Electronic Supplementary Material (ESI) for Chemical Communications
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Supporting information (experimental procedures and spectra data) for

Nickel-Mediated Stereocontrolled Synthesis of Spiroketals via Tandem Cyclization–Coupling of β-Bromo Ketals and Aryl Iodides

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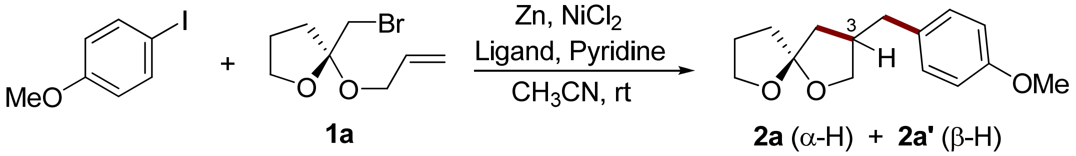
Experimental

General

For product purification by flash column chromatography, silica gel (200~300 mesh) and petroleum ether (bp. 60~90 °C) are used. All solvents were purified and dried by standard techniques, and distilled prior to use. All experiments were conducted under an argon or nitrogen atmosphere in oven-dried or flame-dried glassware with magnetic stirring, unless otherwise specified. All organic extracts were dried over Na_2SO_4 or $MgSO_4$, unless otherwise noted. IR spectra were recorded on a *Nicolet* FT-170SX spectrometer as liquid film. ^1H and ^{13}C NMR spectra were taken on a *Bruker* AM-400, AM-600 and Varian mercury 300 MHz spectrometer with TMS as an internal standard and $CDCl_3$ as solvent unless otherwise noted. EI–MS was obtained on GC/MS QP-2010 SE, and ESI–MS was obtained on *Bruker* esquire 6000 spectrometer. HRMS were determined on a *Bruker Daltonics* APEXII 47e FT-ICR spectrometer with ESI and APCI positive or negative ion mode. Melting points were measured on *Kofler* hot stage and are uncorrected.

The following chemicals were purchased and used as received: Zn (99.9%, dust), $NiCl_2$ (99.9%, powder), Pyridine (99.5%, SuperDry, with molecular sieves), CH_3CN (99.9%, SuperDry, with molecular sieves). Most of the aryl iodides can be synthesized from commercially available corresponding aryl bromides through Br–Li exchange followed by quench of I_2.[1] 7-bromoindole was synthesized from 1-bromo-2-nitrobenzene and vinylmagnesium bromide according to Bartoli's procedure.[2] Following a literature procedure,[3] 4-iodophenylboronic acid pinacol ester (4-IPBPE) was prepared from 4-iodophenyl boronic acid with pinacol.

Table S1. Optimization of Formation of Spiroketal **2a**[a]



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(1) (a) Hsung, R. P.; Chidsey, C. E. D.; Sita, L. R. *Organometallics* **1995**, *14*, 4808–4815. (b) Song, Y.-L.; Morin, C. *Synlett* **2001**, 266–268.

(2) (a) Bartoli, G.; Palmieri, G.; Bosco, M.; Dalpozzo, R.. *Tetrahedron Lett.* **1989**, *30*, 2129–2132. (b) Harrowven, D. C.; Lai, D.; Lucas, M. C. *Synthesis* **1999**, 1300–1302.

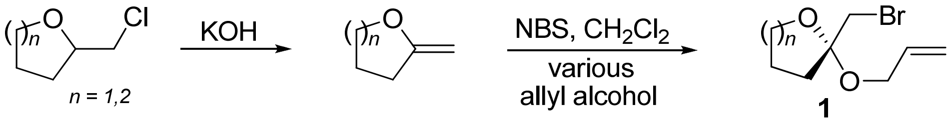
(3) Koolmeister, T.; Södergren, M.; Scobie, M. *Tetrahedron Lett.* **2002**, *43*, 5965–5968.

Entry	ligand	$NiCl_2$ (equiv)	Time (h)	Yield (%) (dr = **2a** : **2a′**)[b]
1	EC	1.0	8	40[c]
2	EC	0.5	8	35[c]
3	2,2′-bipyridine	0.5	8	75 (5 : 1)
4	2,2′-bipyridine	0.3	8	74 (6 : 1)
5	2,2′-bipyridine	0.2	8	72 (6 : 1)
6	2,2′-bipyridine	0.1	8	57 (9 : 1)
7	4,4′-di-*tert*-butyl-2,2′-bipy	0.3	4	80 (8 : 1)
8	4,4′-di-*tert*-butyl-2,2′-bipy	0.1	8	40 (7 : 1)
9	2,2′-bipyridine	0.3	4	52 (5 : 1)
10	2,2′-bipyridine	0.3	8	67 (2 : 1)[d]
11	2,2′-bipyridine	0.3	8	45 (4 : 1)[e]

[a] Reaction conducted on 0.5 mmol scale: A mixture of Zn (1.5 mmol, 3 equiv), $NiCl_2$ (indicated by table), EC (ethyl crotonate) (3 equiv to Ni) or 2,2′-bipyridine or 4,4′-di-*tert*-butyl-2,2′-bipyridine (1.2 equiv to Ni), and pyridine (0.5 mL) were employed for generation of active Ni^0 catalyst at 55 °C; then a solution of *p*-iodoanisole (0.6 mmol, 1.2 equiv) and **1a** (0.5 mmol) in CH_3CN (5 mL) was added to the above Ni^0 complex dropwise over a 10-min period at room temperature. [b] The isolated yield was shown and dr value was estimated by ^1H NMR spectroscopic analysis. [c] Only a diastereomer could be detected by ^1H NMR. [d] Reaction conducted at 50 °C. [e] DMF as the solvent.

Preparation of β-Bromo Ketals 1

General Procedure A



To an oven-dried round bottom flask was added various allyl alcohol (12 mmol) and dry CH_2Cl_2 (15 mL). The resulting solution was cooled to –40 °C and freshly prepared 2-methylenetetrahydrofuran(or -pyran)[4]] (10 mmol) was was introduced followed by the addition of *N*-bromosuccinimide (1.9 g, 11 mmol, recrystallized from acetone). The reaction mixture was slowly warmed to room temperature over a 2 h period and then was diluted with Et_2O (100 mL) and poured into a separatory funnel that contained H_2O (10 mL). The aqueous layer was extracted with Et_2O (2 × 20 mL),

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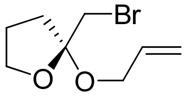
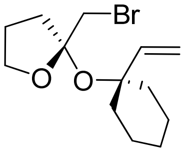
(4) Prepared from commercially available 2-(chloromethyl)tetrahydrofuran [CAS: 3003-84-7] or 2-(chloromethyl)tetrahydropyran [CAS: 18420-41-2] through β-elimination of HCl under strong base condition, see: Cuzzupe, A. N.; Hutton, C. A.; Lilly, M. J.; Mann, R. K.; McRae, K. J.; Zammit, S. C.; Rizzacasa, M. A. *J. Org. Chem.* **2001**, *66*, 2382–2393.

and the combined organic layers were washed with water (3 × 20 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography on silica gel to furnish the desired *β*-bromo ketal **1**.



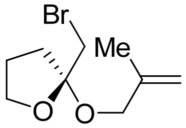
1a

1a was prepared as a colorless oil (55% yield, over two steps) according to General Procedure A. $R_f = 0.52$ (petroleum ether/EtOAc = 10 : 1); IR (film): ν_{max} = 2924, 2854, 1649, 1558, 1458, 1372, 1258, 1154, 1069, 1025, 926 cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ = 5.89–5.78 (m, 1H), 5.22 (dd, J = 16.0, 1.6 Hz, 1H), 5.00 (dd, J = 10.4, 1.6 Hz, 1H), 3.94 (dd, J = 12.8, 4.0 Hz, 1H), 3.83 (ddt, J = 12.8, 5.2, 1.6 Hz, 1H), 3.60 (q, J = 7.6 Hz, 1H), 3.61 (q, J = 7.6 Hz, 1H), 3.37 (d, J = 10.8 Hz, 1H), 3.17 (d, J = 10.8 Hz, 1H), 1.98 (ddd, J = 12.8, 8.4, 4.4 Hz, 1H), 1.98 (dt, J = 12.8, 8.4 Hz, 1H), 1.73–1.62 (m, 1H), 1.47–1.35 (m, 1H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 136.2, 115.7, 108.0, 69.8, 62.7, 36.6, 34.4, 25.2 ppm; HRMS (ESI): *m*/*z* calcd for $C_8H_{13}O_2BrNa^+$ $[M+Na]^+$: 242.9991, found: 243.0000.



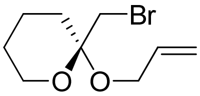
1l

1l was prepared as a colorless oil (44% yield, over two steps) according to General Procedure A. $R_f = 0.43$ (petroleum ether/EtOAc = 8 : 1); ^1H NMR (400 MHz, C_6D_6): δ = 6.15 (dd, J = 18.0, 11.2 Hz, 1H), 5.06 (d, J = 18.0 Hz, 1H), 4.97 (d, J = 11.2 Hz, 1H), 3.78 (dd, J = 8.4, 4.8 Hz, 1H), 3.66–3.55 (m, 1H), 3.62 (d, J = 10.8 Hz, 1H), 3.51 (d, J = 10.8 Hz, 1H), 2.06–1.92 (m, 2H), 1.90–1.76 (m, 3H), 1.74–1.63 (m, 3H), 1.51 (t, J = 9.2 Hz, 2H), 1.44 (brs, 4H) ppm; ^{13}C NMR (150 MHz, C_6D_6): δ = 144.9, 114.0, 109.4, 76.7, 70.1, 39.1, 38.3, 37.5, 37.2, 26.2, 25.0, 22.8, 22.7 ppm; EI–MS (70 eV): *m/z* 165 $[M-C_8H_{13}O]^+$, 163 $[M-C_8H_{13}O]^+$, 121, 109, 84, 67, 55.



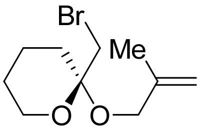
1m

1m was prepared as a colorless oil (42% yield, over two steps) according to General Procedure A. R_f = 0.51 (petroleum ether/EtOAc = 10 : 1); ^{1}H NMR (300 MHz, C_6D_6): δ = 5.05 (s, 1H), 4.83 (s, 1H), 3.88 (d, J = 12.0 Hz, 1H), 3.73 (d, J = 12.0 Hz, 1H), 3.72–3.58 (m, 2H), 3.39 (d, J = 11.1 Hz, 1H), 3.19 (d, J = 11.1 Hz, 1H), 2.04–1.95 (m, 1H), 1.86–1.79 (m, 1H), 1.76–1.56 (m, 1H), 1.64 (s, 3H), 1.48–1.31 (m, 1H) ppm; ^{13}C NMR (75 MHz, C_6D_6): δ = 142.9, 111.2, 107.6, 69.4, 65.2, 36.2, 34.0, 24.9, 19.7 ppm; EI–MS (70 eV): *m/z* 234 $[M]^+$, 163 $[M-C_4H_7O]^+$, 141, 121, 55.



1n

1n was prepared as a colorless oil (45% yield, over two steps) according to General Procedure A. R_f = 0.51 (petroleum ether/EtOAc = 10 : 1); IR (film): ν_{max} = 2946, 2876, 1648, 1433, 1379, 1228, 1200, 1155, 1079, 1024, 924 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6): δ = 5.90–5.80 (m, 1H), 5.27 (dd, J = 17.2, 2.0 Hz, 1H), 5.03 (dd, J = 10.8, 2.0 Hz, 1H), 3.88–3.75 (m, 2H), 3.50–3.39 (m, 2H), 3.23 (d, J = 11.2 Hz, 1H), 3.09 (d, J = 11.2 Hz, 1H), 2.06–1.98 (m, 1H), 1.80–1.68 (m, 1H), 1.38–1.21 (m, 3H), 1.07 (d, J = 12.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 135.7, 115.8, 97.6, 62.7, 61.2, 36.2, 33.0, 25.5, 19.2 ppm; HRMS (ESI): *m/z* calcd for $C_9H_{15}O_2BrNa^+$ $[M+Na]^+$: 257.0148, found: 257.0149.



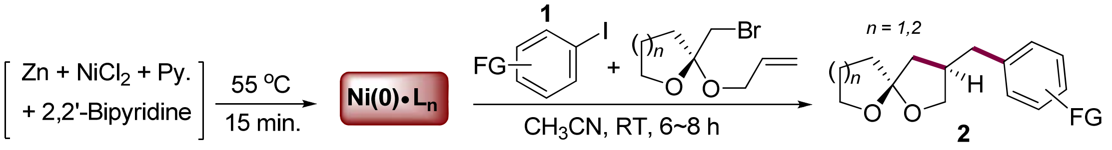
1q

1q was prepared as a colorless oil (44% yield, over two steps) according to General Procedure A. R_f = 0.50 (petroleum ether/EtOAc = 10 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.06 (s, 1H), 4.87 (s, 1H), 3.92 (d, J = 12.0 Hz, 1H), 3.83 (d, J = 12.0 Hz, 1H), 3.67 (dd, J = 9.0, 2.4 Hz, 2H), 3.43 (d, J = 10.8 Hz, 1H), 3.30 (d, J = 10.8 Hz, 1H), 2.07–2.00 (m, 1H), 1.89–1.75 (m, 1H), 1.78 (s, 3H), 1.65–1.48 (m, 4H) ppm; ^{13}C

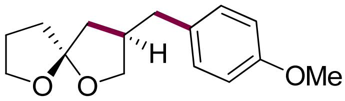
NMR (75 MHz, $CDCl_3$): δ = 142.1, 111.2, 97.1, 63.5, 62.5, 35.6, 32.4, 24.8, 19.9, 18.5 ppm; ESI–MS: *m/z* 271.0 $[M+Na]^+$.

Stereoselective Cyclization–*Intermolecular* Cross-Coupling

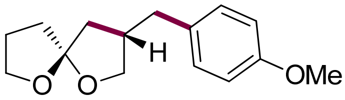
General Procedure B



To a stirred slurry of Zn (100 mg, 1.5 mmol) and $NiCl_2$ (20 mg, 0.15 mmol) in pyridine (0.5 mL) was added 2,2′-bipyridine (28 mg, 0.18 mmol) at room temperature. Then the temperature rose to 55 °C and vigorous stirring was continued for 15 min. The resulting black Ni(0) complex was cooled to room temperature, to which the solution of aryl iodide (0.6 mmol) and *β*-bromo ketal **1** (0.5 mmol) in CH_3CN (5 mL) was added dropwise over a 10-min period. After stirring for 6~8 h, the mixture was filtered with a short plug of silica (elution with 25 mL Et_2O) and washed with water and brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography on silica gel to afford desired spiroketal **2**.



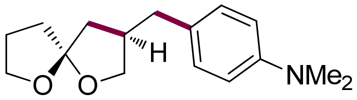
2a



2a′

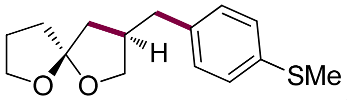
2a and **2a′** was prepared as the colorless oil (57% yield, dr = 9 : 1) according to General Procedure B. (**2a**) R_f = 0.43 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 2941, 2880, 1612, 1583, 1513, 1461, 1341, 1300, 1246, 1178, 1113, 1022, 953, 920, 826 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.09 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 3.97–3.93 (m, 1H), 3.90 (t, J = 8.4 Hz, 2H), 3.78 (s, 3H), 3.62 (t, J = 8.4 Hz, 1H), 2.72 (d, J = 8.0 Hz, 2H), 2.51 (heptet, J = 8.0 Hz, 1H), 2.14 (dd, J = 13.2, 9.2 Hz, 1H), 2.07–2.00 (m, 2H), 2.07–2.00 (m, 3H) ppm; ^{13}C/DEPT NMR (100 MHz, $CDCl_3$): δ = 157.9 (s), 132.9 (s), 129.5 (d, 2C), 115.1 (s), 113.8 (d, 2C), 72.1 (t), 67.2 (t), 55.2

(q), 40.9 (t), 40.7 (d), 38.4 (t), 35.8 (t), 24.4 (t) ppm; HRMS (ESI): *m*/*z* calcd for $C_{15}H_{20}O_3Na^+$ $[M+Na]^+$: 271.1310, found: 271.1312. (**2a′**) R_f = 0.46 (petroleum ether/EtOAc = 4 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.07 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 3.99 (t, J = 8.0 Hz, 1H), 3.95–3.88 (m, 1H), 3.82 (t, J = 8.0 Hz, 1H), 3.78 (s, 3H), 3.62 (dd, J = 8.0, 6.8 Hz, 1H), 2.51 (heptet, J = 8.0 Hz, 1H), 2.65–2.60 (m, 2H), 2.12 (dd, J = 12.8, 7.2 Hz, 1H), 2.09–2.00 (m, 2H), 1.94–1.85 (m, 2H), 1.71 (dd, J = 12.8, 7.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.0, 132.6, 129.5 (2C), 115.0, 113.9 (2C), 72.1, 67.1, 55.3, 41.5, 40.0, 38.9, 35.1, 24.6 ppm.



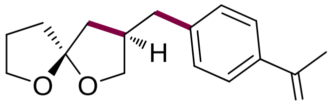
2b

2b was prepared as a colorless oil (75% yield, dr = 8 : 1) according to General Procedure B. R_f = 0.34 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 3070, 2973, 2940, 2880, 2799, 1615, 1522, 1444, 1344, 1226, 1162, 1020, 949, 804 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.05 (d, J = 8.4 Hz, 2H), 6.68 (d, J = 8.4 Hz, 2H), 3.95–3.88 (m, 3H), 3.62 (t, J = 8.0 Hz, 1H), 2.91 (s, 6H), 2.68 (d, J = 7.6 Hz, 2H), 2.51 (heptet, J = 7.6 Hz, 1H), 2.15 (dd, J = 13.2, 9.2 Hz, 1H), 2.05–2.01 (m, 2H), 1.91–1.84 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.1, 129.2 (2C), 129.0, 115.1, 112.9 (2C), 72.2, 67.2, 41.0 (2C), 40.8 (2C), 38.3, 35.9, 24.4 ppm; HRMS (ESI): calcd. for $C_{16}H_{24}NO_2^+$ $[M+H]^+$: 262.1802, found: 262.1811.

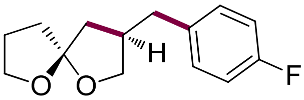


2c

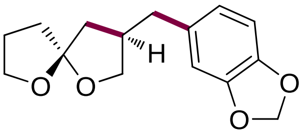
2c was prepared as a colorless oil (72% yield, dr = 5 : 1) according to General Procedure B. R_f= 0.42 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 2974, 2923, 2877, 1600, 1494, 1440, 1341, 1152, 1095, 1019, 953, 827 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 3.97–3.91 (m, 1H), 3.90 (t, J = 7.2 Hz, 2H), 3.62 (t, J = 8.0 Hz, 1H), 2.75 (d, J = 7.6 Hz, 2H), 2.52 (heptet, J = 7.6 Hz, 1H), 2.47 (s, 3H), 2.14 (dd, J = 13.2, 8.8 Hz, 1H), 2.08–2.01 (m, 2H), 1.92–1.84 (m, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 137.9, 135.6, 129.2 (2C), 127.1 (2C), 115.0, 72.1, 67.3, 40.8, 40.4, 38.8, 35.8, 24.4, 16.2 ppm; HRMS (ESI): calcd. for $C_{15}H_{21}O_2S^+$ [M+H]$^+$: 265.1257, found: 265.1259.


2d

2d was prepared as a colorless oil (75% yield, dr = 4 : 1) according to General Procedure B. R_f = 0.23 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 2971, 2940, 2877, 1682, 1606, 1438, 1357, 1267, 1019, 955, 832 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.89 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 3.98–3.93 (m, 1H), 3.91 (t, J = 8.0 Hz, 2H), 3.64 (t, J = 8.0 Hz, 1H), 2.86 (d, J = 8.0 Hz, 2H), 2.59 (s, 3H), 2.58 (heptet, J = 7.6 Hz, 1H), 2.15 (dd, J = 13.2, 9.2 Hz, 1H), 2.08–2.02 (m, 2H), 1.92–1.84 (m, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 197.8, 146.5, 135.3, 128.9 (2C), 128.6 (2C), 115.0, 71.9, 67.3, 40.7, 40.0, 39.4, 35.7, 26.6, 24.4 ppm; HRMS (ESI): calcd. for $C_{16}H_{21}O_3^+$ [M+H]$^+$: 261.1485, found: 261.1484.

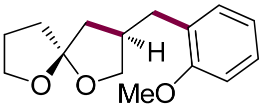

2e

2e was prepared as a colorless oil (76% yield, dr = 6 : 1) according to General Procedure B. R_f = 0.38 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 3040, 2974, 2942, 2880, 1603, 1510, 1443, 1342, 1222, 1156, 1107, 1021, 953, 824 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.13 (dd, J = 8.4, 5.6 Hz, 2H), 6.96 (t, J = 8.4 Hz, 2H), 3.97–3.92 (m, 1H), 3.90 (t, J = 8.0 Hz, 2H), 3.62 (t, J = 8.0 Hz, 1H), 2.75 (d, J = 8.0 Hz, 2H), 2.51 (heptet, J = 7.6 Hz, 1H), 2.14 (dd, J = 13.2, 9.2 Hz, 1H), 2.09–2.01 (m, 2H), 1.94–1.82 (m, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 161.3 (d, J_{C-F} = 242.0 Hz), 136.4 (d, J_{C-F} = 3.0 Hz), 130.0 (d, J_{C-F} = 7.0 Hz, 2C), 115.1 (d, J_{C-F} = 22.0 Hz, 2C), 115.0, 72.0, 67.3, 40.7, 40.5, 38.5, 35.8, 24.4 ppm; ^{19}F NMR (376 MHz, CDCl$_3$): δ = −117.38 ppm; HRMS (ESI): calcd. for $C_{14}H_{18}FO_2^+$ [M+H]$^+$: 237.1285, found: 237.1281.



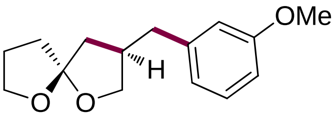
2f

2f was prepared as a colorless oil (80% yield, dr = 8 : 1) according to General Procedure B. R_f = 0.31 (petroleum ether/EtOAc = 5 : 1); IR (film): $\nu_{\max}$ = 3069, 2973, 2940, 2882, 2778, 1608, 1490, 1442, 1342, 1246, 1190, 1101, 1038, 926, 810 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.72 (d, J = 8.0 Hz, 1H), 6.67 (s, 1H), 6.63 (d, J = 8.0 Hz, 1H), 5.92 (s, 2H), 3.97–3.92 (m, 1H), 3.90 (t, J = 8.0 Hz, 2H), 3.61 (t, J = 8.0 Hz, 1H), 2.71 (d, J = 8.0 Hz, 2H), 2.49 (heptet, J = 8.0 Hz, 1H), 2.14 (dd, J = 13.2, 9.2 Hz, 1H), 2.06–2.00 (m, 2H), 1.92–1.82 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6, 145.7, 134.6, 121.5, 115.0, 109.0, 108.1, 100.8, 72.0, 67.2, 40.7, 40.6, 39.0, 35.8, 24.4 ppm; HRMS (ESI): calcd. for $C_{15}H_{19}O_4^+$ $[M+H]^+$: 263.1278, found: 263.1279.



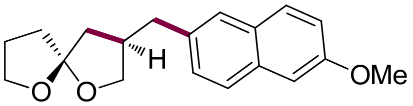
2g

2g was prepared as a colorless oil (74% yield, dr = 8 : 1) according to General Procedure B. R_f = 0.41 (petroleum ether/EtOAc = 4 : 1); IR (film): $\nu_{\max}$ = 3068, 2941, 2881, 1597, 1493, 1462, 1339, 1243, 1117, 1023, 953, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18 (t, J = 8.0 Hz, 1H), 7.13 (d, J = 7.2 Hz, 1H), 6.87 (t, J = 7.2 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 3.97–3.90 (m, 1H), 3.88 (t, J = 8.0 Hz, 2H), 3.81 (s, 3H), 3.64 (t, J = 8.0 Hz, 1H), 2.78 (d, J = 8.0 Hz, 2H), 2.62 (heptet, J = 8.0 Hz, 1H), 2.14 (dd, J = 13.2, 8.8 Hz, 1H), 2.08–2.00 (m, 2H), 1.94–1.82 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 130.3, 129.2, 127.3, 120.3, 115.1, 110.2, 72.3, 67.2, 55.2, 41.1, 38.8, 36.0, 33.7, 24.4 ppm; HRMS (ESI): calcd. for $C_{15}H_{21}O_3^+$ $[M+H]^+$: 249.1485, found: 249.1481.



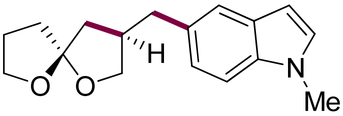
2h

2h was prepared as a colorless oil (70% yield, dr = 8 : 1) according to General Procedure B. R_f = 0.42 (petroleum ether/EtOAc = 4 : 1); IR (film): $\nu_{\max}$ = 2942, 2881, 1601, 1489, 1455, 1318, 1262, 1153, 1020, 953, 782 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6): *δ* = 7.08 (t, *J* = 8.0 Hz, 1H), 6.76 (s, 1H), 6.69 (t, *J* = 8.0 Hz, 2H), 3.91 (dt, *J* = 8.0, 5.6 Hz, 1H), 3.85 (t, *J* = 8.0 Hz, 1H), 3.73 (dt, *J* = 14.8, 7.2 Hz, 2H), 3.33 (s, 3H), 2.72–2.61 (m, 2H), 2.33 (heptet, *J* = 8.0 Hz, 1H), 1.97–1.82 (m, 4H), 1.58–1.47 (m, 2H) ppm; ^{13}C NMR (100 MHz, C_6D_6): *δ* = 160.4, 143.0, 129.6, 121.4, 114.98, 114.93, 111.7, 72.3, 67.1, 54.6, 40.8, 40.7, 39.9, 35.8, 24.7 ppm; HRMS (ESI): calcd. for $C_{15}H_{21}O_3^+$ [M+H]$^+$: 249.1485, found: 249.1482.



