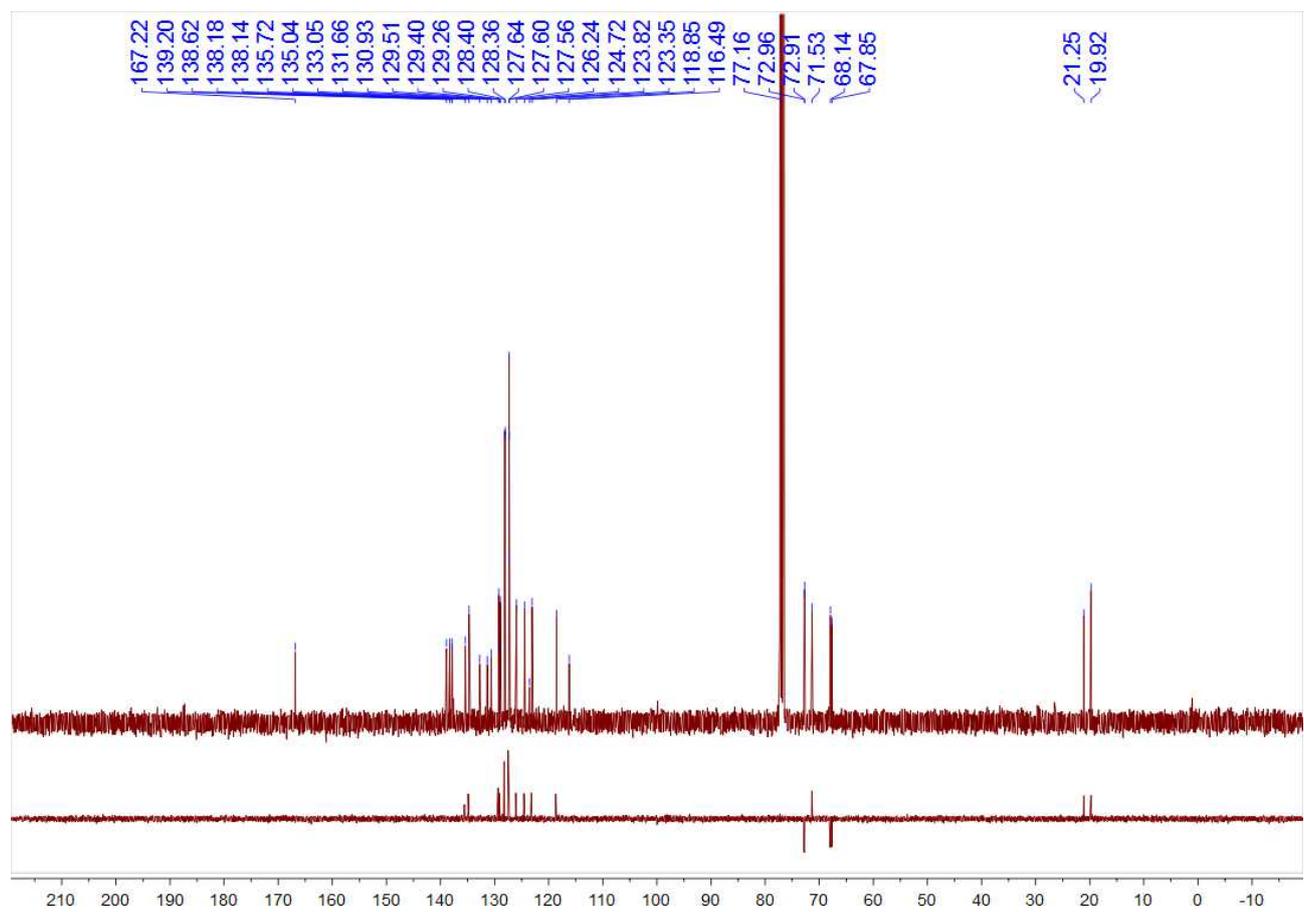
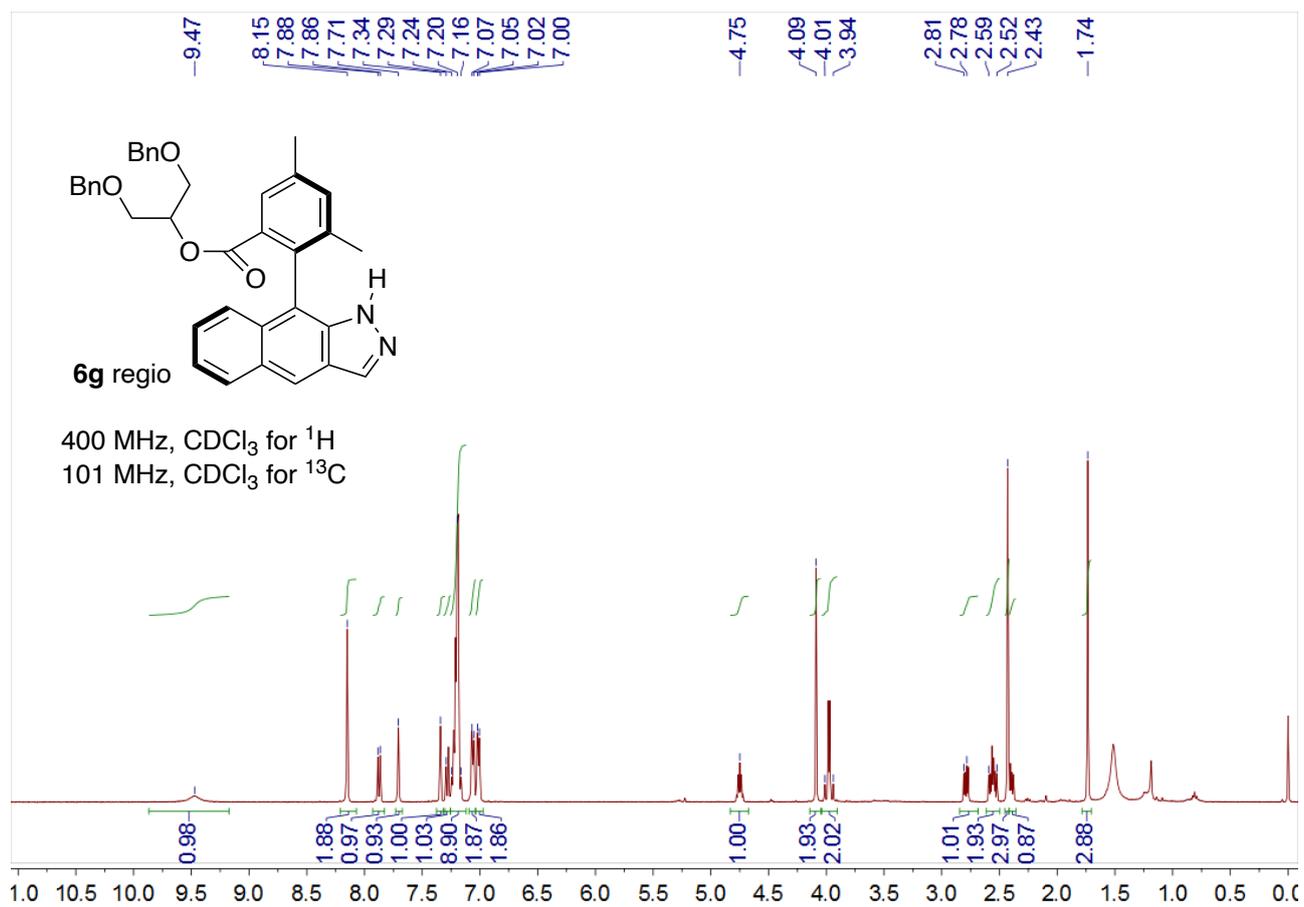
400 MHz, CDCl₃ for ¹H
 101 MHz, CDCl₃ for ¹³C

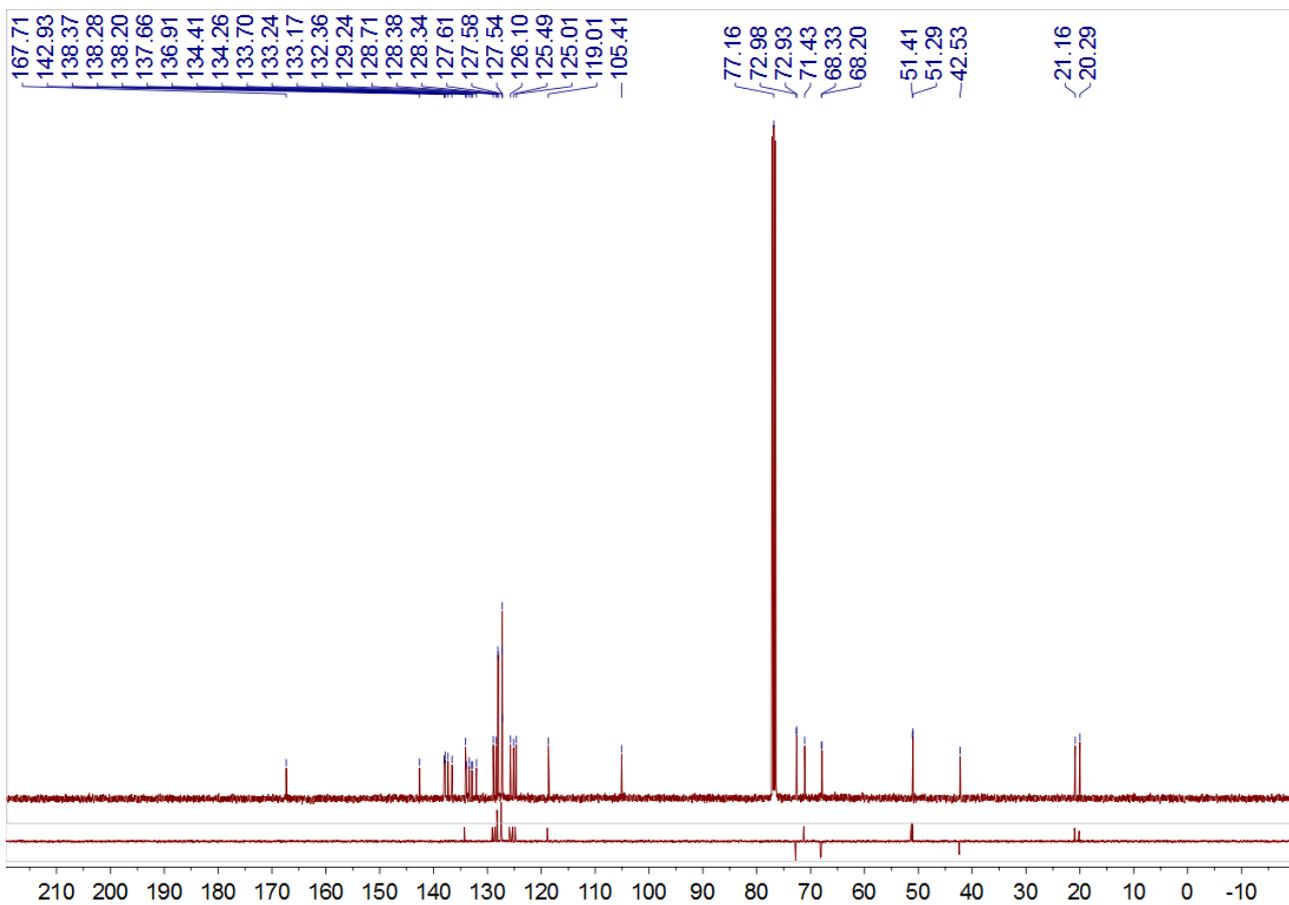
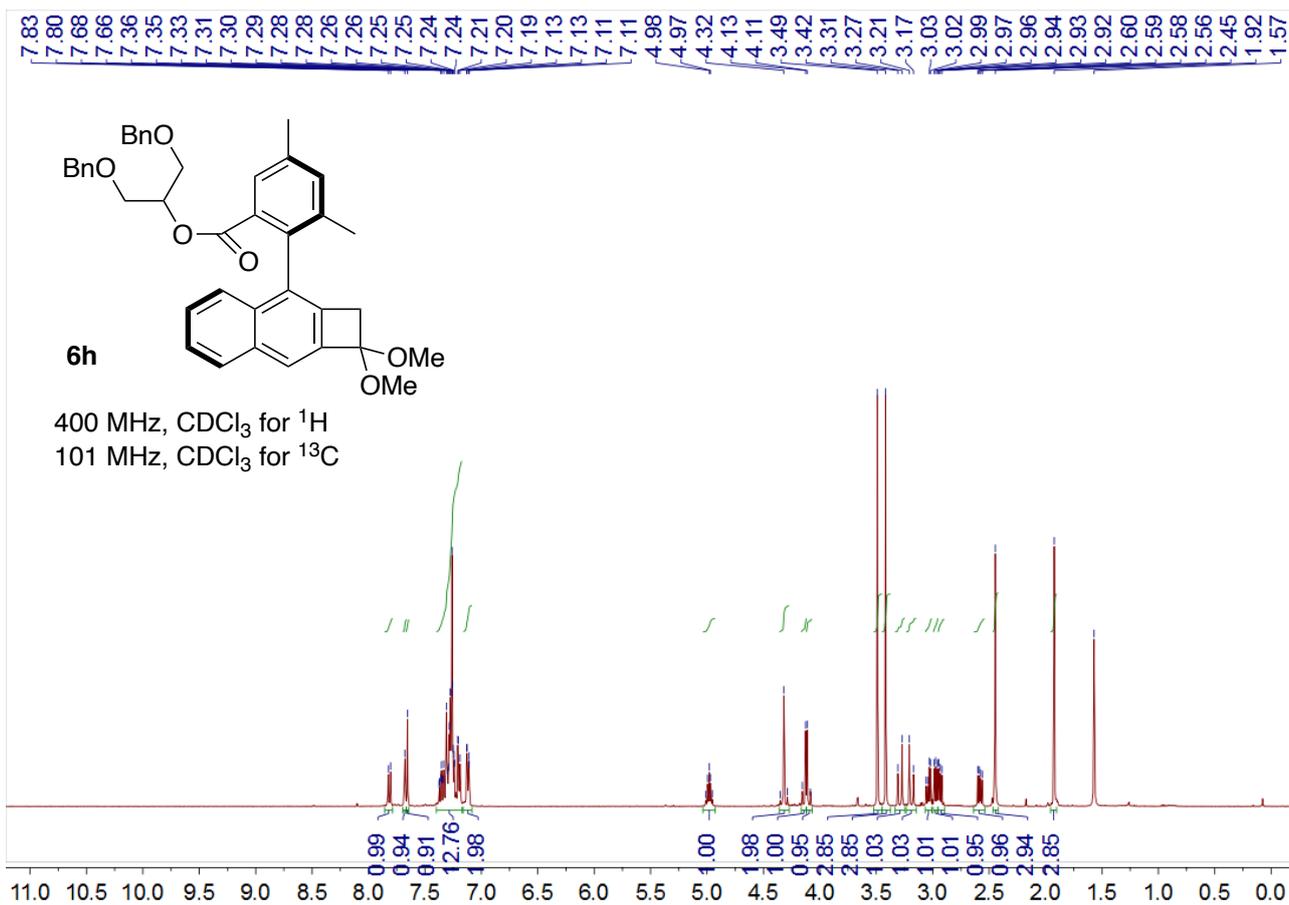


