

Asymmetric Kita spirolactonisation catalysed by *anti*-dimethanoanthracene-based iodoarenes

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Supporting Information

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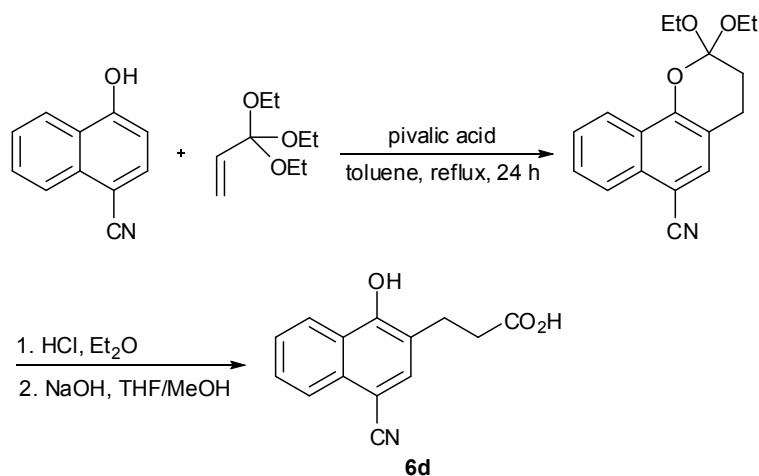
General remarks

NMR spectra were recorded on Varian Inova 300 MHz, Varian Inova 400 MHz and Varian 500 MHz FT spectrometers at 30 °C with CDCl₃, MeOD or DMSO-d₆ as the solvent. Chemical shifts are reported in ppm relative to the residual solvent signal. High resolution mass spectra were measured on a Waters/Micromass GCT and Waters 2996 Photodiode Array Detector instrument. Infrared spectra were recorded on a Varian 3100 FT-IR spectrometer at room temperature. Melting points were recorded in open capillaries on a digital Barnsted Electro Thermal 9300 melting point apparatus and are uncorrected.

Materials

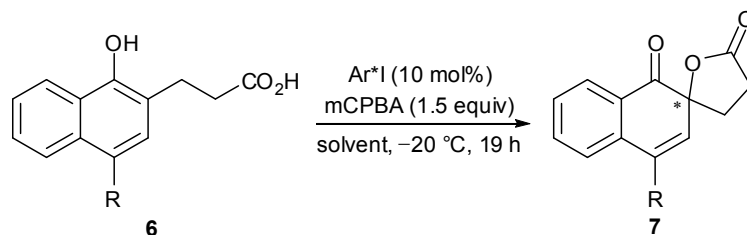
All reagents were obtained from commercial suppliers and used without further purification. All dry solvents were obtained from a dry solvent purification system. Thin Layer Chromatography was performed on Merck Aluminium sheets (silica gel 60 F₂₅₄). Detection was carried out by UV and by colouration with ceric ammonium molybdate (CAM). Flash column chromatography was performed using Merck silica gel 60 (230-400 mesh). 1-Naphthols **6a-c** and **6e**,¹ and aldehyde (+)-**3**² were synthesised according to literature procedures. Iodoarenes **5** were considered light sensitive and were shielded from light by covering with aluminium foil.

3-(4-Cyano-1-hydroxynaphthalen-2-yl)propanoic acid 6d



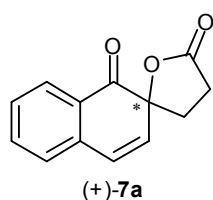
To a solution of 4-cyano-1-naphthol (5.08 g, 30 mmol) and triethylorthoacrylate (6.0 mL, 48 mmol) in toluene (100 mL) was added pivalic acid (1.53 g, 15 mmol). The mixture was left to reflux for 24 h. After cooling, the reaction mixture was poured into 1N NaOH (30 mL), extracted with Et₂O (2 x 30 mL) and washed with brine. The combined organic layers were dried over anhydrous Na₂SO₄ and removed *in vacuo*. The residue was used directly in the next step without further purification. To a solution of this residue (30 mmol) in Et₂O (80 mL) was added 2N HCl (40 mL) and the resulting red solution was left to stir for 12 h. The mixture was extracted with EtOAc (2 x 30 mL) and washed with brine. The combined organic layers were dried over anhydrous MgSO₄ and concentrated *in vacuo*. This material was then dissolved in THF (30 mL) and MeOH (30 mL). After the addition of 2N NaOH (40 mL) the mixture was vigorously stirred at room temperature for 12 h. The reaction mixture was poured into 1N HCl (100 mL), extracted with EtOAc (2 x 30 mL) and washed with brine. The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated *in vacuo*. The oily residue was purified by flash column chromatography (SiO₂; pentane/EtOAc/AcOH, 79.5:19.5:1) to yield the title compound as a white powder (4.41 g, 61% overall yield). Mp: 182-185 °C; IR (KBr, cm⁻¹): 3370 (s), 3208 (s), 2242 (m), 1692 (s), 1595 (w), 1378 (w), 1241 (m), 870 (m); ¹H NMR (400 MHz, DMSO-d₆): δ 2.59 (t, *J* = 7.5 Hz, 2 H, CH₂), 3.02 (t, *J* = 7.5 Hz, 2 H, CH₂), 7.63 (t, *J* = 7.5 Hz, 1 H, ArH), 7.71 (t, *J* = 7.2 Hz, 1 H, ArH), 7.95 (s, 1 H, ArH) 7.98 (d, *J* = 8.2 Hz, 1 H, ArH), 8.37 (d, *J* = 8.2 Hz, 1 H, ArH), 10.51 (brs, 1 H, OH), 12.17 (brs, 1 H, OH); ¹³C NMR (100 MHz, DMSO-d₆): δ 25.3, 34.1, 99.4, 118.8, 122.2, 123.4, 124.5, 125.1, 126.8, 128.8, 132.7, 136.7, 155.4, 174.4; HRMS (ESI): C₁₄H₁₂NO₃ [M + H]⁺ calculated: 242.0817, found: 242.0815.

General procedure for the catalytic asymmetric spirolactonisation of 1-naphthols



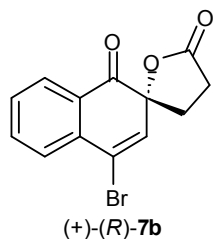
*m*CPBA (184 mg, 0.75 mmol, 70% purity) was added to a stirred solution of Ar*I **5** (0.05 mmol) and the appropriate 1-naphthol **6** (0.50 mmol) in the appropriate solvent (4 mL) at -20 °C. The mixture was allowed to stir at this temperature for 19 h at which point sat. aq NaHCO₃ (5 mL) was added to quench the reaction. The aqueous layer was extracted with CH₂Cl₂ (3 x 5 mL) and the combined organic layers were washed with brine (5 mL), dried over MgSO₄ and concentrated *in vacuo* to yield the crude product. This material was purified by flash column chromatography (SiO₂; pentane/EtOAc, 100:0→80:20) to give the pure spirolactone **7**.

(+)-1'*H*,3*H*-spiro[furan-2,2'-naphthalene]-1',5(4*H*)-dione (+)-**7a**



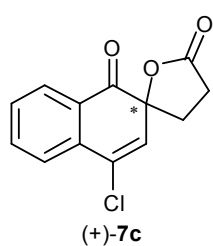
According to the GP using 1-naphthol **6a** in CHCl₃ at 0 °C, the title compound was obtained as a white powder (38 mg, 36%). Enantiomeric excess was determined by chiral HPLC analysis (Chiralpack IB, *n*-heptane/EtOH, 98:2, 1.0 mL/min, 254 nm); *t*_r = 23.1 min (major); *t*_r = 24.8 (minor): 40% ee; [α]_D²⁰ = +36.7 (*c* = 0.5, CHCl₃). All analytical data are consistent with those reported in the literature.¹

(+)-(R)-4'-Bromo-1'*H*,3*H*-spiro[furan-2,2'-naphthalene]-1',5(4*H*)-dione (+)-(R)-**7b**



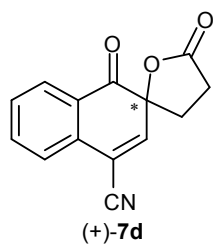
According to the GP using 1-naphthol **6b** in CHCl₃/MeNO₂ (2:1) at -20 °C, the title compound was obtained as a white powder (92 mg, 63%). Enantiomeric excess was determined by chiral HPLC analysis (Chiralpack IB, *n*-heptane/EtOH, 95:5, 1.0 mL/min, 254 nm); (*R*)-enantiomer, *t*_r = 22.6 min (major); (*S*)-enantiomer, *t*_r = 23.9 (minor): 67% ee; [α]_D²⁰ = +42.9 (*c* = 0.5, CHCl₃). All analytical data are consistent with those reported in the literature.¹

(+)-4'-Chloro-1'*H*,3*H*-spiro(furan-2,2'-naphthalene)-1',5(4*H*)-dione (+)-7c



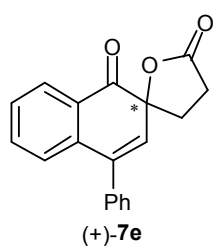
According to the GP using 1-naphthol **6c** in CHCl_3 at $-20\text{ }^\circ\text{C}$, the title compound was obtained as a white powder (70 mg, 57%). Enantiomeric excess was determined by chiral HPLC analysis (Chiralpack AS-H, *n*-heptane/EtOH, 85:15, 1.0 mL/min, 254 nm); $t_r = 16.9$ min (minor); $t_r = 23.7$ (major): 42% ee; $[\alpha]_{\text{D}}^{20} = +30.7$ ($c = 1.0$, CHCl_3). All analytical data are consistent with those reported in the literature.¹

(+)-4'-Cyano -1'*H*,3*H*-spiro[furan-2,2'-naphthalene]-1',5(4*H*)-dione (+)-7d



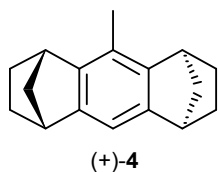
According to the GP using 1-naphthol **6d** in CHCl_3/TFE (2:1) at $-20\text{ }^\circ\text{C}$, the title compound was obtained as a white powder (52 mg, 44%). Enantiomeric excess was determined by chiral HPLC analysis (Chiralpack AS-H, *n*-heptane/EtOH, 75:25, 1.0 mL/min, 254 nm); $t_r = 19.1$ min (minor); $t_r = 29.1$ (major): 48% ee; $[\alpha]_{\text{D}}^{20} = +33.6$ ($c = 0.5$, CHCl_3); Mp: $157\text{--}158\text{ }^\circ\text{C}$; IR (KBr, cm^{-1}): 3241 (m), 2251 (s), 1710, 1675, 1642 (m), 1534 (s), 1297 (s), 834 (m); ^1H NMR (500 MHz, MeOD): δ 2.43–2.49 (m, 1 H, CH_2), 2.51–2.58 (m, 1 H, CH_2), 2.69–2.76 (m, 1 H, CH_2), 2.80–2.89 (m, 1 H, CH_2), 7.30 (s, 1 H, $\text{C}=\text{CH}$), 7.70 (t, $J = 8.1$ Hz, 1 H, ArH), 7.76 (d, $J = 7.4$ Hz, 1 H, ArH), 7.93 (t, $J = 8.1$ Hz, 1 H, ArH), 8.16 (d, $J = 7.4$ Hz, 1 H, ArH); ^{13}C NMR (125 MHz, MeOD): δ 26.9, 31.6, 84.4, 114.9, 115.9, 127.4, 128.3, 129.3, 132.0, 133.0, 137.5, 146.3, 178.0, 195.5; HRMS (ESI): $\text{C}_{14}\text{H}_9\text{NO}_3\text{Na}$ $[\text{M} + \text{Na}]^+$ calculated: 262.0480, found: 262.0471.