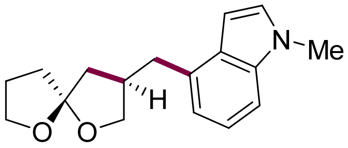
2i

2i was prepared as a colorless oil (57% yield, dr = 10 : 1) according to General Procedure B. R_f = 0.40 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 3055, 2940, 2883, 1633, 1607, 1506, 1484, 1390, 1266, 1229, 1027, 951, 852 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.66 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.54 (s, 1H), 7.28 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.13 (d, *J* = 2.4 Hz, 1H), 7.12 (brs, 1H), 3.98–3.91 (m, 3H), 3.90 (s, 3H), 3.68 (t, *J* = 8.0 Hz, 1H), 2.90 (d, *J* = 8.0 Hz, 2H), 2.63 (heptet, *J* = 7.6 Hz, 1H), 2.16 (dd, *J* = 13.2, 8.8 Hz, 1H), 2.08–2.01 (m, 2H), 1.94 (dd, *J* = 13.2, 6.0 Hz, 1H), 1.91–1.82 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 157.3, 136.0, 133.1, 129.1, 128.9, 127.8, 126.8, 126.7, 118.7, 115.1, 105.7, 72.2, 67.2, 55.3, 40.9, 40.4, 39.3, 35.8, 24.4 ppm; HRMS (ESI): calcd. for $C_{19}H_{23}O_3^+$ [M+H]$^+$: 299.1642, found: 299.1640.



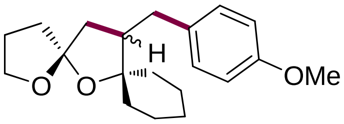
2j

2j was prepared as a colorless oil (61% yield, dr = 7 : 1) according to General Procedure B. R_f = 0.38 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 3070, 2973, 2940, 2880, 1615, 1522, 1444, 1344, 1226, 1162, 1020, 949, 805 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.42 (s, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 7.01 (d, *J* = 3.2 Hz, 1H), 6.40 (d, *J* = 3.2 Hz, 1H), 3.98–3.92 (m, 1H), 3.90 (t, *J* = 8.0 Hz, 2H), 3.75 (s, 3H), 3.67 (t, *J* = 8.0 Hz, 1H), 2.87 (d, *J* = 7.6 Hz, 2H), 2.60 (heptet, *J* = 7.6 Hz, 1H), 2.15 (dd, *J* = 13.2, 8.8 Hz, 1H), 2.06–2.00 (m, 2H), 1.94 (dd, *J* = 13.2, 6.8 Hz, 1H), 1.91–1.84 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 135.4, 131.6, 128.9, 128.6, 122.6, 120.3, 115.1, 109.0, 100.4, 72.3, 67.2, 41.2, 41.0, 39.4, 35.9, 32.8, 24.4 ppm; HRMS (ESI): calcd for $C_{17}H_{22}NO_2^+$ $[M+H]^+$: 272.1645, found: 272.1640.



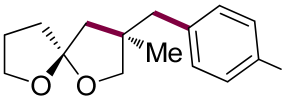
2k

2k was prepared as a colorless oil (82% yield, dr = 8 : 1) according to General Procedure B. R_f = 0.36 (petroleum ether/EtOAc = 5 : 1); IR (film): ν_{max} = 3098, 3046, 2942, 2879, 1670, 1606, 1581, 1498, 1444, 1341, 1299, 1267, 1241, 1154, 1018, 950, 824, 751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.21 (d, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 3.2 Hz, 1H), 6.95 (d, *J* = 6.8 Hz, 1H), 6.55 (d, *J* = 3.2 Hz, 1H), 3.99–3.89 (m, 3H), 3.79 (s, 3H), 3.74 (t, *J* = 8.0 Hz, 1H), 3.08 (d, *J* = 7.6 Hz, 2H), 2.77 (heptet, *J* = 8.0 Hz, 1H), 2.17 (dd, *J* = 13.2, 8.8 Hz, 1H), 2.09–1.98 (m, 3H), 1.94–1.84 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 136.7, 133.1, 128.3, 127.9, 121.6, 119.0, 115.1, 107.3, 99.3, 72.5, 67.2, 41.2, 39.7, 36.8, 35.9, 32.9, 24.4 ppm; HRMS (ESI): calcd for $C_{17}H_{22}NO_2^+$ $[M+H]^+$: 272.1645, found: 272.1639.



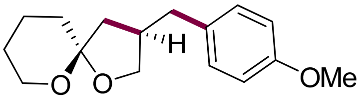
2l

2l was prepared as a white solid (65% yield, dr = 1.2 : 1) according to General Procedure B. R_f= 0.56 (petroleum ether/EtOAc = 5 : 1); Mp. 82–83 °C; IR (film): ν_{max} = 3070, 3035, 2932, 2856, 1609, 1584, 1510, 1445, 1334, 1285, 1245, 1178, 1112, 1034, 998, 847, 818, 759, 634 cm^{-1}; (*one isomer*) ^{1}H NMR (400 MHz, C_6D_6): *δ* = 6.98 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 3.92 (dt, *J* = 8.0, 2.0 Hz, 1H), 3.63 (q, *J* = 5.6 Hz, 1H), 3.36 (s, 3H), 2.64–2.56 (m, 2H), 2.29–2.21 (m, 1H), 2.07–1.82 (m, 6H), 1.72–1.62 (m, 3H), 1.61–1.49 (m, 4H), 1.48–1.35 (m, 1H), 1.25–1.10 (m, 2H) ppm; ^{13}C NMR (100 MHz, C_6D_6): *δ* = 158.5, 133.4, 129.9 (2C), 114.2 (2C), 112.4, 83.5, 66.6, 54.7, 50.2, 41.5, 38.6, 38.1, 35.7, 33.0, 26.4, 24.9, 23.6, 22.5 ppm; HRMS (ESI): calcd for $C_{20}H_{29}O_3^+$ $[M+H]^+$: 317.2111, found: 317.2112.



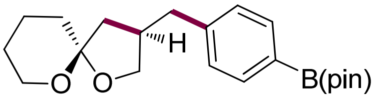
2m

2m was prepared as a colorless oil (51% yield, dr > 20 : 1) according to General Procedure B. R_f = 0.31 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 3079, 2976, 2934, 2875, 1612, 1517, 1456, 1400, 1362, 1324, 1273, 1146, 1090, 1022, 858, 666 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.72 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 3.97–3.88 (m, 2H), 3.85 (d, J = 8.4 Hz, 1H), 3.44 (d, J = 8.4 Hz, 1H), 2.84 (d, J = 12.8 Hz, 1H), 2.77 (d, J = 12.8 Hz, 1H), 2.20 (d, J = 13.6 Hz, 1H), 2.10–2.02 (m, 2H), 1.96–1.85 (m, 2H), 1.76 (d, J = 13.2 Hz, 1H), 1.34 (s, 12H), 1.00 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 142.4, 134.5 (2C), 129.8, 129.6, 115.3, 83.7 (2C), 78.0, 67.1, 48.1, 45.2, 43.4, 36.8, 24.86, 24.85 (4C), 24.5 ppm (The boron-bound carbon was not detected due to quadrupolar relaxation of boron); ESI–MS: m/z [M+H]$^+$: 359.3.



2n

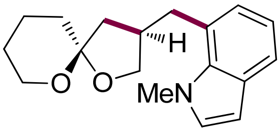
2n was prepared as a colorless oil (87% yield, dr = 8 : 1) according to General Procedure B. R_f= 0.42 (petroleum ether/EtOAc = 10 : 1); IR (film): ν_{max} = 2940, 2868, 1612, 1512, 1246, 1178, 1077, 1037, 1013, 979, 808 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.08 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.4 Hz, 2H), 3.94 (t, J = 8.0 Hz, 1H), 3.87 (td, J = 11.6, 3.2 Hz, 1H), 3.78 (s, 3H), 3.64–3.62 (m, 1H), 3.61 (t, J = 8.4 Hz, 1H), 2.70 (d, J = 8.0 Hz, 2H), 2.51 (heptet, J = 8.0 Hz, 1H), 1.89 (dd, J = 13.2, 9.6 Hz, 1H), 1.84–1.75 (m, 1H), 1.72 (d, J = 6.0 Hz, 1H), 1.69–1.26 (m, 5H) ppm; ^{13}C / DEPT NMR (100 MHz, CDCl$_3$): δ = 157.9 (s), 133.1 (s), 129.5 (d, 2C), 113.8 (d, 2C), 106.3 (s), 72.1 (t), 61.7 (t), 55.2 (q), 44.2 (t), 40.2 (d), 38.8 (t), 34.2 (t), 25.1 (t), 20.0 (t) ppm; HRMS (APCI): m/z calcd for $C_{16}H_{23}O_3^+$ [M+H]$^+$: 263.1642, found: 263.1635.



2o

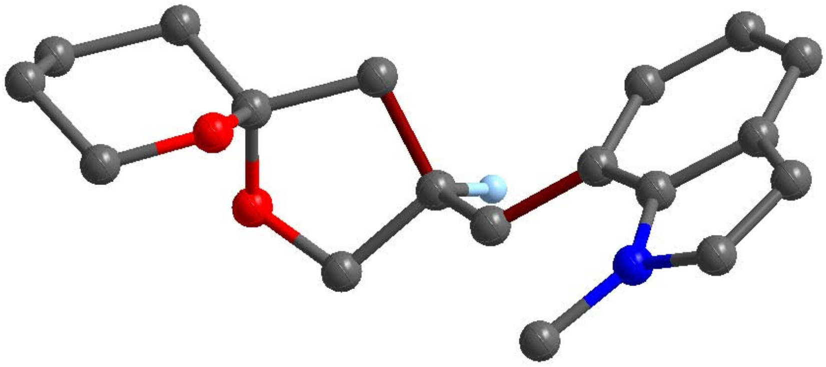
2o was prepared as a colorless oil (72% yield, dr = 6 : 1) according to General

Procedure B. R_f = 0.33 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 3046, 2979, 2940, 2868, 1611, 1518, 1444, 1361, 1270, 1144, 1090, 1024, 964, 859, 737, 661 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6): δ = 8.12 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 3.98 (td, *J* = 12.0, 2.0 Hz, 1H), 3.86 (t, *J* = 8.0 Hz, 1H), 3.62 (t, *J* = 8.0 Hz, 1H), 3.60–3.55 (m, 1H), 2.62–2.52 (m, 2H), 2.31–2.25 (m, 1H), 1.94–1.88 (m, 1H), 1.77 (dd, *J* = 9.2, 5.6 Hz, 1H), 1.63 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.56 (dd, *J* = 11.6, 4.0 Hz, 2H), 1.48–1.40 (m, 2H), 1.30–1.21 (m, 1H), 1.12 (s, 12H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 145.3, 136.0 (2C), 128.9 (2C), 106.5, 84.0 (2C), 72.6, 61.9, 44.9, 40.7, 40.5, 34.9, 26.0, 25.3 (4C), 20.9 ppm (The boron-bound carbon was not detected due to quadrupolar relaxation of boron); HRMS (ESI): calcd. for $C_{21}H_{32}BO_4^+$ [M+H]$^+$: 359.2392, found: 359.2389.



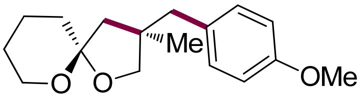
2p

2p was prepared as a colorless solid (58% yield, dr = 6 : 1) according to General Procedure B. R_f = 0.43 (petroleum ether/EtOAc = 5 : 1); Mp. 90–91 °C; IR (film): ν_{max} = 3053, 2940, 2870, 1628, 1519, 1445, 1316, 1221, 1168, 1080, 1017, 978, 808, 721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 7.6 Hz, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 2.8 Hz, 1H), 6.45 (d, *J* = 2.8 Hz, 1H), 4.03 (s, 3H), 4.00 (t, *J* = 8.0 Hz, 1H), 3.90 (td, *J* = 11.2, 2.8 Hz, 1H), 3.73 (t, *J* = 8.0 Hz, 1H), 3.65 (dt, *J* = 11.6, 2.0 Hz, 1H), 3.32 (dd, *J* = 14.4, 8.0 Hz, 1H), 3.22 (dd, *J* = 14.4, 7.6 Hz, 1H), 2.69 (heptet, *J* = 6.0 Hz, 1H), 1.94 (dd, *J* = 13.2, 9.6 Hz, 1H), 1.84 (dd, *J* = 13.2, 5.6 Hz, 1H), 1.82–1.76 (m, 1H), 1.72 (dd, *J* = 12.8, 4.0 Hz, 1H), 1.68–1.60 (m, 2H), 1.59–1.51 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.7, 130.9, 130.3, 124.5, 123.4, 119.5, 119.3, 106.3, 101.1, 72.0, 61.7, 44.1, 40.1, 37.0, 36.1, 34.1, 25.1, 20.0 ppm; HRMS (ESI): calcd. for $C_{18}H_{24}NO_2^+$ [M+H]$^+$: 286.1802, found: 286.1801. This spiroketal product was dissolved in CH_2Cl_2. After a few days, colorless single crystals were obtained by slow evaporation of solvent at room temperature.



X-ray crystal data of **2p** (selected H atoms have been omitted for clarity)

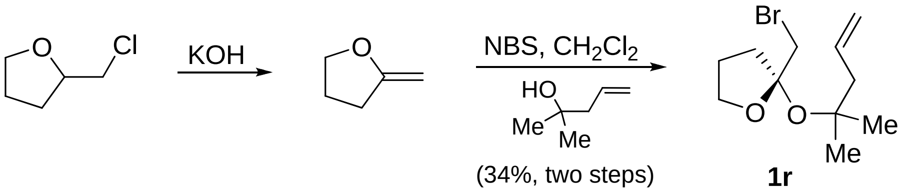
Empirical formula	$C_{18}H_{23}NO_2$
Temperature (K)	296(2)
Crystal color	colorless
Formula weight	285.37
Crystal system	Monoclinic
Space group	$P2_1/n$
a (Å)	7.335(4)
b (Å)	11.239(6)
c (Å)	18.641(10)
α (°)	90.00
β (°)	98.321(6)
γ (°)	90.00
V (Å ^{3})	1520.6(15)
Z	4
Density (calculated) (g/cm^3)	1.247
F (000)	616
λ (Å)	0.71073
Reflections collected	10164
Independent reflections	2639
θ Range for data collection (°)	2.12—24.92
Index range	$-8 \leq h \leq 8$ $-13 \leq k \leq 13$ $-21 \leq l \leq 22$
Final R indices [I>2σ(I)]	$R_1 = 0.1046$, $wR_2 = 0.2537$
Largest difference peak and hole [e Å $^{-3}$]	0.630, –0.223



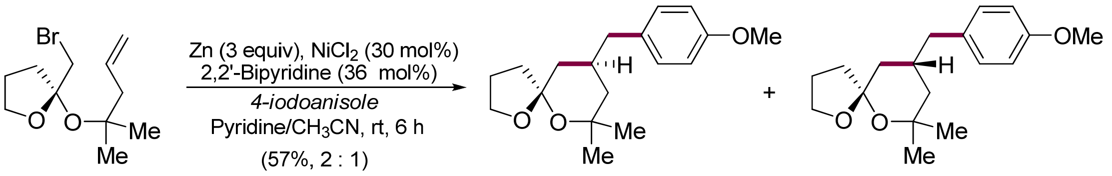
2q

2q was prepared as a colorless oil (38% yield, dr > 20 : 1) according to General Procedure B. R_f = 0.18 (petroleum ether/EtOAc = 10 : 1); IR (film): ν_{max} = 2933, 2867, 1611, 1582, 1512, 1460, 1366, 1247, 1176, 1079, 1021, 837, 809 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.07 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 3.90 (td, J = 11.2, 3.2 Hz, 1H), 3.86 (d, J = 8.0 Hz, 1H), 3.79 (s, 3H), 3.63 (dt, J = 11.2, 2.4 Hz, 1H), 3.47 (d, J = 8.0 Hz, 1H), 2.74 (d, J = 13.6 Hz, 1H), 2.69 (dd, J = 13.6 Hz, 1H), 2.00 (d, J = 13.6 Hz, 1H), 1.86–1.75 (m, 1H), 1.74–1.68 (m, 2H), 1.66–1.60 (m, 1H), 1.58–1.52 (m, 1H), 1.50 (d, J = 13.6 Hz, 2H), 1.00 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.0, 131.3, 130.9 (2C), 113.4 (2C), 106.7, 77.9, 61.8, 55.2, 51.7, 44.8, 43.4, 35.2, 25.7, 25.1, 20.9 ppm; HRMS (ESI): calcd. for $C_{17}H_{25}O_3^+$ [M+H]$^+$: 277.1798, found: 277.1796.

6-*Exo-trig* Cyclization–Coupling



To an oven-dried round bottom flask was added 1,1-dimethyl homoallyl alcohol (600 mg, 6 mmol) and dry CH_2Cl_2 (10 mL). The resulting solution was cooled to –78 °C and freshly prepared 2-methylenetetrahydrofuran[4] (5 mmol) was was introduced followed by the addition of *N*-bromosuccinimide (980 mg, 5.5 mmol, recrystallized from acetone) portionwise. The reaction mixture was stirred for 20 min at this temperature and then quenched by H_2O (10 mL). The aqueous layer was extracted with Et_2O (2 × 50 mL), and the combined organic layers were washed with water (3 × 10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether/EtOAc = 50 : 1) on silica gel (basified with 1% Et_3N) to furnish the desired β-bromo ketal **1r** (447 mg, 34%, over two steps) as the pale yellow oil. R_f = 0.64 (petroleum ether/EtOAc = 5 : 1); ^{1}H NMR (400 MHz, C_6D_6): δ = 5.99–5.88 (m, 1H), 5.05 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.01 (dd, *J* = 17.2, 1.2 Hz, 1H), 3.76 (td, *J* = 11.6, 4.0 Hz, 1H), 3.60 (q, *J* = 8.0 Hz, 1H), 3.47 (d, *J* = 10.4 Hz, 1H), 3.39 (d, *J* = 10.4 Hz, 1H), 2.29 (dd, *J* = 13.6, 7.2 Hz, 1H), 2.18 (dd, *J* = 13.6, 7.6 Hz, 1H), 2.01–1.87 (m, 2H), 1.77–1.67 (m, 1H), 1.42–1.33 (m, 1H), 1.23 (s, 3H), 1.22 (s, 3H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 135.7, 117.1, 108.9, 76.6, 70.4, 49.3, 39.6, 38.3, 27.9, 27.4, 24.8 ppm; ESI–MS: *m/z* 301.1 $[M+K]^+$.



1r **2r** **2r'**

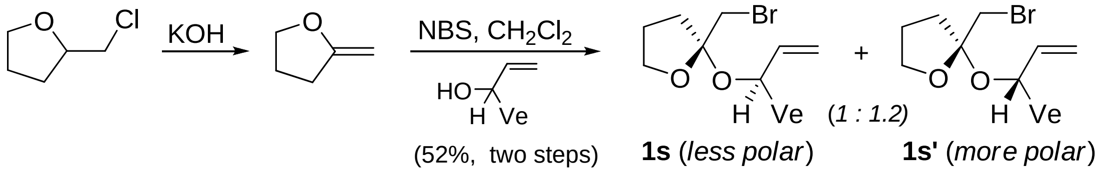
To a stirred slurry of Zn (78 mg, 1.2 mmol) and $NiCl_2$ (16 mg, 0.12 mmol) in pyridine (0.5 mL) was added 2,2′-bipyridine (22 mg, 0.15 mmol) at room temperature. Then the temperature rose to 55 °C and vigorous stirring was continued for 15 min. The resulting black Ni(0) complex was cooled to room temperature, to which the solution of 4-iodoanisole (112 mg, 0.48 mmol) and β-bromo ketal **1r** (105 mg, 0.4 mmol) in CH_3CN (4 mL) was added dropwise over a 10-min period. After stirring for 6 h, the mixture was filtered with a short plug of silica (elution with 30 mL Et_2O) and washed with water and brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography (petroleum ether/EtOAc = 20 : 1) on silica gel to afford desired spiroketal **2r** (*less polar*) and **2r′** (*more polar*) as the colorless oils (66 mg, 57%, dr = 2:1).

(**2r**): a colorless oil; R_f = 0.56 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 3050, 2968, 2934, 2839, 1610, 1584, 1509, 1462, 1376, 1270, 1246, 1179, 1038, 1001, 972, 824, 738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.07 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 3.87 (dd, *J* = 8.0, 6.8 Hz, 1H), 3.85 (t, *J* = 6.8 Hz, 1H), 3.79 (s, 3H), 2.51 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.40 (dd, *J* = 13.2, 7.6 Hz, 1H), 2.35–2.24 (m, 1H), 2.08–1.98 (m, 1H), 1.89 (td, *J* = 8.8, 3.6 Hz, 1H), 1.83–1.74 (m, 1H), 1.71 (dd, *J* = 11.2, 2.0 Hz, 1H), 1.63 (dd, *J* = 8.4, 2.0 Hz, 1H), 1.54 (dd, *J* = 16.0, 2.8 Hz, 1H), 1.32

(t, *J* = 12.8 Hz, 1H), 1.26 (s, 3H), 1.13 (s, 3H), 1.04 (t, *J* = 12.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.8, 132.1, 130.0 (2C), 113.6 (2C), 106.6, 73.0, 66.6, 55.2, 42.9, 42.7, 40.1, 39.3, 32.8, 30.3, 26.5, 23.7 ppm; HRMS (ESI): calcd. for $C_{18}H_{26}NaO_3^+$ $[M+Na]^+$: 313.1774, found: 313.1775.

(**2r′**): a colorless oil; R_f = 0.41 (petroleum ether/EtOAc = 4 : 1); IR (film): ν_{max} = 2970, 2930, 1612, 1584, 1512, 1461, 1364, 1299, 1246, 1177, 1035, 1021, 999, 825 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.08 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.96 (t, *J* = 7.2 Hz, 1H), 3.88–3.83 (m, 1H), 3.80 (s, 3H), 2.53 (d, *J* = 8.0 Hz, 2H), 2.07–1.96 (m, 3H), 1.89–1.81 (m, 2H), 1.69–1.63 (m, 1H), 1.49 (ddd, *J* = 13.2, 4.0, 1.6 Hz, 1H), 1.40 (dd, *J* = 13.6, 10.8 Hz, 2H), 1.26 (s, 3H), 1.14 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.8, 132.3, 139.9 (2C), 113.6 (2C), 107.5, 73.3, 66.9, 55.2, 42.5, 41.2, 40.1, 38.5, 32.1, 31.6, 28.0, 24.7 ppm; HRMS (ESI): calcd. for $C_{18}H_{26}NaO_3^+$ $[M+Na]^+$: 313.1774, found: 313.1774.

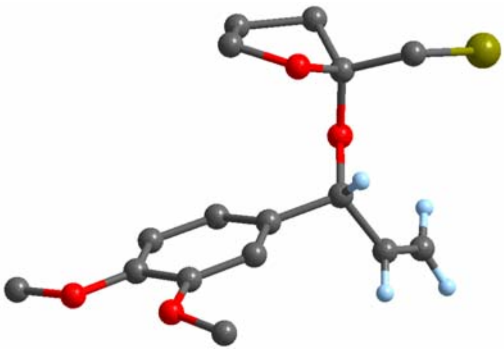
***Stereospecific* Cyclization–Intermolecular Cross-Coupling**



To an oven-dried round bottom flask was added 1-veratryl allyl alcohol (1.2 g, 6 mmol, prepared from veratraldehyde and vinylmagnesium bromide in 95% yield) and dry CH_2Cl_2 (15 mL). The resulting solution was cooled to –40 °C and freshly prepared 2-methylenetetrahydrofuran[4] (5 mmol) was was introduced followed by the addition of *N*-bromosuccinimide (980 mg, 5.5 mmol, recrystallized from acetone). The reaction mixture was stirred for 1 h then slowly warmed to room temperature over a 2 h period. The reaction mixture was diluted with Et_2O (30 mL) and poured into a separatory funnel that contained H_2O (10 mL). The aqueous layer was extracted with Et_2O (2 × 30 mL), and the combined organic layers were washed with water (3 × 10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether/EtOAc = 20 : 1) on silica gel to furnish the desired β-bromo ketal **1s** (*less polar*) and **1s′** (*more polar*) (930 mg, 52%, dr = 1:1.2, over two steps).

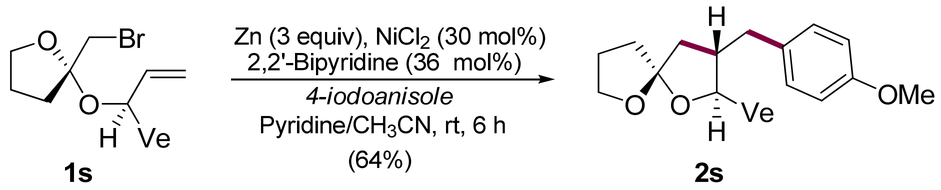
(**1s**): a colorless oil; R_f = 0.43 (petroleum ether/EtOAc = 5 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.91 (d, J = 1.6 Hz, 1H), 6.87 (dd, J = 8.0, 1.6 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 5.94 (ddd, J = 17.2, 10.4, 5.6 Hz, 1H), 5.23 (d, J = 5.6 Hz, 1H), 5.16 (dd, J = 17.2, 1.6 Hz, 1H), 5.08 (dd, J = 10.4, 1.2 Hz, 1H), 4.07–4.03 (m, 2H), 3.90 (s, 3H), 3.87 (s, 3H), 3.36 (d, J = 10.8 Hz, 1H), 3.26 (d, J = 10.8 Hz, 1H), 2.22–2.10 (m, 3H), 2.02–1.94 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.0, 148.4, 140.3, 134.9, 118.9, 114.1, 110.9, 110.0, 108.3, 73.9, 69.8, 55.86, 55.85, 36.2, 35.0, 24.5 ppm; HRMS (ESI): calcd. for $C_{16}H_{21}BrNaO_4^+$ $[M+Na]^+$: 379.0515, found: 379.0508.