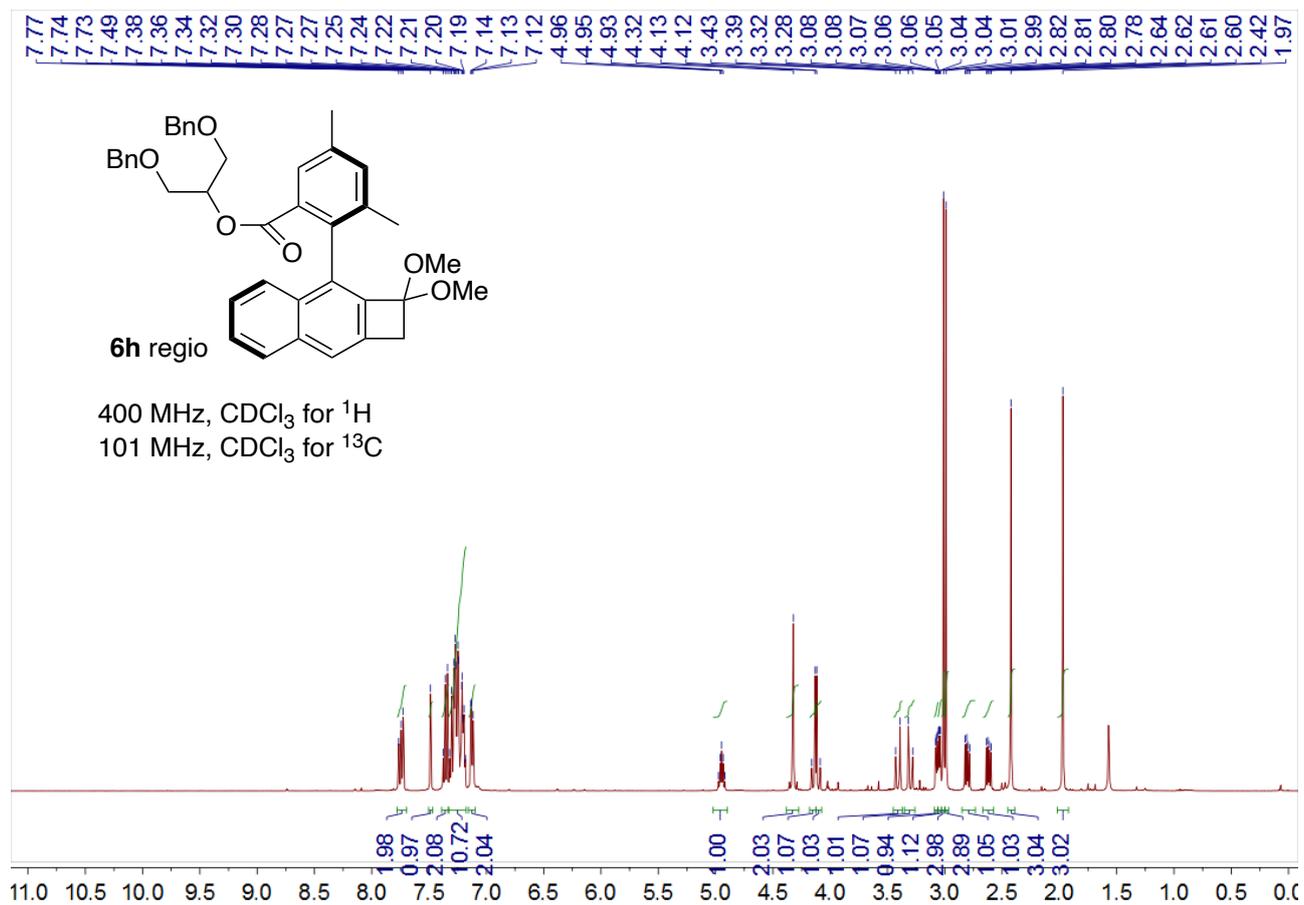


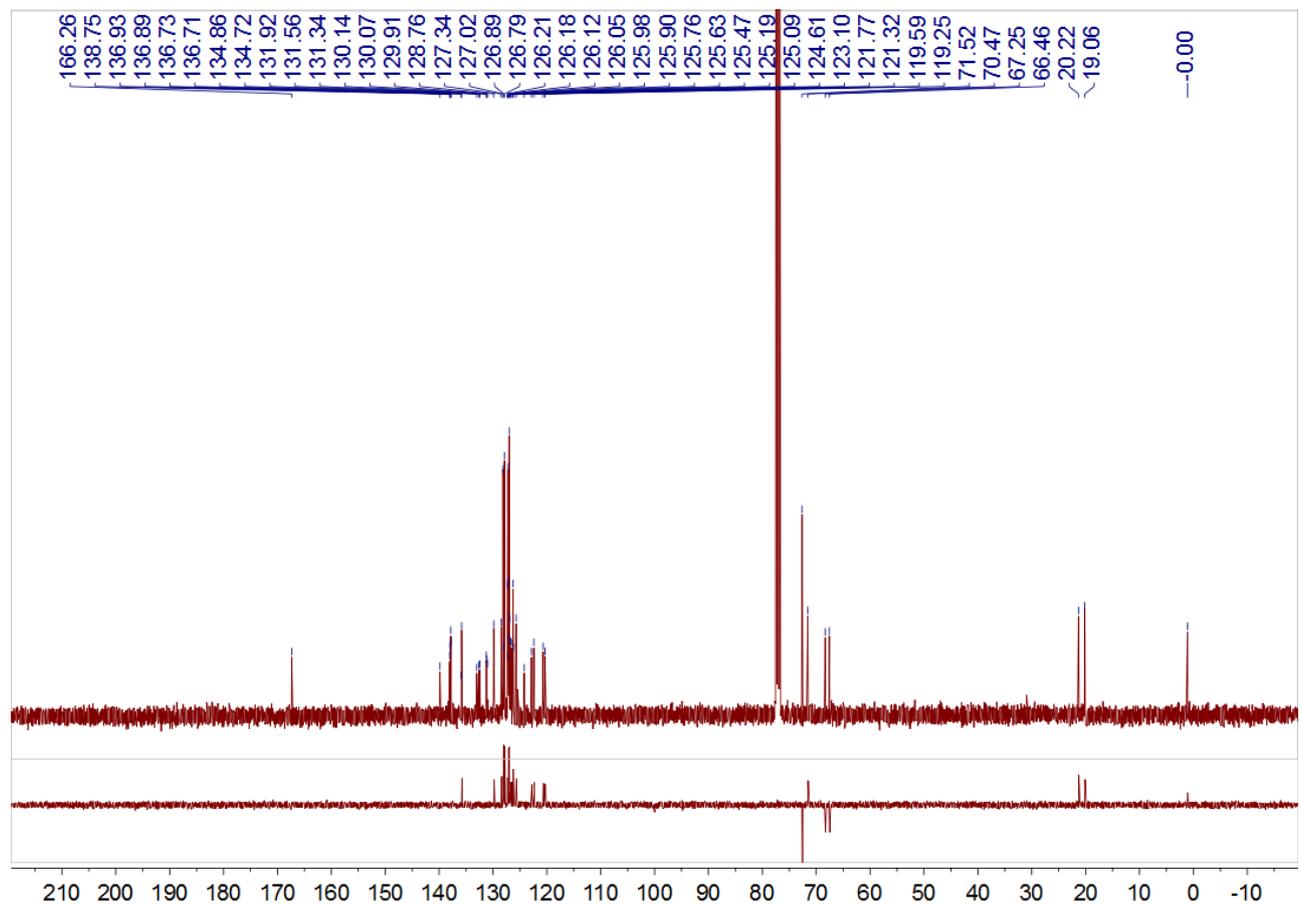
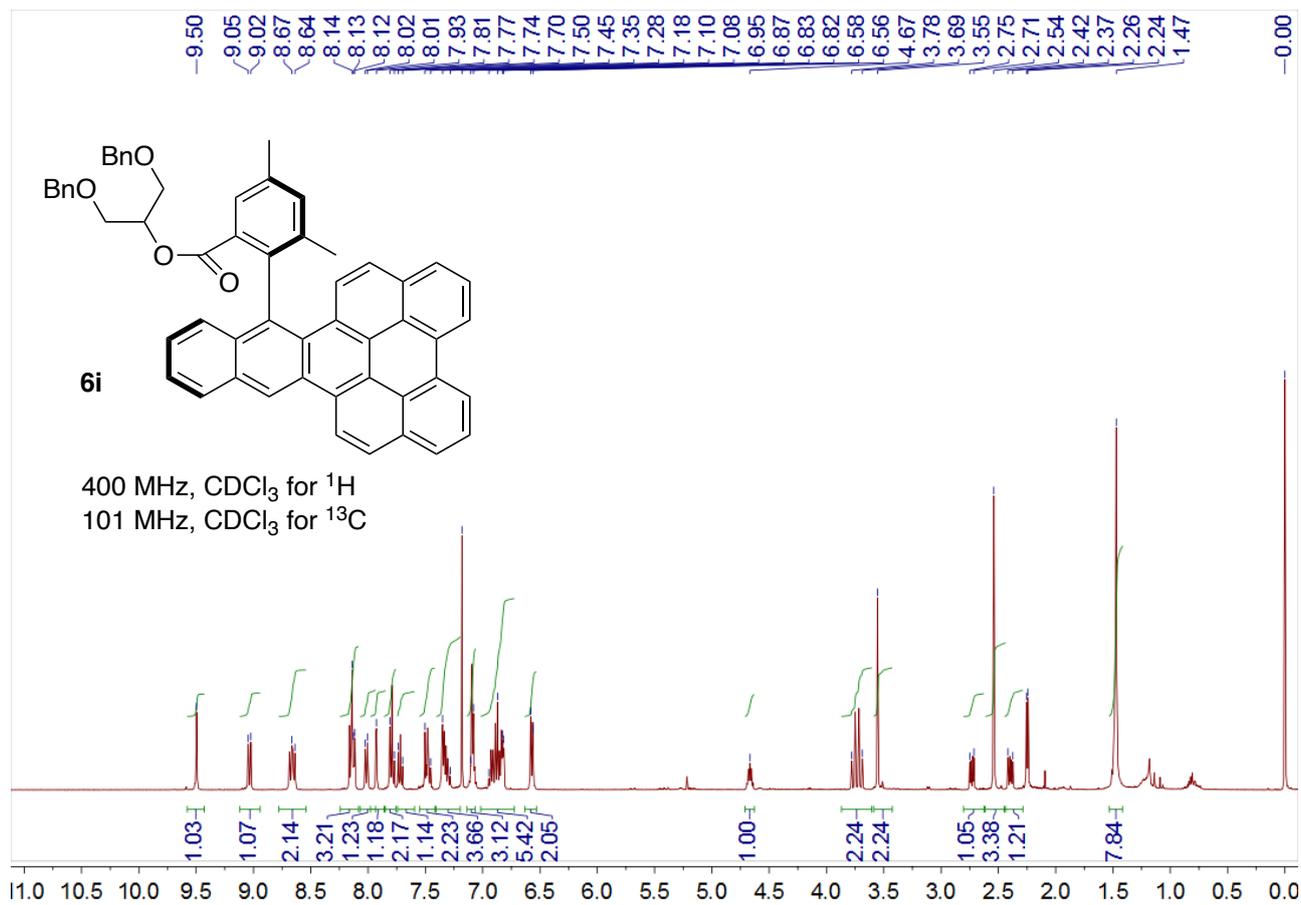