(+)-4'-Phenyl-1'*H*,3*H*-spiro[furan-2,2'-naphthalene]-1',5(4*H*)-dione (+)-7e



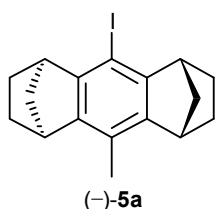
According to the GP using 1-naphthol **6e** in CHCl_3 at $-20\text{ }^\circ\text{C}$, the title compound was obtained as a white powder (89 mg, 62%). Enantiomeric excess was determined by chiral HPLC analysis (Chiralpack IB, *n*-heptane/EtOH, 96:4, 1.0 mL/min, 254 nm); $t_r = 23.8$ min (minor); $t_r = 28.3$ (major): 57% ee; $[\alpha]_{\text{D}}^{20} = +48.6$ ($c = 1.0$, CHCl_3). All analytical data are consistent with those reported in the literature.¹

(+)-(1*S*,4*R*,5*R*,8*S*)-9-Methyl-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene
(+)-4



In a 100 mL glass insert, (+)-3 (2.19 g, 9.20 mmol) was dissolved in EtOAc (40 mL) and 10% Pd/C (0.40 g) was added to the mixture. The insert was placed in a Parr reactor which was pressurised with 50 bar of H₂. After stirring the reaction mixture for 12 h at room temperature, the reactor was slowly vented and the insert was removed and the mixture was set to one side for 10 min while the evolution of dissolved H₂ occurred. This mixture was then directly applied to a pad of silica gel and was eluted with EtOAc. Removal of the solvent *in vacuo* yielded the product as a white solid (2.05 g, 99%). $[\alpha]_D^{25} = +60$ ($c = 1$, CHCl₃); Mp: 188-191 °C; IR (KBr, cm⁻¹): 2961 (s), 2863 (w), 1618 (w), 1110 (m); ¹H NMR (400 MHz, CDCl₃): δ 1.09–1.11 (m, 4 H, CH₂), 1.44–1.46 (m, 2 H, CHCH₂CH), 1.68–1.71 (m, 2 H, CHCH₂CH), 1.84–1.86 (m, 4 H, CH₂), 2.28 (s, 3 H, CH₃), 3.28 (brs, 2 H, CH), 3.42 (brs, 2 H, CH), 6.82 (s, 1 H, ArH); ¹³C NMR (100 MHz, CDCl₃): δ 14.9, 26.7, 27.4, 41.4, 44.3, 49.1, 110.9, 122.4, 143.7, 145.0; HRMS (EI): C₁₇H₂₀ [M]⁺ calculated: 224.1565, found: 224.1562.

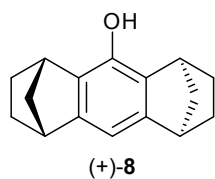
(-)-(1*S*,4*R*,5*R*,8*S*)-9-Methyl-10-iodo-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene (-)-5a



Arene (+)-4 (211 mg, 0.94 mmol) was dissolved in EtOAc (15 mL). To this solution (diacetoxy)iodobenzene (443 mg, 1.37 mmol) and iodine (210 mg, 1.74 mmol) were added. The purple solution was then heated to 70 °C and left for 12 h until TLC analysis (SiO₂; pentane) showed the starting material had been consumed. Sat. aq Na₂S₂O₃ (10 mL) was then added and the mixture stirred until the purple colour faded. The organic layer was washed with H₂O (2 x 10 mL), dried over MgSO₄ and concentrated *in vacuo* to yield the product as a white powder (231 mg, 70%). $[\alpha]_D^{25} = -66.5$ ($c = 1$, CHCl₃), Mp: 125-127 °C; IR (KBr, cm⁻¹): 2921 (s), 2855 (m), 1423 (m), 1077 (m); ¹H NMR (300 MHz, CDCl₃): δ 1.06–1.16 (m, 4 H, CH₂), 1.43 (d, $J = 9.0$ Hz, 2 H, CHCH₂CH), 1.71 (d, $J = 9.0$ Hz, 2 H, CHCH₂CH), 1.81–1.94 (m, 4 H, CH₂), 2.21 (s, 3 H, CH₃), 3.39 (s, 2 H, CH), 3.59 (s, 2 H, CH); ¹³C NMR (100 MHz, CDCl₃): δ 14.3, 26.2, 26.4, 43.2, 48.1, 48.3, 81.8, 122.5, 145.3, 148.3; HRMS (EI): C₁₇H₁₉I [M]⁺ calculated: 350.0532, found: 350.0544.

(+)-(1*S*,4*R*,5*R*,8*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene-9-ol

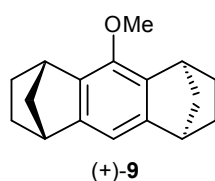
(+)-8



*m*CPBA (1.72 g, 6.9 mmol, 70% purity) was added in one portion to a stirred solution of (+)-**3** (200 mg, 0.84 mmol) in CH₂Cl₂ (20 mL) at 0 °C. The solution was allowed to reach room temperature and stirred for an additional 1 h. The mixture was diluted with Et₂O (45 mL) and washed with sat. aq Na₂SO₃ (2 x 15 mL), sat. aq NaHCO₃ (2 x 15 mL) and brine. After drying with MgSO₄ the solvents were removed *in vacuo* to yield the crude formate. The residue was dissolved in MeOH (35 mL) and K₂CO₃ (175 mg, 1.2 mmol) was added. The mixture was left to stir at room temperature for 30 min, then diluted with Et₂O (40 mL). The organic layer was washed with H₂O (20 mL), brine (20 mL) and dried over MgSO₄. The solvents were removed *in vacuo* to yield the title compound as a white solid. The product was sufficiently pure to be used in the next step but analytically pure (+)-**8** was obtained after flash column chromatography (SiO₂; pentane/CH₂Cl₂, 80:20) as a white solid (138 mg, 73%). $[\alpha]_D^{20} = +79.2$ ($c = 1$, CHCl₃); Mp 139-140 °C; IR (KBr, cm⁻¹) 3279 (s), 2962 (m), 1447 (w), 725 (m); ¹H NMR (300 MHz, CDCl₃): δ 1.07–1.19 (m, 4 H, CH₂), 1.44–1.48 (m, 2 H, CHCH/HCH), 1.68–1.72 (m, 2 H, CHCH/HCH), 1.81–1.86 (m, 4 H, CH₂), 3.28 (brs, 2 H, CH), 3.48 (brs, 2 H, CH), 4.63 (brs, 1 H, OH), 6.64 (s, 1 H, ArH); ¹³C NMR (100 MHz, CDCl₃): δ 26.9, 27.4, 39.3, 44.3, 49.3, 106.9, 130.1, 142.5, 147.9; HRMS (ESI): C₁₆H₁₉O [M + H]⁺ calculated: 227.1436, found: 227.1441.

(+)-(1*S*,4*R*,5*R*,8*S*)-9-Methoxy-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene

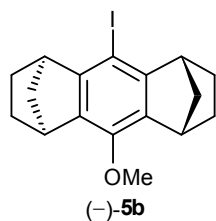
(+)-9



2N NaOH (1.5 mL) was added to a solution of (+)-**8** (100 mg, 0.44 mmol) in THF (3 mL). Dimethyl sulphate (0.4 mL, 531 mg, 2.57 mmol) was then added. After stirring the solution at room temperature for 5 min another aliquot of 2N NaOH (1.5 mL) was added at which point the reaction mixture was heated to reflux for 4 h. After cooling to room temperature, the aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with H₂O (10 mL), brine (10 mL) and dried over MgSO₄. The organic layer was then concentrated *in vacuo* to yield the title compound as a white solid (98 mg, 93%). The product was sufficiently pure to be used directly in the next step, but an analytically pure sample was obtained following purification by flash column chromatography (SiO₂; pentane/CH₂Cl₂, 1:1). $[\alpha]_D^{20} = +52.5$ ($c = 1$, CHCl₃); Mp: 58-59 °C; IR (KBr, cm⁻¹) 2955 (s), 2866 (s), 1572 (w), 1301 (s),

1058, 952 (m), 857 (m); ^1H NMR (300 MHz, CDCl_3): δ 1.05–1.20 (m, 4 H, CH_2), 1.42–1.44 (m, 2 H CHCHHCH), 1.64–1.71 (m, 2 H, CHCHHCH), 1.77–1.90 (m, 4 H, CH_2), 3.24 (brs, 2 H, CH), 3.56 (brs, 2 H, CH), 3.87 (brs, 3 H, OMe), 6.71 (s, 1 H, ArH). ^{13}C NMR (75 MHz, CDCl_3): δ 27.2, 27.4, 40.6, 44.1, 49.2, 60.9, 109.1, 135.0, 147.5, 148.1; HRMS (ESI): $\text{C}_{17}\text{H}_{21}\text{O}$ $[\text{M} + \text{H}]^+$ calculated: 241.1592, found: 241.1603.