(**1s′**): a colorless solid; R_f = 0.39 (petroleum ether/EtOAc = 5 : 1); Mp. 46–48 °C; ^{1}H NMR (400 MHz, C_6D_6): δ = 6.94 (s, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.61 (d, J = 8.0 Hz, 1H), 6.06 (ddd, J = 16.0, 10.4, 6.8 Hz, 1H), 5.23 (d, J = 6.8 Hz, 1H), 5.20 (d, J = 16.0 Hz, 1H), 5.01 (d, J = 10.4 Hz, 1H), 3.57–3.52 (m, 2H), 3.45 (s, 3H), 3.40 (s, 3H), 3.47–3.39 (m, 2H), 2.06 (ddd, J = 12.0, 8.4, 3.6 Hz, 1H), 1.93 (dt, J = 12.8, 9.2 Hz, 1H), 1.71–1.61 (m, 1H), 1.42–1.33 (m, 1H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 150.5, 149.8, 141.5, 136.1, 119.7, 114.6, 112.4, 111.6, 109.1, 75.0, 70.2, 56.0, 55.9, 36.9, 35.4, 25.0 ppm; HRMS (ESI): calcd. for $C_{16}H_{21}BrNaO_4^+$ $[M+Na]^+$: 379.0515, found: 379.0508. This product was dissolved in EtOAc and hexane (8 : 1). After a few days, colorless single crystals were obtained by slow evaporation of solvent at room temperature.

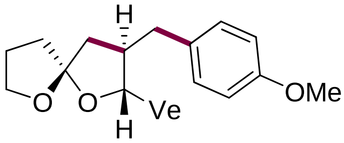


X-ray crystal data of **1s′** (selected H atoms have been omitted for clarity)

Empirical formula	$C_{16}H_{21}BrO_4$
Temperature (K)	296(2)
Crystal color	colorless
Formula weight	357.24
Crystal system	Monoclinic
Space group	$P2_1/n$
a (Å)	8.3184(19)
b (Å)	10.279(2)
c (Å)	19.396(4)
α (°)	90.00
β (°)	99.917(2)
γ (°)	90.00
V (Å^3)	1633.7(6)
Z	4
Density (calculated) (g/cm^3)	1.452
F (000)	736
λ (Å)	0.71073
Reflections collected	11523
Independent reflections	3031
θ Range for data collection (°)	2.25—25.50
Index range	$-10 \leq h \leq 10$ $-12 \leq k \leq 11$ $-22 \leq l \leq 23$
Final R indices [I>2σ(I)]	$R_1 = 0.0461$, $wR_2 = 0.0932$
Largest difference peak and hole [e Å^{-3}]	0.547, –0.366

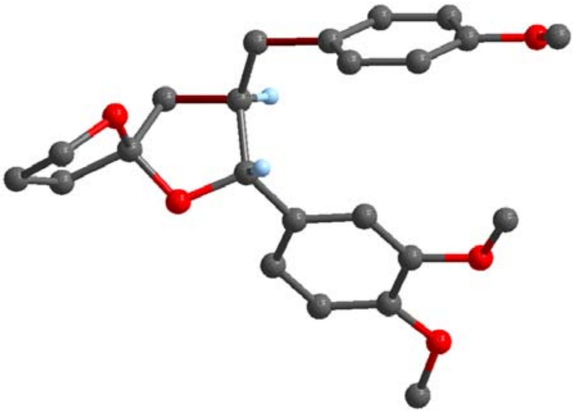


To a stirred slurry of Zn (40 mg, 0.6 mmol) and $NiCl_2$ (8 mg, 0.06 mmol) in pyridine (0.5 mL) was added 2,2′-bipyridine (11 mg, 0.07 mmol) at room temperature. Then the temperature rose to 55 °C and vigorous stirring was continued for 10 min. The resulting black Ni(0) complex was cooled to room temperature, to which the solution of 4-iodoanisole (57 mg, 0.24 mmol) and β-bromo ketal **1s** (71 mg, 0.2 mmol) in CH_3CN (4 mL) was added dropwise over a 10-min period. After stirring for 6 h, the mixture was filtered with a short plug of silica (elution with 30 mL Et_2O) and washed with water and brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash column chromatography (petroleum ether/EtOAc = 10 : 1) on silica gel to afford the desired spiroketal **2s** (49 mg, 64%) as a colorless oil. $R_f = 0.30$ (petroleum ether/EtOAc = 3 : 1); IR (film): ν_{max} = 3061, 2934, 2836, 1610, 1513, 1592, 1513, 1462, 1344, 1246, 1159, 1136, 1030, 935, 815 cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ = 7.35 (d, J = 1.6 Hz, 1H), 7.05 (dd, J = 8.4, 1.6 Hz, 1H), 6.85 (d, J = 8.4 Hz, 2H), 6.72 (d, J = 8.4 Hz, 2H), 6.67 (d, J = 8.4 Hz, 1H), 4.62 (d, J = 8.8 Hz, 1H), 4.02 (dt, J = 8.0, 5.6 Hz, 1H), 3.71 (q, J = 7.6 Hz, 1H), 3.59 (s, 3H), 3.44 (s, 3H), 3.31 (s, 3H), 2.96–2.83 (m, 2H), 2.30 (dd, J = 12.8, 9.6 Hz, 1H), 2.14 (dd, J = 11.6, 5.6 Hz, 1H), 2.06 (ddd, J = 12.0, 8.4, 3.6 Hz, 1H), 1.98–1.89 (m, 1H), 1.72 (t, J = 12.0 Hz, 1H), 1.67 (dd, J = 12.0, 8.0 Hz, 1H), 1.60–1.52 (m, 1H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 159.0, 150.9, 150.1, 136.8, 133.0, 130.3 (2C), 120.0, 114.6, 114.5 (2C), 112.3, 111.8, 88.0, 67.3, 56.1, 55.9, 55.1, 51.0, 42.9, 37.8, 35.7, 25.2 ppm; HRMS (ESI): calcd. for $C_{23}H_{29}O_5^+$ $[M+H]^+$: 385.2010, found: 385.2017.



2s′

2s′ was prepared as a colorless solid (73% yield) starting from **1s′** (*more polar isomer*) according to the above procedure for **2s**. $R_f = 0.23$ (petroleum ether/EtOAc = 3 : 1); Mp. 71–73 °C; IR (film): ν_{max} = 3068, 2953, 2873, 2835, 1612, 1592, 1515, 1462, 1329, 1253, 1158, 1132, 1027, 810, 762 cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ = 6.96 (dd, J = 8.4, 2.0 Hz, 1H), 6.93 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 2.0 Hz, 1H), 6.73 (dd, J = 6.8, 2.0 Hz, 2H), 6.65 (d, J = 8.4 Hz, 1H), 4.95 (d, J = 7.2 Hz, 1H), 4.00 (dt, J = 8.0, 6.0 Hz, 1H), 3.82 (dt, J = 8.0, 6.0 Hz, 1H), 3.46 (s, 3H), 3.41 (s, 3H), 3.30 (s, 3H), 3.00 (dd, J = 13.6, 6.0 Hz, 1H), 2.69 (dd, J = 13.6, 9.6 Hz, 1H), 2.47–2.37 (m, 1H), 2.21–2.10 (m, 1H), 2.16 (t, J = 8.0 Hz, 2H), 1.98–1.87 (m, 1H), 1.73–1.65 (m, 1H), 1.62–1.53 (m, 1H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 159.0, 150.6, 150.1, 135.6, 133.5, 130.6 (2C), 119.4, 115.0, 114.6 (2C), 112.6, 111.4, 85.7, 67.6, 56.04, 56.00, 55.1, 50.9, 41.8, 39.1, 36.5, 25.2 ppm; HRMS (ESI): calcd. for $C_{23}H_{29}O_5^+$ $[M+H]^+$: 385.2010, found: 385.2009. This spiroketal product was dissolved in EtOAc and hexane (4 : 1). After a few days, colorless single crystals were obtained by slow evaporation of solvent at room temperature.

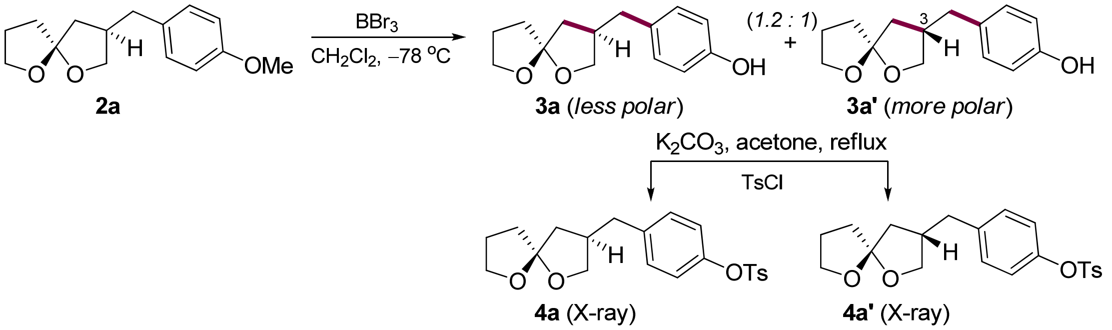


X-ray crystal data of **2s′** (selected H atoms have been omitted for clarity)

Empirical formula	$C_{23}H_{28}O_5$
Temperature (K)	296(2)
Crystal color	colorless
Formula weight	384.45
Crystal system	Triclinic
Space group	*P*-1
a (Å)	6.143(14)
b (Å)	8.81(2)
c (Å)	19.64(4)
α (°)	83.80(2)
β (°)	83.37(2)
γ (°)	76.77(2)
V (Å^3)	1024(4)
Z	2
Density (calculated) (g/cm^3)	1.247
F (000)	412
λ (Å)	0.71073

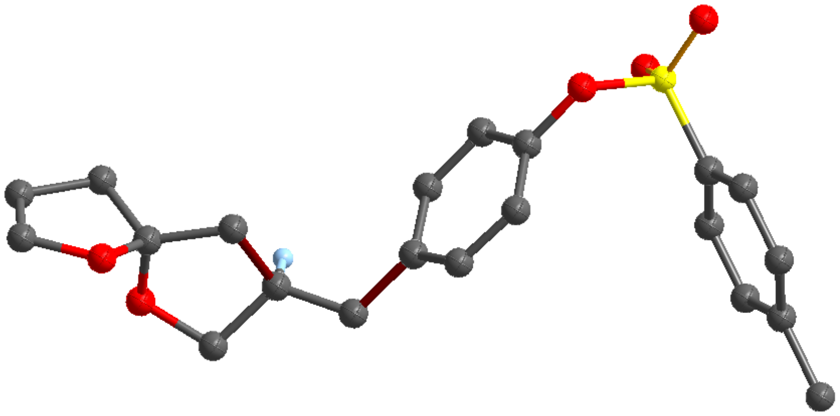
Reflections collected	5691
Independent reflections	3531
θ Range for data collection (°)	2.38—25.10
Index range	$-5 \leq h \leq 7$ $-10 \leq k \leq 10$ $-23 \leq l \leq 23$
Final R indices [I>2σ(I)]	$R_1 = 0.0963$, $wR_2 = 0.2607$
Largest difference peak and hole [e Å^{-3}]	0.272, –0.271

Epimerization



To the solution of spiroketal **2a** (140 mg, 0.56 mmol) in CH_2Cl_2 (2 mL) was added BBr_3 (0.1 M in CH_2Cl_2, 17 mL, 3 equiv) dropwise at –78 °C. The reaction mixture was kept for 2 h at this temperature and then quenched carefully by saturated aqueous $NaHCO_3$ (5 mL) and diluted with CH_2Cl_2 (10 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic layers were washed with water and brine (5 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (petroleum/EtOAc = 3 : 1) on silica gel to afford free phenol **3a** (70 mg, *less polar*) and C(3) isomerized **3a′** (58 mg, *more polar*) as the colorless oils.

To the solution of the above free phenol **3a** (40 mg, 0.17 mmol) in acetone (2 mL) was added K_2CO_3 (164 mg, 1.19 mmol, 7 equiv) followed by the addition of TsCl (37 mg, 0.19 mmol, 1.1 equiv) after 10 min. The resulting mixture was heated at reflux for 4 h and quenched by saturated aqueous $NaHCO_3$ (5 mL) and diluted with EtOAc (15 mL) and poured into a separatory funnel. The aqueous layer was extracted with EtOAc (3 × 10 mL), and the combined organic layers were washed with water and brine (5 mL) respectively, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether/EtOAc = 8 : 1) on silica gel to furnish the desired **4a** (61 mg, 92%), which was dissolved in EtOAc and hexane. After a few days, colorless single crystals were obtained by slow evaporation of solvent at room temperature. R_f = 0.22 (petroleum ether/EtOAc = 4 : 1); Mp. 84–86 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 3.95–3.86 (m, 1H), 3.87 (t, J = 8.0 Hz, 2H), 3.58 (t, J = 8.0 Hz, 1H), 2.75 (dd, J = 8.0, 3.2 Hz, 2H), 2.49 (heptet, J = 7.2 Hz, 1H), 2.45 (s, 3H), 2.12 (dd, J = 13.6, 9.2 Hz, 1H), 2.06–1.99 (m, 2H), 1.94–1.84 (m, 2H), 1.83 (dd, J = 8.0, 3.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.9, 145.2, 139.8, 132.5, 129.71 (2C), 129.67 (2C), 128.5 (2C), 122.3 (2C), 115.0, 71.9, 67.3, 40.6, 40.1, 38.7, 35.7, 24.4, 21.7 ppm.

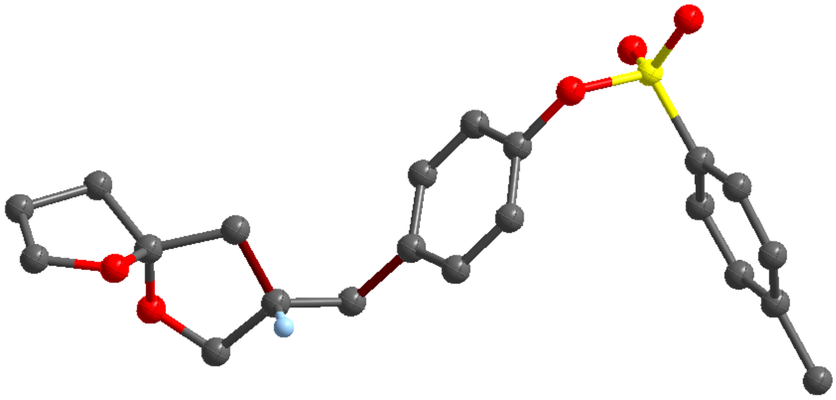


X-ray crystal data of **4a** (selected H atoms have been omitted for clarity)

Empirical formula	$C_{21}H_{24}O_5S$
Temperature (K)	293(2)
Crystal color	colorless
Formula weight	388.46
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	11.215(18)
b (Å)	9.284(15)
c (Å)	19.41(3)

α (°)	90.00
β (°)	90.341(19)
γ (°)	90.00
V (Å^3)	2021(6)
Z	4
Density (calculated) (g/cm^3)	1.277
F (000)	824
λ (Å)	0.71073
Reflections collected	7900
Independent reflections	3511
θ Range for data collection (°)	2.10—25.00
Index range	$-7 \leq h \leq 13$ $-11 \leq k \leq 10$ $-23 \leq l \leq 19$
Final R indices [I>2σ(I)]	$R_1 = 0.1031$, $wR_2 = 0.2647$
Largest difference peak and hole [e Å^{-3}]	1.022, –0.389

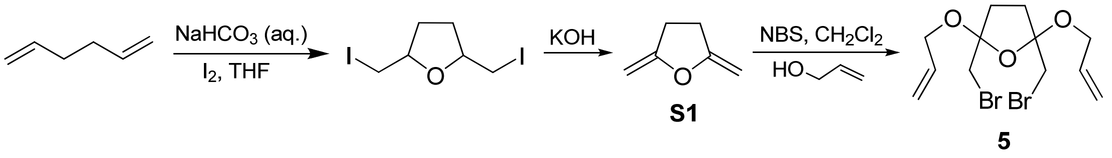
4a′ was prepared as a white solid starting from **3a′** (*more polar isomer*) according to the above procedure for **4a**. R_f = 0.20 (petroleum ether/EtOAc = 4 : 1); Mp. 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 3.97 (t, J = 8.0 Hz, 1H), 3.94–3.88 (m, 1H), 3.82 (t, J = 8.0 Hz, 1H), 3.48 (t, J = 8.0 Hz, 1H), 2.72 (heptet, J = 7.6 Hz, 1H), 2.66–2.61 (m, 2H), 2.45 (s, 3H), 2.09 (dd, J = 12.8, 7.2 Hz, 1H), 2.05 (d, J = 7.2 Hz, 1H), 2.09–1.99 (m, 1H), 1.95–1.86 (m, 2H), 1.68 (dd, J = 12.8, 9.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.0, 145.3, 139.5, 132.5, 129.7 (2C), 129.6 (2C), 128.5 (2C), 122.3 (2C), 114.9, 71.9, 67.2, 41.4, 39.7, 39.0, 35.0, 24.5, 21.7 ppm; HRMS (ESI): m/z calcd for $C_{21}H_{25}O_5S^+$ [M+H]$^+$: 389.1417, found: 389.1435. This spiroketal product was dissolved in EtOAc and hexane (4 : 1). After a few days, colorless single crystals were obtained by slow evaporation of solvent at room temperature.



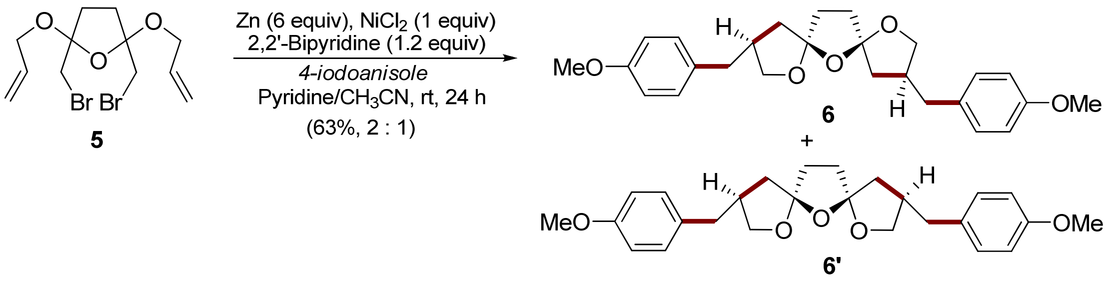
X-ray crystal data of **4a′** (selected H atoms have been omitted for clarity)

Empirical formula	$C_{21}H_{24}O_5S$
Temperature (K)	296(2)
Crystal color	colorless
Formula weight	388.46
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	11.137(11)
b (Å)	9.246(9)
c (Å)	18.976(18)
α (°)	90.00
β (°)	90.813(11)
γ (°)	90.00
V (Å ^{3})	1954(3)
Z	4
Density (calculated) (g/cm^3)	1.321
F (000)	824
λ (Å)	0.71073
Reflections collected	13647
Independent reflections	3616
θ Range for data collection (°)	2.15—25.50
Index range	$-13 \leq h \leq 13$ $-11 \leq k \leq 11$ $-22 \leq l \leq 21$
Final R indices [I>2σ(I)]	$R_1 = 0.1190$, $wR_2 = 0.3704$
Largest difference peak and hole [e Å $^{-3}$]	0.559, –0.644

Stereocontrolled Synthesis of [5,5,5]-Bisspiroketal



To an oven-dried round bottom flask was added allyl alcohol (1.2 g, 20 mmol) and dry CH_2Cl_2 (15 mL). The resulting solution was cooled to –40 °C and freshly prepared bismethylenetetrahydrofuran **S1**[5] (ca.1.0 g, 10 mmol) was introduced followed by the addition of *N*-bromosuccinimide (3.6 g, 20 mmol, recrystallized from acetone) portionwise. The reaction mixture was stirred at –40 °C for 0.5 h then diluted with Et_2O (60 mL) and poured into a separatory funnel that contained H_2O (10 mL). The aqueous layer was extracted with Et_2O (2 × 60 mL), and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was purified by flash column chromatography (petroleum ether/EtOAc = 50 : 1) on silica gel to furnish the desired β-bromo ketal **5** (*ca.* 1.8:1, 930 mg, 25% yield, over two steps) as a colorless oil. $R_f = 0.57$ (petroleum ether/EtOAc = 10 : 1); IR (film): ν_{max} = 3080, 2981, 2959, 2923, 2868, 1648, 1455 1437, 1328, 1268, 1120, 1073, 1003, 925, 882 cm^{-1}; (*major isomer*) ^1H NMR (400 MHz, $CDCl_3$): δ = 5.96–5.86 (m, 2H), 5.31 (dd, J = 17.2, 1.6 Hz, 2H), 5.17 (dd, J = 10.4, 1.6 Hz, 2H), 4.16–4.00 (m, 4H), 3.64 (d, J = 10.8 Hz, 2H), 3.41 (d, J = 11.2 Hz, 2H), 2.33–2.18 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.3 (2C), 116.6 (2C), 109.1 (2C), 62.7 (2C), 34.8 (2C), 34.2 (2C) ppm; ESI–MS: *m/z* 391.3 $[M+Na]^+$.



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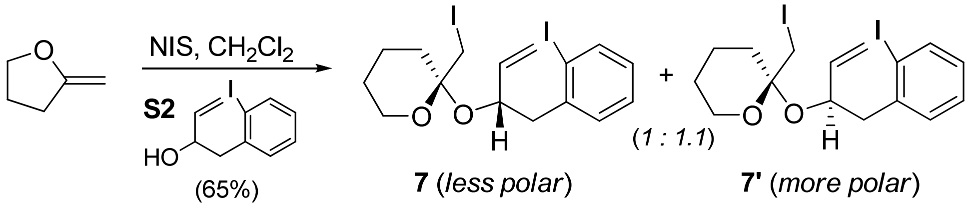
(5) Prepared through DBU (5 g, 33 mmol)-promoted β-elimination of HI in 2,5-bisiodomethyl tetrahydrofuran (4.6 g, 13 mmol) which was synthesized from 1,5-hexadiene according to known procedure: Iqbal, J.; Srivastava, R. R. *Tetrahedron* **1991**, *47*, 3155–3170. Characterization data for labile **S1**: ^1H NMR (400 MHz, C_6D_6): δ = 4.56 (s, 2H), 3.88 (s, 2H), 2.05 (s, 4H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 161.6 (2C), 82.5 (2C), 27.5 (2C).

To a stirred slurry of Zn (117 mg, 1.8 mmol) and $NiCl_2$ (39 mg, 0.3 mmol) in pyridine (1.0 mL) was added 2,2′-bipyridine (56 mg, 0.36 mmol) at room temperature. Then the temperature rose to 55 °C and vigorous stirring was continued for 15 min. The resulting Ni(0) complex was cooled to room temperature, to which the solution of **5** (111 mg, 0.3 mmol) and 4-iodoanisole (281 mg, 1.2 mmol, 4 equiv) in CH_3CN (5 mL) was added dropwise over a 10 min period. Then the reaction mixture was further stirred for 24 h and filtered with a short plug of silica (elution with 100 mL Et_2O). The filtrate was washed with water (2 × 10 mL) and brine (10 mL), dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography (petroleum/EtOAc = 5 : 1) on silica gel to afford separable bisspiroketal **6** (*less polar*, 53 mg, 42%) and **6′** (*more polar*, 26 mg, 21%) as the colorless oils.

(**6**): $R_f = 0.49$ (petroleum ether/EtOAc = 2 : 1); IR (film): $\nu_{max} = 3030, 2942, 2836, 1612, 1583, 1512, 1443, 1349, 1245, 1179, 1116, 1036, 993, 829, 734$ cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.12$ (d, $J = 8.4$ Hz, 4H), 6.83 (d, $J = 8.8$ Hz, 4H), 3.91 (t, $J = 8.0$ Hz, 2H), 3.79 (s, 6H), 3.70 (dd, $J = 8.4, 6.8$ Hz, 2H), 2.80 (dd, $J = 8.0, 6.0$ Hz, 4H), 2.53 (heptet, $J = 7.2$ Hz, 2H), 2.20–2.10 (m, 4H), 2.07–1.97 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 157.9$ (2C), 132.9 (2C), 129.7 (4C), 115.3 (2C), 113.8 (4C), 72.4 (2C), 55.2 (2C), 42.1 (2C), 40.3 (2C), 38.6 (2C), 35.3 (2C) ppm; HRMS (ESI): calcd. for $C_{26}H_{33}O_5^+$ $[M+H]^+$: 425.2323, found: 425.2331.

(**6′**): $R_f = 0.35$ (petroleum ether/EtOAc = 2 : 1); IR (film): $\nu_{max} = 3030, 2939, 2859, 1612, 1583, 1512, 1443, 1300, 1246, 1178, 1036, 989, 882$ cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.11$ (d, $J = 8.8$ Hz, 4H), 6.84 (d, $J = 8.8$ Hz, 4H), 3.99 (t, $J = 8.0$ Hz, 2H), 3.80 (s, 6H), 3.72 (t, $J = 8.0$ Hz, 2H), 2.76 (d, $J = 8.0$ Hz, 4H), 2.51 (heptet, $J = 8.0$ Hz, 2H), 2.22 (q, $J = 6.4$ Hz, 2H), 2.06 (dd, $J = 12.8, 8.4$ Hz, 2H), 1.96 (q, $J = 6.4$ Hz, 2H), 1.88 (dd, $J = 12.8, 6.4$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 157.9$ (2C), 132.9 (2C), 129.6 (4C), 115.3 (2C), 113.8 (4C), 72.7 (2C), 55.2 (2C), 42.4 (2C), 40.4 (2C), 38.4 (2C), 36.1 (2C) ppm; HRMS (ESI): calcd. for $C_{26}H_{33}O_5^+$ $[M+H]^+$: 425.2323, found: 425.2327.

Stereospecific Cyclization-*Intramolecular* Coupling



To an oven-dried round bottom flask was added *N*-iodosuccinimide (1.5 g, 6.7 mmol, 1.3 equiv) and dry CH_2Cl_2 (20 mL). The resulting suspension was cooled to –40 °C and the solution of allyl alcohol **S2**[6] (1.42 g, 5.2 mmol) in CH_2Cl_2 (4 mL) was added dropwise over a 5 min period. After 2 min, the solution of 2-methylenetetrahydrofuran[4] (750 mg, 8.8 mmol, 1.7 equiv) in CH_2Cl_2 (4 mL) was added dropwise over a 5 min period. The reaction mixture was stirred for 30 min then was diluted with Et_2O (60 mL) and poured into a separatory funnel that contained H_2O (10 mL). The aqueous layer was extracted with Et_2O (2 × 30 mL), and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude residue was carefully purified by flash column chromatography (petroleum ether/EtOAc = 50 : 1) on silica gel to furnish the desired β-iodo ketal **7** (*less polar*) and **7′** (*more polar*) (1.68 g, 65%, dr = 1 : 1.1).