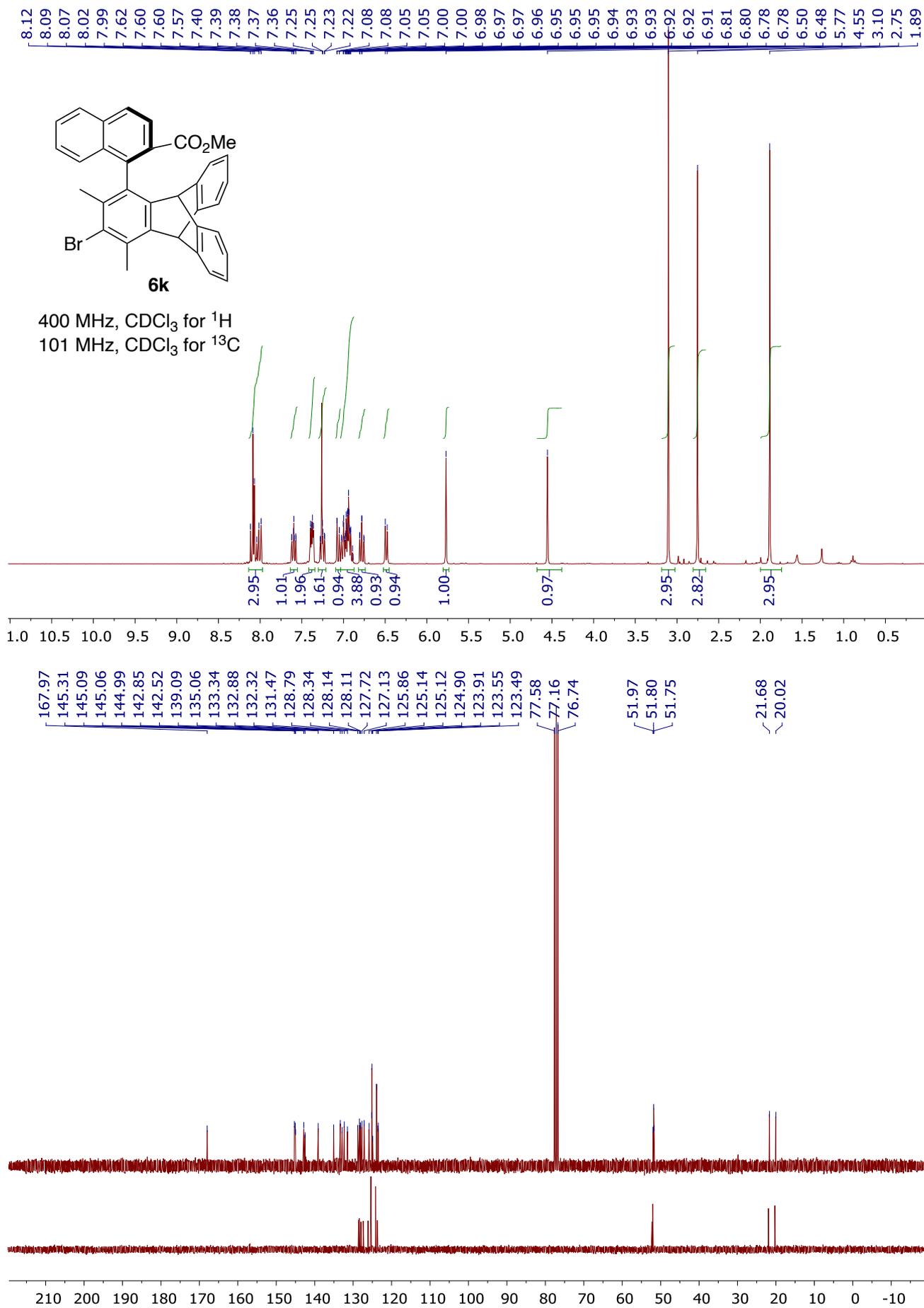


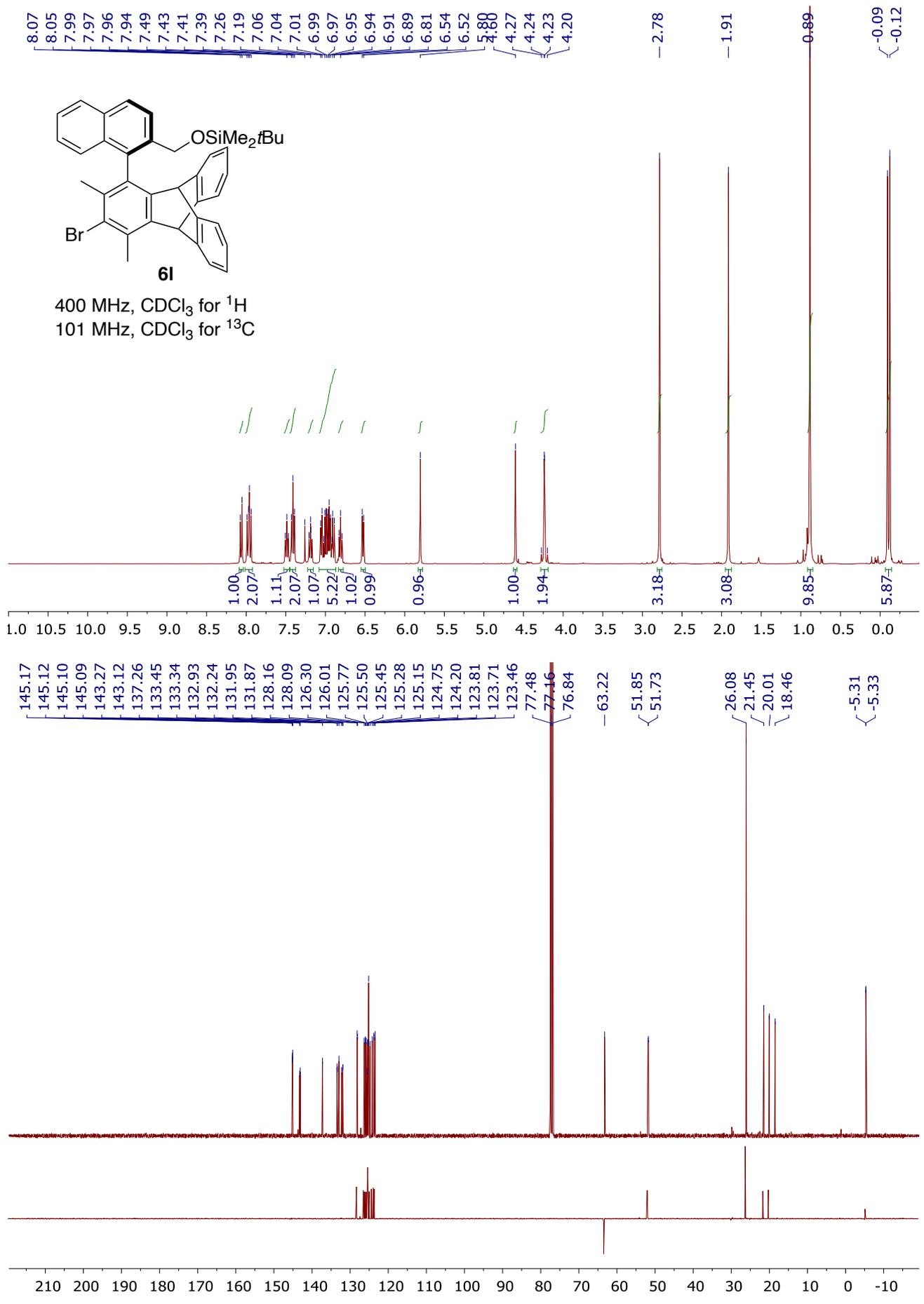


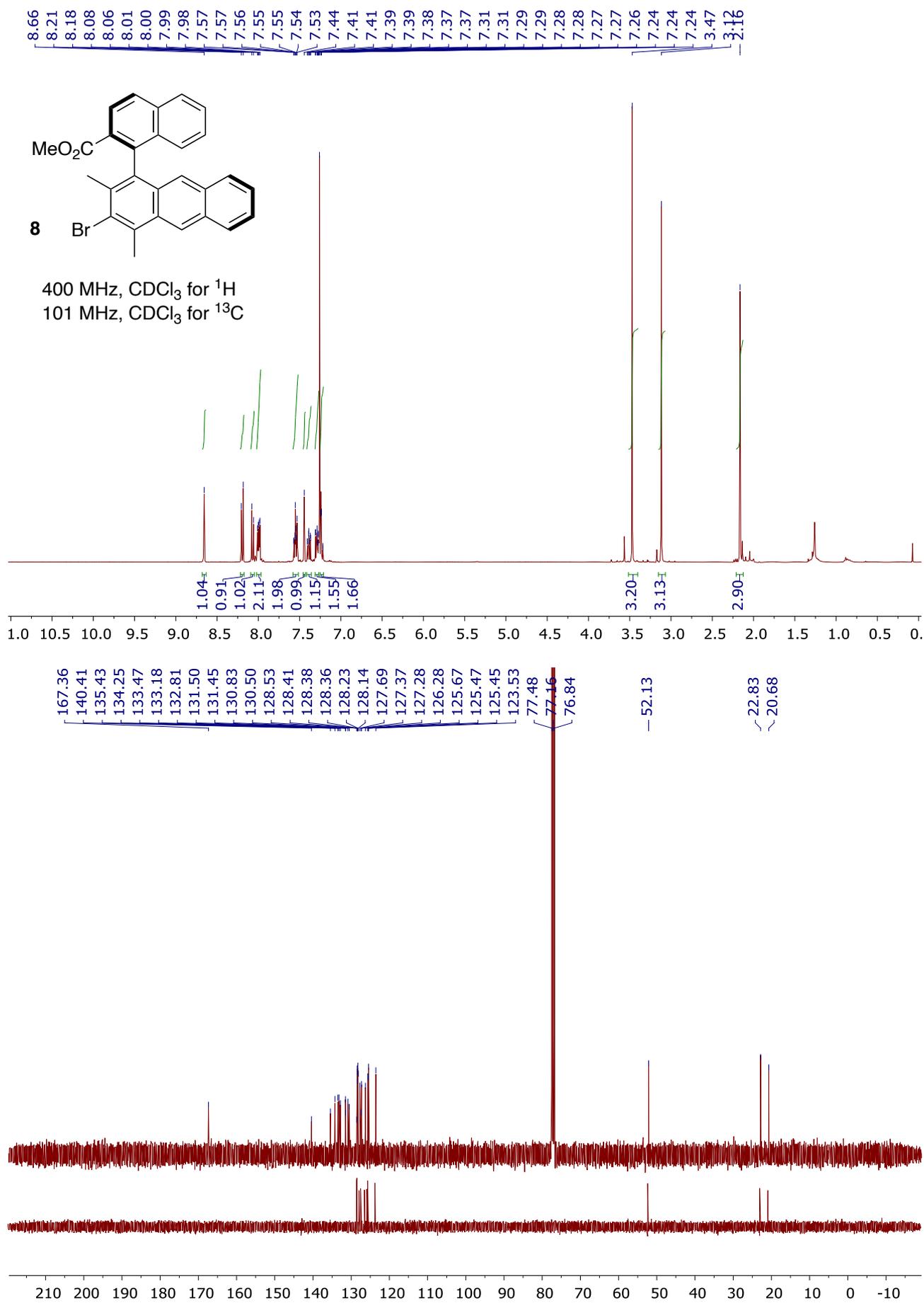






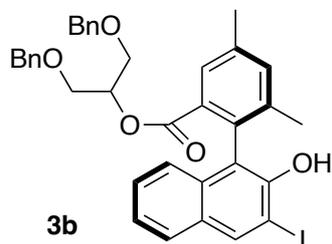




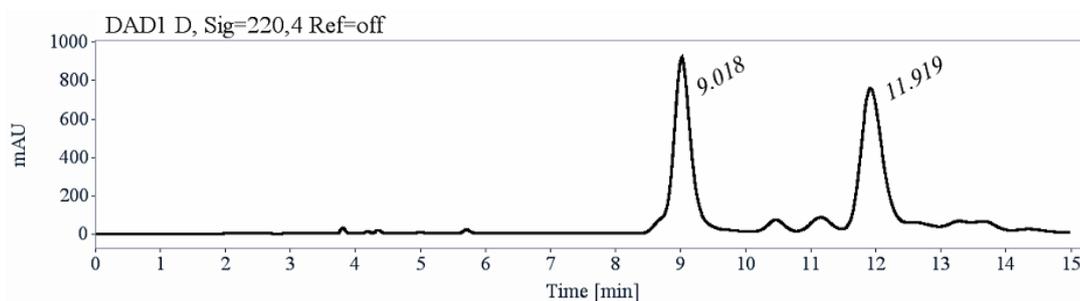


Chromatograms from analytical HPLC on chiral stationary phases of all enantio-enriched products: racemic material (top) and enantio-enriched material (bottom)

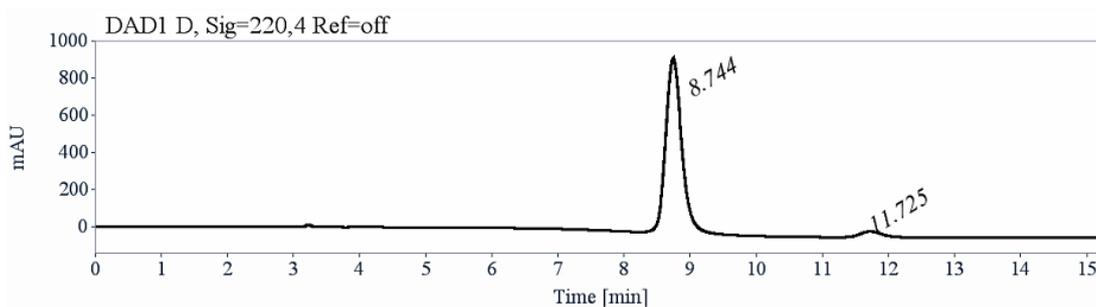
Note: for the chromatograms of the racemic materials, only the two signals of interest are noted with their retention times. All other signals can be attributed to the presence of unidentified inseparable impurities and/or the other diastereomer/regioisomer.



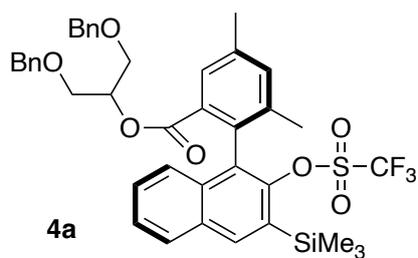
Chiralpak IF column, heptane/ethanol = 90:10, 1 mL/min



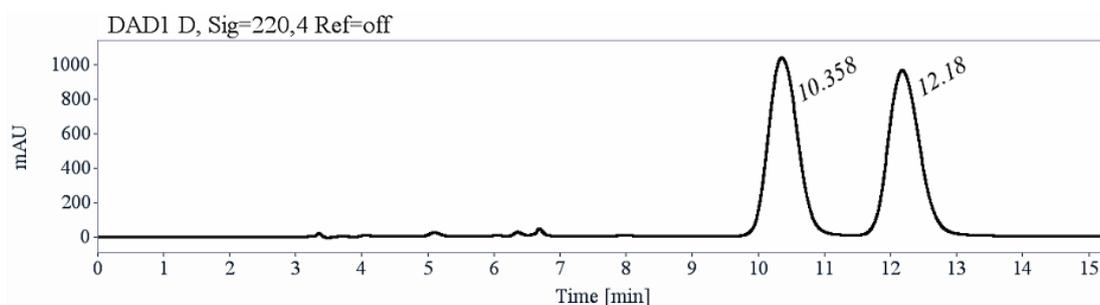
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
9.02	17246	51.95	2.06		
11.92	15951	48.05	3.04	1.48	5.50
Totals	33198	100.00			



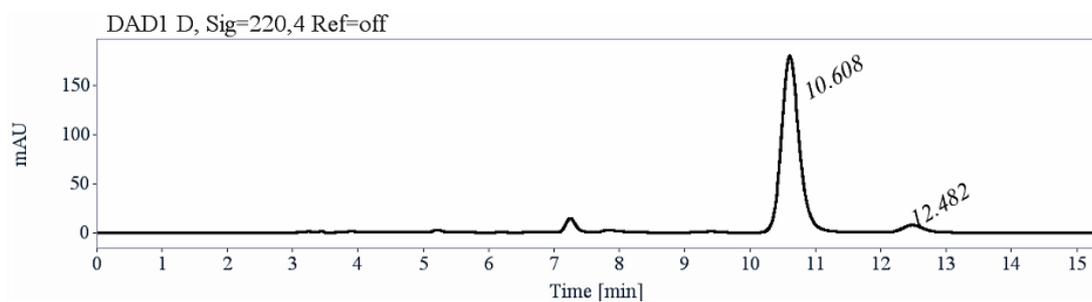
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
8.74	15823	95.31	1.96		
11.73	778	4.69	2.97	1.51	5.69
Totals	16602	100.00			



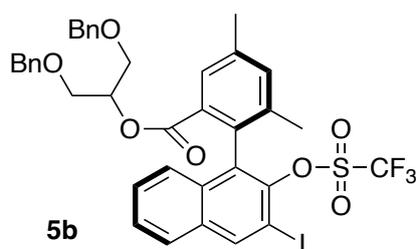
(S,S) Whelk-O1, heptane/isopropanol = 95:5, 1 mL/min



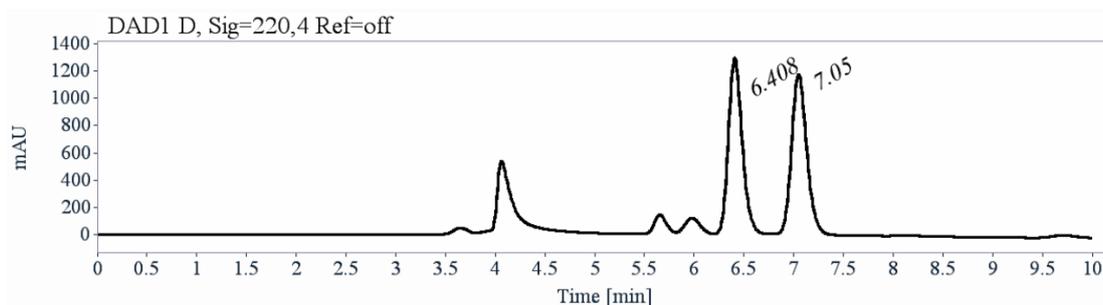
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
10.36	32193	50.05	2.51		
12.18	32125	49.95	3.13	1.25	2.19
Totals	64318	100.00			



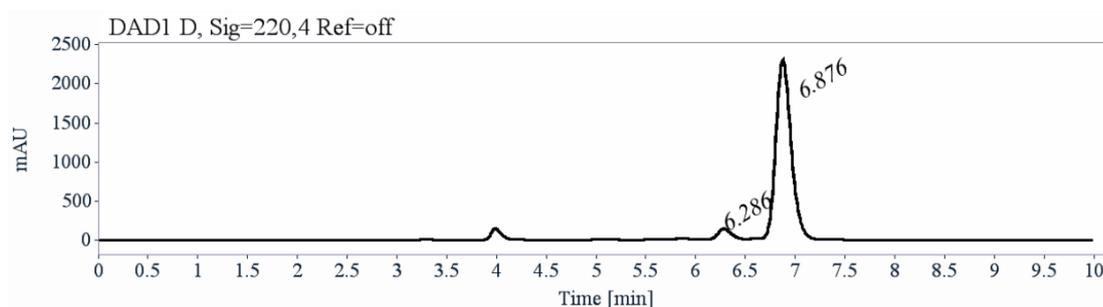
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
10.61	3461	96.03	2.51		
12.48	143	3.97	3.13	1.25	2.19
Totals	3605	100.00			



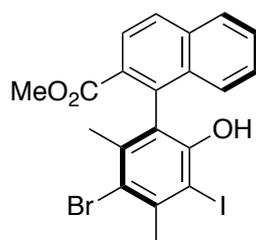
Chiralpak IE, heptane/ethanol = 90:10, 1 mL/min



Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
6.41	12504	49.88	1.17		
7.05	12564	50.12	1.39	1.19	2.42
Totals	25068	100.00			

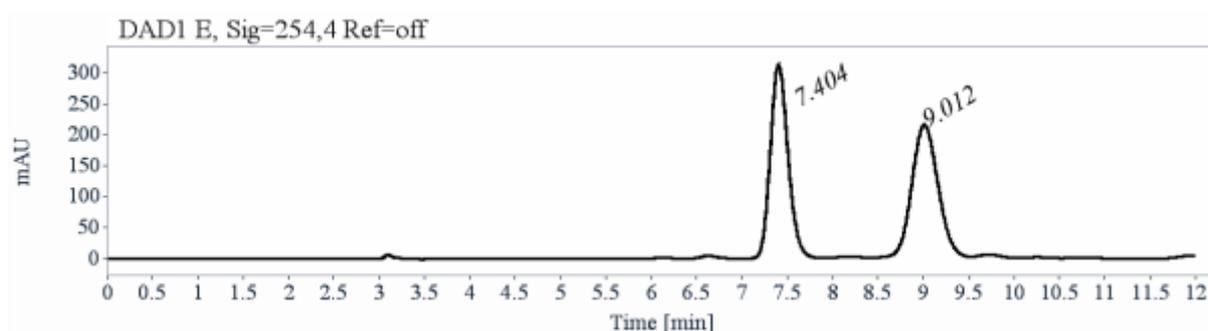


Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
6.29	1366	5.19	1.13		
6.88	24942	94.81	1.33	1.18	2.21
Totals	26308	100.00			



Semi-preparative separation of the enantiomers in *rac*-**3c**

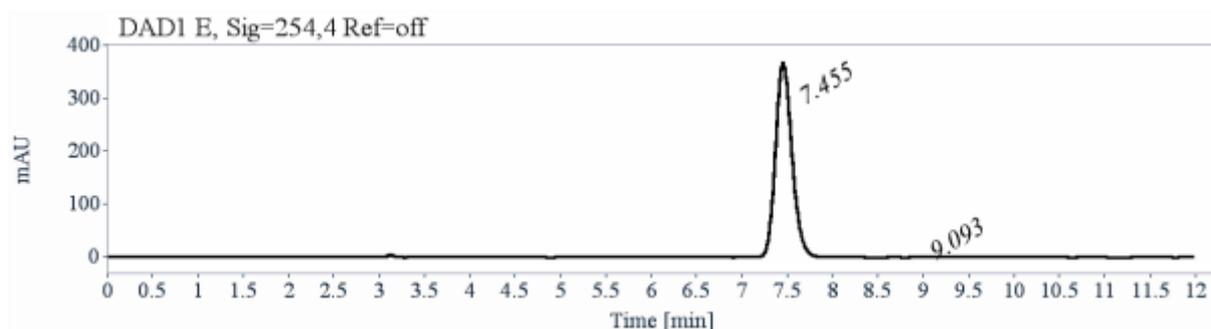
Chiralpak IG, heptane/ethanol = 90:10, 1 mL/min



RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
7.40	4239	49.87	1.51		
9.01	4260	50.13	2.05	1.36	3.63
Sum	8499	100.00			

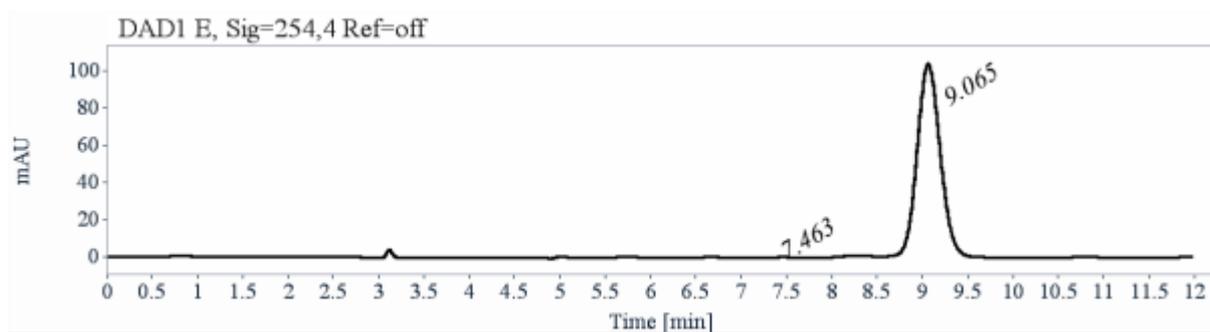
- Sample preparation: About 480 mg of racemic **3c** were dissolved in 9.2 mL of dichloromethane/ethanol (1:2).
- Chromatographic conditions: Chiralpak IG (250 x 10 mm), hexane/ethanol (9:1) as mobile phase, flow-rate = 5 mL/min, UV detection at 254 nm.
- Injections (stacked): 184 times 50 μ L, every 3 minutes.