(-)-(1*S*,4*R*,5*R*,8*S*)-9-Methoxy-10-iodo-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene (-)-5b



(+)-9 (50 mg, 0.21 mmol) was added in one portion to a mixture of NIS (33 mg, 0.25 mmol) and trifluoroacetic acid (1.5 μL , 2 mg, 0.02 mmol) in MeCN (2.5 mL). The resulting mixture was stirred at room temperature for 12 h. Sat. aq $\text{Na}_2\text{S}_2\text{O}_3$ was added and the mixture was stirred vigorously for 10 min. The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic extracts were washed with brine, dried over MgSO_4 and concentrated *in vacuo* to yield the product as an off-white solid (60 mg, 79%). $[\alpha]_{\text{D}}^{20} = -37.5$ ($c = 1$, CHCl_3); Mp: 87–89 $^{\circ}\text{C}$; IR (KBr, cm^{-1}) 2990 (m), 1589 (w), 1241 (s), 1072 (m), 732 (m); ^1H NMR (400 MHz, CDCl_3): δ 1.13–1.19 (m, 4 H, CH_2), 1.41–1.43 (m, 2 H CHCHHCH), 1.71–1.73 (m, 2 H, CHCHHCH), 1.82–1.92 (m, 4 H, CH_2), 3.39 (brs, 2 H, CH), 3.76 (brs, 2 H, CH), 3.86 (s, 3 H, OMe); ^{13}C NMR (100 MHz, CDCl_3): δ 25.1, 25.7, 41.1, 46.7, 47.2, 60.0, 76.7, 135.7, 146.7, 149.8; HRMS (EI): $\text{C}_{17}\text{H}_{19}\text{IO}$ $[\text{M}]^+$ calculated: 366.0481, found: 366.0469.

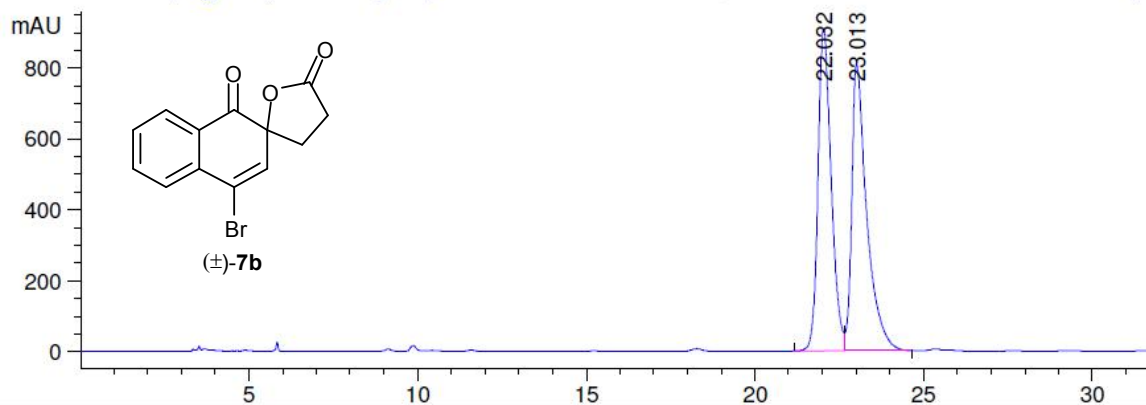
References

1. (a) M. Uyanik, T. Yasui and K. Ishihara, *Angew. Chem. Int. Ed.*, 2010, **49**, 2175; (b) M. Uyanik, T. Yasui and K. Ishihara, *Tetrahedron*, 2010, **66**, 5841.
2. (a) R. L. Halterman and S. T. Jan, *J. Org. Chem.*, 1991, **56**, 5253; (b) R. L. Halterman, S.-T. Jan, H. L. Nimmons, D. J. Standlee and M. A. Khan, *Tetrahedron*, 1997, **53**, 11257.

HPLC traces

Table 2, entry 6: 67% ee

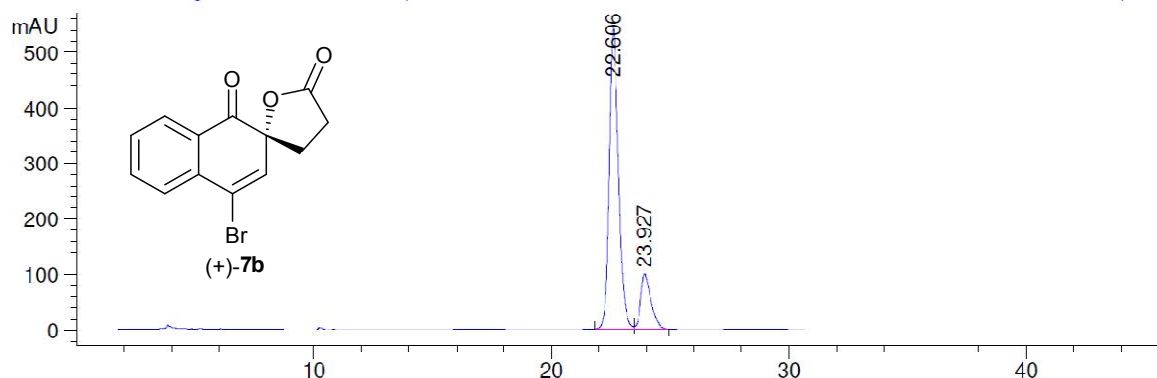
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Signal 3: DAD1 D, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.032	BV	0.4135	2.47558e4	909.78601	49.6850
2	23.013	VB	0.4495	2.50697e4	809.17493	50.3150

DAD1 D, Sig=230,8 Ref=360,100 (C:\CHEM32\1\DATA\DGG\RUN QUEUE 2011-03-29 20-10-53\SM-676-P.D)

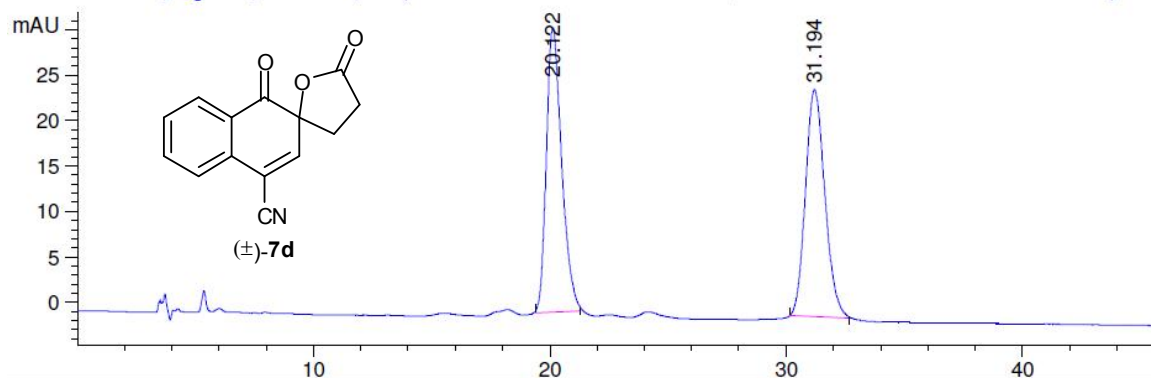


Signal 1: DAD1 A, Sig=254,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.606	BB	0.4140	2533.21118	92.92855	83.5839
2	23.928	BB	0.4384	497.52853	16.95256	16.4161