(**7**): a white solid; $R_f = 0.28$ (petroleum ether/EtOAc = 10 : 1); Mp. 55–57 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.81$ (d, $J = 8.0$ Hz, 1H), 7.29–7.23 (m, 2H), 6.89 (td, $J = 8.0, 2.4$ Hz, 1H), 6.06 (ddd, $J = 17.2, 10.4, 8.0$ Hz, 1H), 5.15 (d, $J = 17.2$ Hz, 1H) 5.06 (d, $J = 10.4$ Hz, 1H), 4.53 (dt, $J = 8.0, 5.6$ Hz, 1H), 3.43–3.38 (m, 1H), 3.36 (d, $J = 10.8$ Hz, 1H), 3.23 (d, $J = 10.4$ Hz, 1H), 3.11 (dd, $J = 13.2, 8.4$ Hz, 1H), 2.92–2.84 (m, 2H), 1.88 (dd, $J = 10.0, 2.8$ Hz, 1H), 1.67–1.60 (m, 1H), 1.59–1.50 (m, 1H), 1.49–1.42 (m, 1H), 1.41–1.33 (m, 1H), 1.11 (d, $J = 12.0$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 141.4$, 141.0, 139.4, 132.5, 128.2, 127.8, 115.7, 101.3, 97.7, 71.7, 62.2, 47.7, 34.3, 24.5, 18.7, 14.3 ppm; HRMS (ESI): calcd for $C_{16}H_{20}I_2NaO_2^+$ $[M+Na]^+$: 520.9445, found: 520.9455. This spiroketal product was dissolved in

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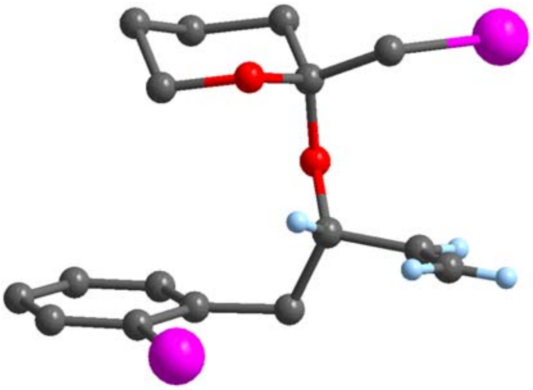
(6) For its preparation, see: Yan, C.-S.; Peng, Y.; Xu, X.-B.; Wang, Y.-W. *Chem.–Eur. J.* **2012**, *18*, 6039.

EtOAc and Hexane (3 : 1). After a few days, colorless single crystals were obtained by slow evaporation of solvent at room temperature.

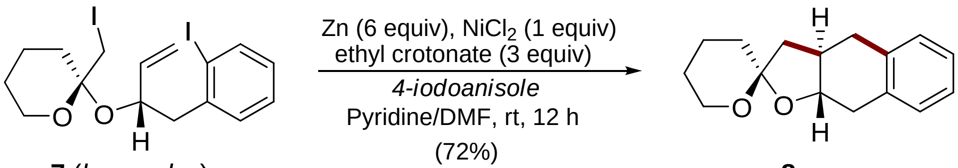


X-ray crystal data of **7** (selected H atoms have been omitted for clarity)

Empirical formula	$C_{16}H_{20}I_2O_2$
Temperature (K)	296(2)
Crystal color	colorless
Formula weight	498.12
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	8.616(4)
b (Å)	22.680(12)
c (Å)	18.209(9)
α (°)	90.00
β (°)	96.020(6)
γ (°)	90.00
V (Å^3)	3539(3)
Z	8
Density (calculated) (g/cm^3)	1.870
F (000)	1904
λ (Å)	0.71073
Reflections collected	13784
Independent reflections	6458
θ Range for data collection (°)	2.12—25.50
Index range	$-10 \leq h \leq 10$ $-26 \leq k \leq 27$ $-12 \leq l \leq 22$

Final *R* indices [I>2σ(*I*)]	$R_1 = 0.0423$, $wR_2 = 0.0718$
Largest difference peak and hole [e Å^{-3}]	0.716, –0.871

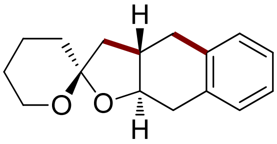
(**7′**): a colorless oil; R_f = 0.23 (petroleum ether/EtOAc = 10 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, J = 8.0 Hz, 1H), 7.23 (d, J = 7.2 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 6.89 (t, J = 8.0 Hz, 1H), 5.92–5.84 (m, 1H), 5.06 (d, J = 17.2 Hz, 1H), 5.04 (d, J = 10.0 Hz, 1H), 4.50 (q, J = 7.8 Hz, 1H), 3.77 (td, J = 12.0, 2.8 Hz, 1H), 3.56–3.53 (m, 1H), 3.29 (d, J = 10.4 Hz, 1H), 3.15 (dd, J = 13.6, 7.6 Hz, 1H), 3.01 (d, J = 10.8 Hz, 1H), 2.91 (dd, J = 13.6, 7.2 Hz, 1H), 1.86 (d, J = 7.2 Hz, 1H), 1.76–1.70 (m, 2H), 1.54–1.44 (m, 2H), 1.42–1.37 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.9, 139.3 (2C), 132.2, 128.2, 127.8, 115.8, 101.2, 97.6, 72.3, 63.2, 47.8, 33.2, 24.7, 19.0, 12.4 ppm; HRMS (ESI): calcd for $C_{16}H_{20}I_2NaO_2^+$ $[M+Na]^+$: 520.9445, found: 520.9434.



7 (*less polar*) **8**

To a stirred slurry of Zn (47 mg, 0.72 mmol) and $NiCl_2$ (16 mg, 0.12 mmol) in pyridine (0.4 mL) was added ethyl crotonate (0.05 mL, 0.36 mmol) at room temperature. Then the temperature rose to 55 °C and vigorous stirring was continued for 15 min. The resulting Ni(0) complex was cooled to room temperature, to which the solution of **7** (60 mg, 0.12 mmol) in DMF (4 mL) was added dropwise over a 20 min period. Then the reaction mixture was further stirred for 12 h and filtered with a short plug of silica (elution with 50 mL Et_2O). The filtrate was washed with water and brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography (petroleum/EtOAc = 20 : 1) on silica gel to afford desired spiroketal **8** as a white solid (21 mg, 72%). R_f = 0.45 (petroleum ether/EtOAc = 5 : 1); Mp. 96–100 °C; IR (film): ν_{max} = 3062, 3014, 2938, 2873, 2849, 1489, 1446, 1359, 1266, 1069, 1041, 971, 901, 746 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ =

7.16–7.07 (m, 4H), 4.01 (td, *J* = 11.2, 3.2 Hz, 1H), 3.89 (sext, *J* = 5.6 Hz, 1H), 3.66 (dt, *J* = 10.8, 2.0 Hz, 1H), 3.23 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.03 (dd, *J* = 16.0, 4.8 Hz, 1H), 2.86 (t, *J* = 13.2 Hz, 1H), 2.70 (t, *J* = 13.2 Hz, 1H), 2.21 (dd, *J* = 12.8, 8.0 Hz, 1H), 1.96–1.84 (m, 1H), 1.90 (dd, *J* = 12.4, 4.8 Hz, 1H), 1.82–1.70 (m, 3H), 1.69–1.51 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.1, 134.8, 130.2, 129.2, 126.01, 125.95, 106.7, 78.7, 62.6, 44.8, 42.0, 35.9, 35.7, 34.2, 25.1, 19.8 ppm; HRMS (ESI): calcd. for $C_{16}H_{21}O_2^+$ $[M+H]^+$: 245.1536, found: 245.1539.



8′

8′ was prepared as a white solid (70% yield) starting from **7′** (*more polar isomer*) according to the above procedure for **8**. R_f = 0.45 (petroleum ether/EtOAc = 5 : 1); Mp. 40–42 °C; IR (film): ν_{max} = 3017, 2939, 2922, 2849, 1490, 1438, 1363, 1262, 1223, 1077, 1034, 974, 899, 805, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14–7.10 (m, 4H), 3.99 (td, *J* = 11.2, 3.2 Hz, 1H), 3.73 (sext, *J* = 5.6 Hz, 1H), 3.65 (dt, *J* = 9.2, 2.0 Hz, 1H), 3.24 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.07 (dd, *J* = 16.0, 4.8 Hz, 1H), 2.92 (t, *J* = 13.6 Hz, 1H), 2.62 (t, *J* = 13.8 Hz, 1H), 2.32–2.19 (m, 2H), 1.97–1.83 (m, 1H), 1.81–1.65 (m, 3H), 1.64–1.49 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.1, 135.0, 130.3, 129.3, 126.0, 125.9, 106.3, 81.2, 62.1, 44.2, 40.2, 36.8, 35.1, 34.0, 25.1, 20.2 ppm; HRMS (ESI): calcd. for $C_{16}H_{21}O_2^+$ $[M+H]^+$: 245.1536, found: 245.1534.

Supporting Information for

Nickel-Mediated Stereocontrolled Synthesis of Spiroketals via Tandem Cyclization–Coupling of β-Bromo Ketals and Aryl Iodides

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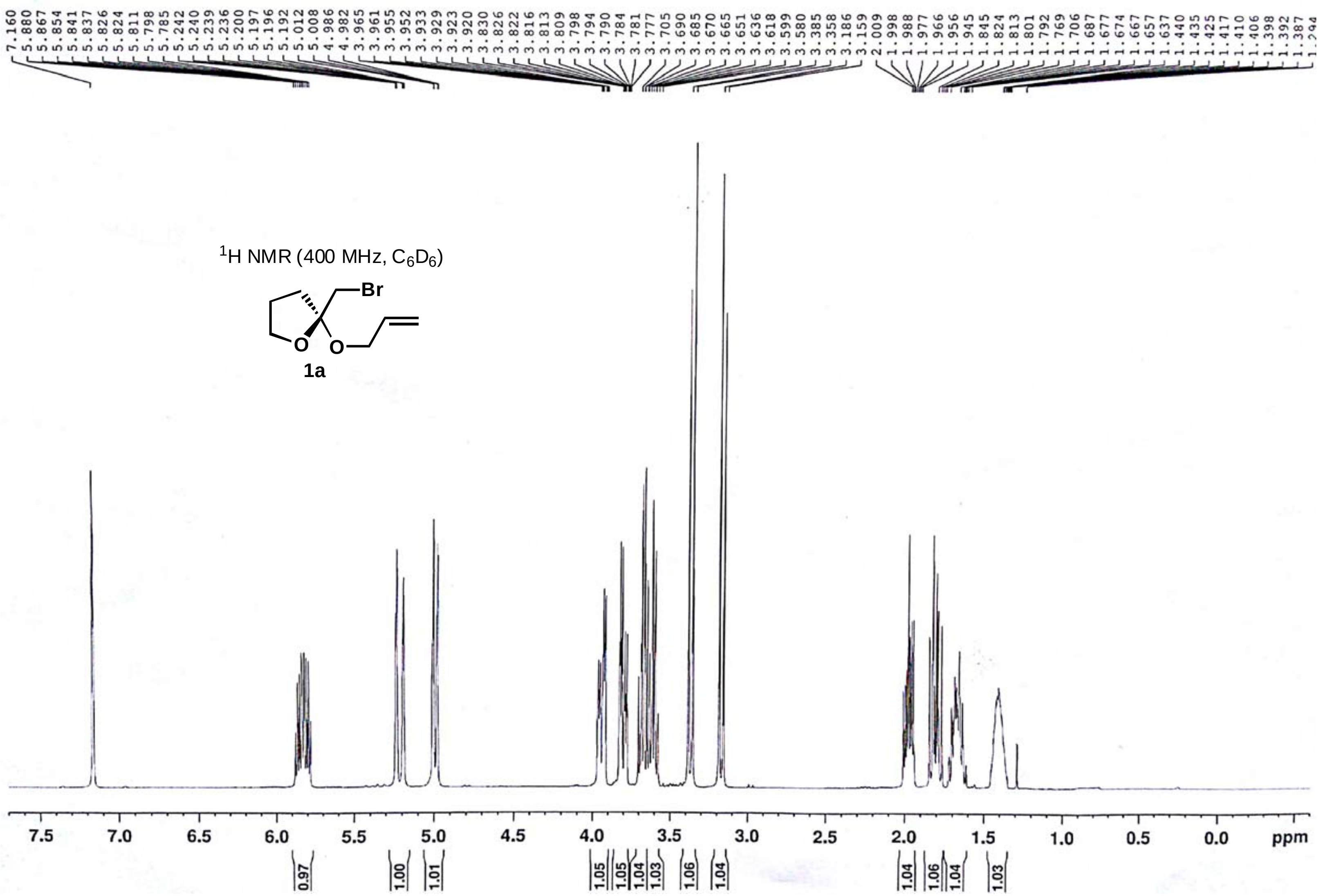
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1.398
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1.387
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O
O
1a
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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1.04
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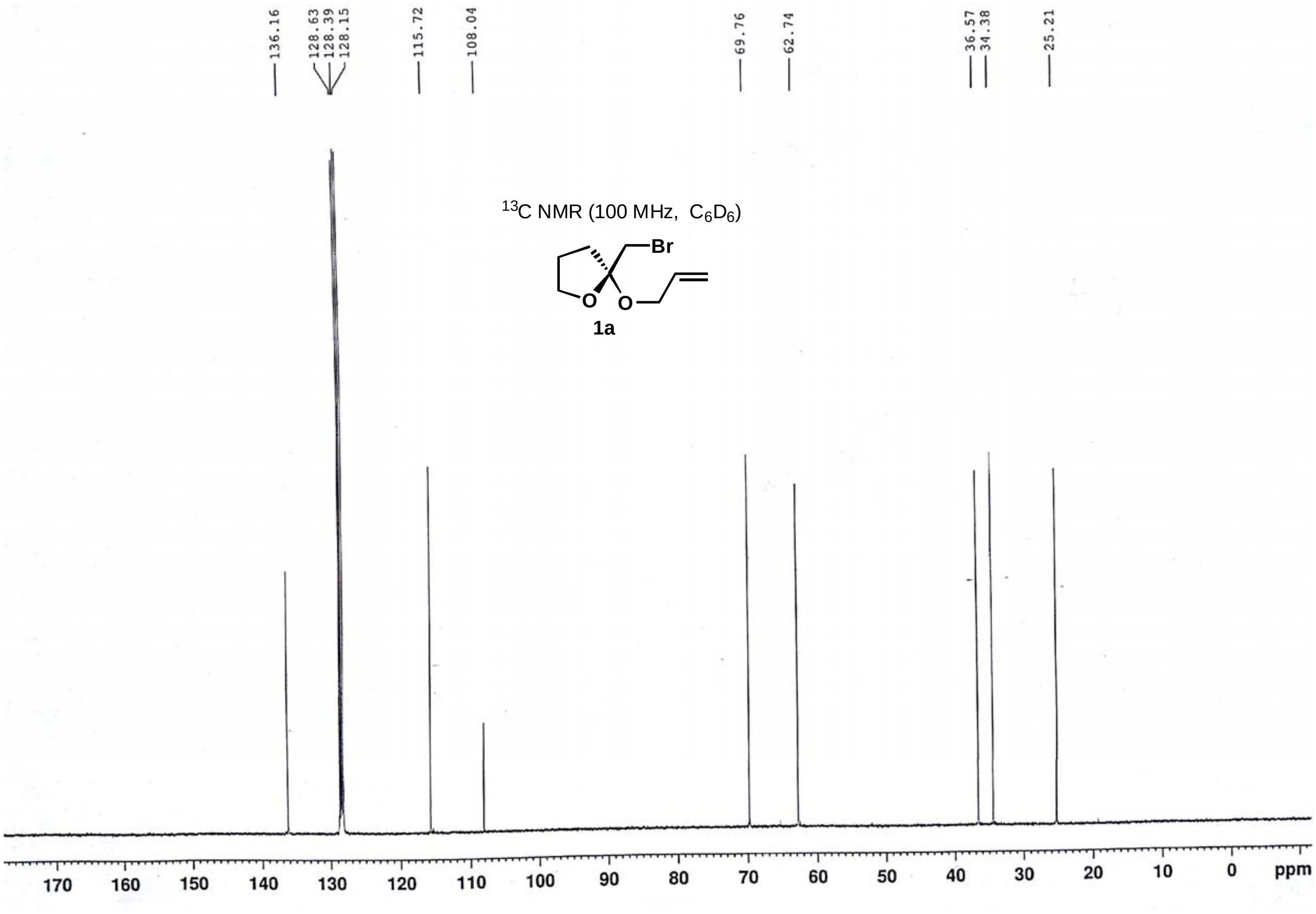
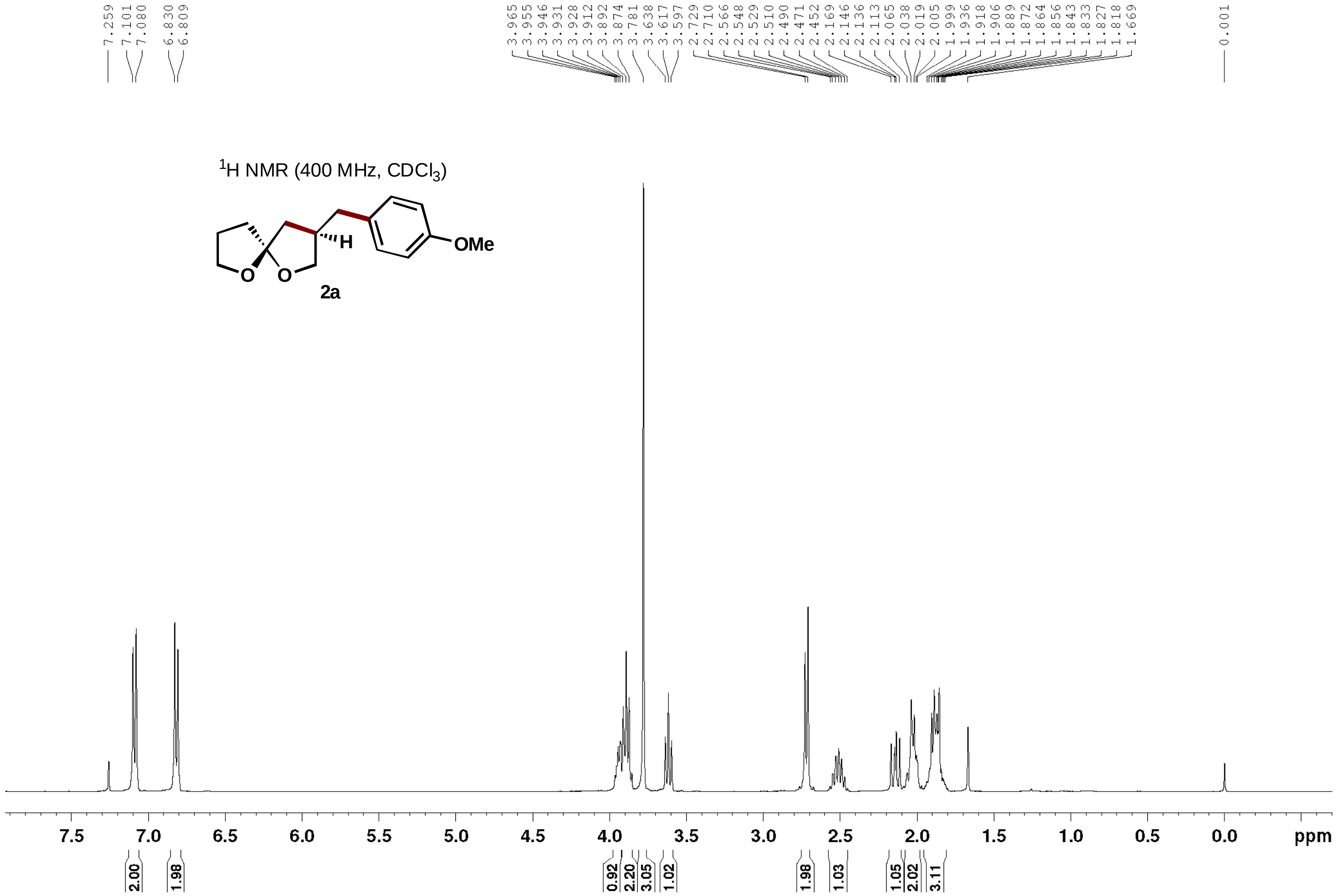
1.03



^{13}C NMR (100 MHz, C_6D_6)

1a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^{1}H NMR (400 MHz, $CDCl_3$)
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OMe
O
O
2a
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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ppm
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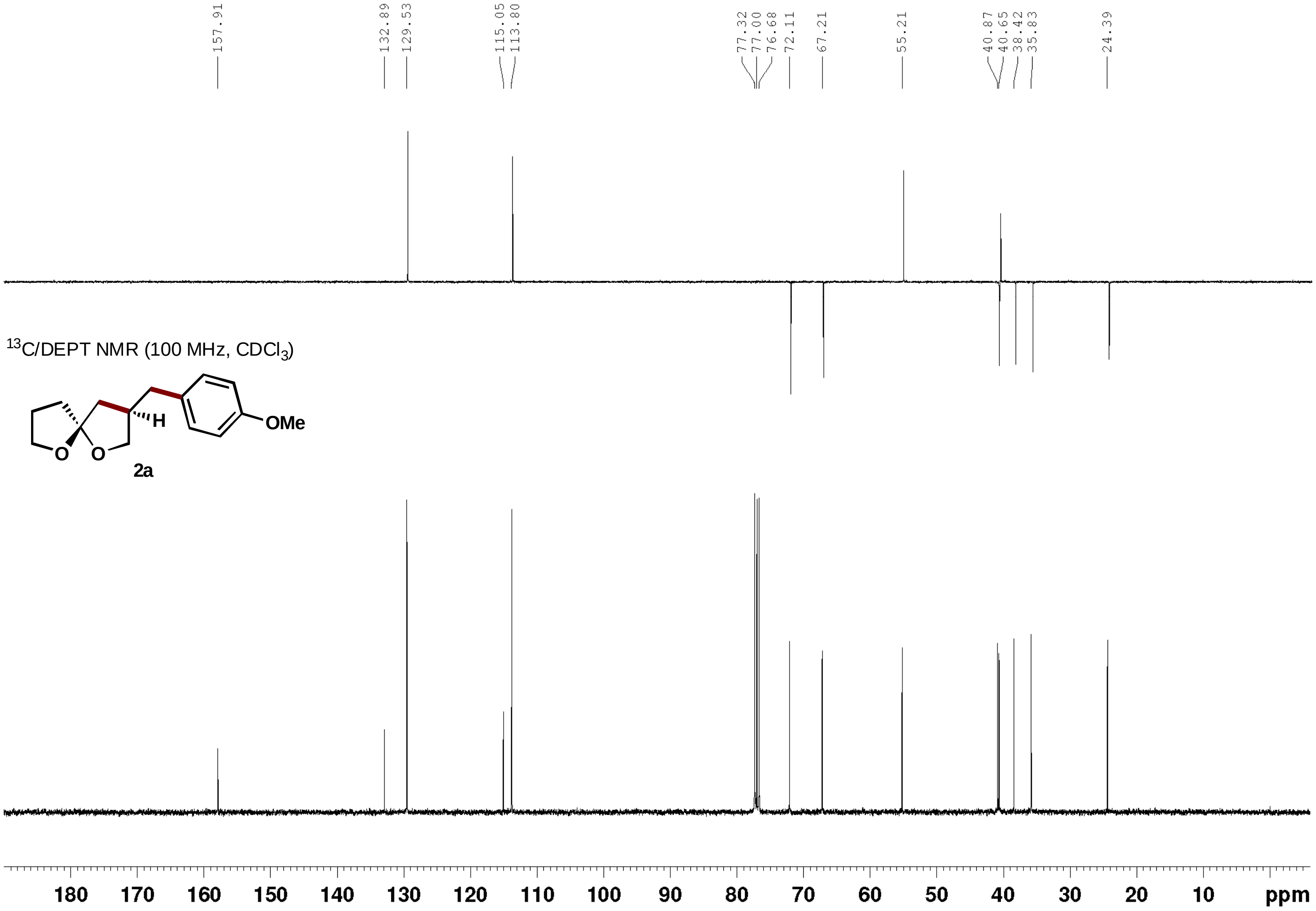
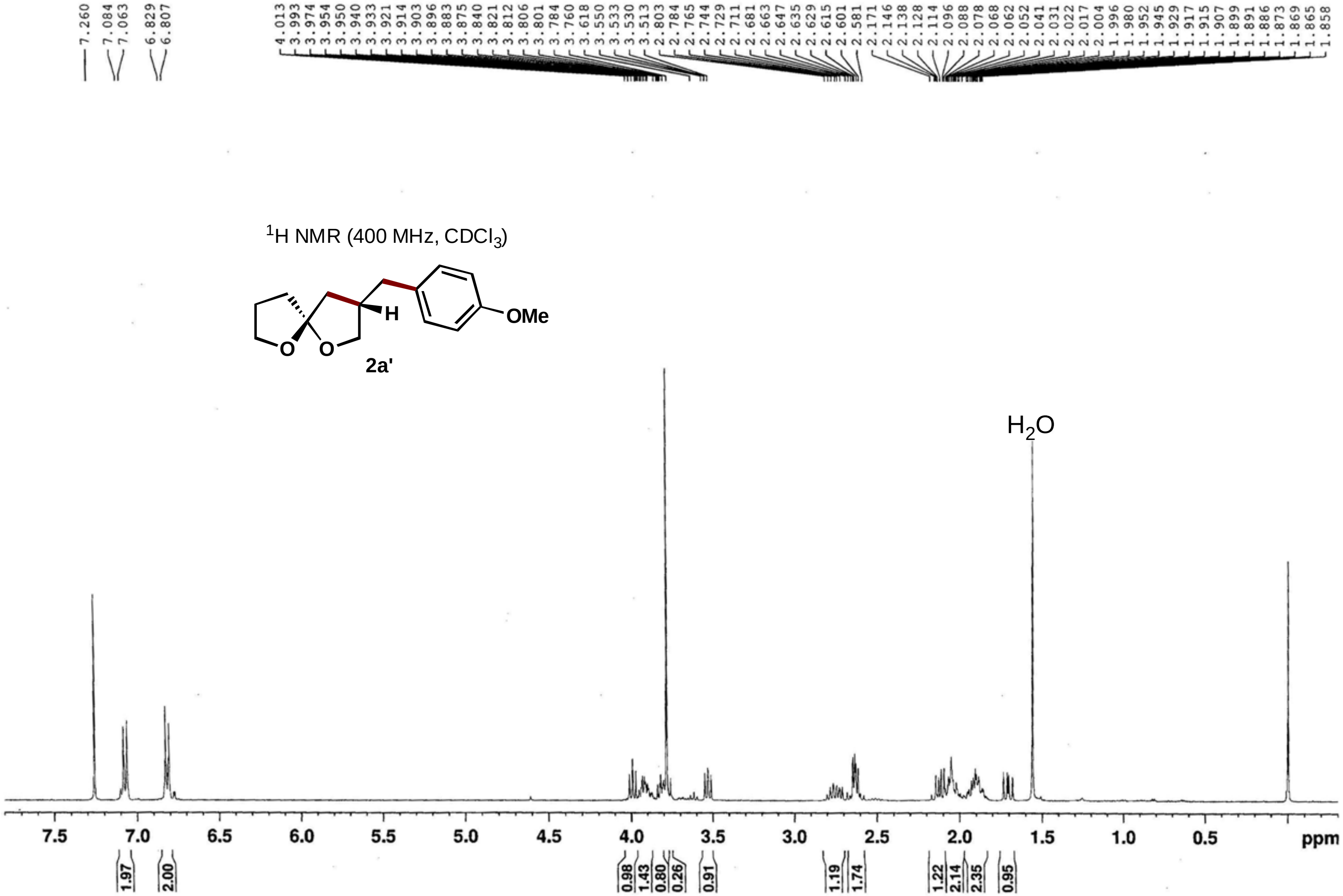