This afforded 205 mg of the first eluted enantiomer with >99.5% ee, and 212 mg of the second eluted enantiomer with >99.5% ee (see chromatograms of the enantiopure materials below)



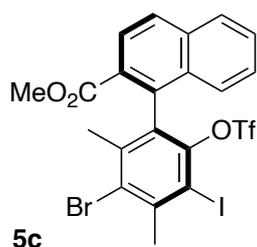
RT [min]	Area	Area%
7.45	4619	99.87
9.09	6	0.13
Sum	4625	100.00

(aS)-3c

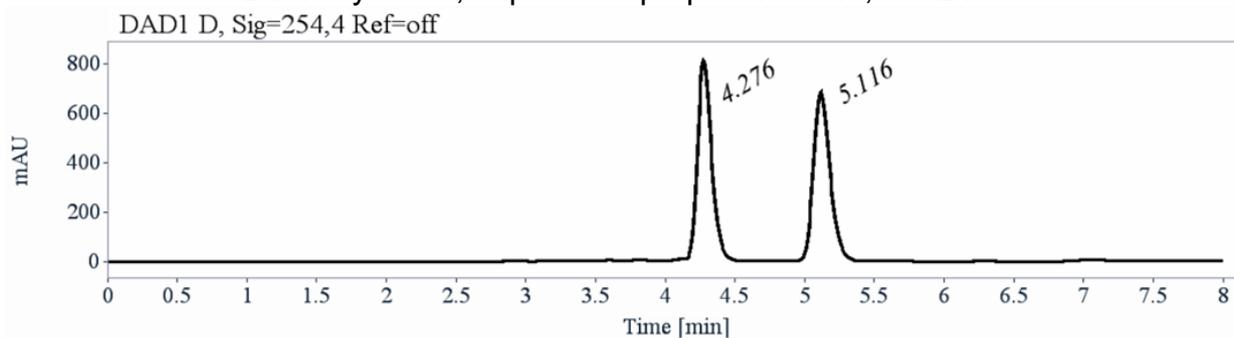


RT [min]	Area	Area%
7.46	3	0.16
9.07	1828	99.84
Sum	1831	100.00

(aR)-3c

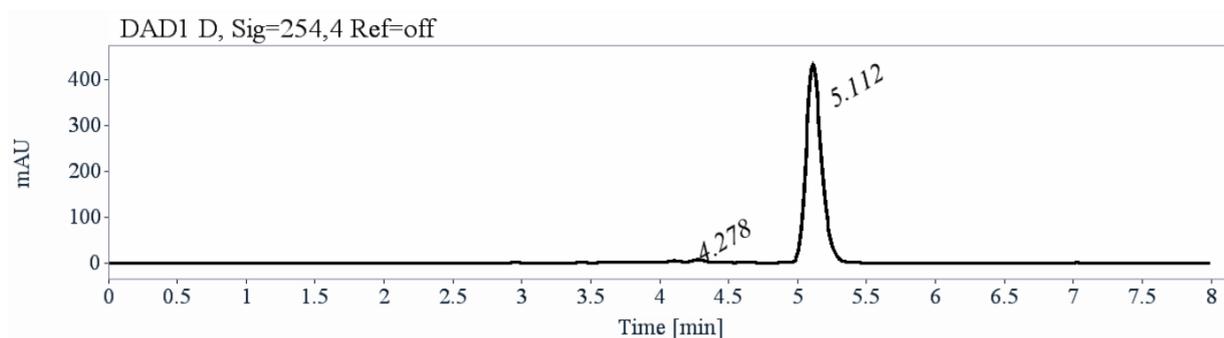


Lux-Amylose-1, heptane/isopropanol = 95:5, 1 mL/min



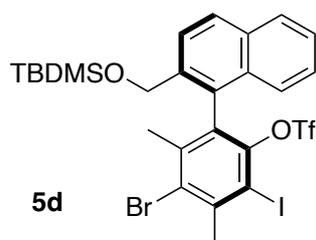
DAD1 D, Sig=254,4 Ref=off

RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
4.28	5746	50.14	0.45		
5.12	5714	49.86	0.73	1.63	4.18
Sum	11460	100.00			

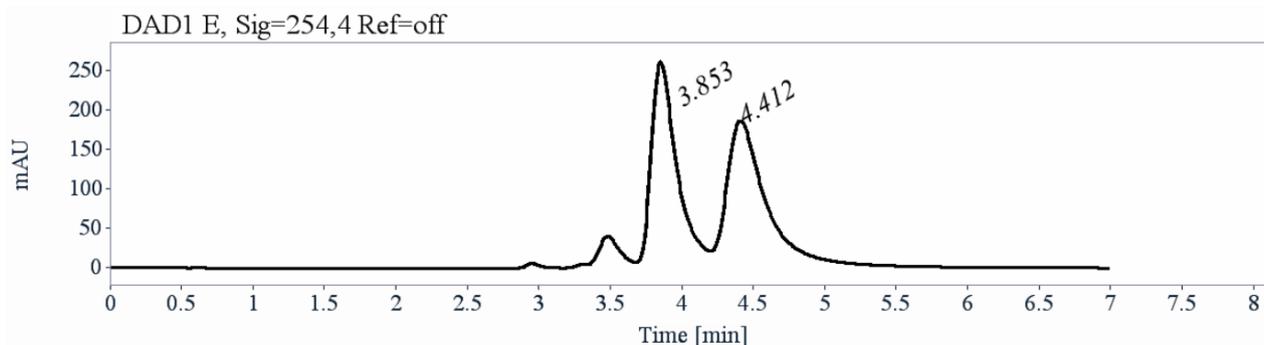


DAD1 D, Sig=254,4 Ref=off

RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
4.28	43	1.26	0.45		
5.11	3388	98.74	0.73	1.63	4.42
Sum	3431	100.00			

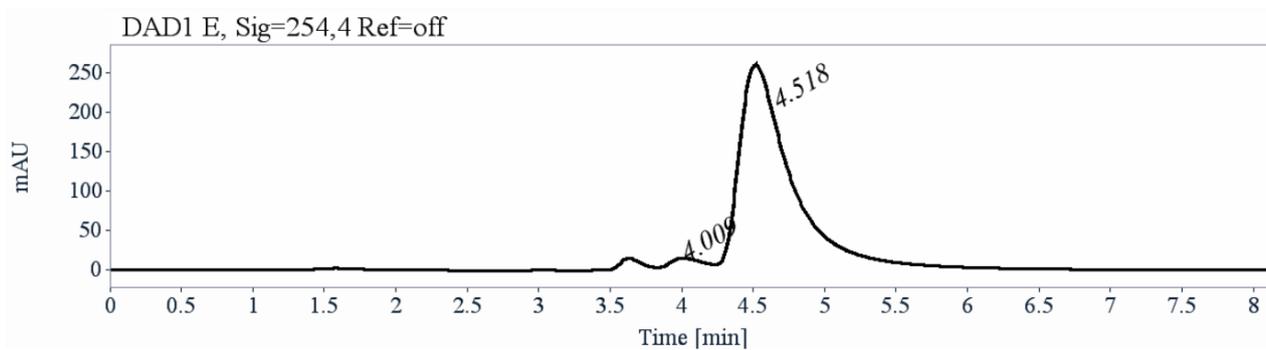


Lux-Amylose-1, heptane/isopropanol = 99.9:0.1, 1 mL/min



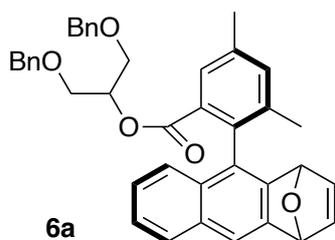
Signal: DAD1 E, Sig=254,4 Ref=off

RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
3.85	3279	47.93	0.31		
4.41	3562	52.07	0.50	1.62	1.47
Sum	6841	100.00			



Signal: DAD1 E, Sig=254,4 Ref=off

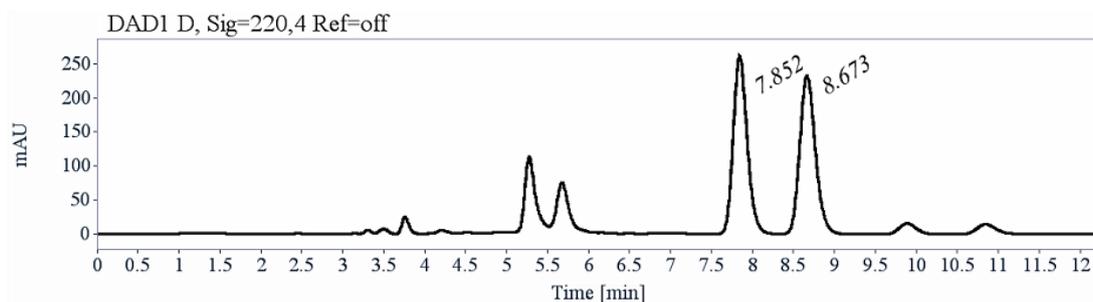
RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
4.01	203	3.17	0.36		
4.52	6197	96.83	0.53	1.48	0.99
Sum	6400	100.00			



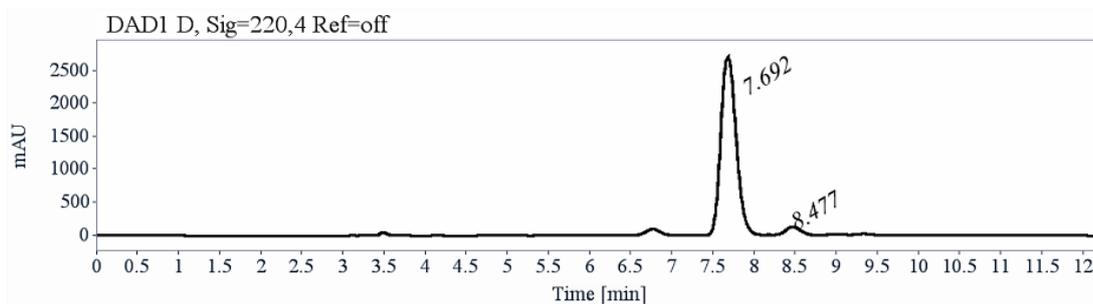
6a

1st eluted diastereomer

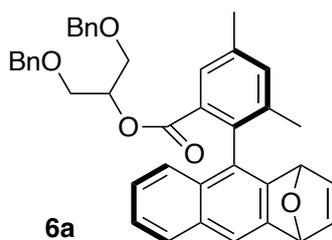
Chiralpak IE, heptane/ethanol = 80:20, 1 mL/min



Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
7.85	3106	50.11	1.66		
8.67	3092	49.89	1.94	1.17	2.49
Totals	6198	100.00			

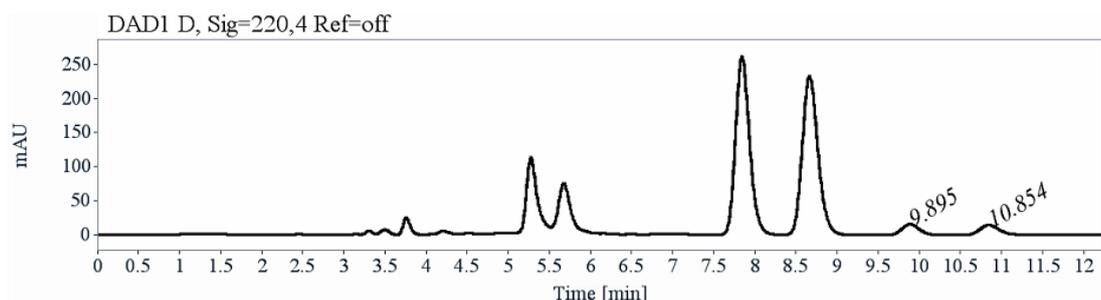


Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
7.69	35418	95.30	1.61		
8.48	1748	4.70	1.87	1.17	2.31
Totals	37166	100.00			

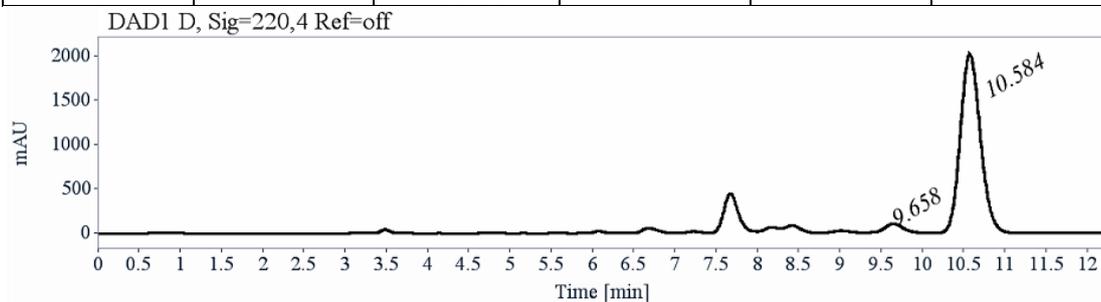


2nd eluted diastereomer
 (contains ca. 10% of the
 1st eluted diastereomer)

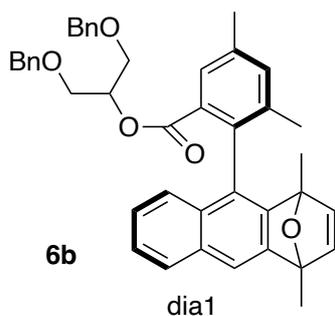
Chiralpak IE, heptane/ethanol = 80:20, 1 mL/min



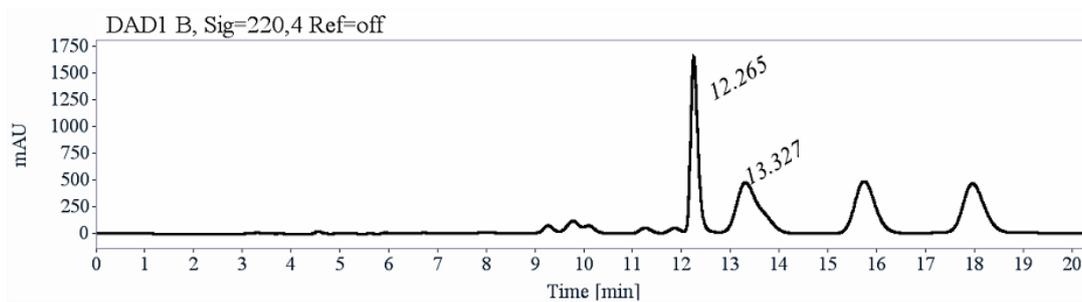
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
9.90	234	49.37	2.35		
10.85	240	50.63	2.68	1.14	2.35
Totals	474	100.00			



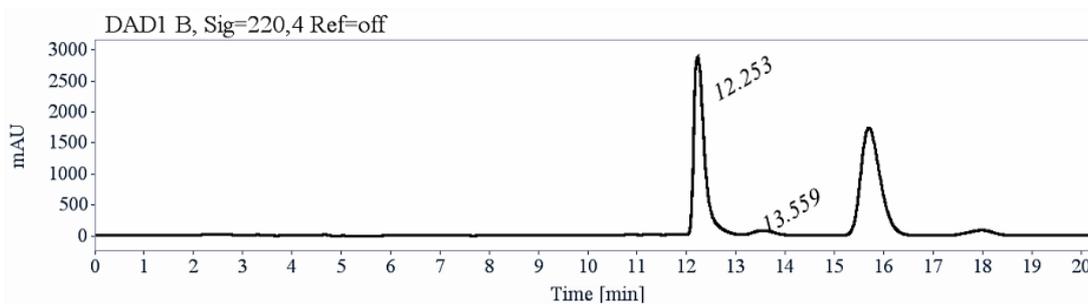
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
9.66	1579	4.41	2.27		
10.58	34185	95.59	2.59	1.14	2.20
Totals	35764	100.00			



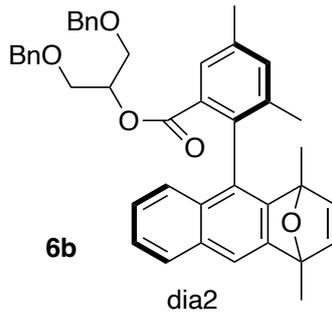
Chiralpak IE, heptane/ethanol = 95:5, 1 mL/min



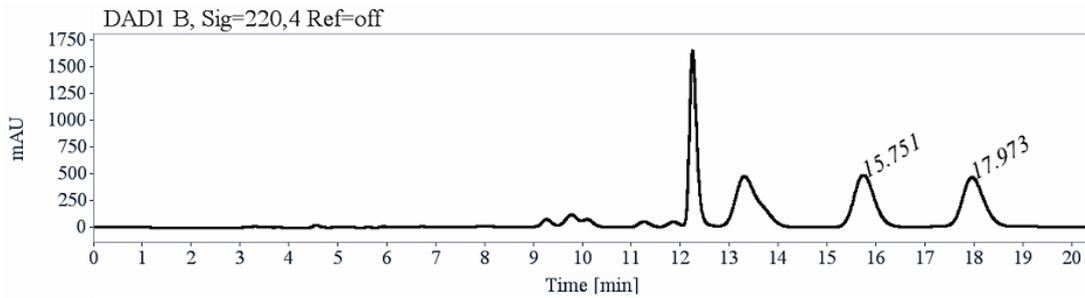
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
12.27	16929	52.25	3.16		
13.33	15471	47.75	3.52	1.11	1.95
Totals	32400	100.00			



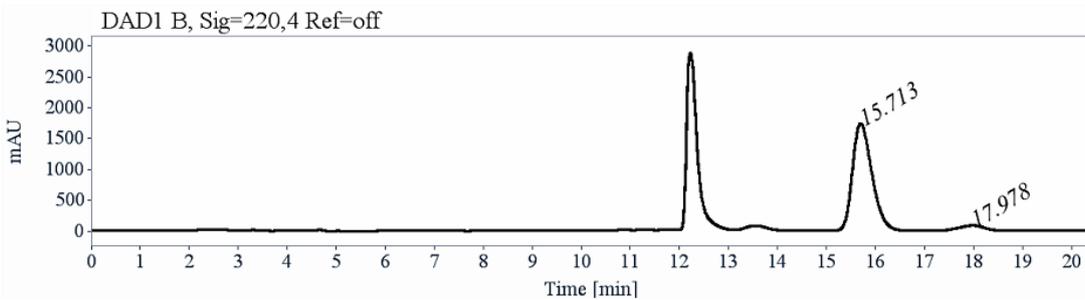
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
12.25	43475	95.23	3.15		
13.56	2178	4.77	3.60	1.14	2.35
Totals	45653	100.00			



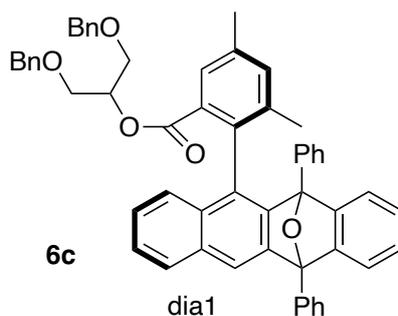
Chiralpak IE, heptane/ethanol = 95:5, 1 mL/min