Table 2, entry 13: 48% ee

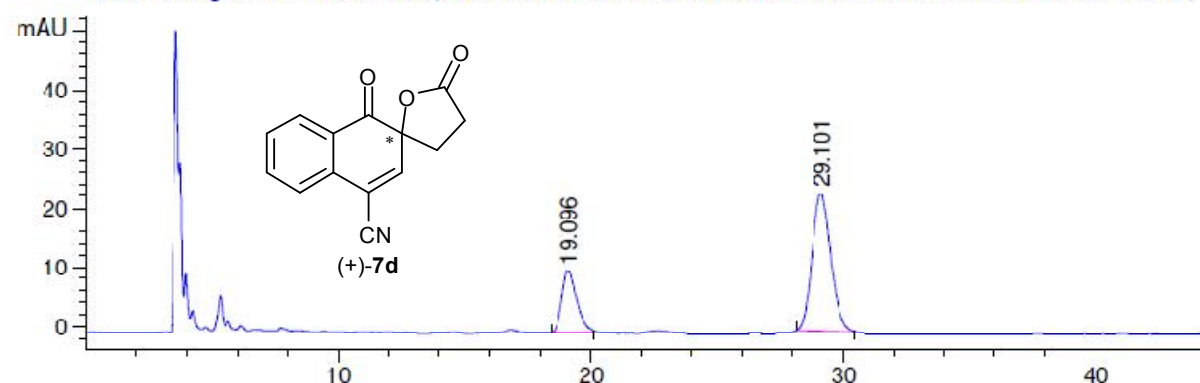
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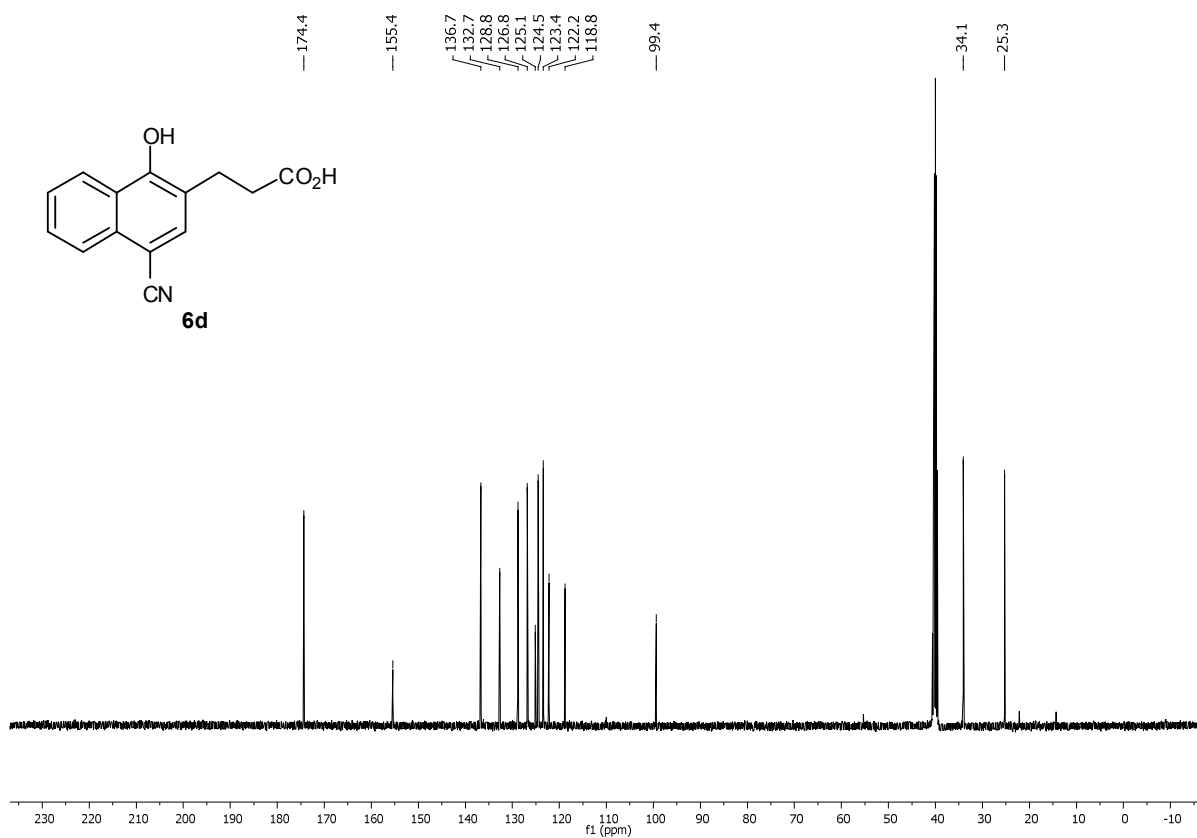
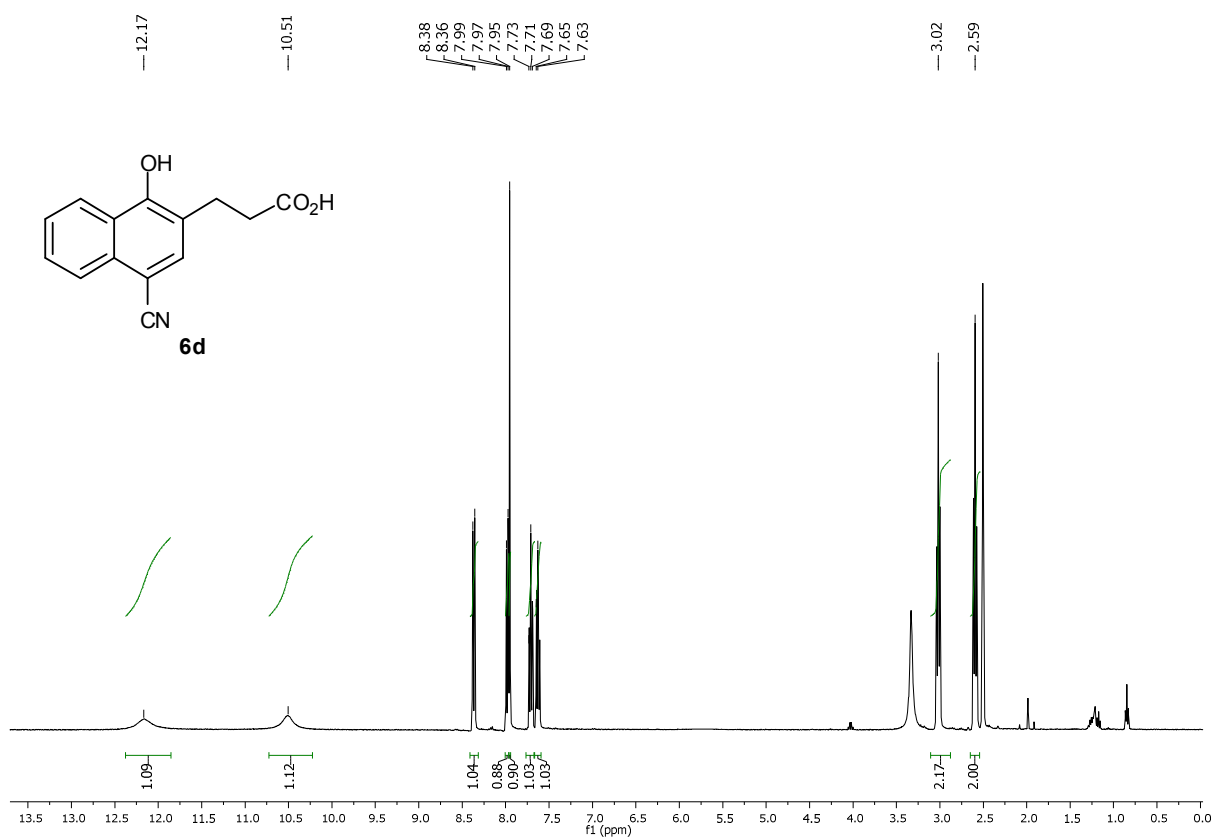
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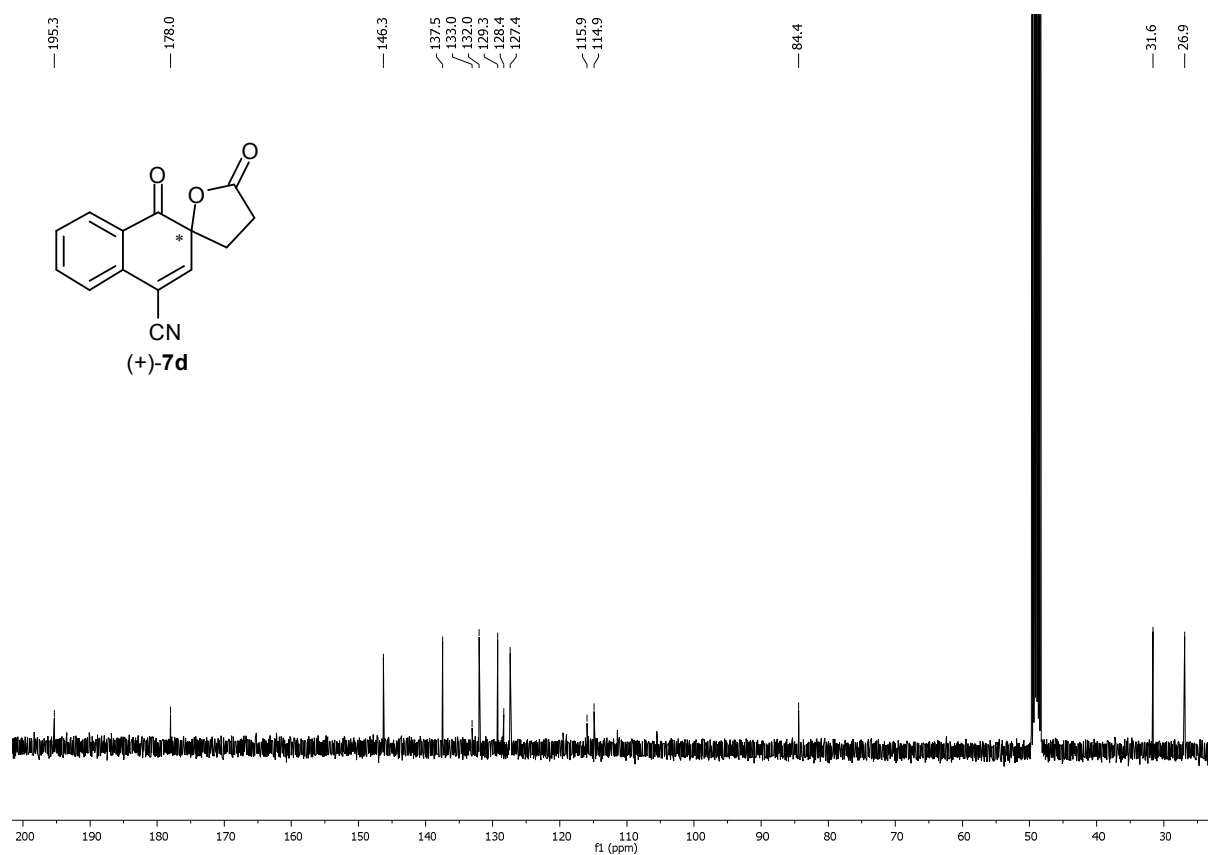
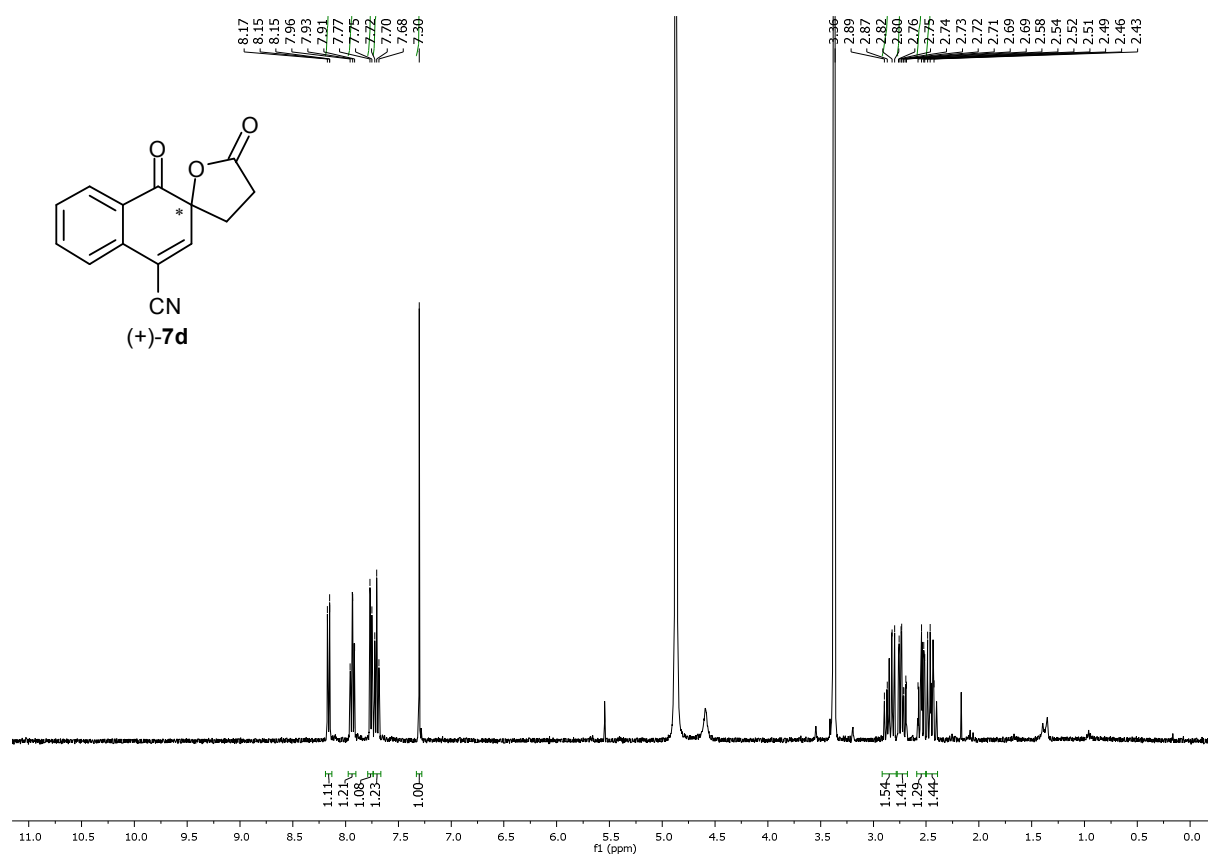
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.122	BB	0.6857	1408.91443	31.26747	49.7309
2	31.194	BB	0.8629	1424.16455	24.98772	50.2691