^{13}C/DEPT NMR (100 MHz, $CDCl_3$)

2a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OMe
O
O
2a'
H_2O
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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2.00
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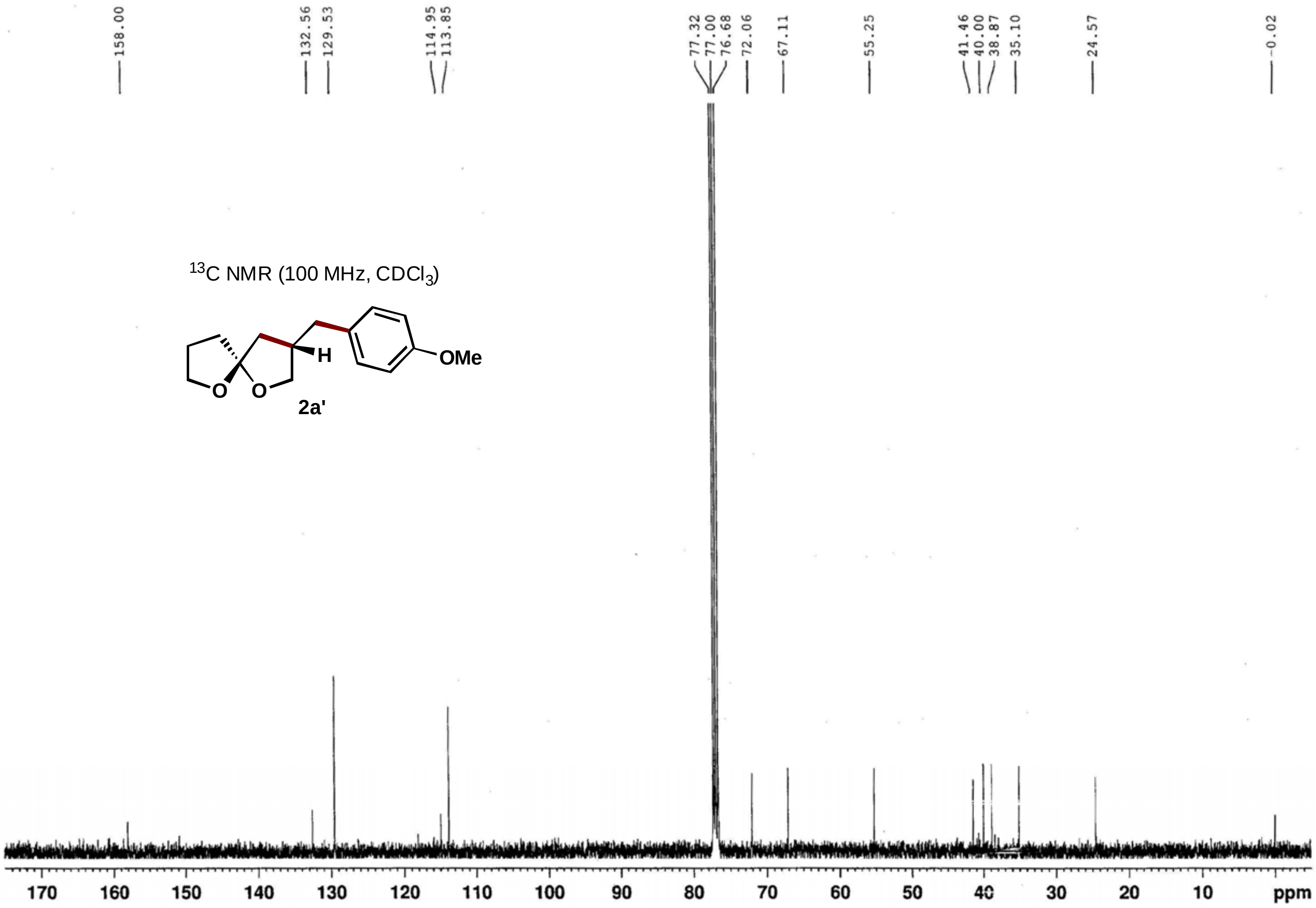
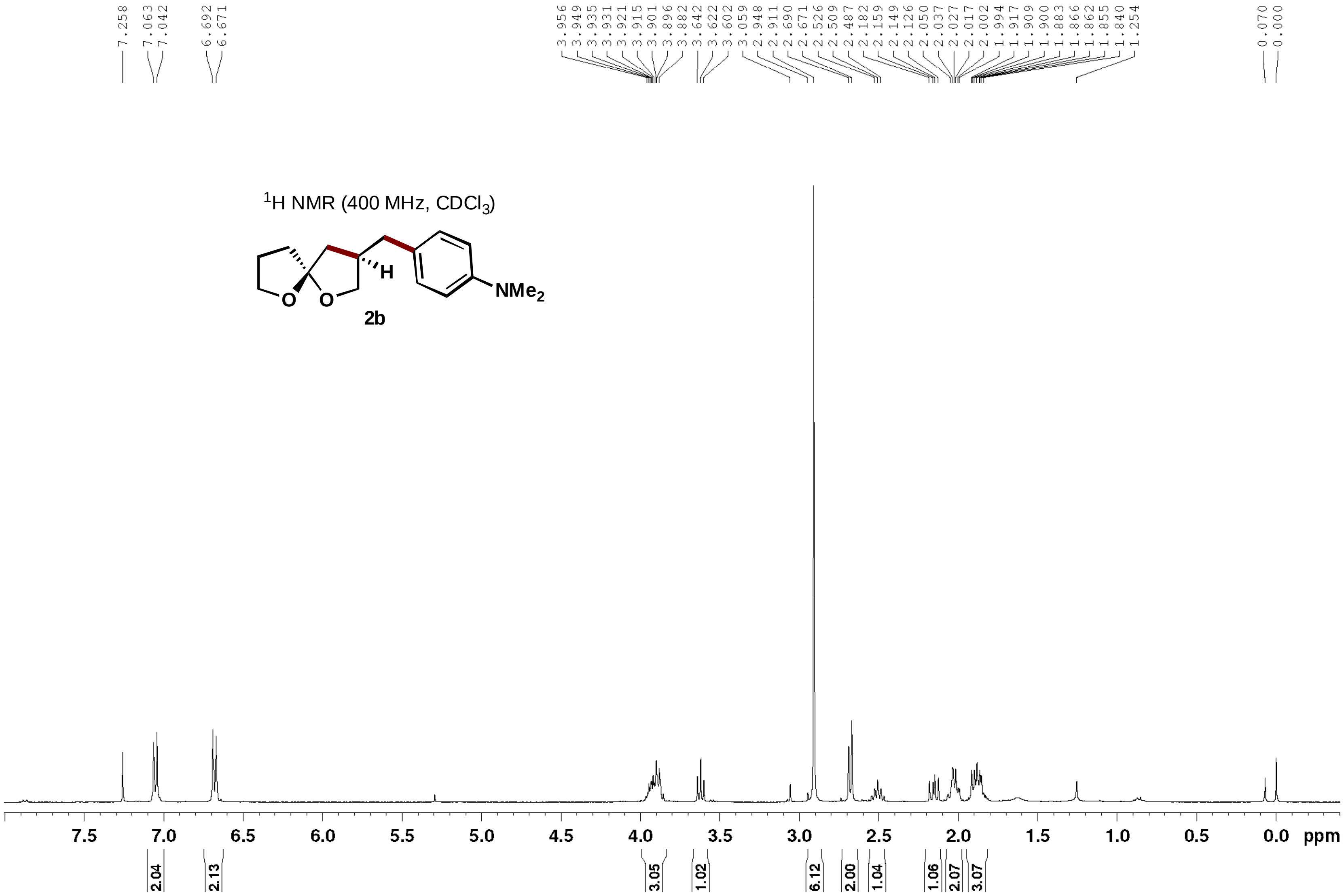
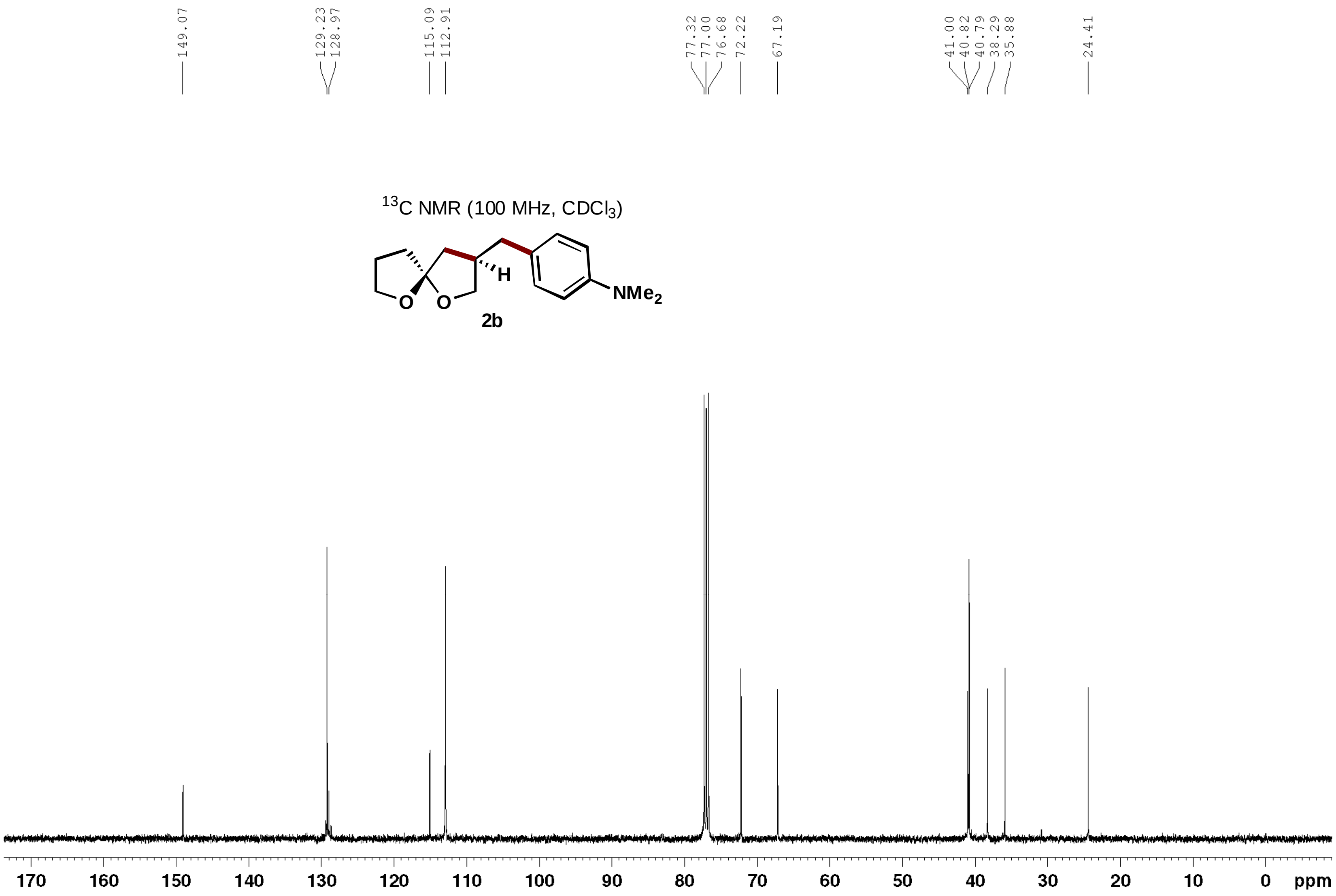
0.95



^{13}C NMR (100 MHz, $CDCl_3$)

2a'

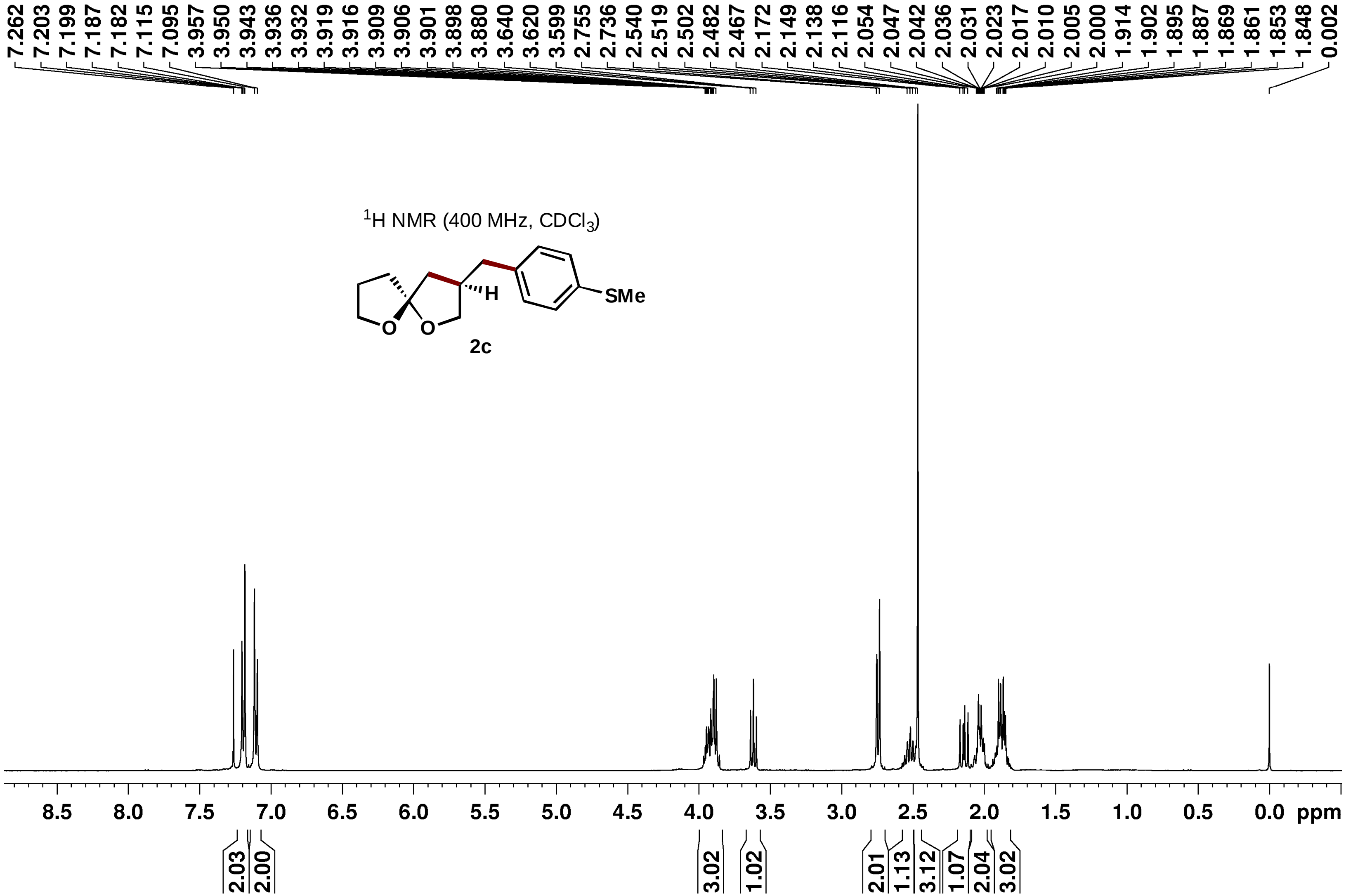

7.258
7.063
7.042
6.692
6.671
3.956
3.949
3.935
3.931
3.921
3.915
3.901
3.896
3.882
3.642
3.622
3.602
3.059
2.948
2.911
2.690
2.671
2.526
2.509
2.487
2.182
2.159
2.149
2.126
2.050
2.037
2.027
2.017
2.002
1.994
1.917
1.909
1.900
1.883
1.866
1.862
1.855
1.840
1.254
0.070
0.000
^{1}H NMR (400 MHz, $CDCl_3$)
H
O
O
NMe_2
2b
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.04
2.13
3.05
1.02
6.12
2.00
1.04
1.06
2.07
3.07

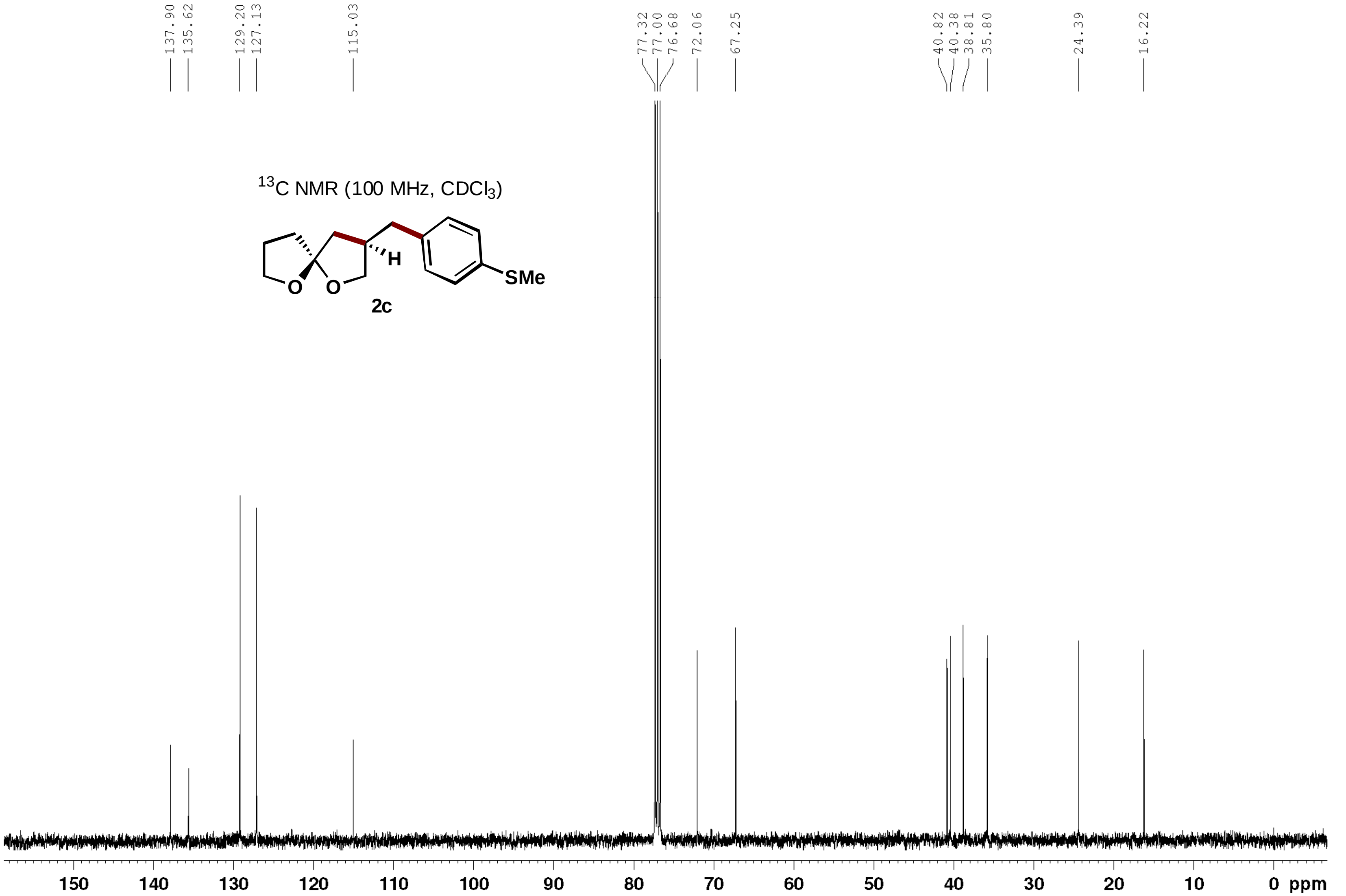


^{13}C NMR (100 MHz, $CDCl_3$)

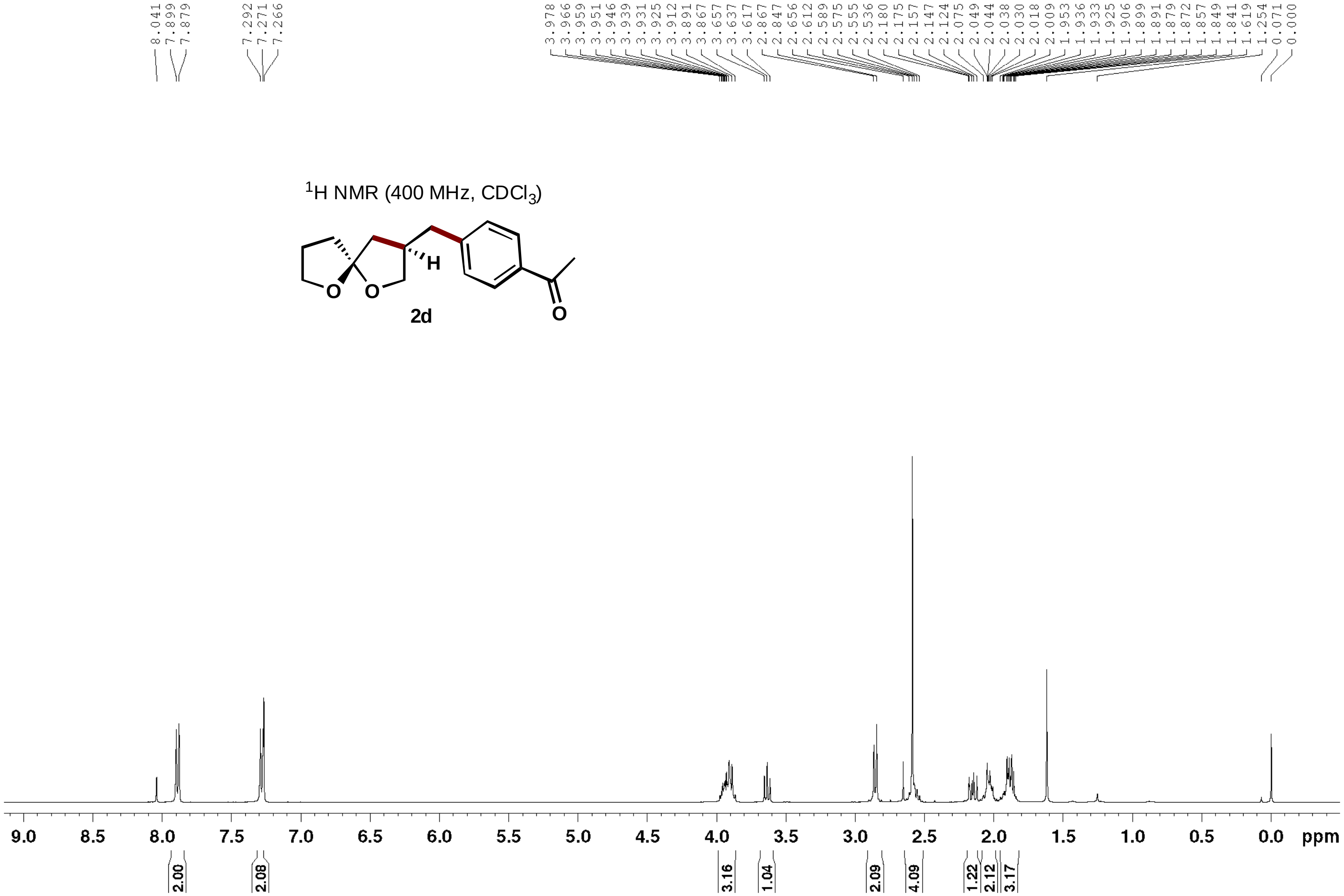
2b

Electronic Supplementary Material (ESI) for Chemical Communications

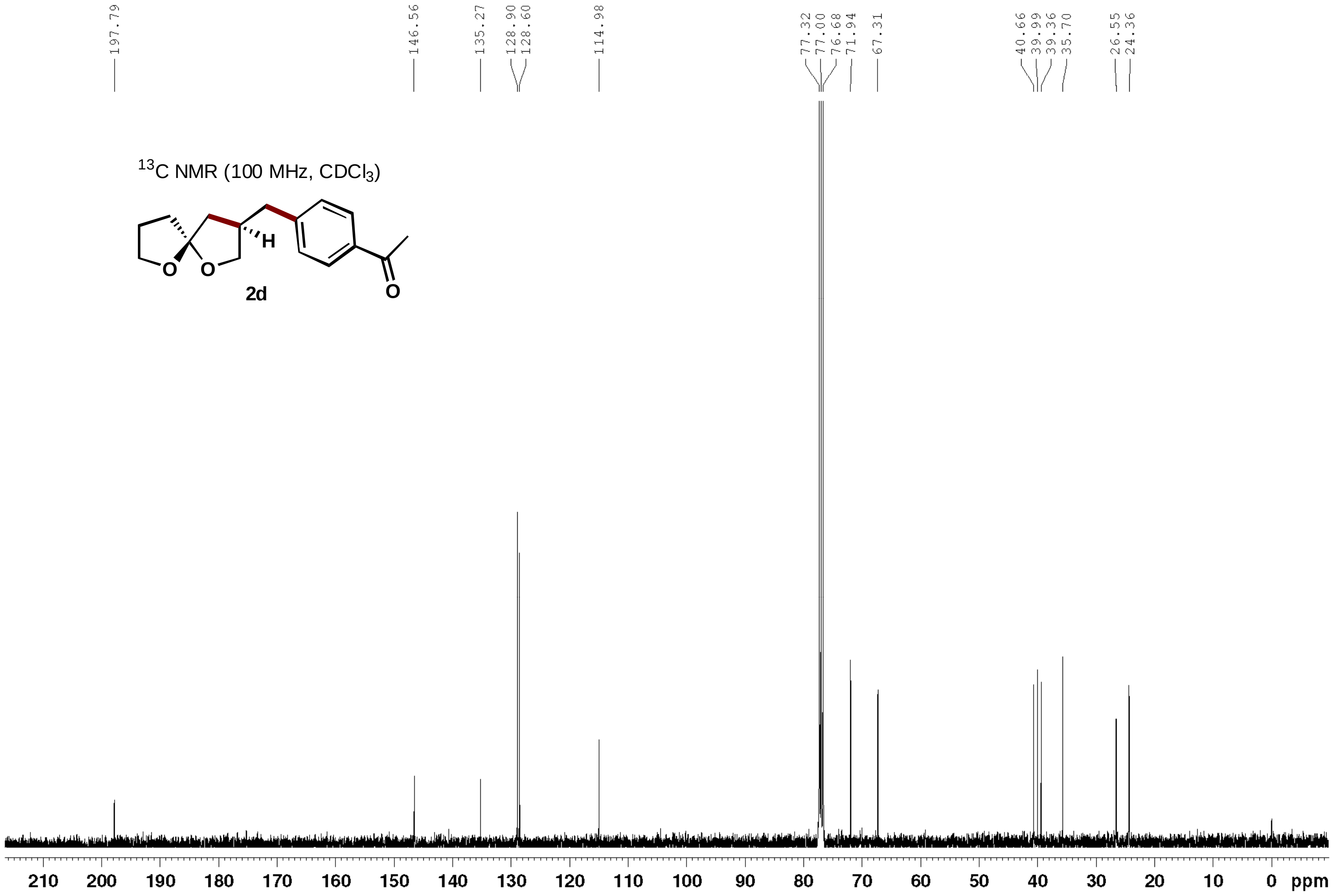

^{1}H NMR (400 MHz, $CDCl_3$)