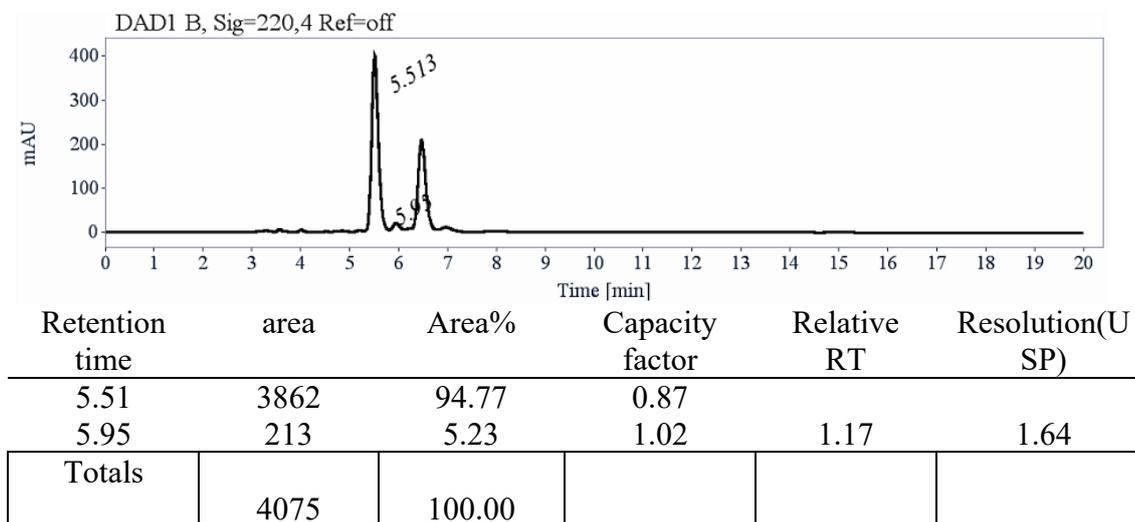
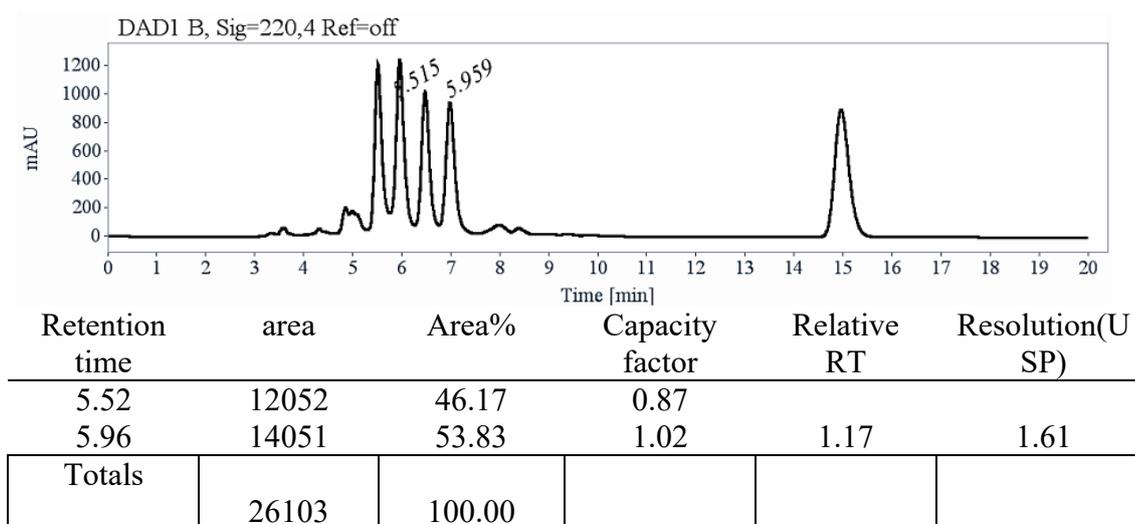
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
15.75	14265	50.12	4.34		
17.97	14198	49.88	5.09	1.17	2.82
Totals	28463	100.00			

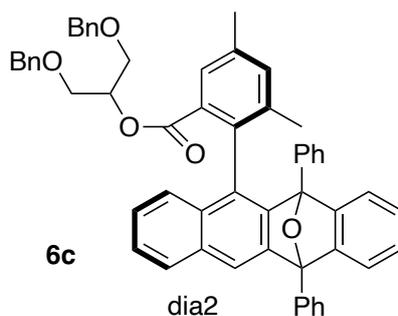


Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
15.71	47662	93.58	4.33		
17.98	3272	6.42	5.09	1.18	2.67
Totals	50934	100.00			

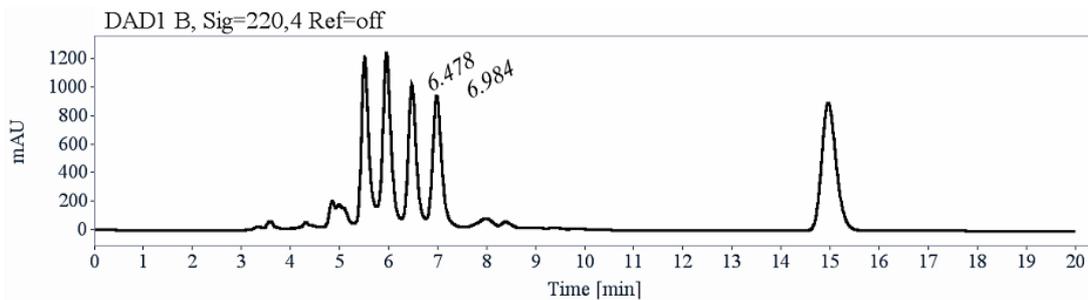


Chiralpak IE, heptane/ethanol = 80:20, 1 mL/min

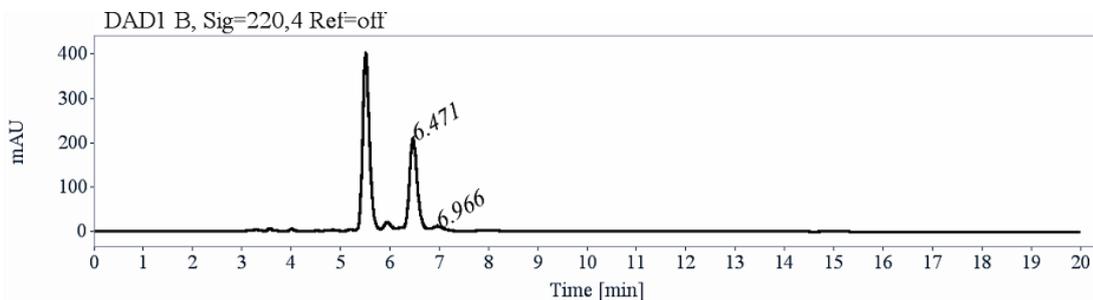




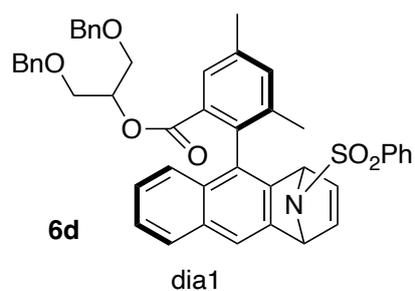
Chiralpak IE, heptane/ethanol = 80:20, 1 mL/min



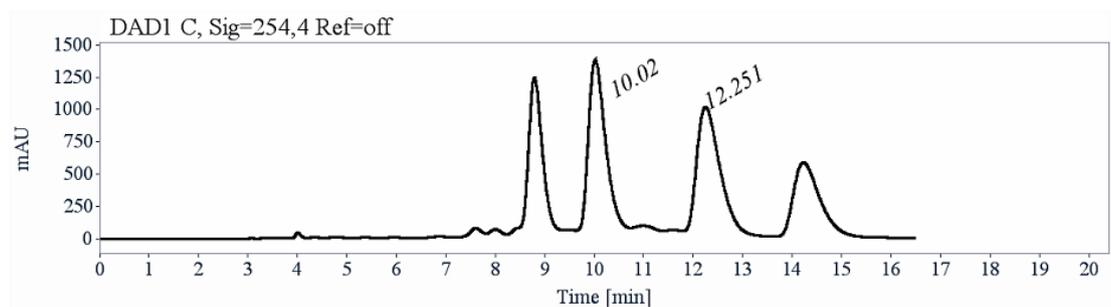
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
6.48	11394	49.33	1.20		
6.98	11705	50.67	1.37	1.14	1.64
Totals	23099	100.00			



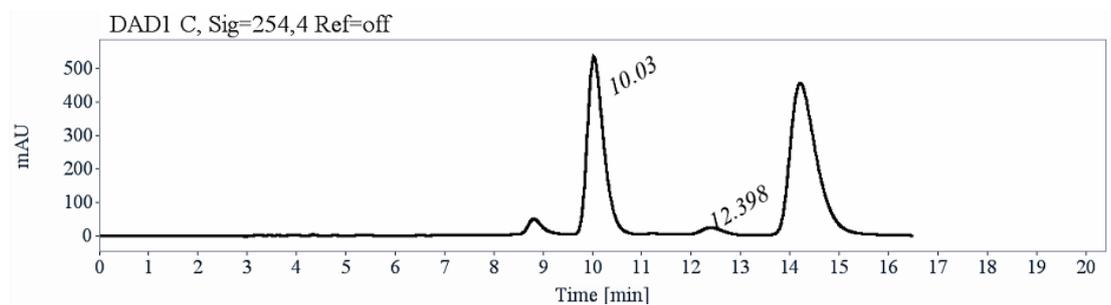
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
6.47	2420	92.61	1.19		
6.97	193	7.39	1.36	1.14	1.33
Totals	2613	100.00			



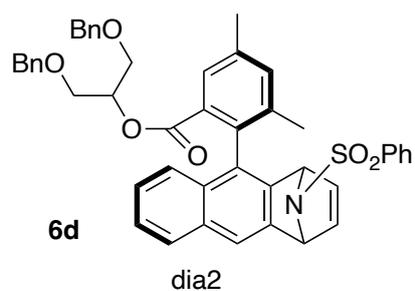
Chiralpak ID, heptane/ethanol = 60:40, 1 mL/min



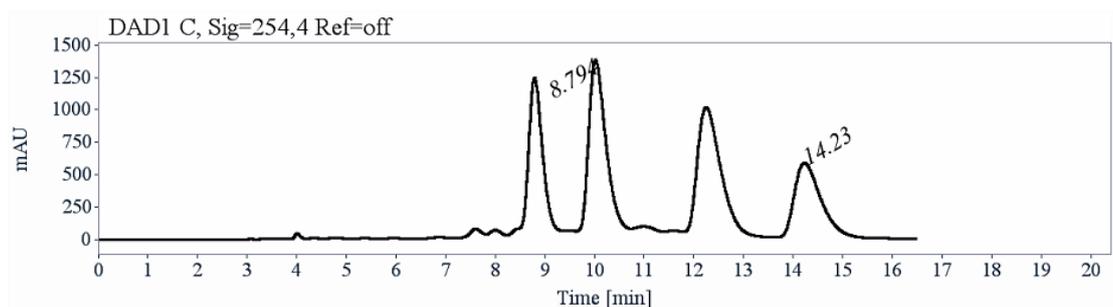
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
10.02	30957	49.78	2.4		
12.25	31230	50.22	3.15	1.32	3.03
Totals	62187	100.00			



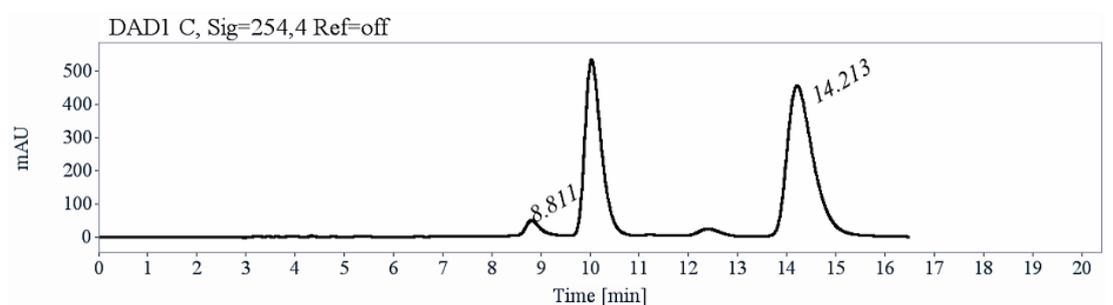
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
10.03	12181	95.07	2.4		
12.40	631	4.93	3.2	1.33	3.38
Totals	12812	100.00			



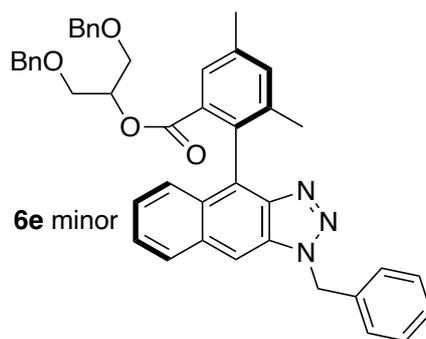
Chiralpak ID, heptane/ethanol = 60:40, 1 mL/min



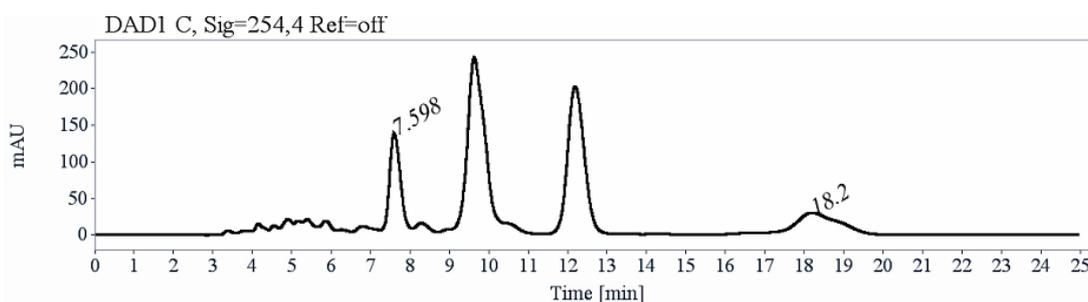
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
8.79	22969	51.71	1.92		
14.23	21445	48.29	3.82	1.93	7.4
Totals	44414	100.00			



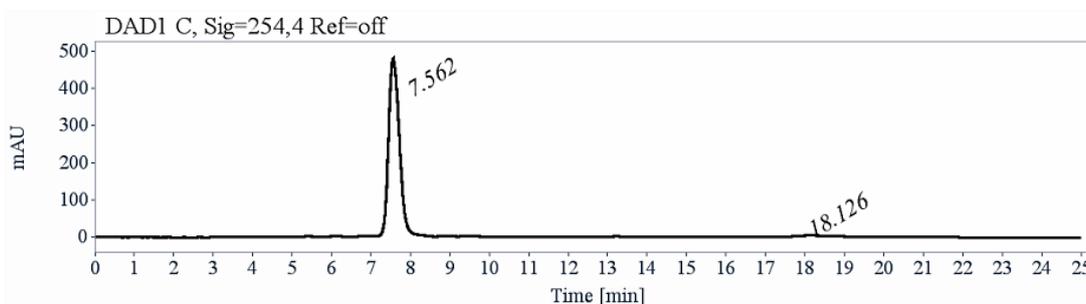
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
8.81	1001	5.69	1.99		
14.21	16592	94.31	3.82	1.92	7.33
Totals	17593	100.00			



Chiralpak IA, heptane/ethanol = 80:20, 1 mL/min

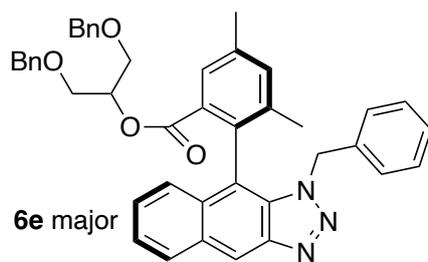


Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
7.60	3789	52.92	1.57		
18.20	3327	47.08	5.71	3.28	8.37
Totals	7161	100.00			

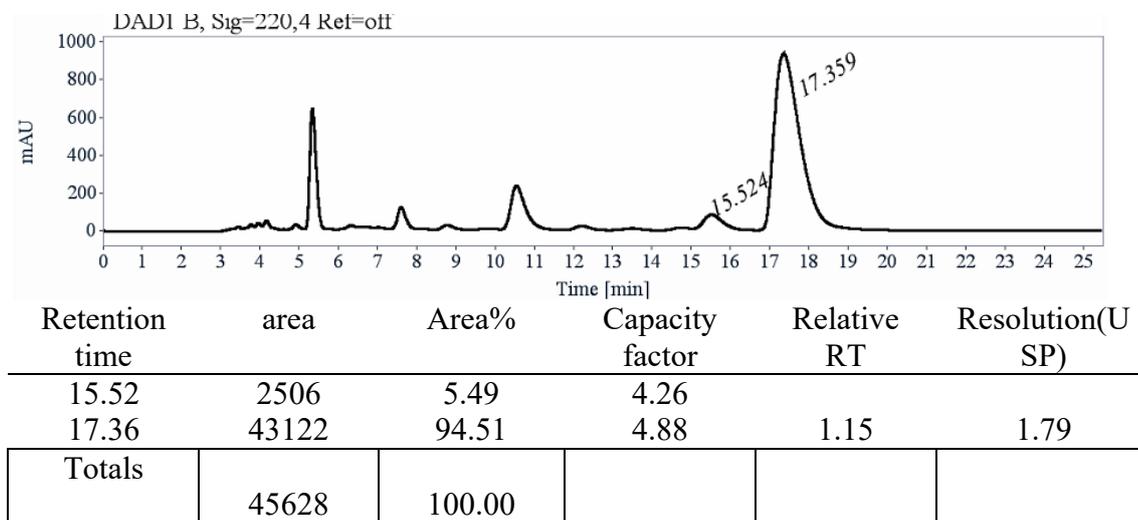
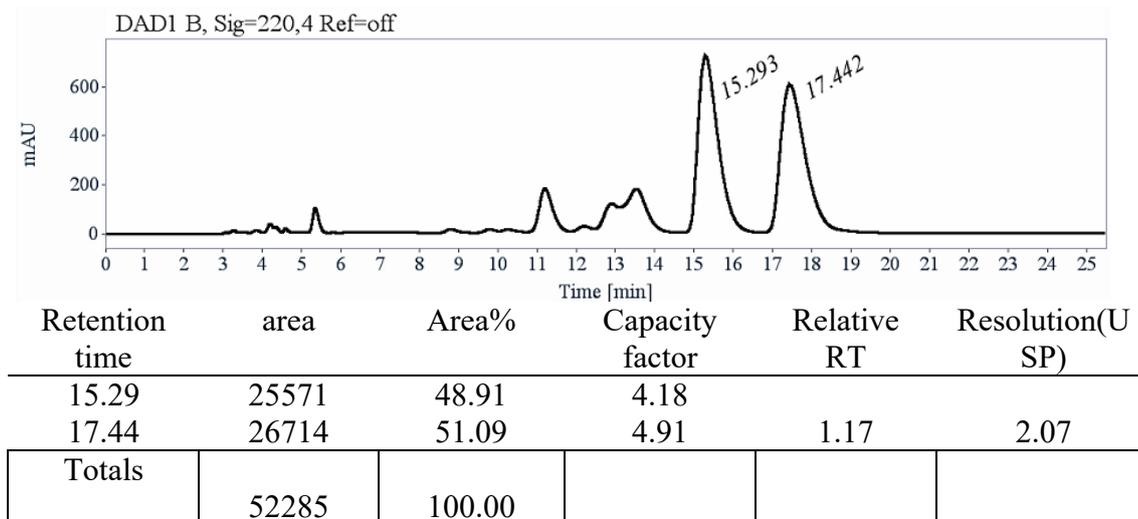


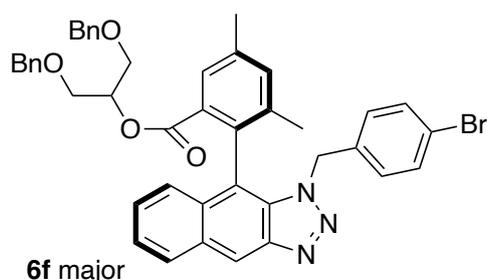
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
7.56	8904	96.44	1.56		
18.13	329	3.56	5.14	3.29	8.70
Totals	9233	100.00			

The experimentally determined ratio of enantiomers accounts for an enantiomeric excess of 93% in this case, which is certainly over-estimated considering the 90% ee recorded for the substrate. The reported ee for **6e minor** has thus been arbitrarily set to 90%. This discrepancy can be attributed to the experimental error inherent to the analytical method (up to 3%).