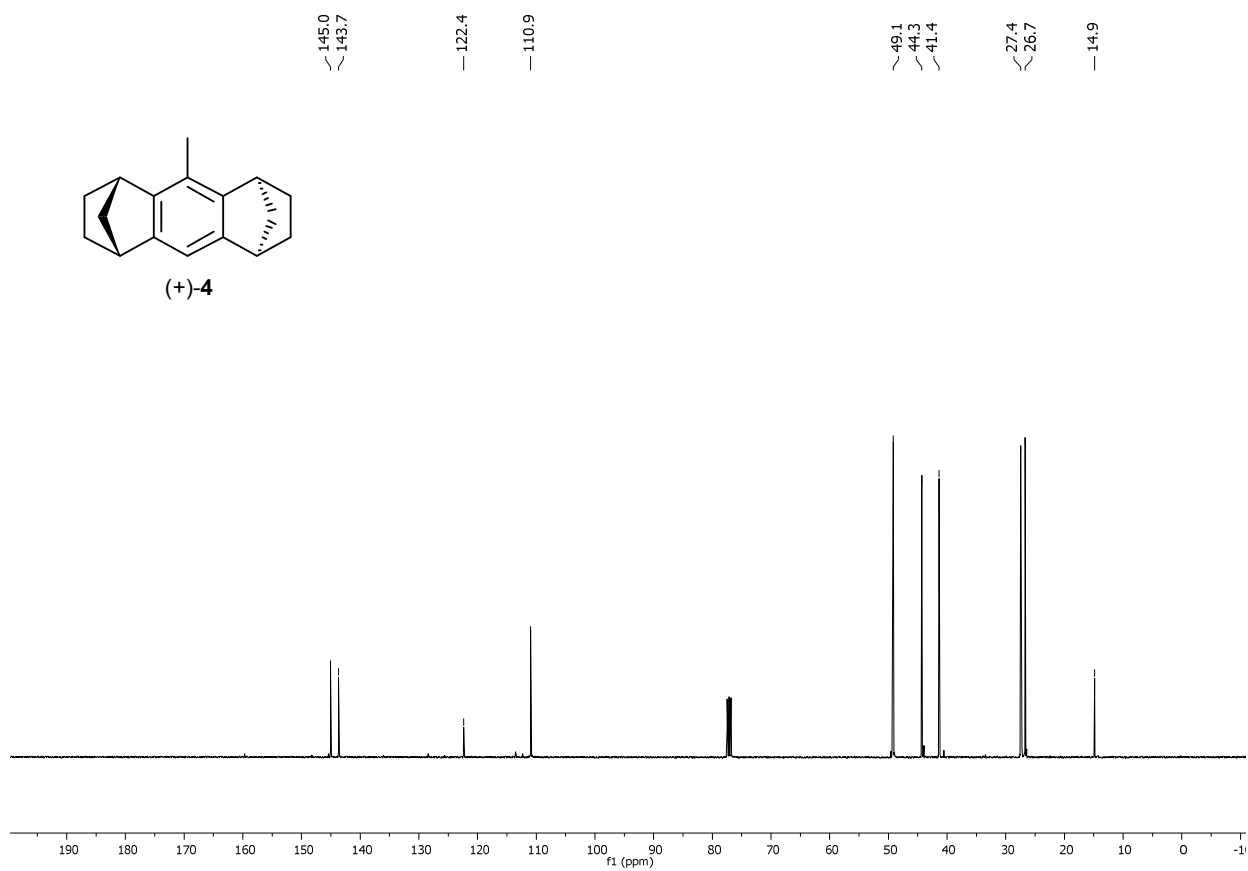
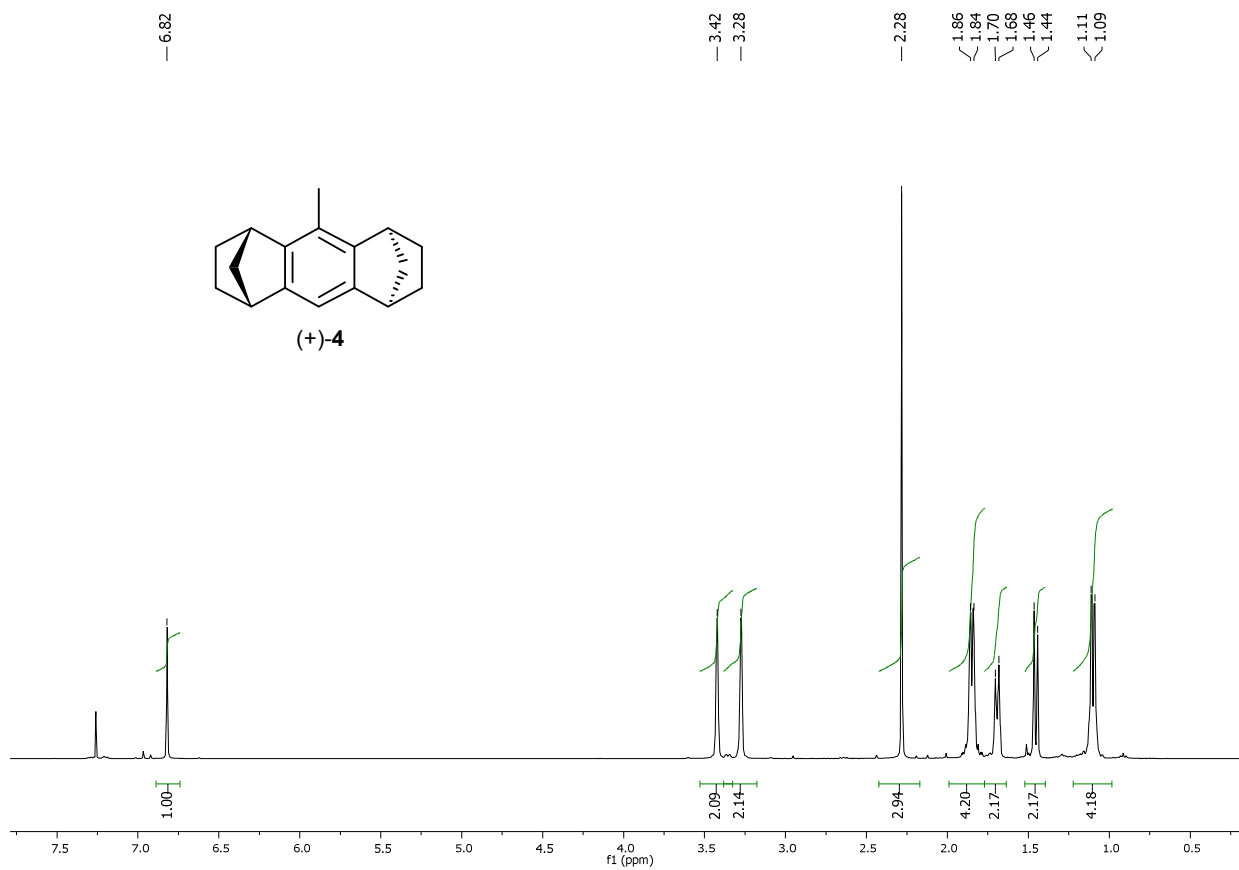
DAD1 C, Sig=210,8 Ref=360,100 (C:\CHEM32\1\DATA\DGG\RUN QUEUE 2011-06-15 16-30-57\100-1201.D)