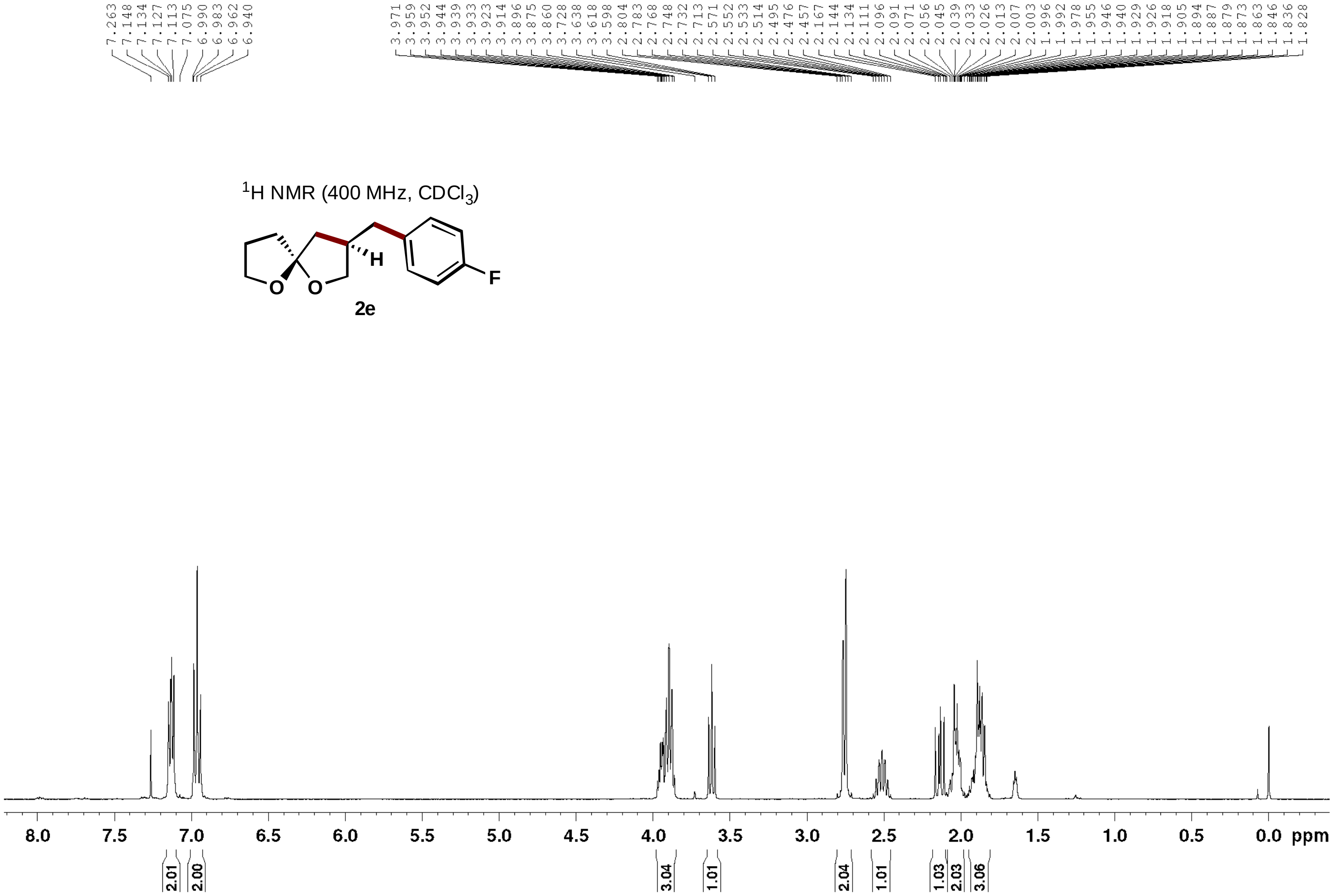

137.90
135.62
129.20
127.13
115.03
77.32
77.00
76.68
72.06
67.25
40.82
40.38
38.81
35.80
24.39
16.22
^{13}C NMR (100 MHz, CDCl$_3$)
O
O
H
SMe
2c
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

^{1}H NMR (400 MHz, CDCl$_3$)



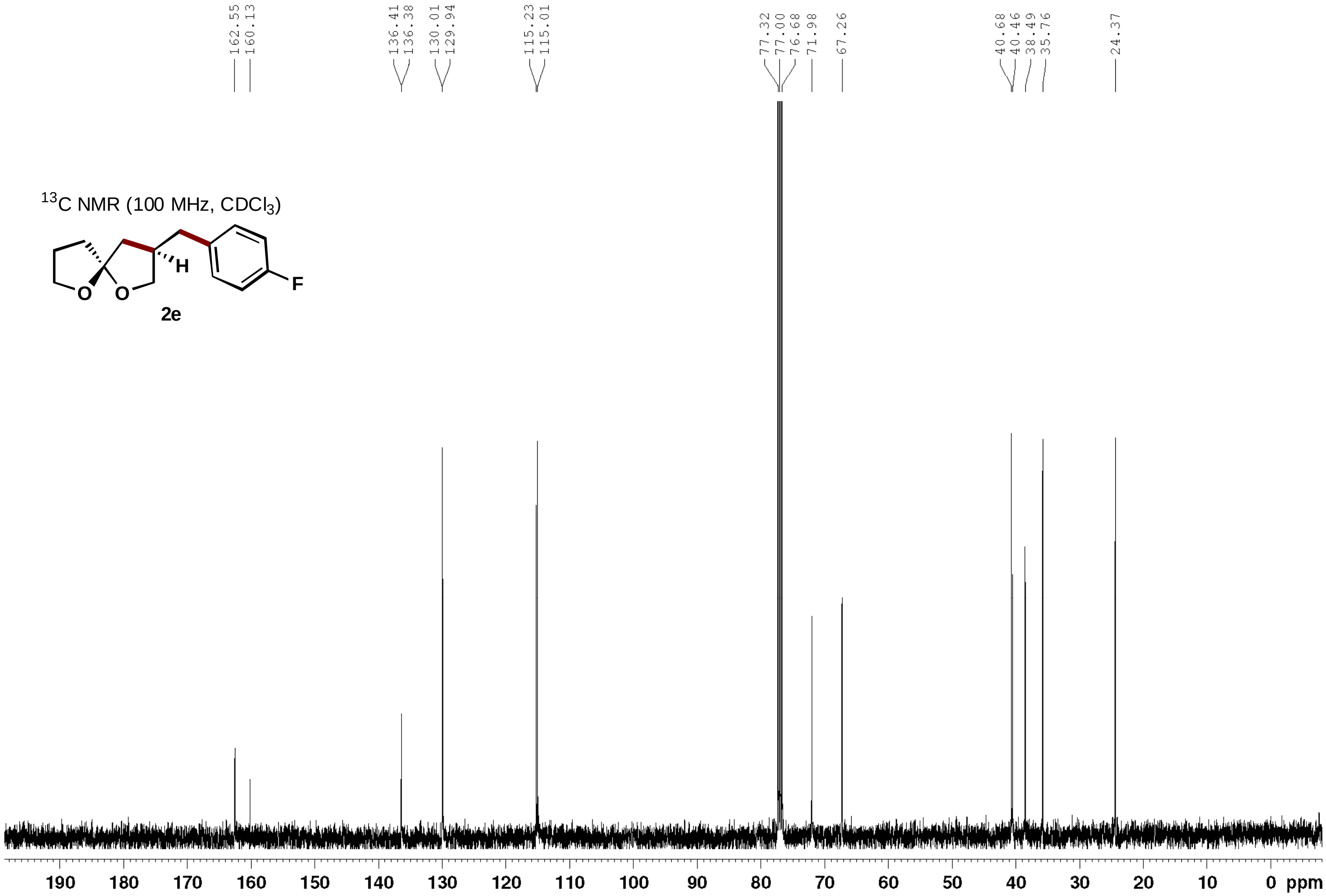
2d


197.79
146.56
135.27
128.90
128.60
114.98
77.32
77.00
76.68
71.94
67.31
40.66
39.99
39.36
35.70
26.55
24.36
^{13}C NMR (100 MHz, CDCl$_3$)
H
O
O
O
2d
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



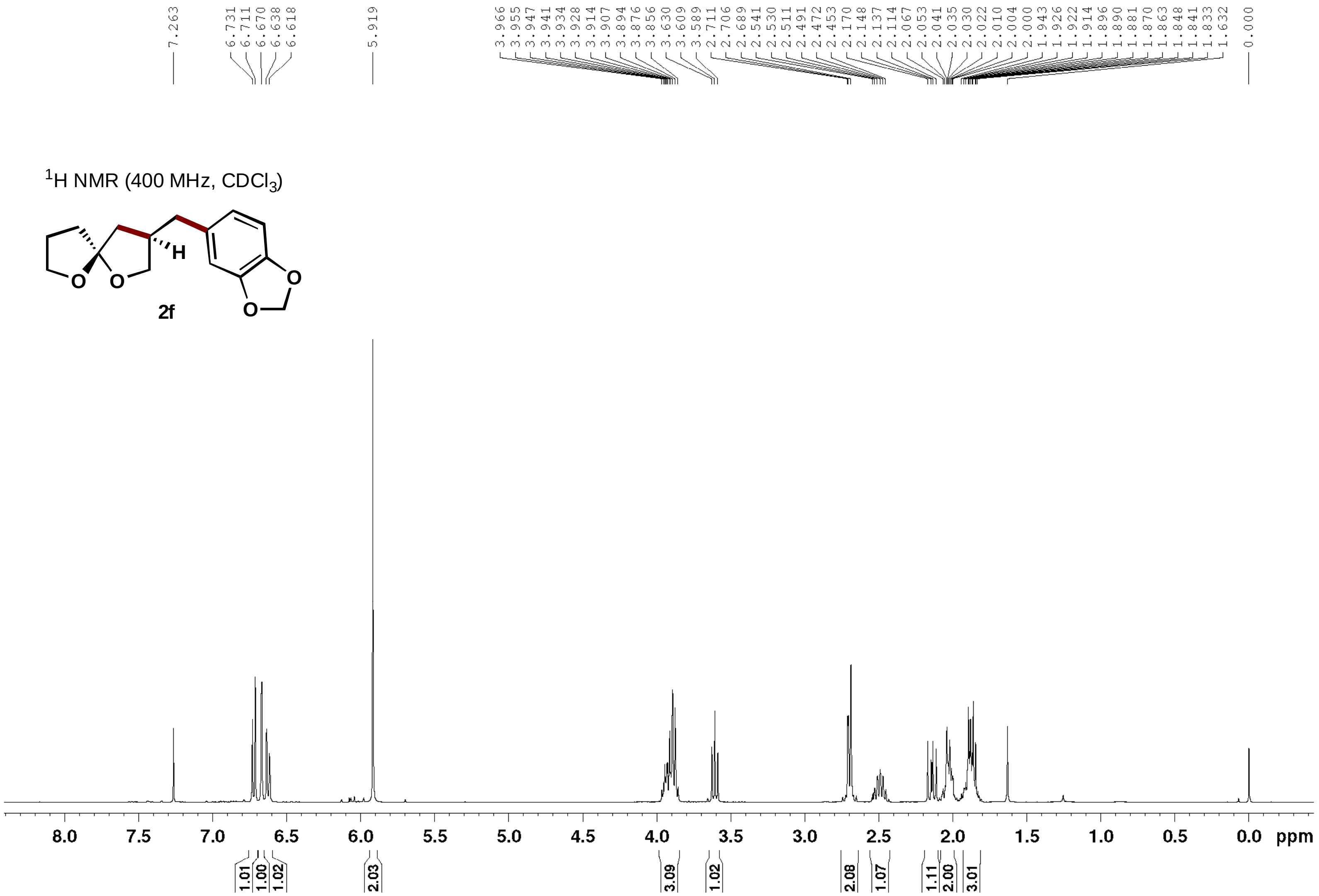
^{1}H NMR (400 MHz, $CDCl_3$)

2e



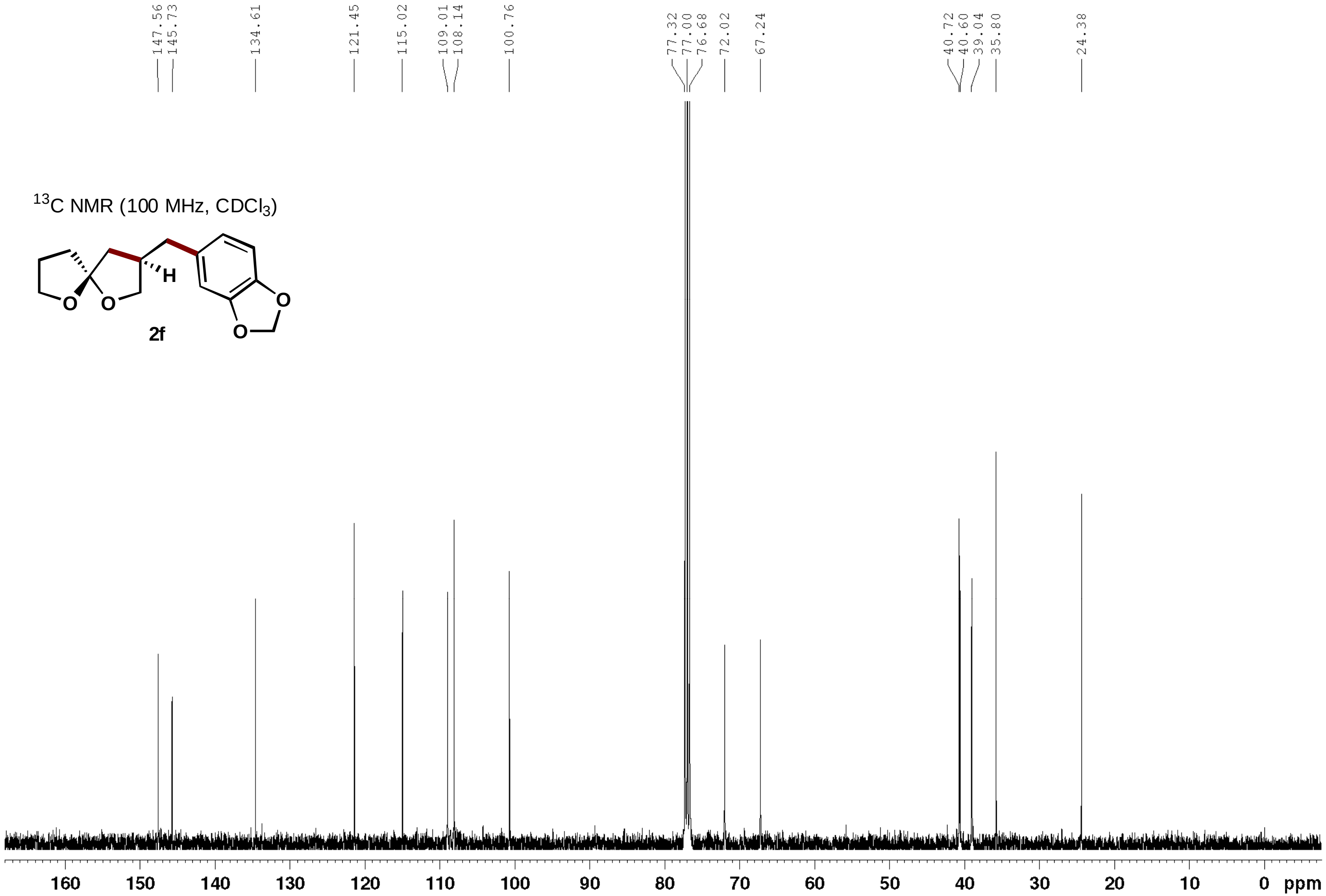
^{13}C NMR (100 MHz, $CDCl_3$)

2e



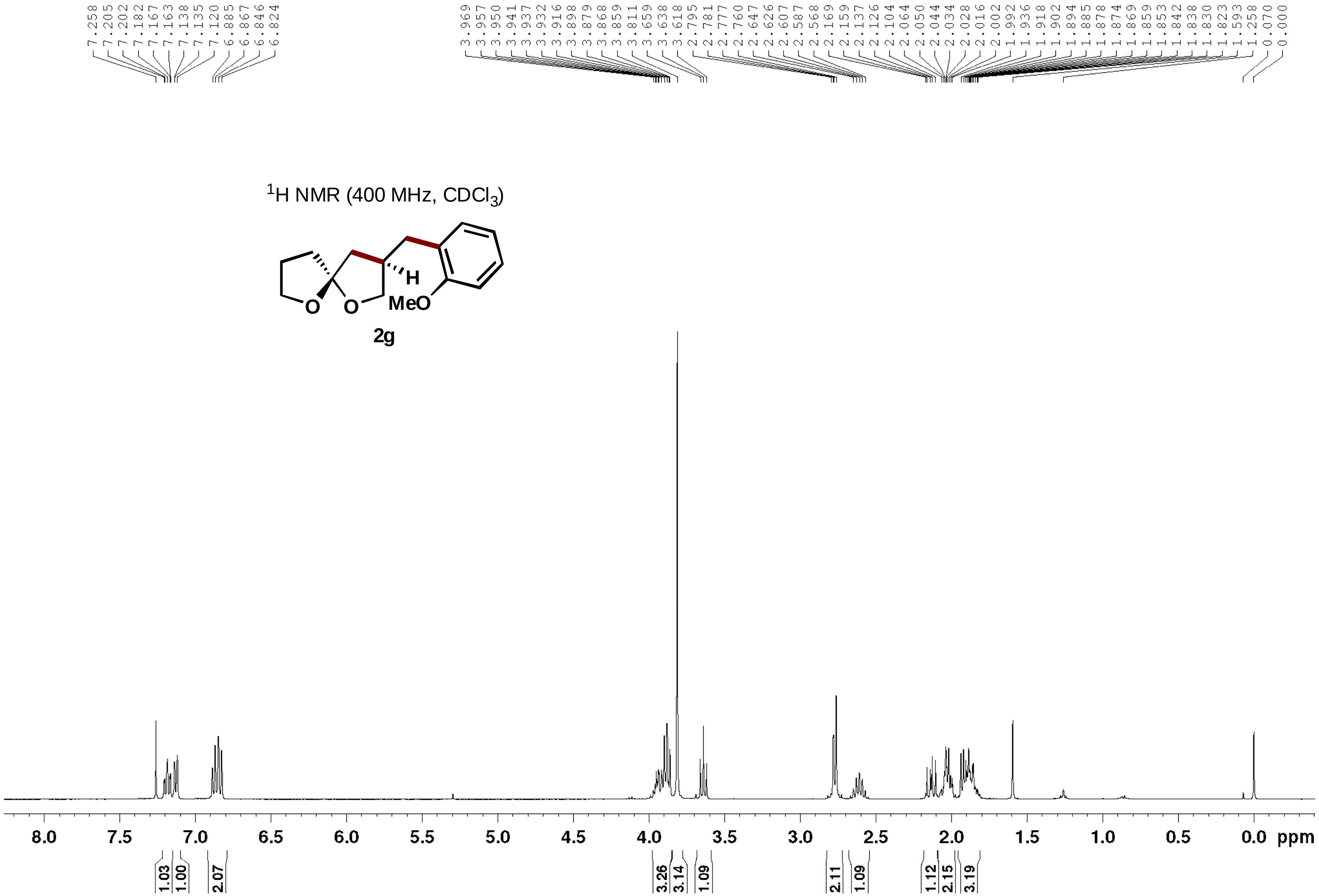
^{1}H NMR (400 MHz, $CDCl_3$)

2f



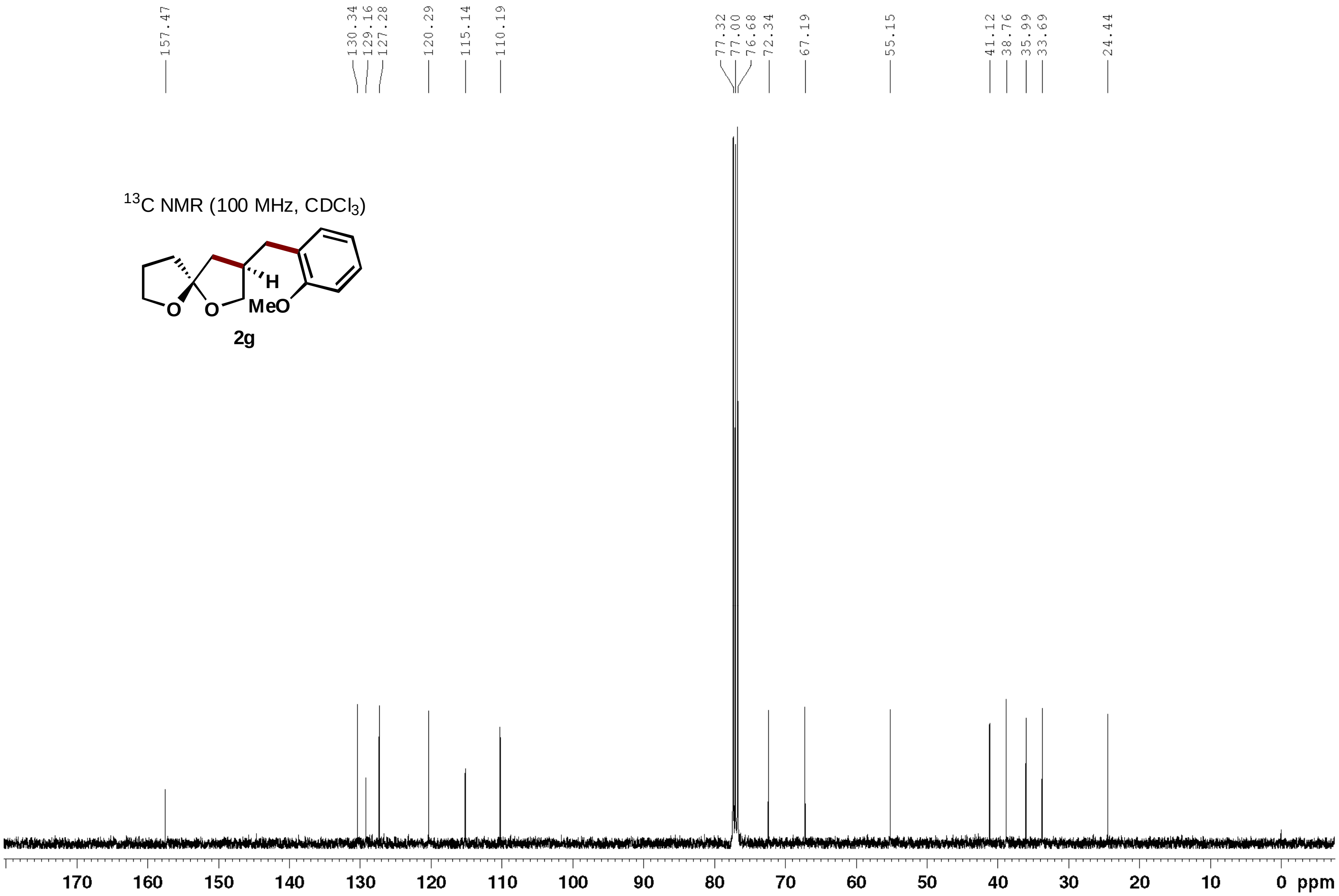
^{13}C NMR (100 MHz, $CDCl_3$)