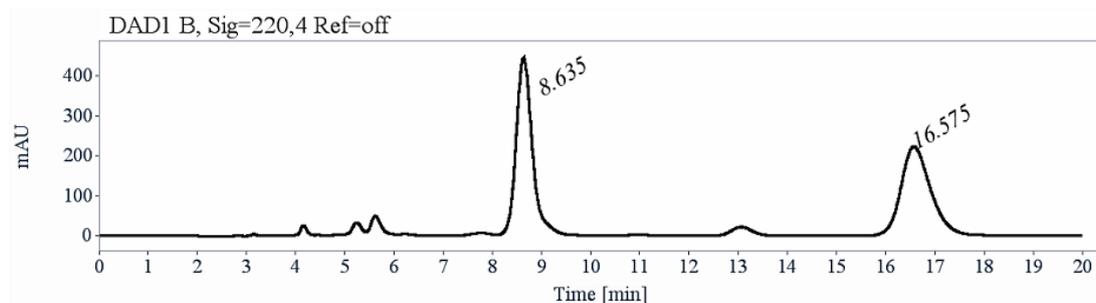


Chiralpak ID, heptane/ethanol = 80:20, 1 mL/min

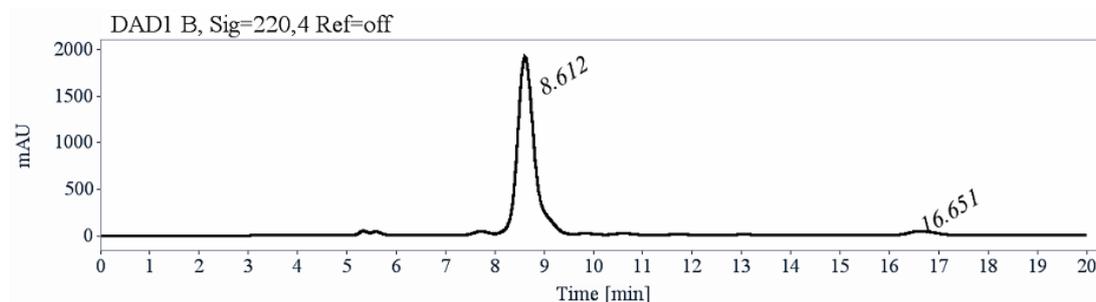




Chiralpak IA, heptane/ethanol = 80:20, 1 mL/min

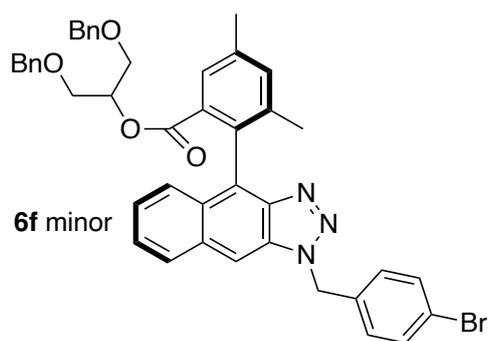


Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
8.64	10144	52.00	1.93		
16.58	9365	48.00	4.62	2.4	9.59
Totals	19509	100.00			

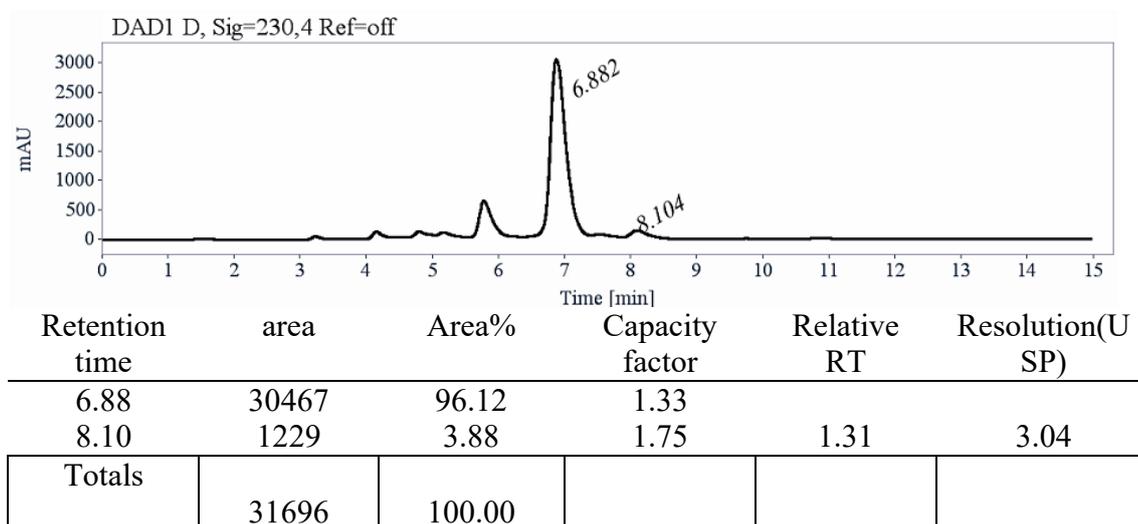
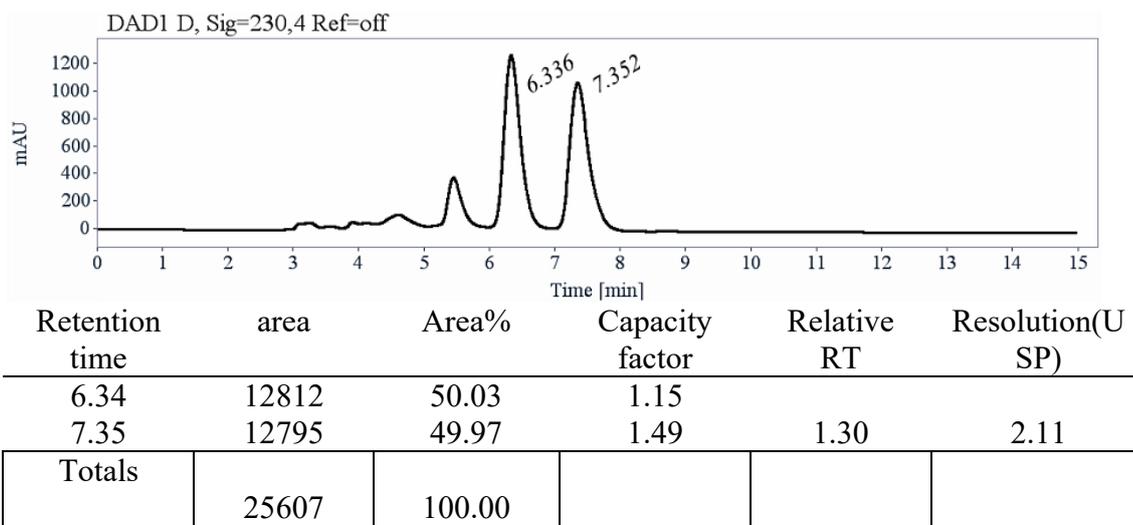


Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
8.61	45264	95.94	1.92		
16.65	1917	4.06	4.64	2.42	9.97
Totals	47181	100.00			

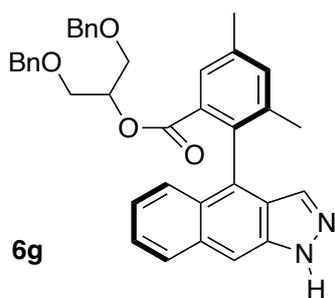
The experimentally determined ratio of enantiomers accounts for an enantiomeric excess of 92% in this case, which is certainly over-estimated considering the 90% ee recorded for the substrate. The reported ee for **6f major** has thus been arbitrarily set to 90%. This discrepancy can be attributed to the experimental error inherent to the analytical method (up to 3%).



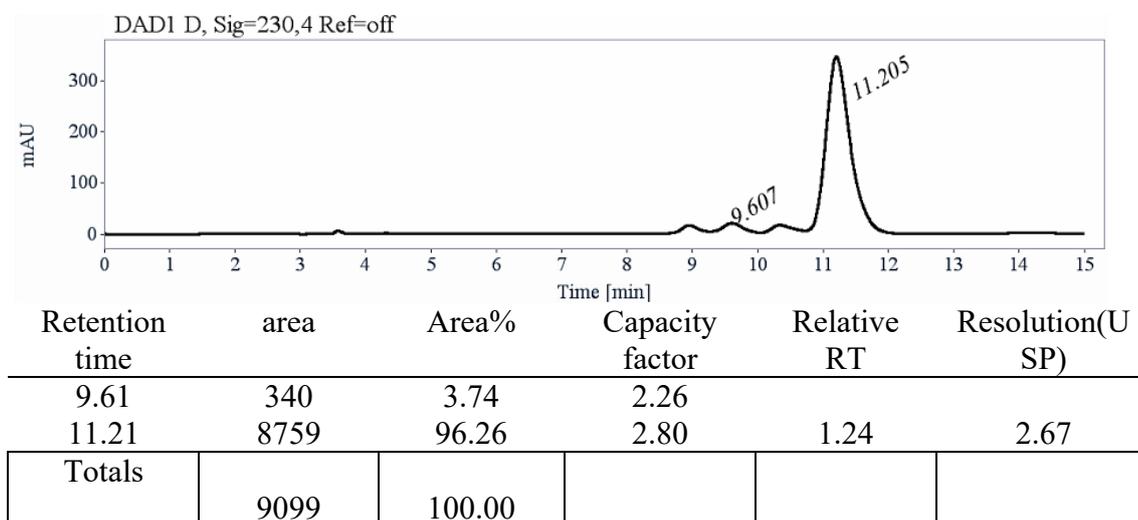
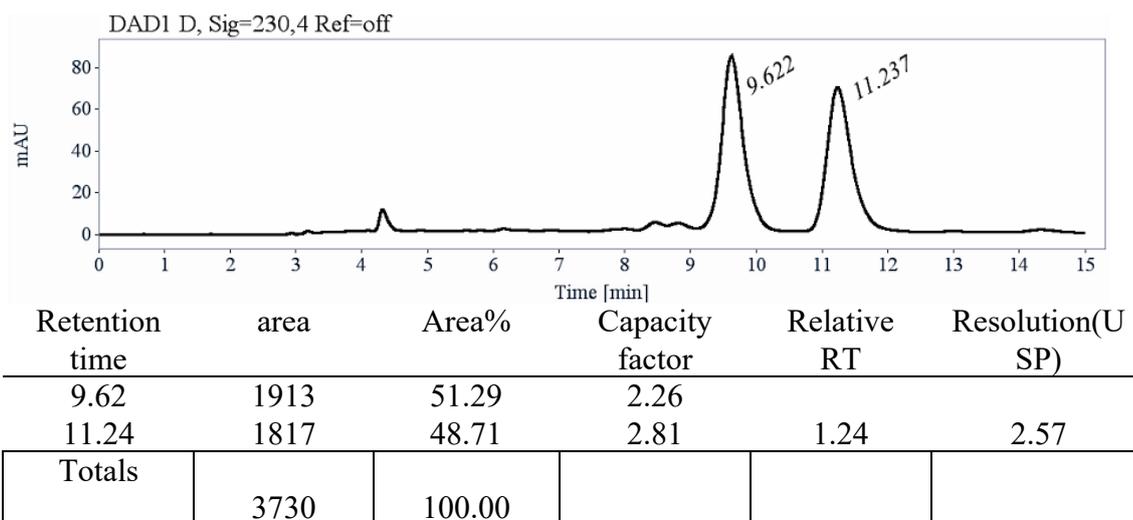
Chiralpak IB, heptane/ethanol = 80:20, 1 mL/min



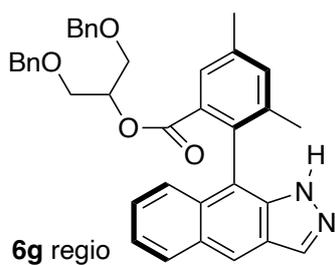
The experimentally determined ratio of enantiomers accounts for an enantiomeric excess of 92% in this case, which is certainly over-estimated considering the 90% ee recorded for the substrate. The reported ee for **6f minor** has thus been arbitrarily set to 90%. This discrepancy can be attributed to the experimental error inherent to the analytical method (up to 3%).



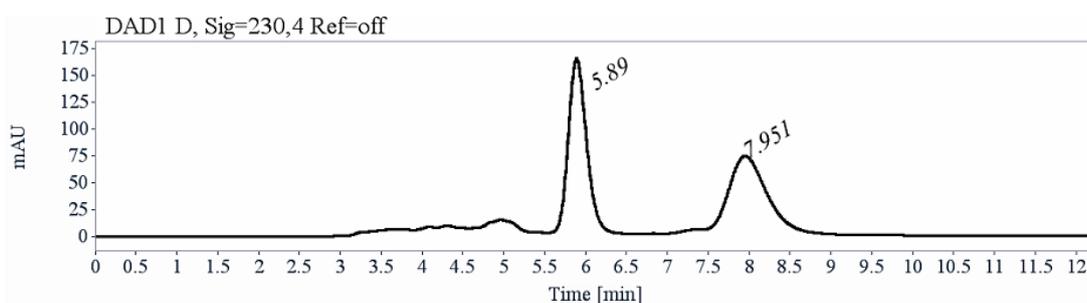
Chiralpak IG, heptane/ethanol = 80:20, 1 mL/min, 220 nm,



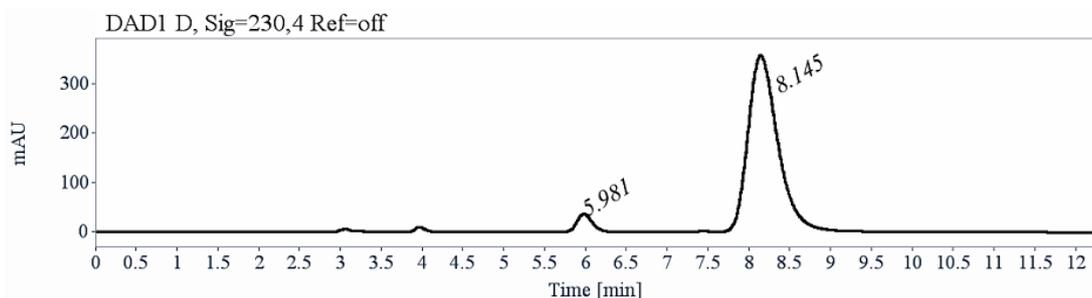
The experimentally determined ratio of enantiomers accounts for an enantiomeric excess of 93% in this case, which is certainly over-estimated considering the 90% ee recorded for the substrate. The reported ee for **6g** has thus been arbitrarily set to 90%. This discrepancy can be attributed to the experimental error inherent to the analytical method (up to 3%).