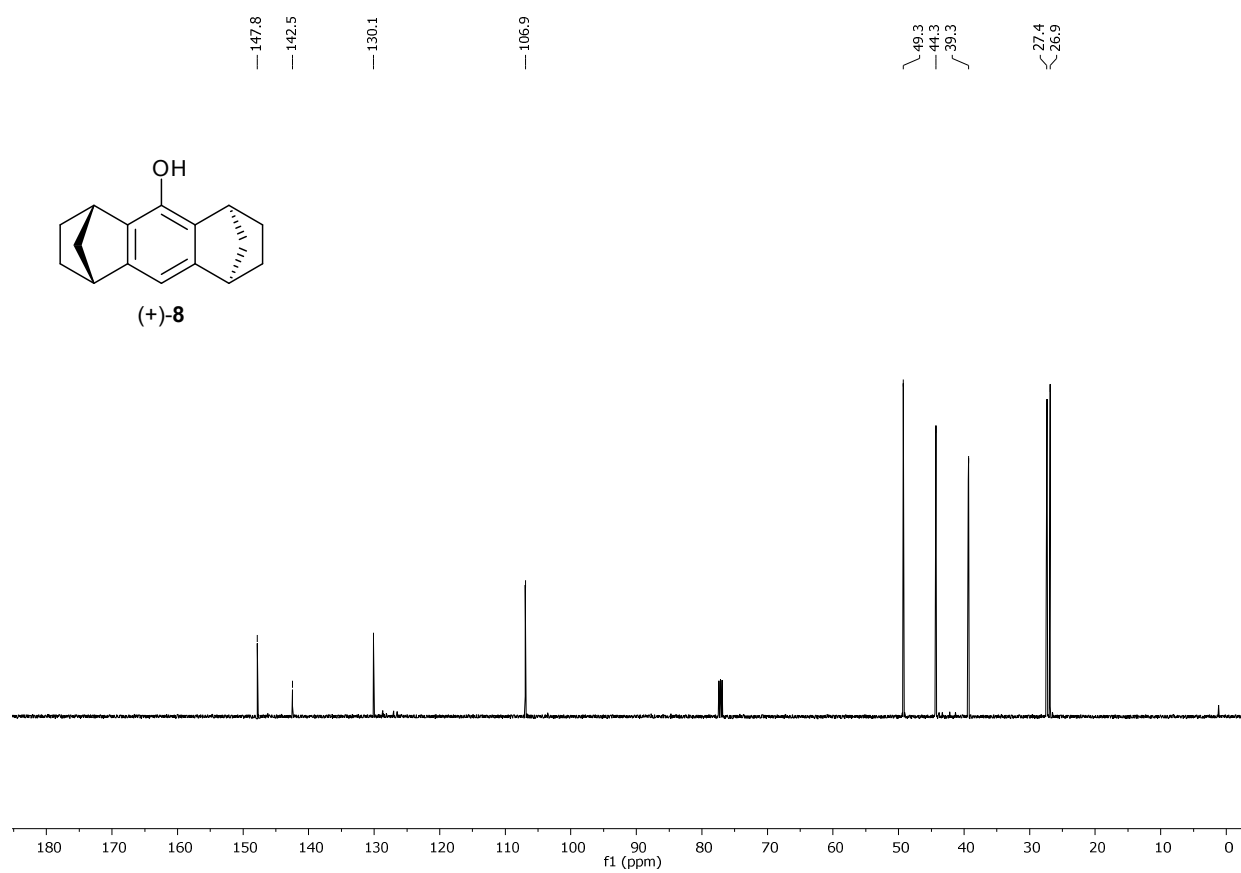
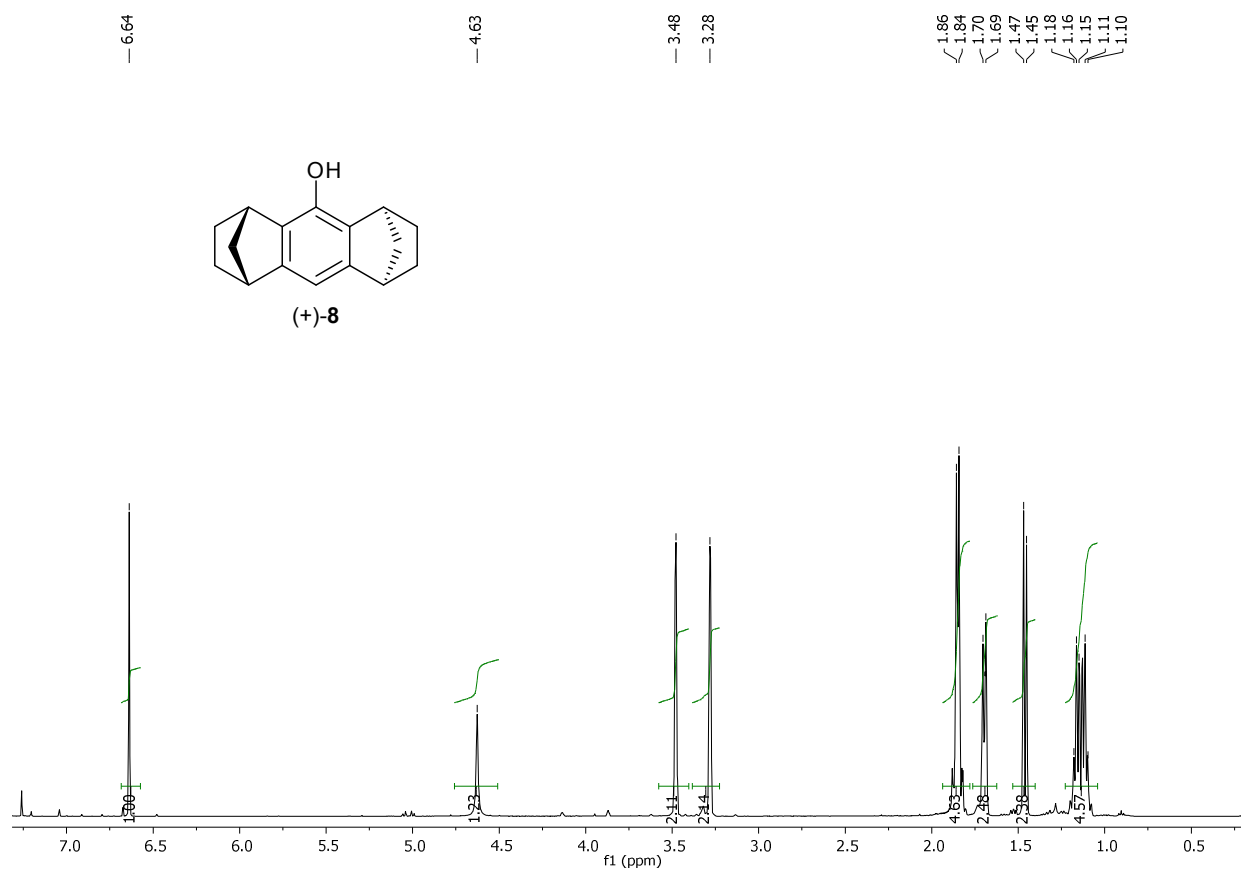


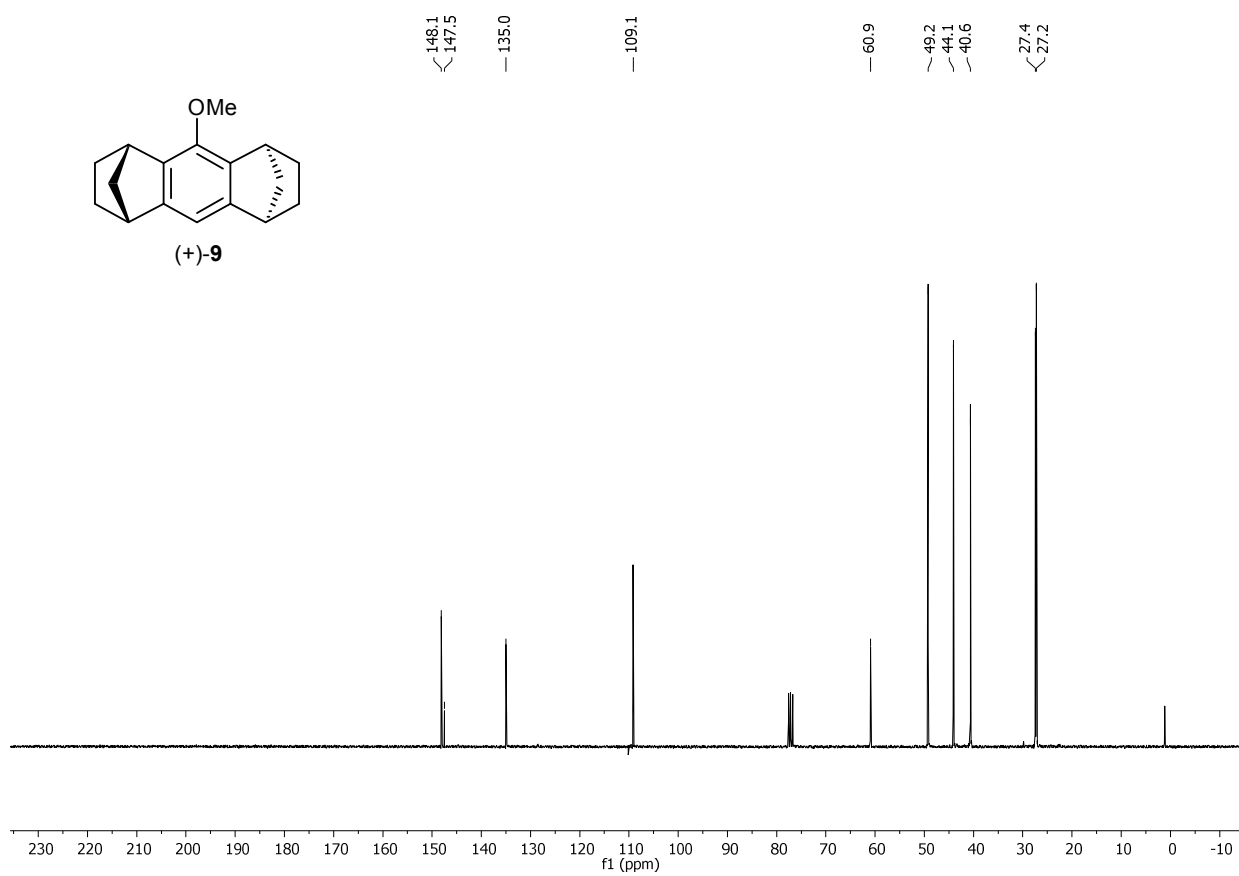
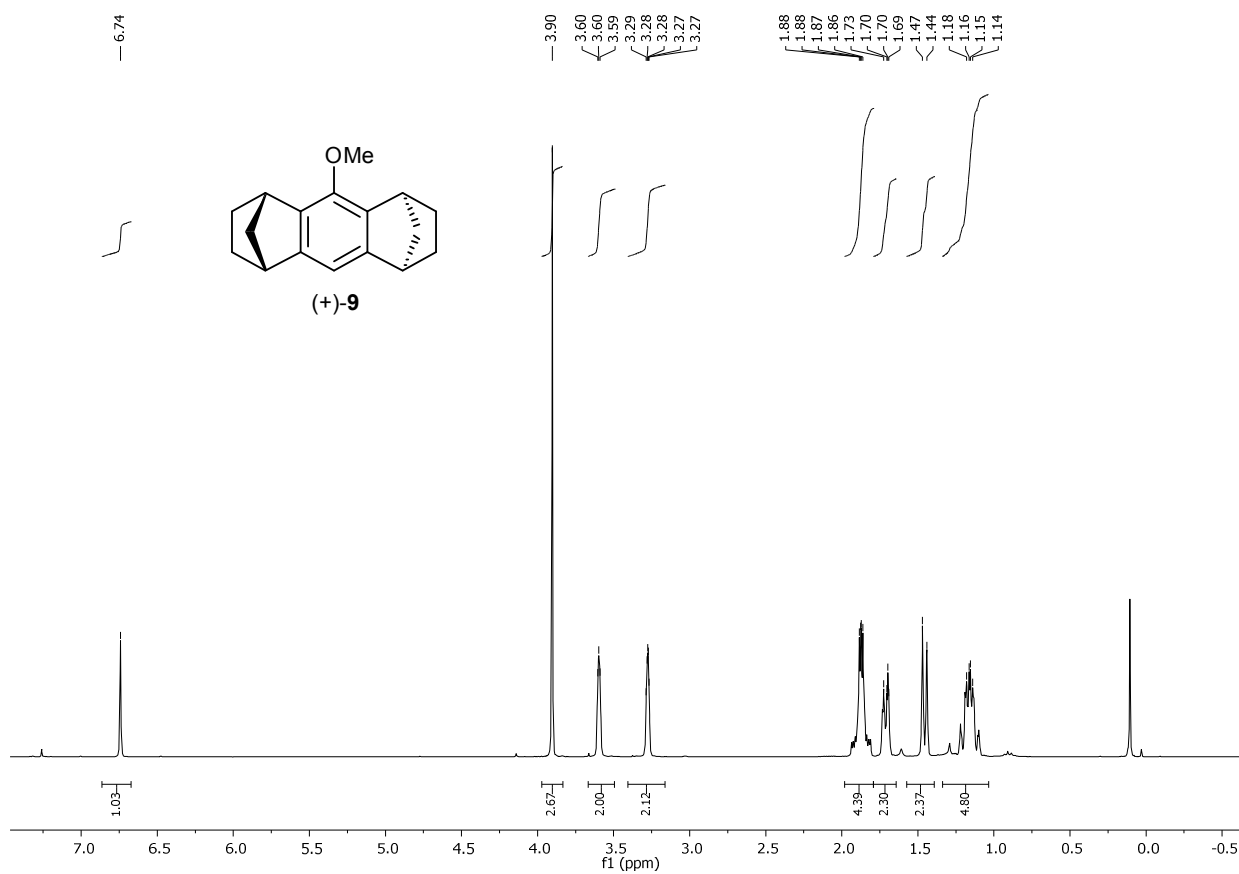
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2	29.101	BB	0.7834	1191.80884	23.27523	74.0491