2f



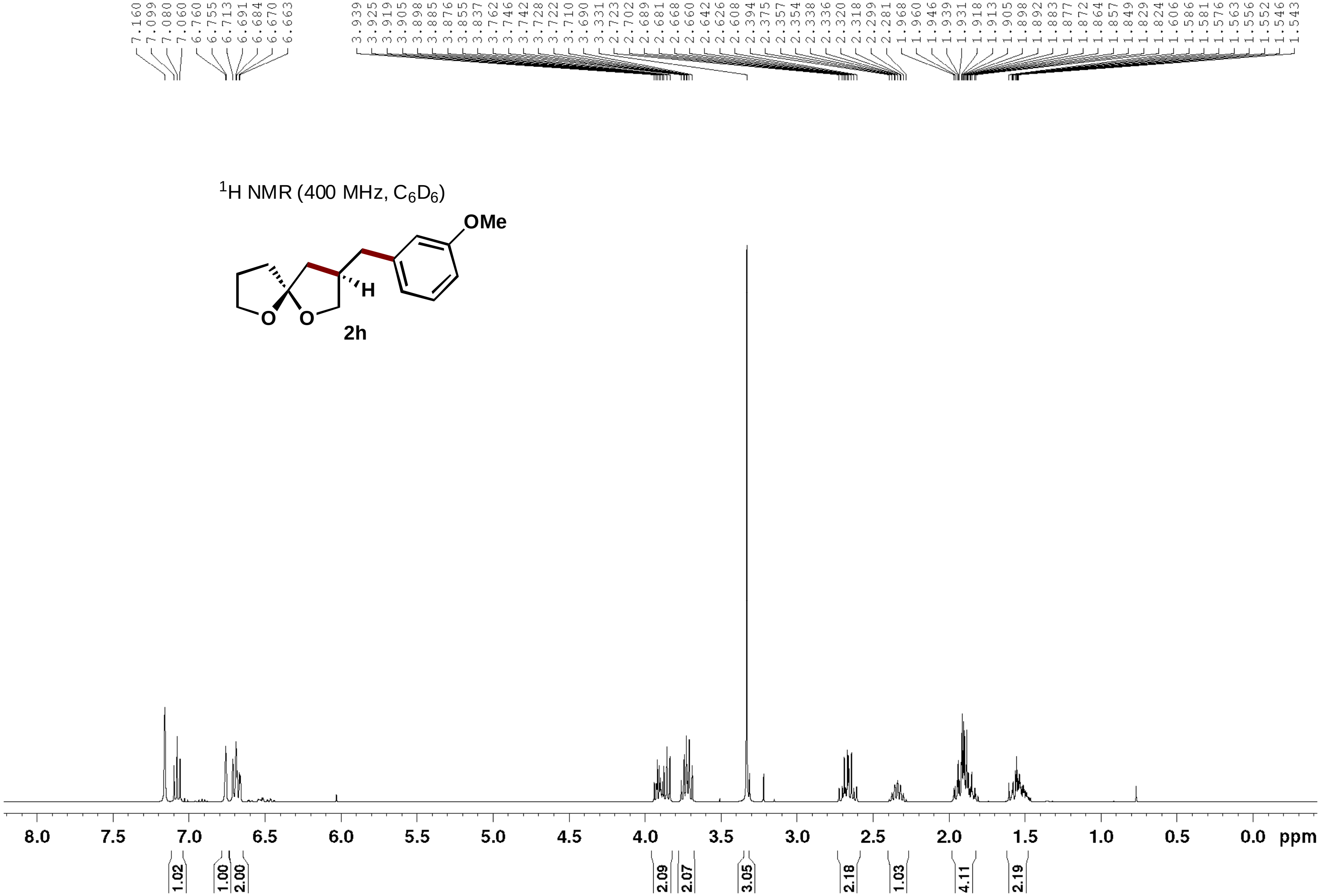
^{1}H NMR (400 MHz, CDCl$_3$)

2g



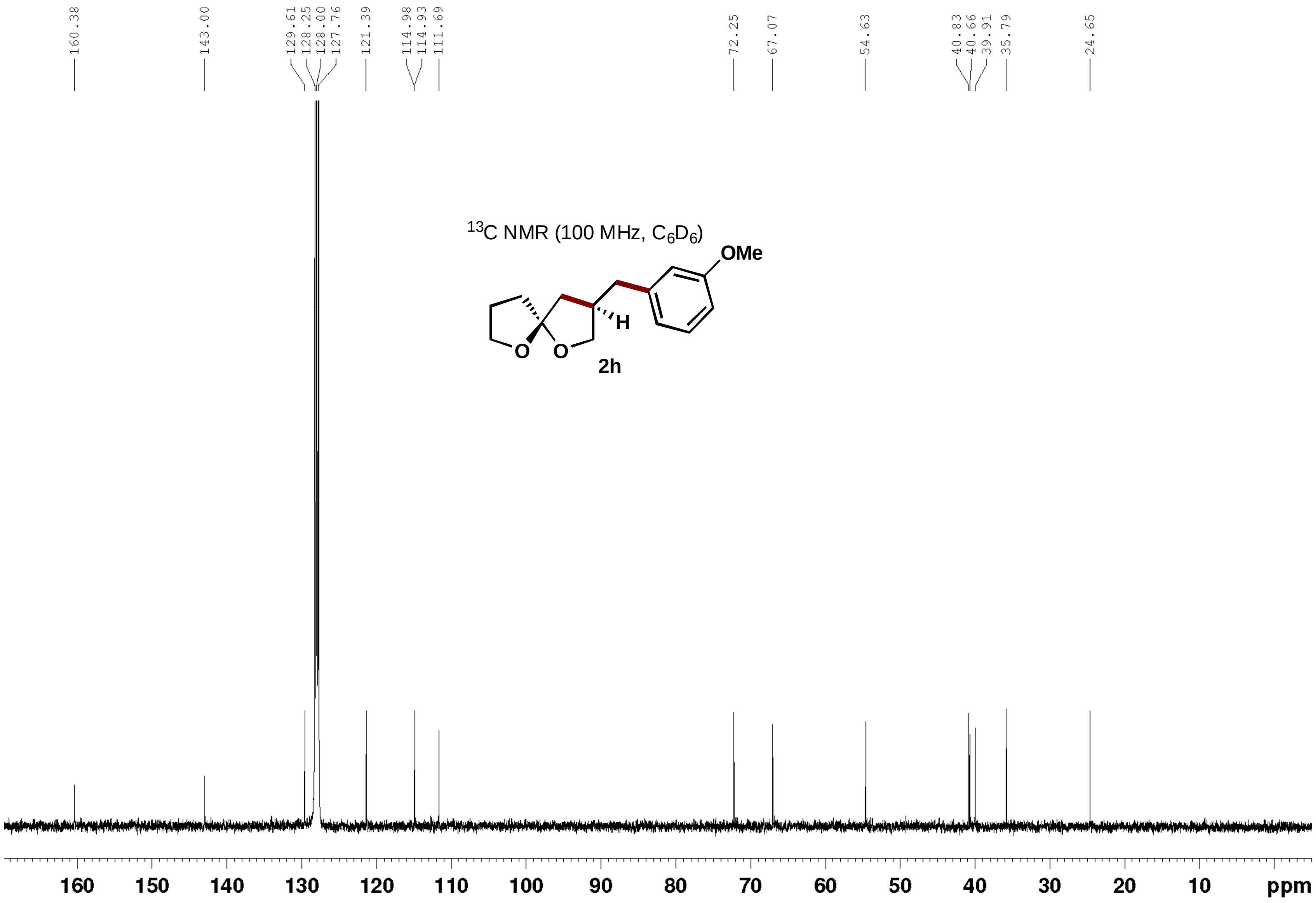
^{13}C NMR (100 MHz, $CDCl_3$)

2g

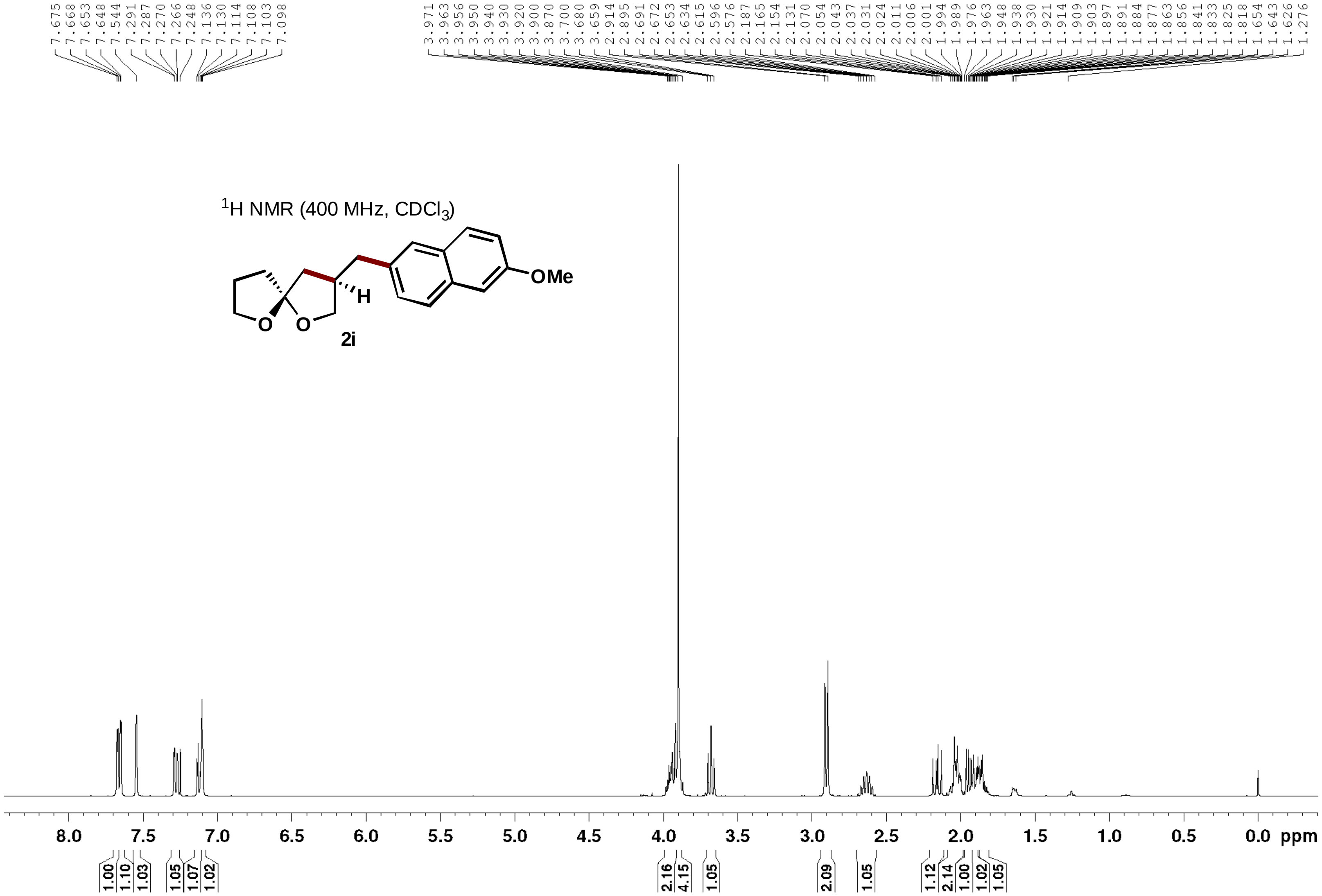


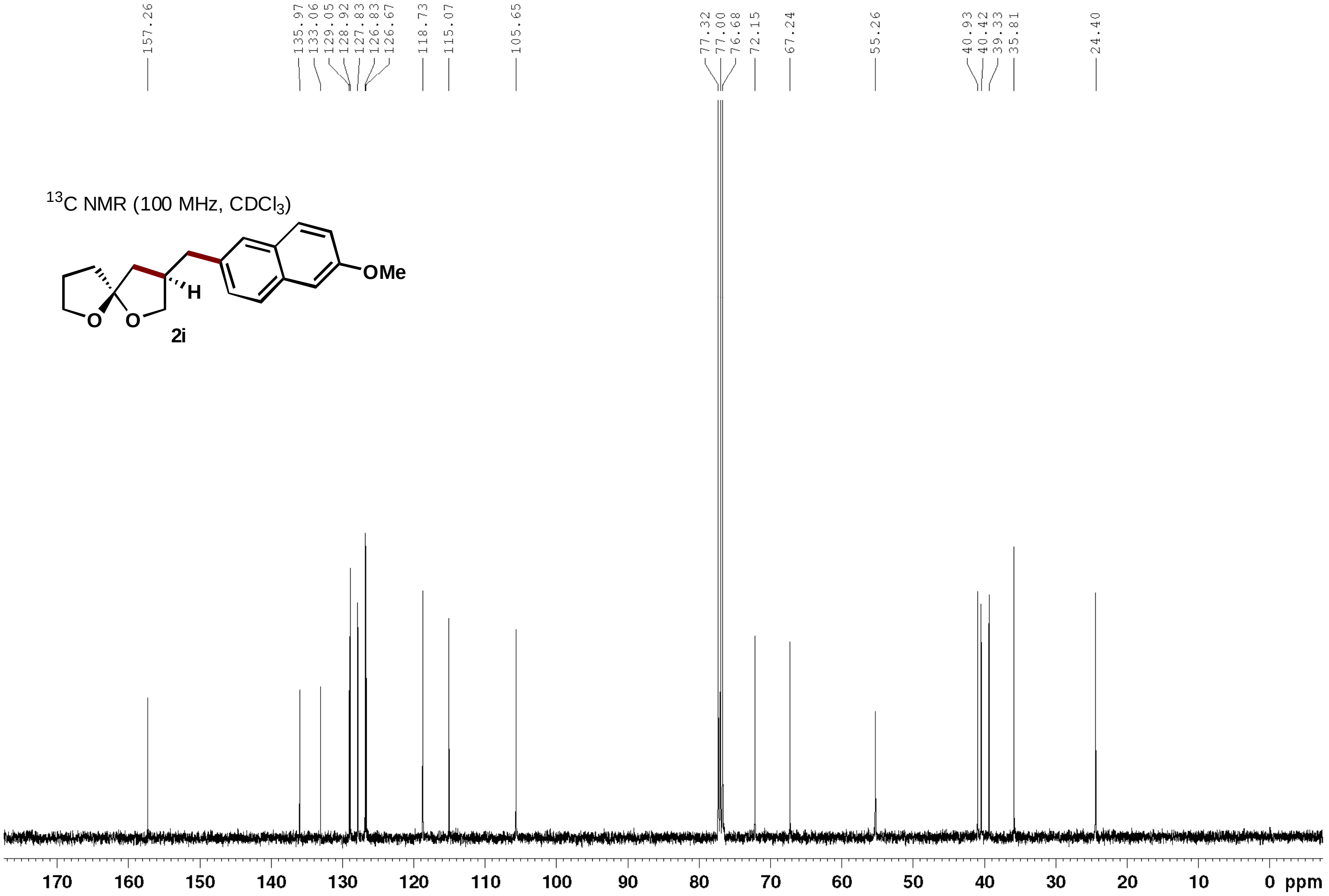
^1H NMR (400 MHz, C_6D_6)

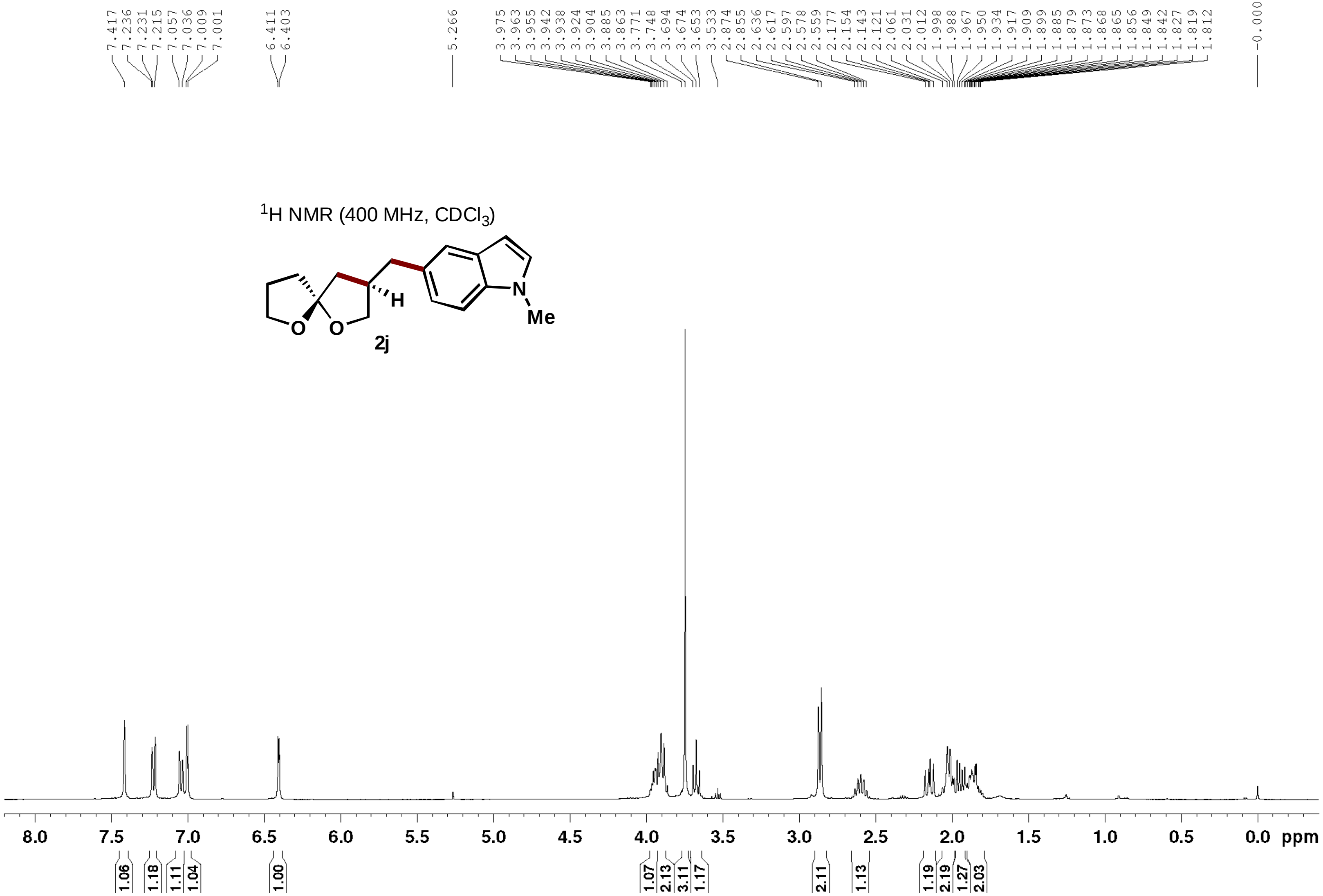
2h

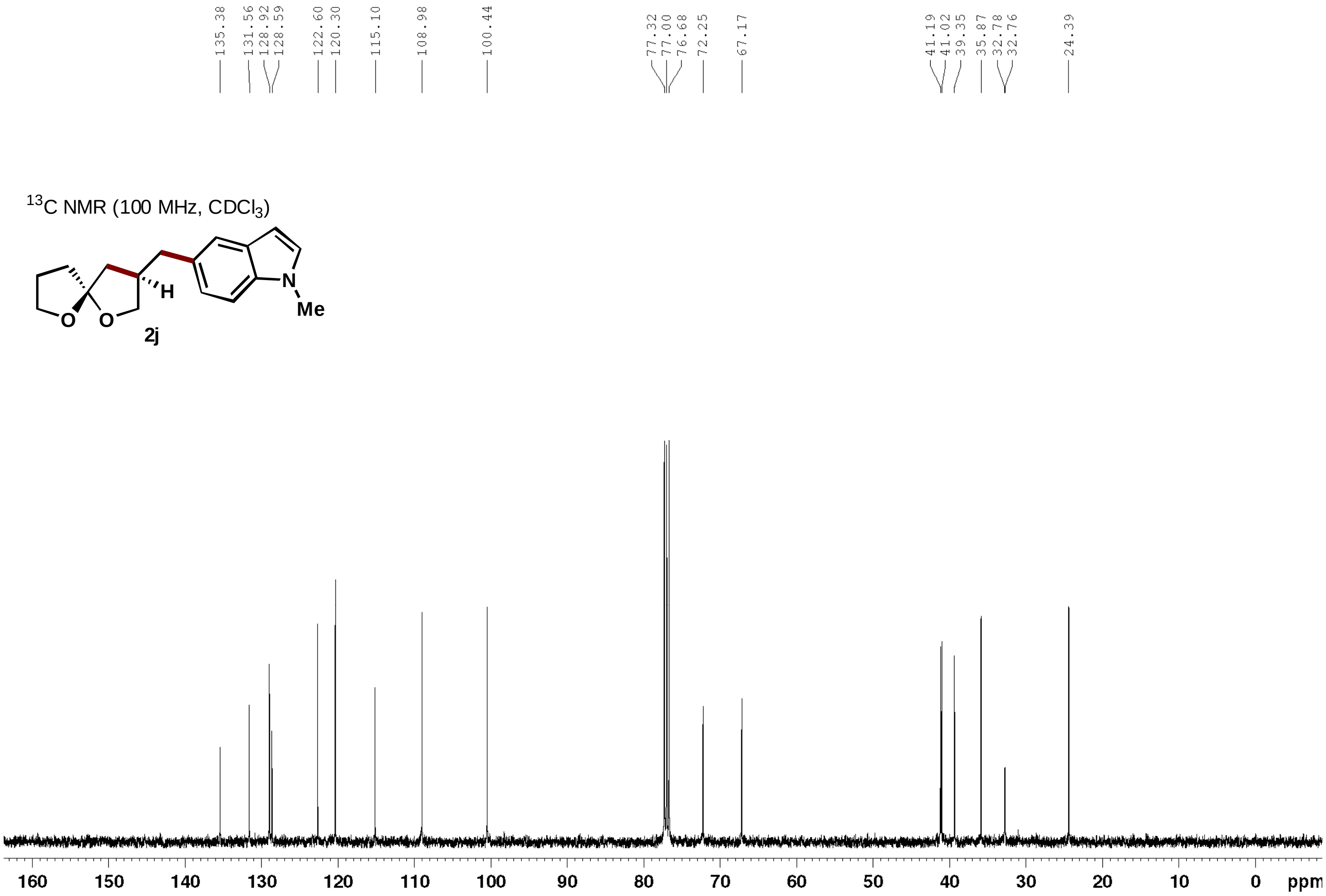

160.38
143.00
129.61
128.25
128.00
127.76
121.39
114.98
114.93
111.69
72.25
67.07
54.63
40.83
40.66
39.91
35.79
24.65
13C NMR (100 MHz, C6D6)
OMe
H
O
O
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