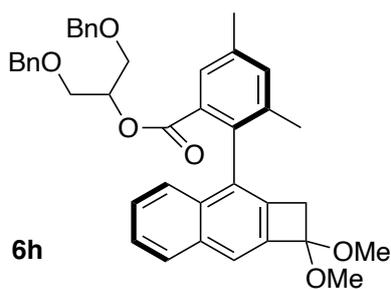
Chiralpak IH, heptane/ethanol = 80:20, 1 mL/min



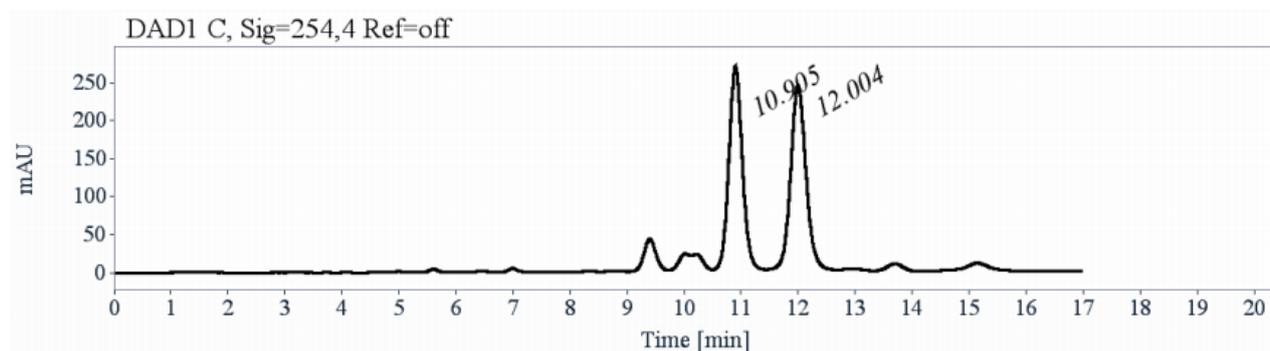
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
5.89	2521	53.3	1.0		
7.95	2209	46.7	1.7	1.7	3.35
Totals	4730	100.00			



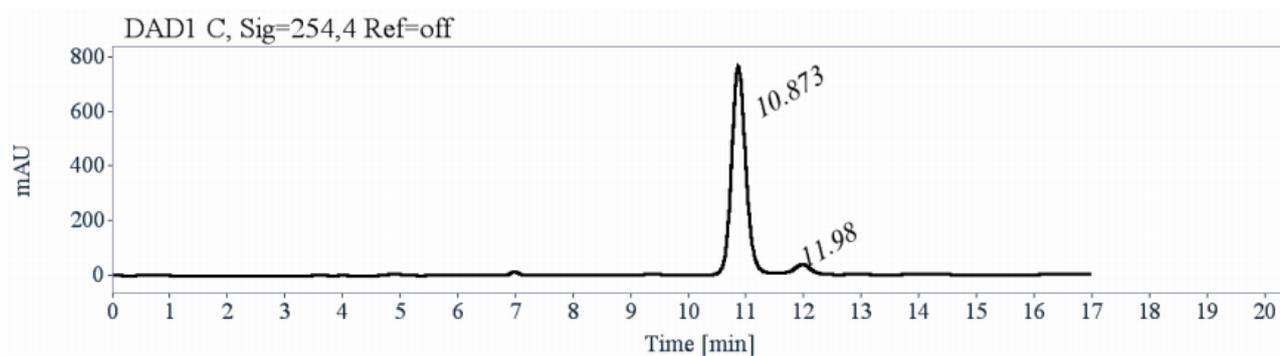
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
5.98	480	5.05	1.03		
8.15	9027	94.95	1.76	1.71	4.37
Totals	9507	100.00			



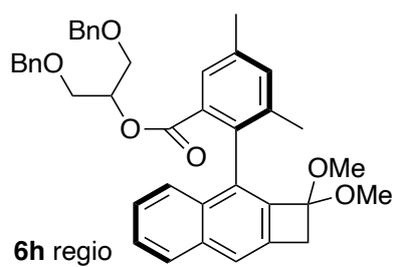
(S,S)-Whelk-O1, heptane/ethanol = 95:5, 1 mL/min



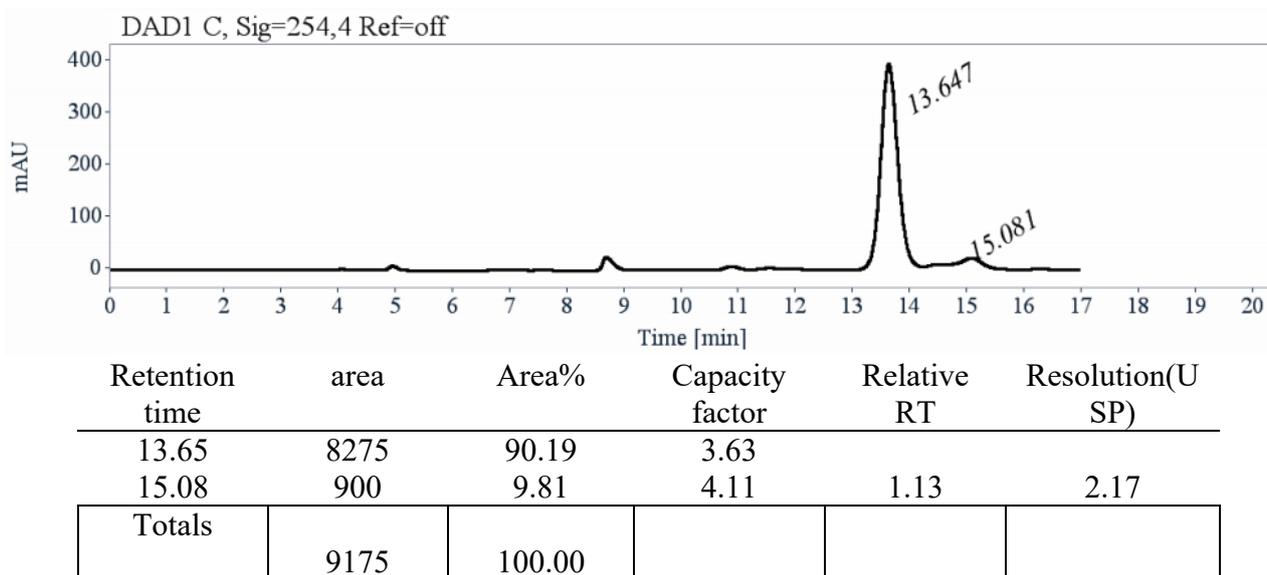
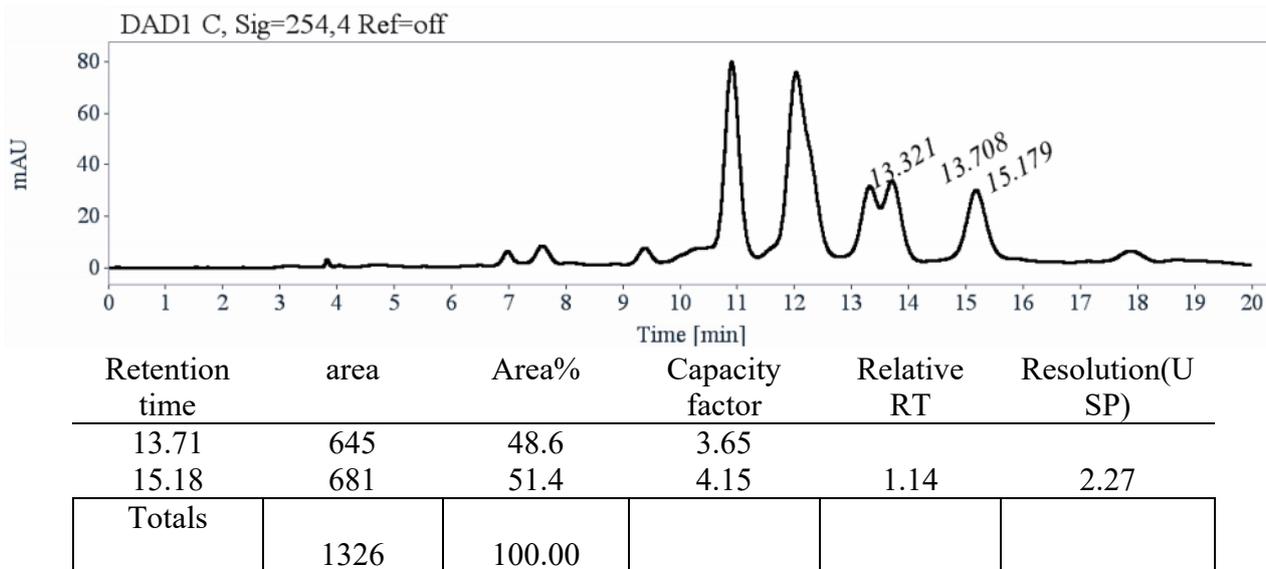
Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
10.90	4371	49.23	2.7		
12.0	4507	50.77	3.07	1.14	2.43
Totals	8878	100.00			

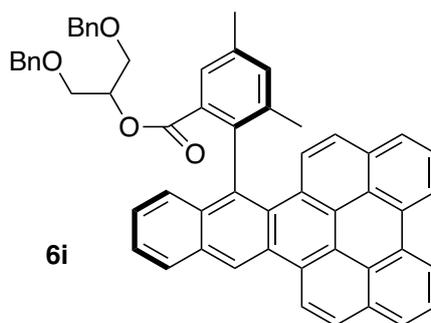


Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
10.87	13056	94.08	2.69		
11.98	822	5.92	3.06	1.14	2.43
Totals	13878	100.00			

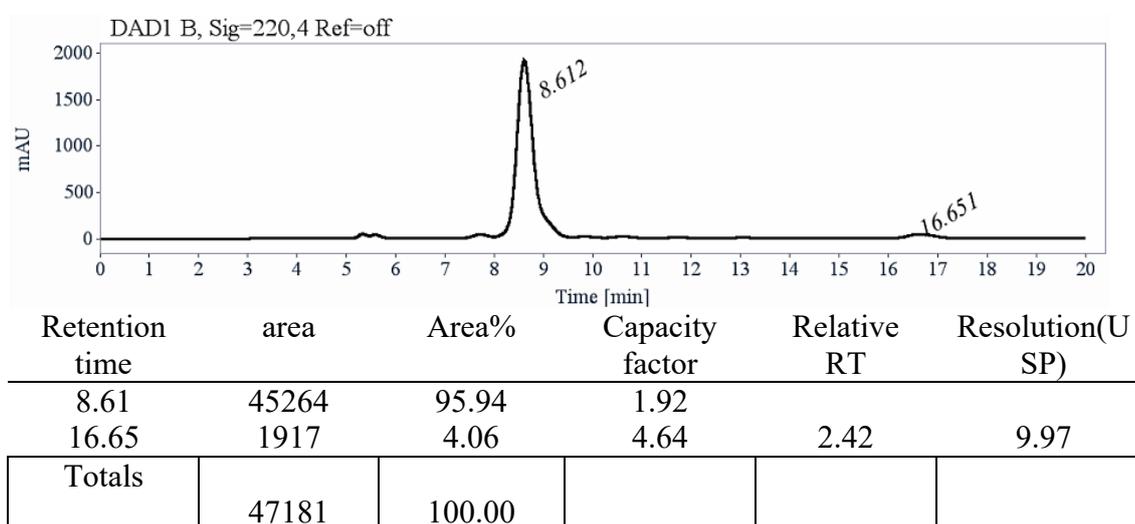
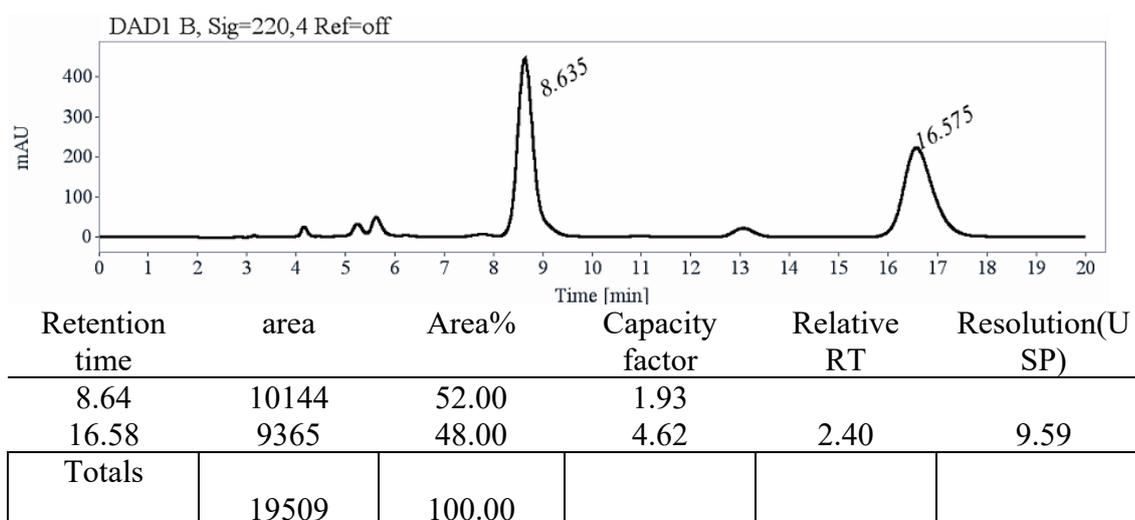


(S,S)-Whelk-O1, heptane/ethanol = 95:5, 1 mL/min

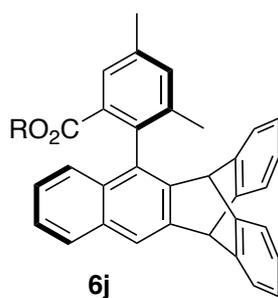




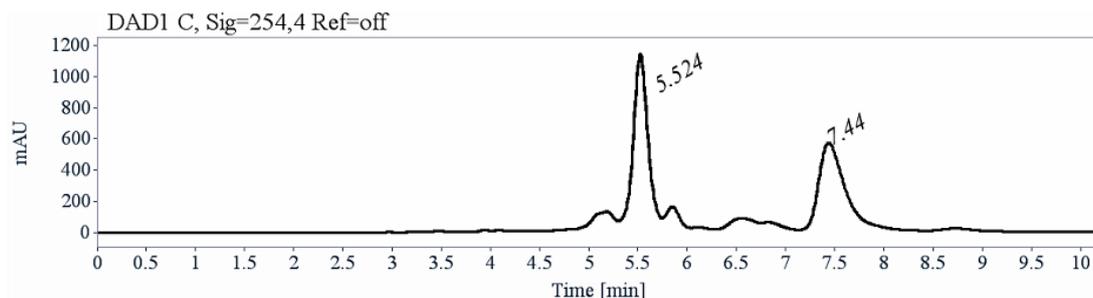
Chiralpak IF, heptane/ethanol = 80:20, 1 mL/min



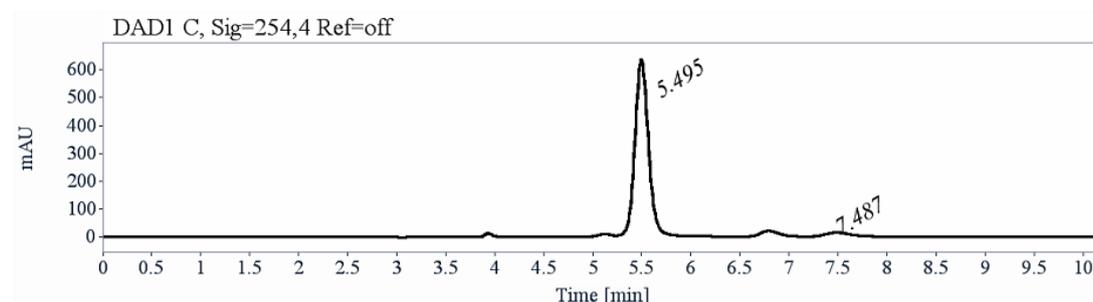
The experimentally determined ratio of enantiomers accounts for an enantiomeric excess of 92% in this case, which is certainly over-estimated considering the 90% ee recorded for the substrate. The reported ee for **6i** has thus been arbitrarily set to 90%. This discrepancy can be attributed to the experimental error inherent to the analytical method (up to 3% ee).



HPLC Chiralpak IF, heptane/ethanol = 80:20, 1 mL/min

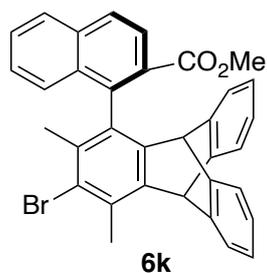


Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
5.52	11691	52.89	0.87		
7.44	10415	47.11	1.52	1.74	5.26
Totals	22106	100.00			

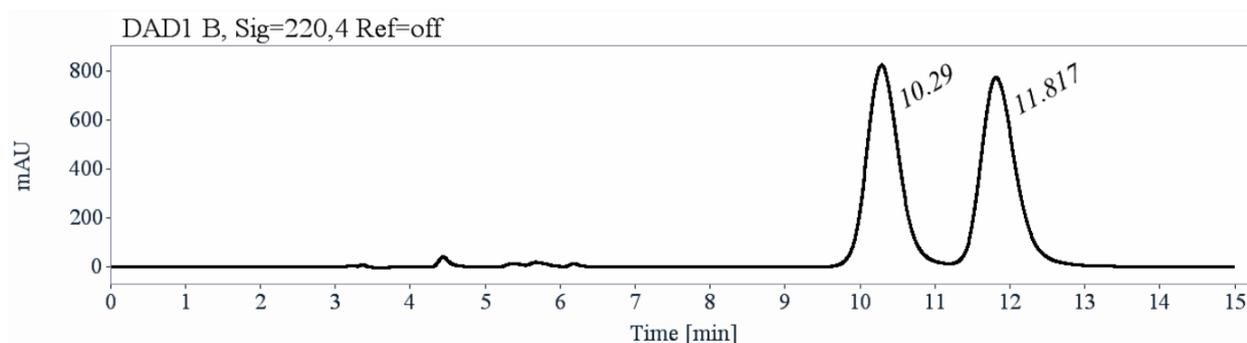


Retention time	area	Area%	Capacity factor	Relative RT	Resolution(U SP)
5.50	6111	95.63	0.86		
7.49	279	4.37	1.54	1.78	5.53
Totals	6390	100.00			

The experimentally determined ratio of enantiomers accounts for an enantiomeric excess of 91% in this case, which is certainly over-estimated considering the 90% ee recorded for the substrate. The reported ee for **6j** has thus been arbitrarily set to 90%. This discrepancy can be attributed to the experimental error inherent to the analytical method (up to 3% ee).