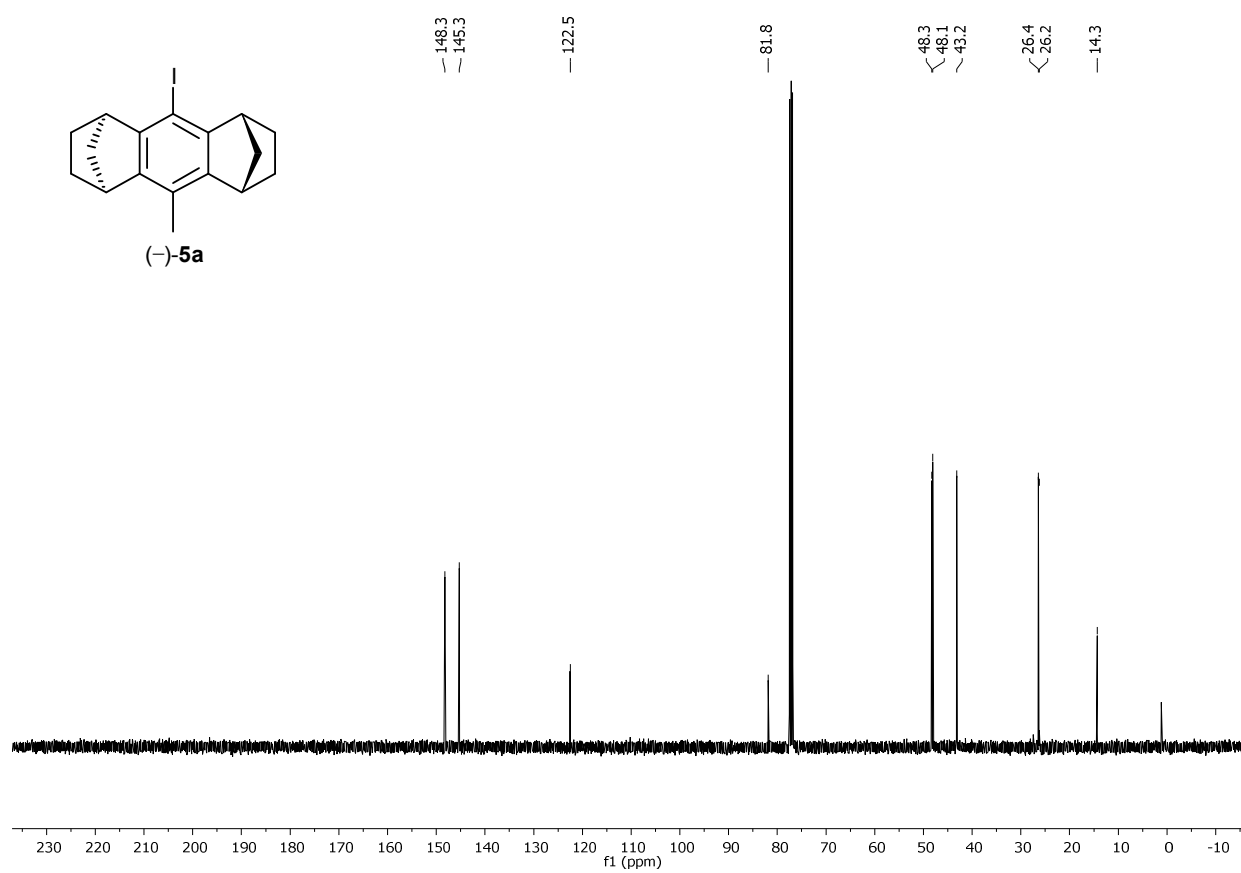
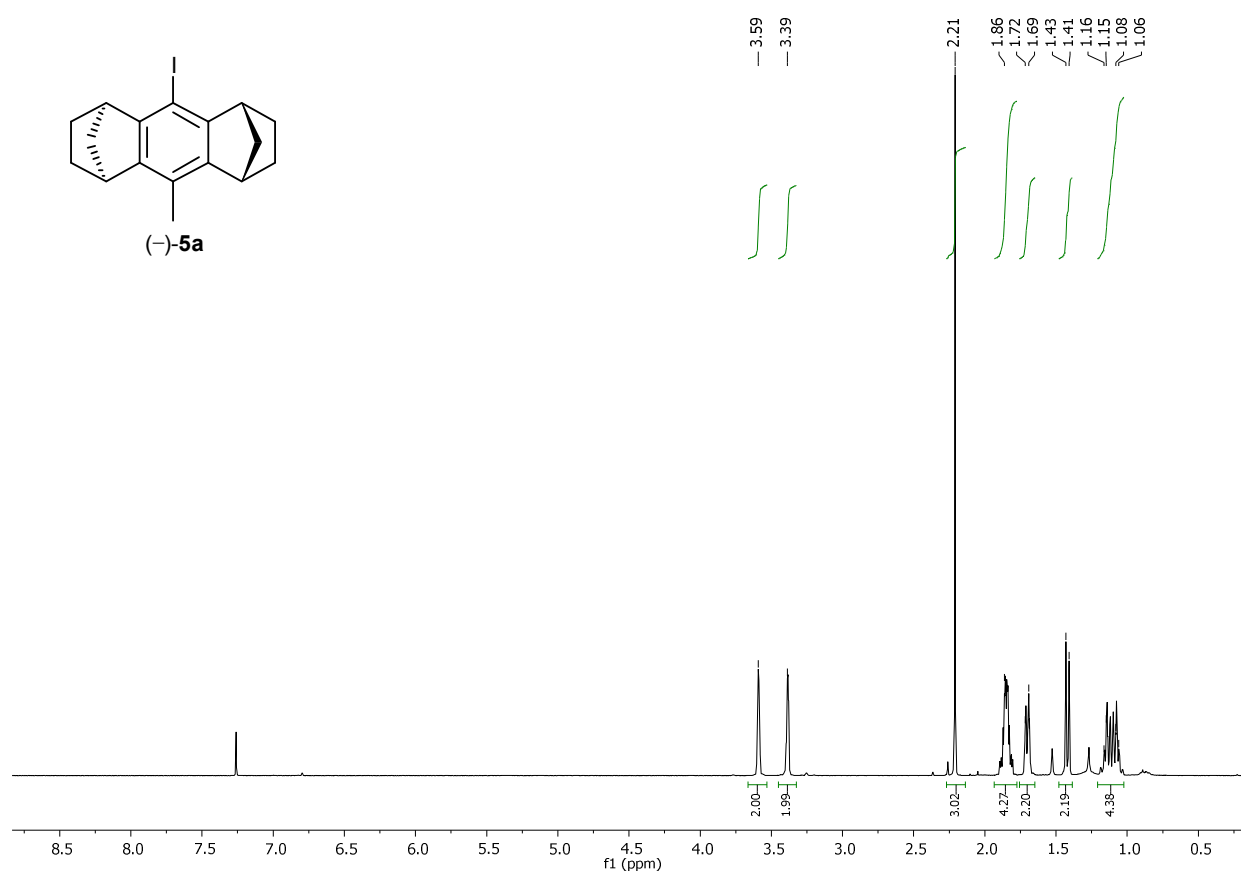


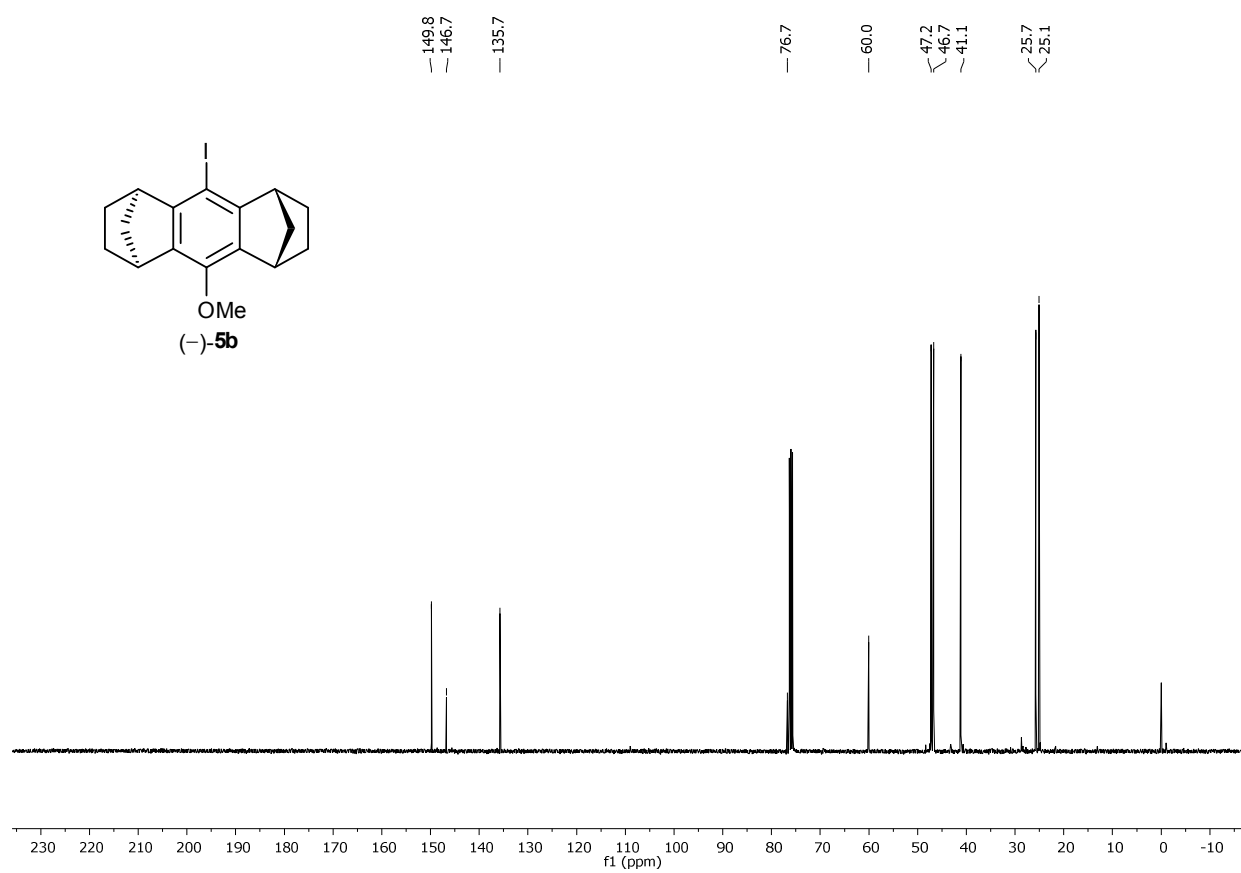
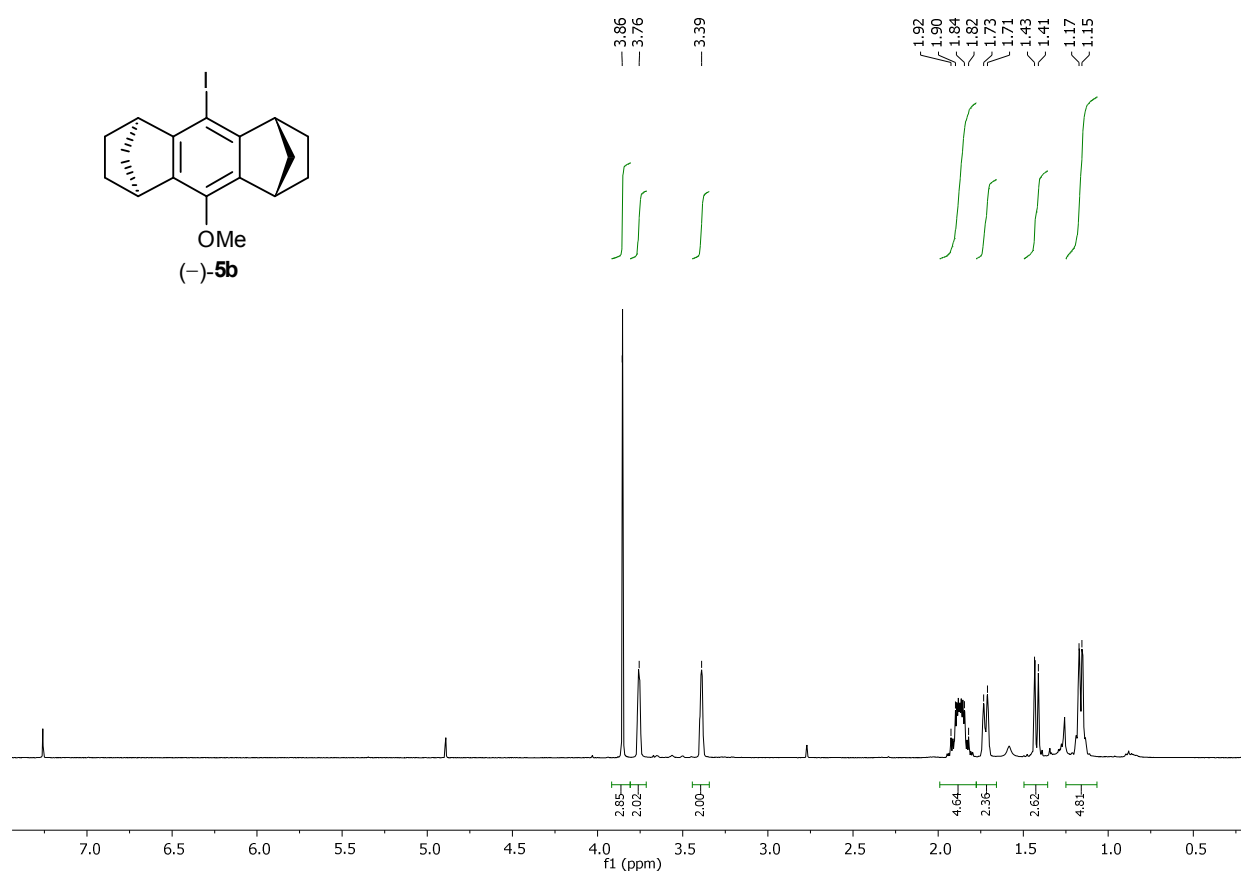




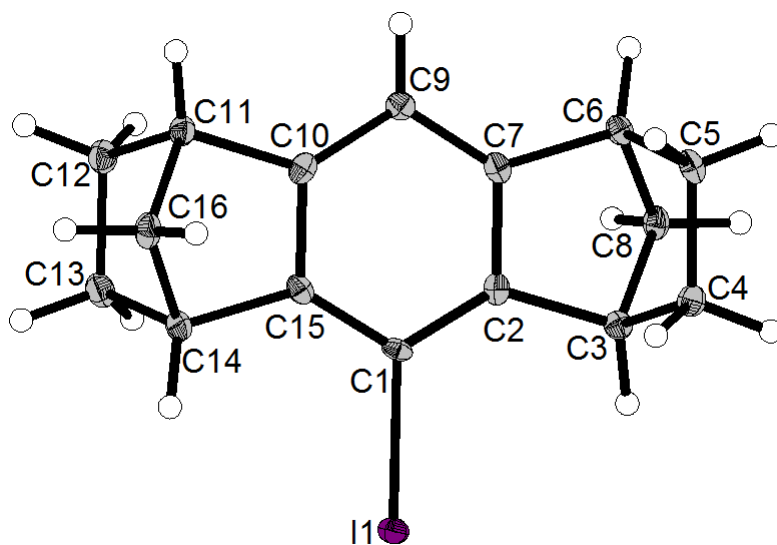




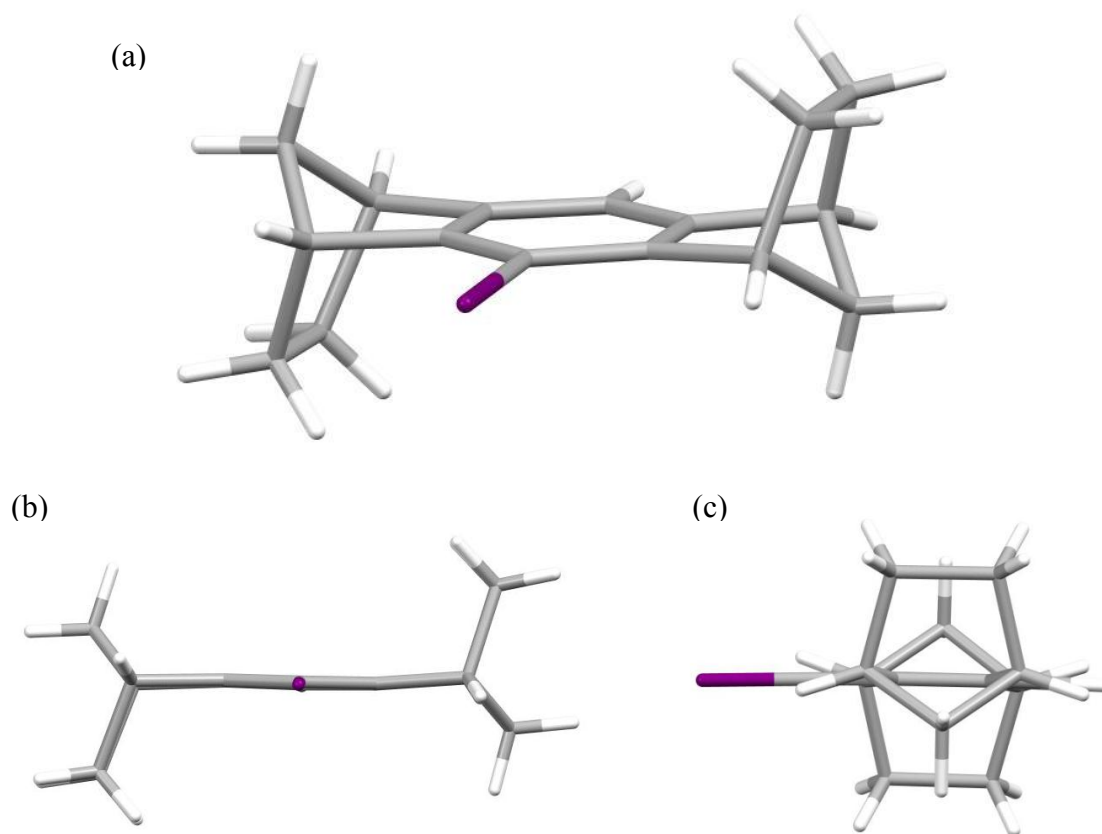




Crystal structure of (\pm)-9-iodo-*anti*-dimethanoanthracene



(thermal ellipsoids are drawn on the 50% probability level)



(a) Structure depicted in an angle similar to Figure 1 in the manuscript. (b) Front view along the arene plane. (c) Side-on view along the arene plane.