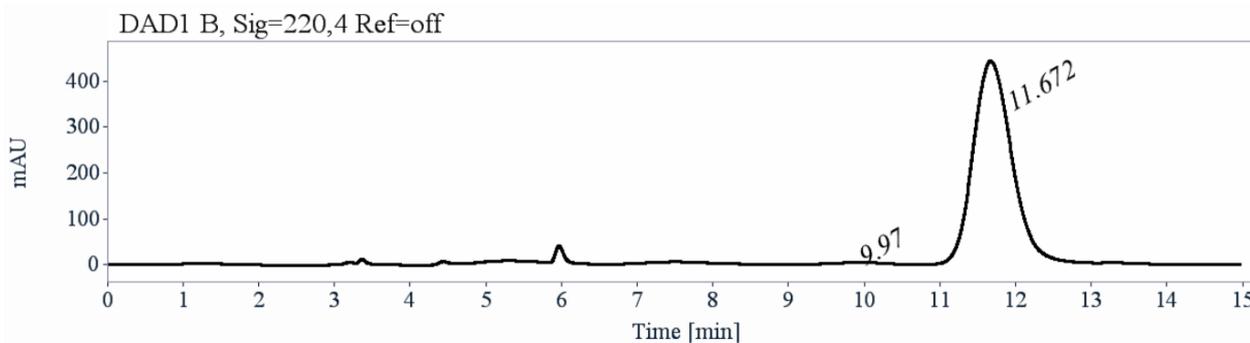


(S,S)-Whelk-O1, heptane/isopropanol = 95:5, 1 mL/min



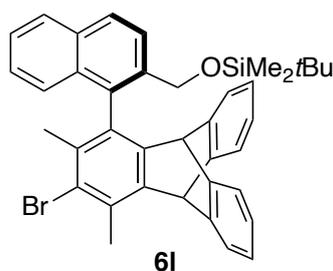
Signal: DAD1 B, Sig=220,4 Ref=off

RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
10.29	25127	49.87	2.49		
11.82	25262	50.13	3.01	1.21	1.88
Sum	50388	100.00			

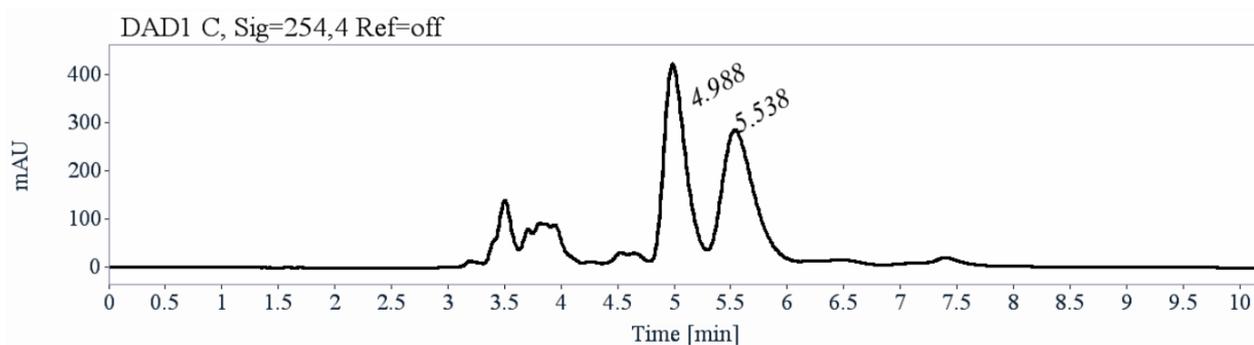


Signal: DAD1 B, Sig=220,4 Ref=off

RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
9.97	179	1.13	2.38		
11.67	15670	98.87	2.96	1.24	1.65
Sum	15849	100.00			

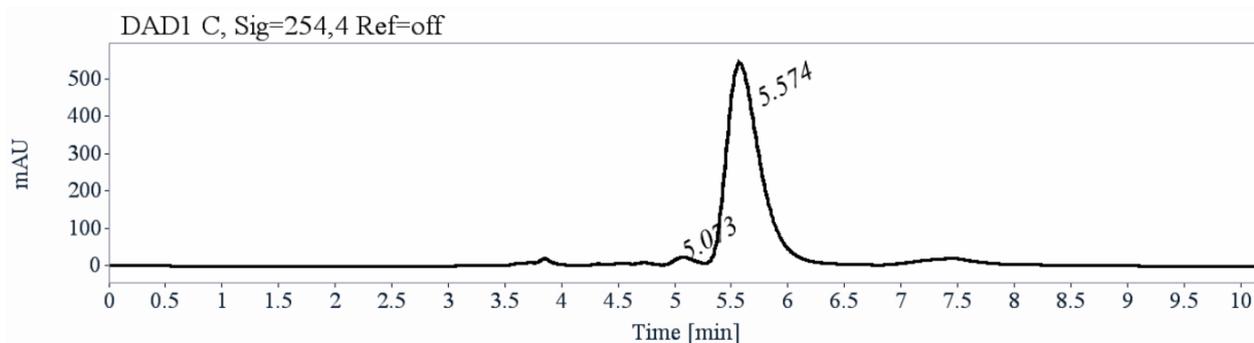


Lux-Cellulose-2, heptane/isopropanol = 99.5:0.5, 1 mL/min



Signal: DAD1 C, Sig=254,4 Ref=off

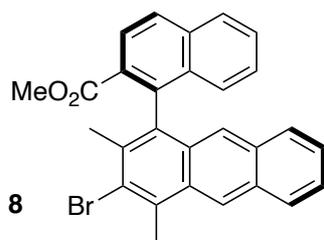
RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
4.99	5340	50.25	0.69		
5.54	5287	49.75	0.88	1.27	1.28
Sum	10626	100.00			



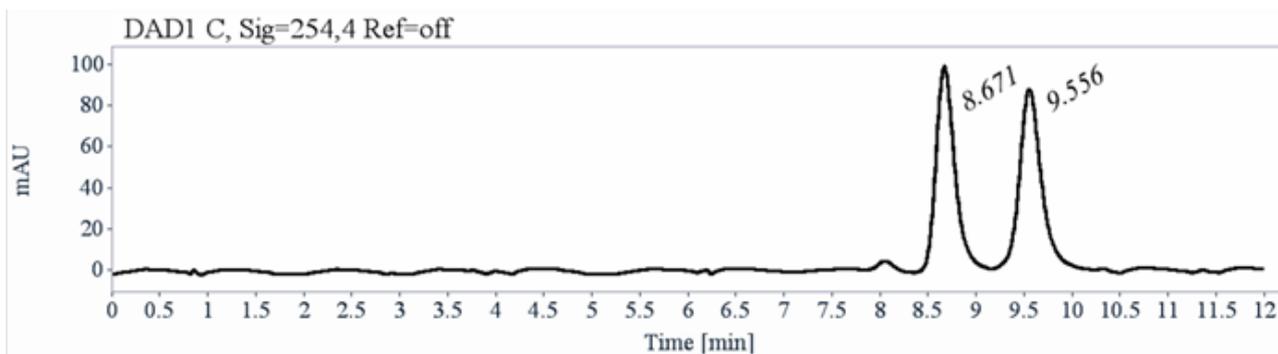
Signal: DAD1 C, Sig=254,4 Ref=off

RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
5.07	247	2.18	0.72		
5.57	11046	97.82	0.89	1.24	1.17
Sum	11292	100.00			

The experimentally determined ratio of enantiomers accounts for an enantiomeric excess of 95.6% in this case, which is certainly over-estimated considering the 93.7% ee recorded for the substrate. The reported ee for **6I** has thus been arbitrarily set to 94%. This discrepancy can be attributed to the experimental error inherent to the analytical method (up to 3% ee).

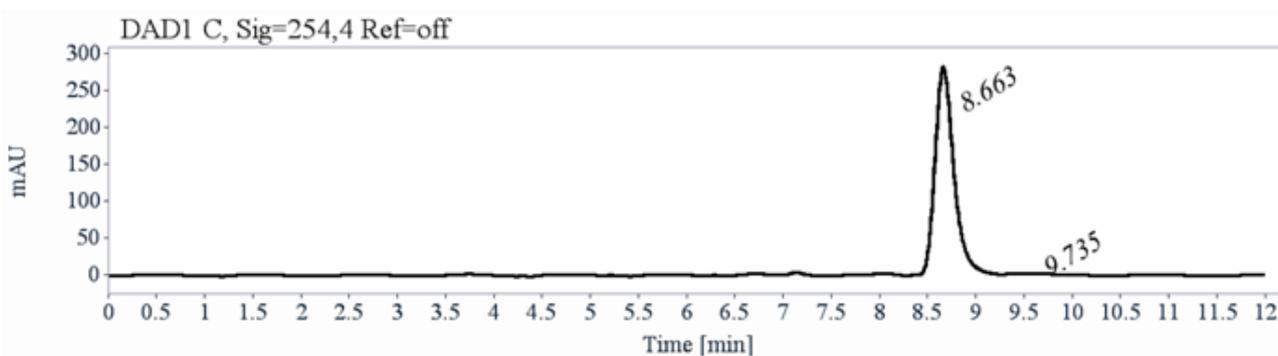


(S,S)-Whehk-O1, heptane/ethanol = 95:5, 1 mL/min



DAD1 C, Sig=254,4 Ref=off

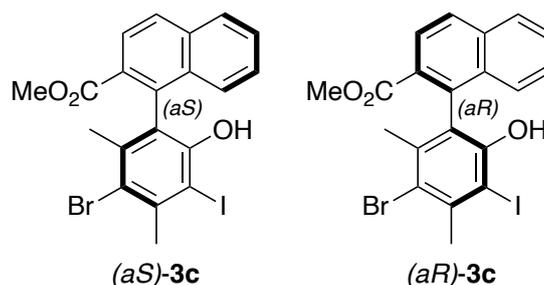
RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
8.67	1385	49.50	1.94		
9.56	1413	50.50	2.24	1.15	2.36
Sum	2799	100.00			



DAD1 C, Sig=254,4 Ref=off

RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
8.66	3852	98.36	1.94		
9.73	64	1.64	2.30	1.19	1.56
Sum	3917	100.00			

VCD and ECD spectroscopic analyses of **3c**



VCD spectra measurements

Infrared (IR) and vibrational circular dichroism (VCD) spectra were recorded on a Bruker PMA 50 accessory coupled to a Vertex70 Fourier transform infrared spectrometer. A photoelastic modulator (Hinds PEM 90) set at $1/4$ retardation was used to modulate the handedness of the circular polarized light at 50 kHz. Demodulation was performed by a lock-in amplifier (SR830 DSP). An optical low-pass filter ($< 1800 \text{ cm}^{-1}$) before the photoelastic modulator was used to enhance the signal/noise ratio. A transmission cell equipped with CaF_2 windows and of 200 μm of optical pathlength was used. Solutions with a concentration of 0.1 mol L^{-1} were prepared by dissolving the solid samples in CD_2Cl_2 . The VCD spectra of the pure enantiomers (1st eluted)-**1** and (2nd eluted)-**1** were measured at room temperature and the baseline of the spectra were corrected using the standard procedure of the half-subtraction of the spectra of each enantiomer. For each individual spectrum, about 16000 scans were averaged at 4 cm^{-1} resolution (corresponding to 4 hours measurement time). For IR absorption spectra, the cell filled with CD_2Cl_2 served as a reference. The spectra are presented without smoothing and further data processing.

ECD spectra measurements

UV-vis and electronic circular dichroism (ECD) spectra were measured on a JASCO J-815 spectrometer equipped with a JASCO Peltier cell holder PTC-423 to maintain the temperature at $20.0 \text{ }^\circ\text{C}$. A quartz photoelastic modulator set at $1/4$ retardation was used to modulate the handedness of the circular polarized light at 50 kHz. A quartz cell of 1 mm of optical path length was used. Solutions with a concentration of $2 \cdot 10^{-4} \text{ mol} \cdot \text{L}^{-1}$ were prepared in acetonitrile (HPLC grade). The CD spectrometer was purged with nitrogen during the recording of spectra. The UV absorption and ECD spectra were recorded using acetonitrile as a reference and are presented without smoothing and further data processing.

Computational work

The calculations were done using the absolute configuration (aS) of molecule **3c** (Figure S10). We performed a systematic search of the conformations of the molecule, by rotation around the $\text{C}_{\text{sp}^2}^{\text{ar}}-\text{C}_{\text{sp}^2}$ bonds of the ester function and $\text{C}_{\text{sp}^2}^{\text{ar}}-\text{O}$ bonds of the alcohol function. We found 5 conformations, 4 of them having a calculated Boltzmann population greater than 10% in dichloromethane and in acetonitrile (Table 1 and 2, figure 2). To establish this result, we used the Density Functional Theory (DFT), with the B3LYP functional with basis function 6-311+G(d,p) for H, C, O and Br atoms, and MWB46 with the associated pseudo potential for the I atom. Solvent effects were taken into account by using the implicit SMD solvation model. It is a polarizable dielectric continuum type model. Dichloromethane and acetonitrile were chosen in analogy with the experiments. All geometries found were characterized by a frequency calculation which confirmed that they were all local minima (no imaginary frequency).

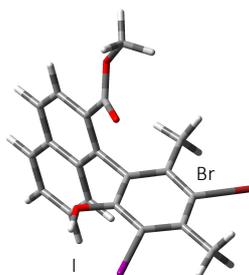


Figure S10. A geometry of (aS)-**3c** obtained by DFT methods

The vibrational frequencies, IR absorption and VCD intensities were calculated using the same theoretical level as for geometries optimization: SMD(CD₂Cl₂)/B3LYP/6-311+G(d,p)-MWB46. For the calculation of IR/VCD spectra, computed harmonic frequencies are generally larger than those experimentally observed. Thus, a scaling factor of 0.98 has been applied homogenously to all calculated frequencies in order to calibrate the spectra. IR absorption and VCD spectra were constructed from calculated dipole and rotational strengths assuming Lorentzian band shape with a half-width of 8 cm⁻¹.

Based on the SMD(CH₃CN)/B3LYP/6-311+G(d,p)-MWB46 optimized geometries, the ECD and UV spectra were calculated using time dependent density functional theory (TD-DFT) with CAM-B3LYP functional and 6-31++G(d,p) basis set. Calculations were performed for vertical 1A singlet excitation using 50 states. For a comparison between theoretical results and the experimental values, the calculated UV and ECD spectra have been modeled with a Gaussian function, using a half-width of 0.37 eV. Due to the approximations of the theoretical model used, an offset almost constant was observed between measured and calculated frequencies. Using UV spectra, all calculated frequencies were calibrated by a factor of 1.02.

Boltzmann populations calculated from enthalpies obtained at SMD(CD₂Cl₂)/B3LYP/6-311+G(d,p)-MWB46 and SMD(CH₃CN)/B3LYP/6-311+G(d,p)-MWB46 levels, are given in respectively Tables S4 and S5.

Table S4. Enthalpies and Boltzmann populations of conformations A₁-A₅ calculated using SMD(CD₂Cl₂)/B3LYP/6-311+G(d,p)-MWB46 level

Conformations	H ^{298K} (in a.u)	ΔH ^{298K} (in kcal.mol ⁻¹)	Distribution of Boltzmann
A ₁	-3582,973771	0,000	0,34
A ₂	-3582,973524	0,155	0,26
A ₃	-3582,973309	0,290	0,21
A ₄	-3582,973175	0,374	0,18
A ₅	-3582,962245	7,233	0,00

Table S5. Enthalpies and Boltzmann populations of conformations B₁-B₅ calculated using SMD(CH₃CN)/B3LYP/6-311+G(d,p)-MWB46 level

Conformations	H ^{298K} (in a.u)	ΔH ^{298K} (in kcal.mol ⁻¹)	Distribution of Boltzmann
B ₁	-3582,972191	0,000	0,34
B ₂	-3582,971874	0,199	0,24
B ₃	-3582,971797	0,247	0,22
B ₄	-3582,971639	0,346	0,19
B ₅	-3582,961807	6,516	0,00

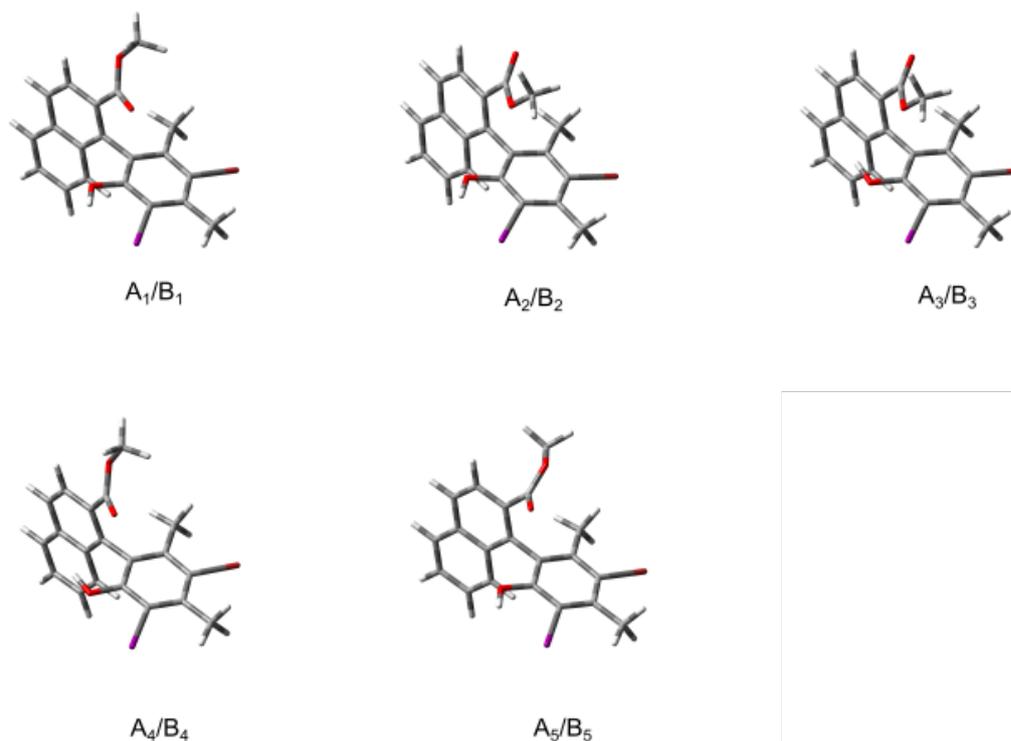


Figure S11. Geometries of calculated conformations of (aS)-**3c** using SMD(CD₂Cl₂)/B3LYP/6-311+G(d,p)-MWB46 and SMD(CH₃CN)/B3LYP/6-311+G(d,p)-MWB46 levels.

Figures S1 on page S15 shows the IR and VCD spectra measured for the two enantiomers (1st eluted)-**3c** and (2nd eluted)-**3c** and calculated for (aS)-**3c**. It can be observed that the IR and VCD spectra calculated for (aS)-**3c** gives the best correlation (signs and intensities of bands) with the spectra measured for the (1st eluted)-**3c** enantiomer.

Figures S2 on page S16 shows the UV and ECD spectra measured for the two enantiomers (1st eluted)-**3c** and (2nd eluted)-**3c** and calculated for (aS)-**3c**. As in IR/VCD, it can be observed, that the UV and ECD spectra calculated for the enantiomer (aS)-**3c** gives the best correlation (signs and intensities of bands) with the spectra measured for the (1st eluted)-**3c** enantiomer.

Altogether, the calculated spectra reproduce well both the high and low-energy bands of the experimental CD spectra allowing the determination of the absolute configuration of (1st eluted)-**3c** as (aS)-**3c** with the greatest confidence.