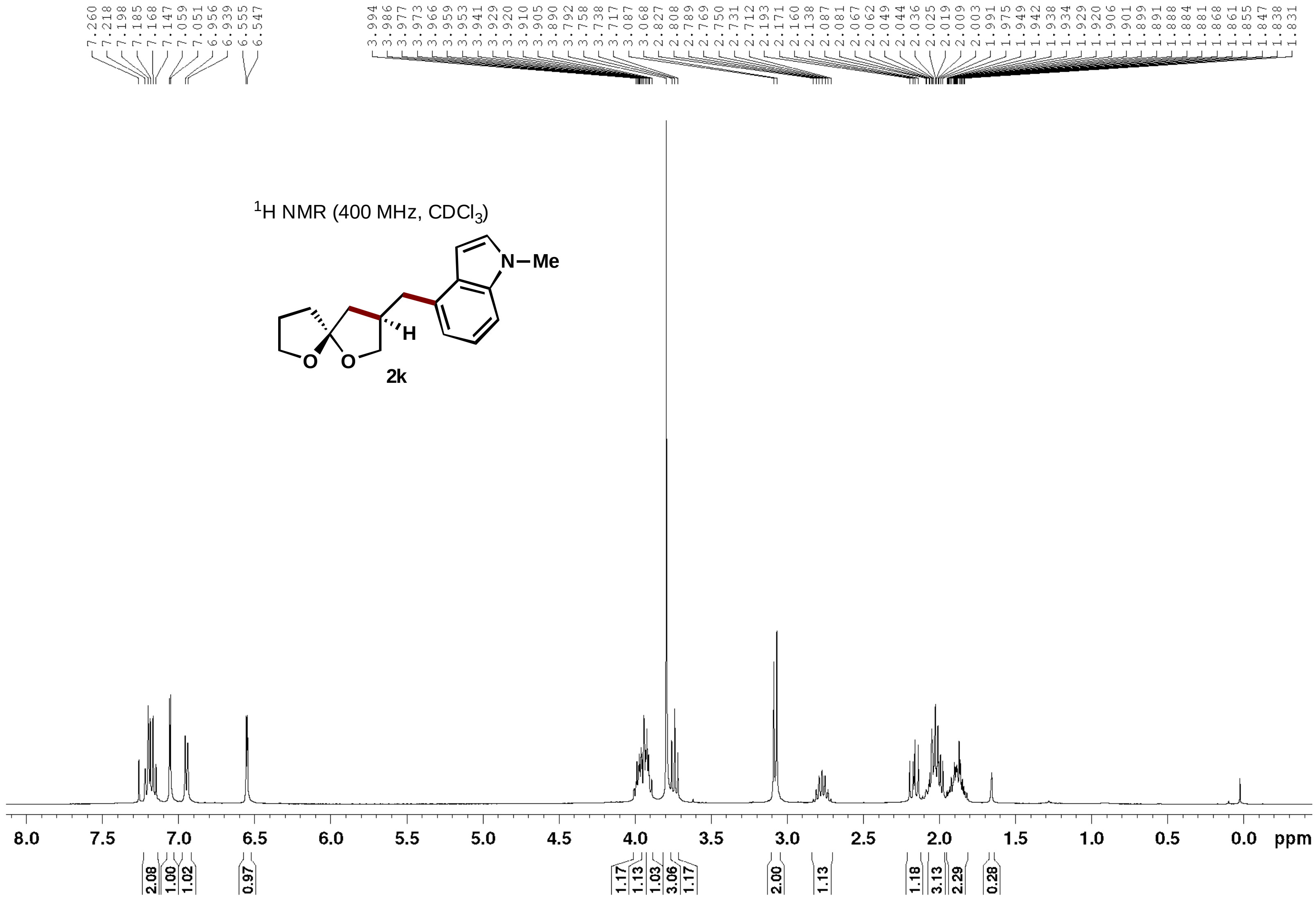
2h

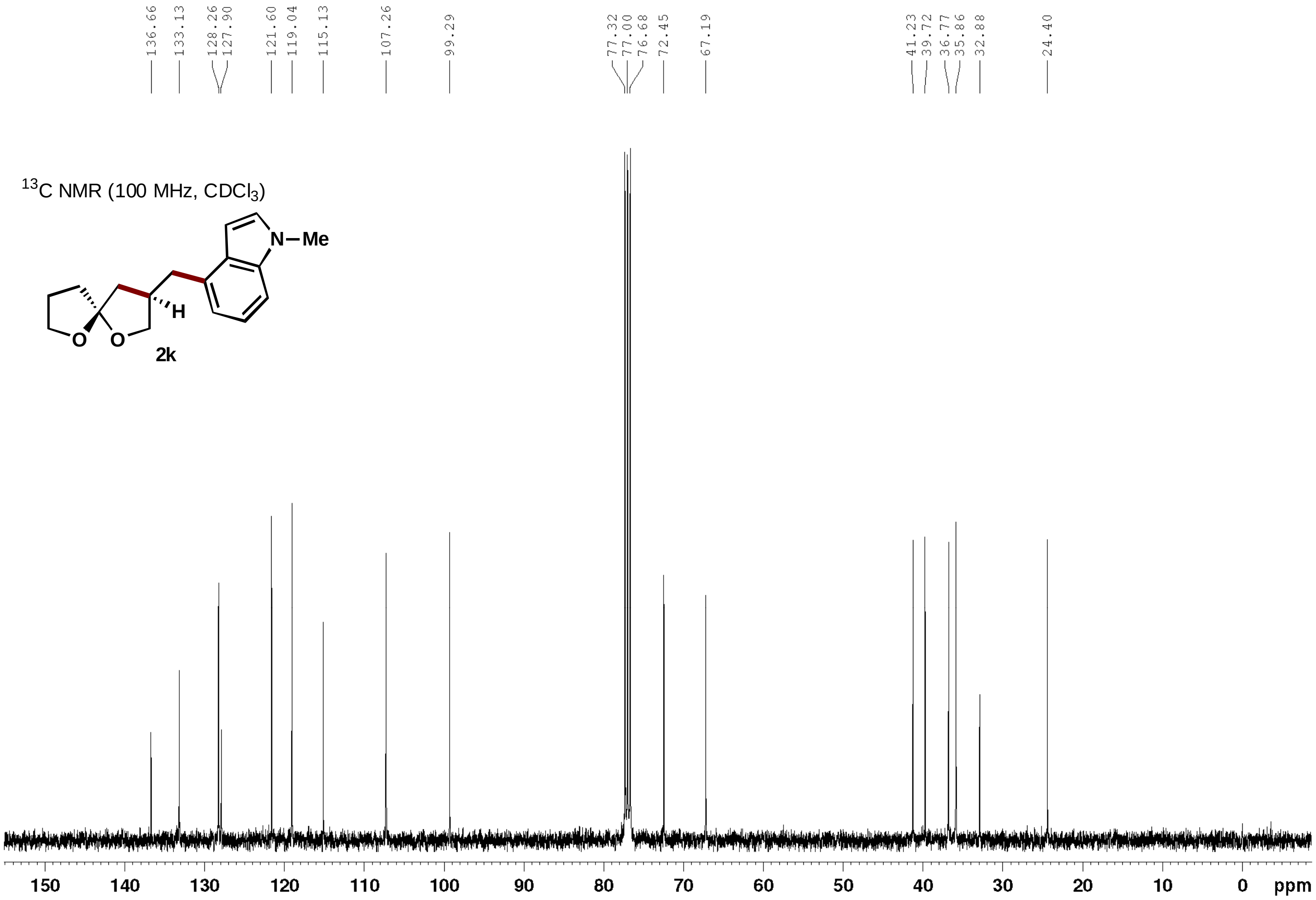

7.675
7.668
7.653
7.648
7.544
7.291
7.287
7.270
7.266
7.248
7.136
7.130
7.114
7.108
7.103
7.098
3.971
3.963
3.956
3.950
3.940
3.930
3.920
3.900
3.870
3.700
3.680
3.659
2.914
2.895
2.691
2.672
2.653
2.634
2.615
2.596
2.576
2.187
2.165
2.154
2.131
2.070
2.054
2.043
2.037
2.031
2.024
2.011
2.006
2.001
1.994
1.989
1.976
1.963
1.948
1.938
1.930
1.921
1.914
1.909
1.903
1.897
1.891
1.884
1.877
1.863
1.856
1.841
1.833
1.825
1.818
1.654
1.643
1.626
1.276
^{1}H NMR (400 MHz, CDCl$_3$)
H
O
O
OMe
2i
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.10
1.03
1.05
1.07
1.02
2.16
4.15
1.05
2.09
1.05
1.12
2.14
1.00
1.02
1.05

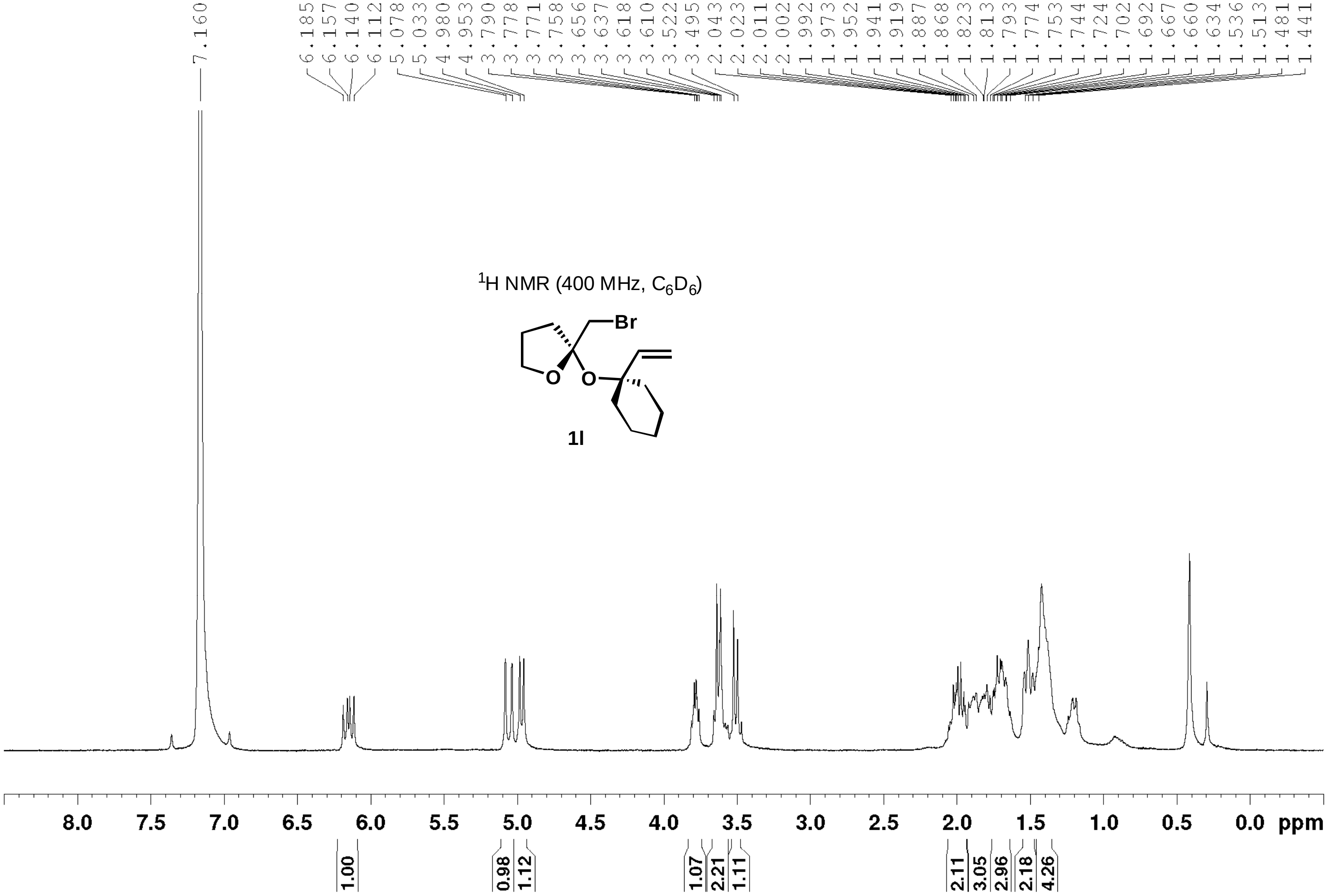

157.26
135.97
133.06
129.05
128.92
127.83
126.83
126.67
118.73
115.07
105.65
77.32
77.00
76.68
72.15
67.24
55.26
40.93
40.42
39.33
35.81
24.40
^{13}C NMR (100 MHz, $CDCl_3$)
H
O
O
OMe
2i
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm


7.417
7.236
7.231
7.215
7.057
7.036
7.009
7.001
6.411
6.403
5.266
3.975
3.963
3.955
3.942
3.938
3.924
3.904
3.885
3.863
3.771
3.748
3.694
3.674
3.653
3.533
2.874
2.855
2.636
2.617
2.597
2.578
2.559
2.177
2.154
2.143
2.121
2.061
2.031
2.012
1.998
1.988
1.967
1.950
1.934
1.917
1.909
1.899
1.885
1.879
1.873
1.868
1.865
1.856
1.849
1.842
1.827
1.819
1.812
-0.000
^{1}H NMR (400 MHz, CDCl$_3$)
O
O
H
N
Me
2j
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.06
1.18
1.11
1.04
1.00
1.07
2.13
3.11
1.17
2.11
1.13
1.19
2.19
1.27
2.03


135.38
131.56
128.92
128.59
122.60
120.30
115.10
108.98
100.44
77.32
77.00
76.68
72.25
67.17
41.19
41.02
39.35
35.87
32.78
32.76
24.39
^{13}C NMR (100 MHz, CDCl$_3$)
H
O
O
N
Me
2j
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

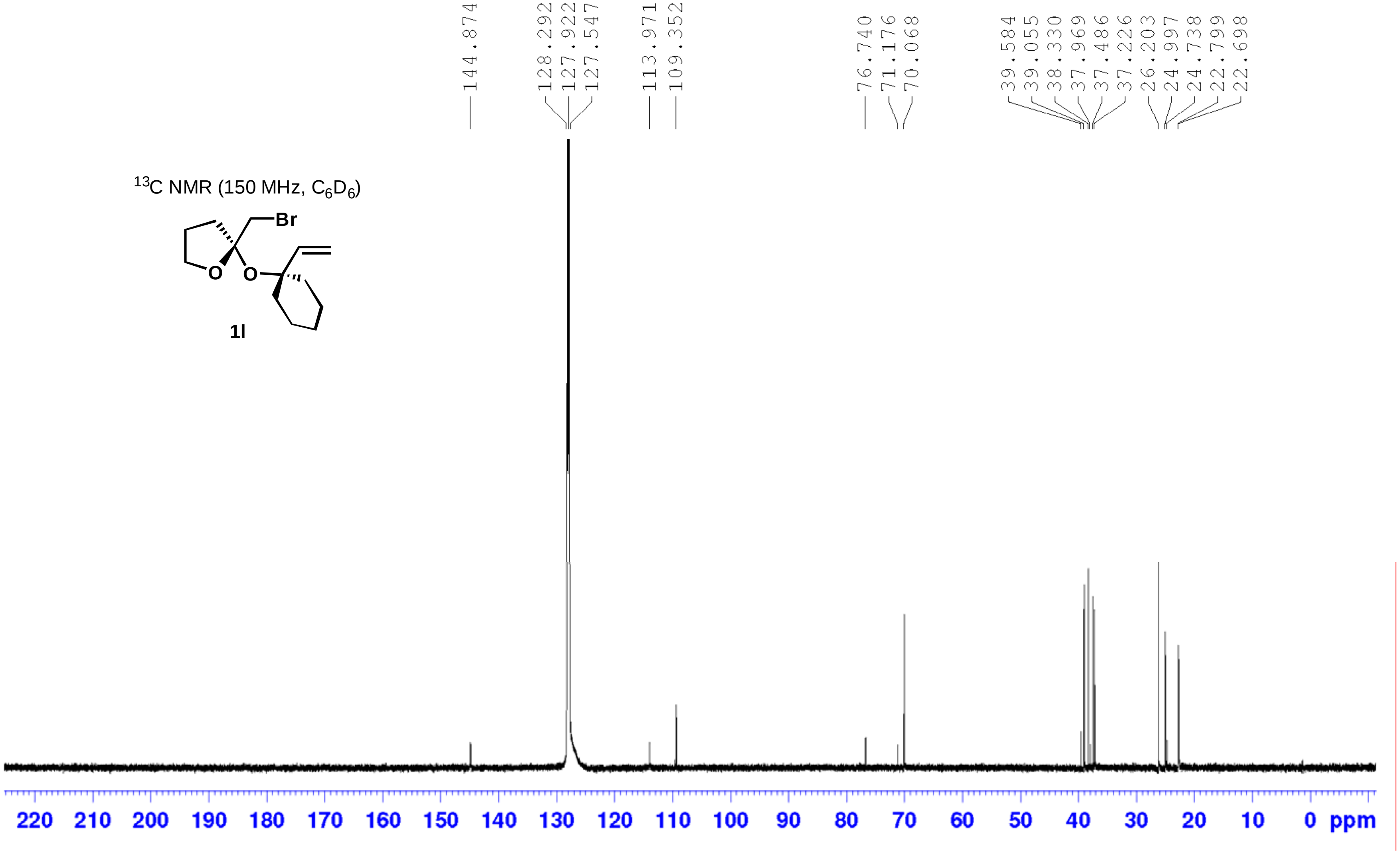

7.260
7.218
7.198
7.185
7.168
7.147
7.059
7.051
6.956
6.939
6.555
6.547
3.994
3.986
3.977
3.973
3.966
3.959
3.953
3.941
3.929
3.920
3.910
3.905
3.890
3.792
3.758
3.738
3.717
3.087
3.068
2.827
2.808
2.789
2.769
2.750
2.731
2.712
2.193
2.171
2.160
2.138
2.087
2.081
2.067
2.062
2.049
2.044
2.036
2.025
2.019
2.009
2.003
1.991
1.975
1.949
1.942
1.938
1.934
1.929
1.920
1.906
1.901
1.899
1.891
1.888
1.884
1.881
1.868
1.861
1.855
1.847
1.838
1.831
^{1}H NMR (400 MHz, $CDCl_3$)
N–Me
H
O
O
2k
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.08
1.00
1.02
0.97
1.17
1.13
1.03
3.06
1.17
2.00
1.13
1.18
3.13
2.29
0.28

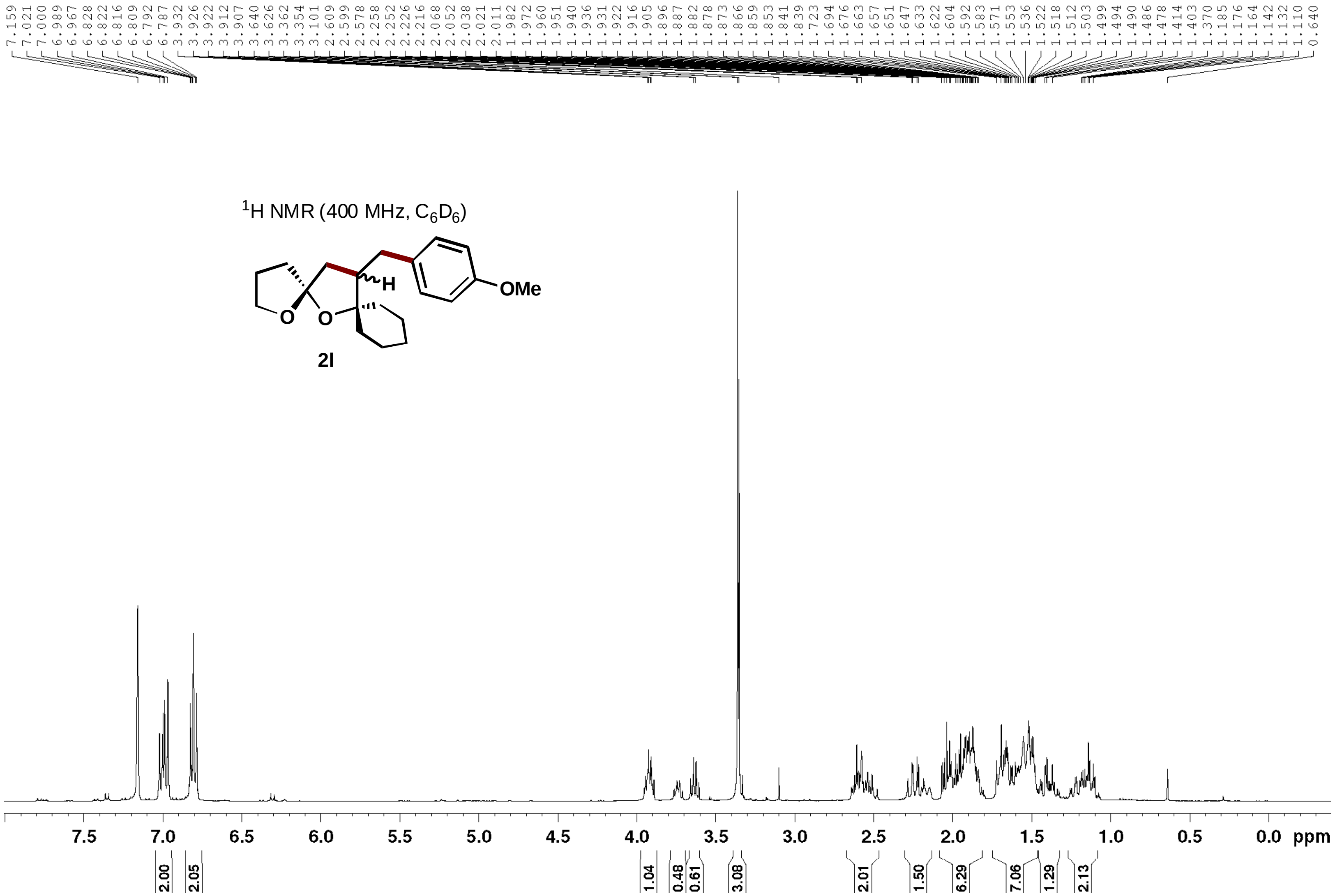

136.66
133.13
128.26
127.90
121.60
119.04
115.13
107.26
99.29
77.32
77.00
76.68
72.45
67.19
41.23
39.72
36.77
35.86
32.88
24.40
^{13}C NMR (100 MHz, CDCl$_3$)
N–Me
H
O
O
2k
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

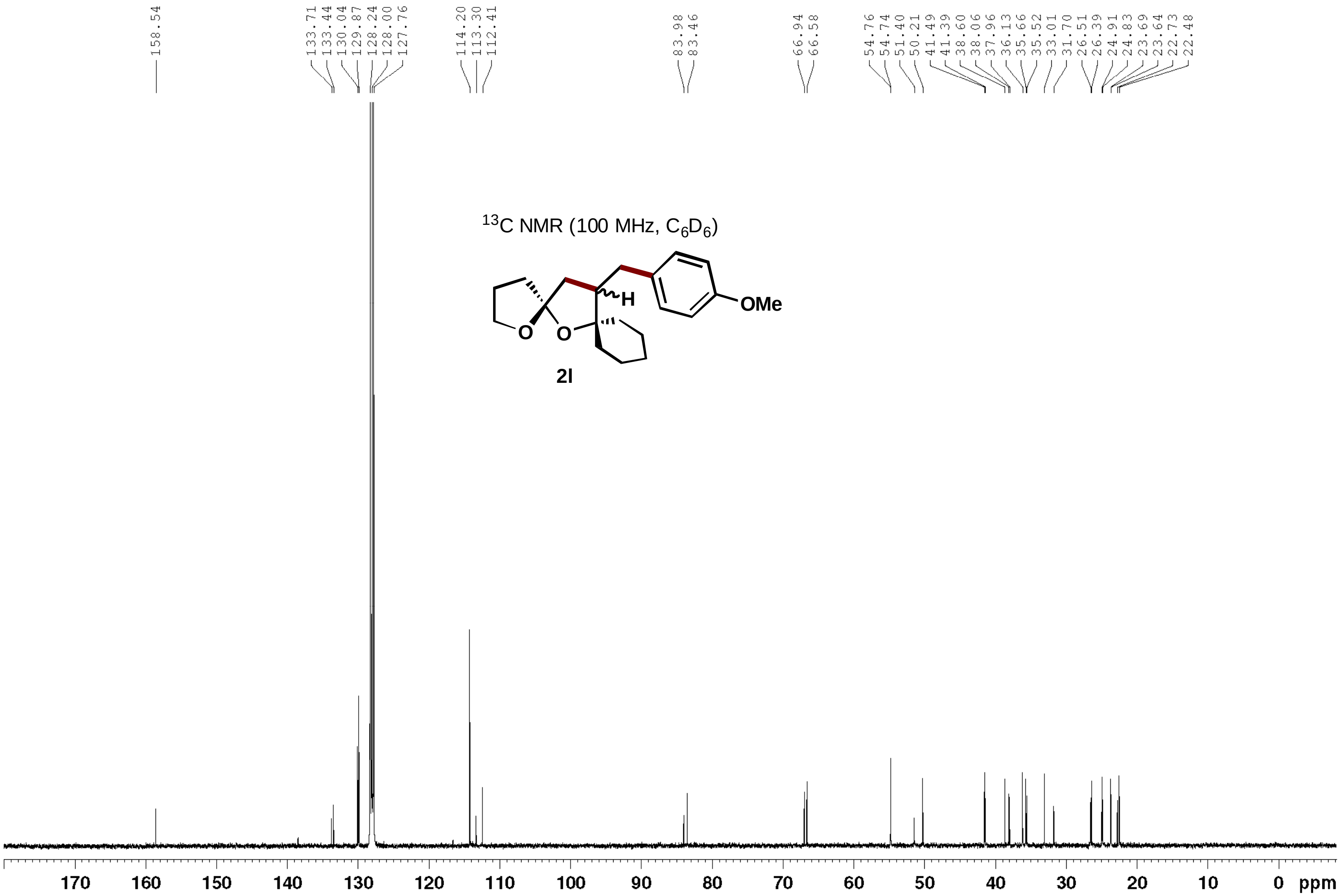


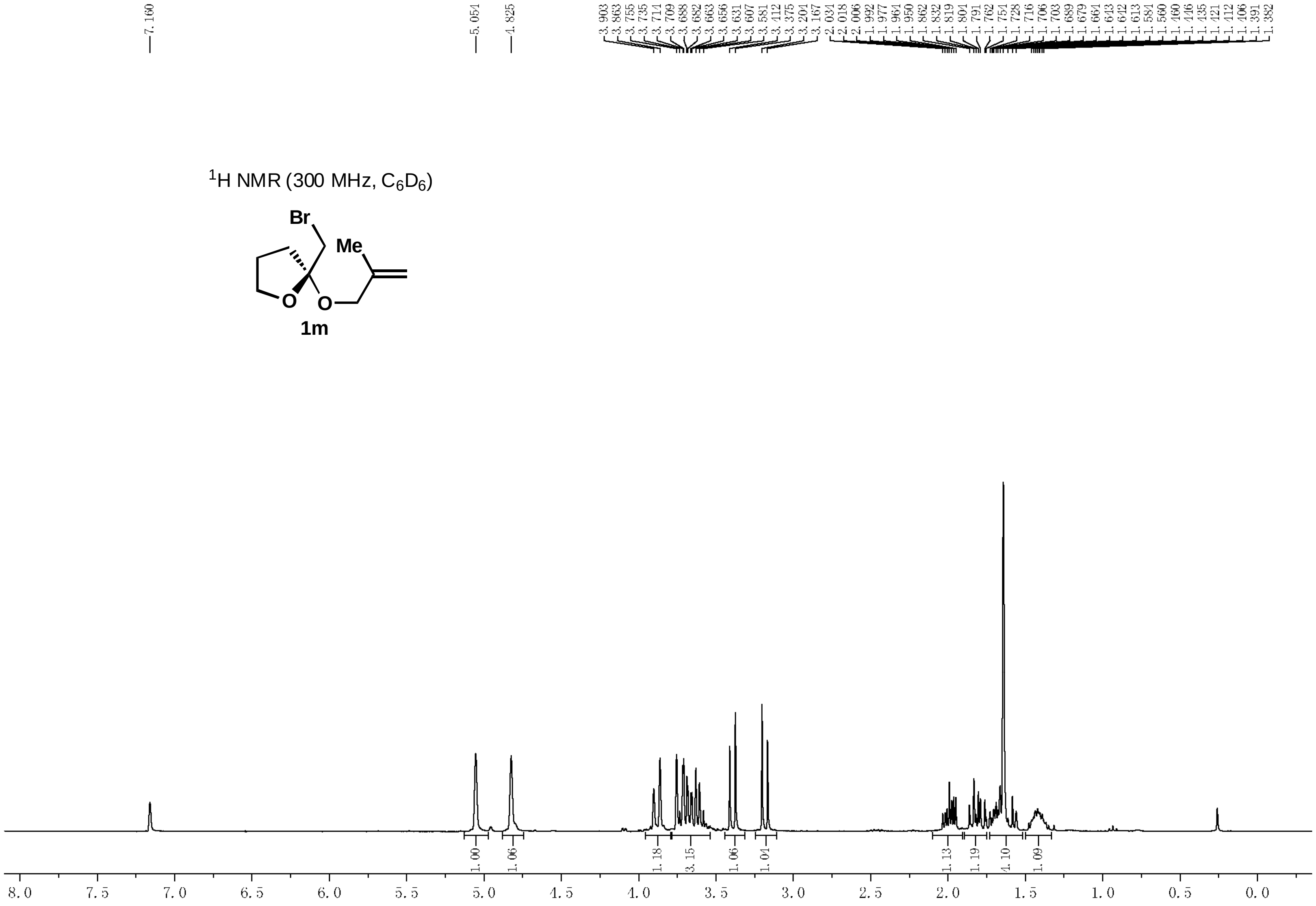
^{1}H NMR (400 MHz, C_6D_6)

1l


144.874
128.292
127.922
127.547
113.971
109.352
76.740
71.176
70.068
39.584
39.055
38.330
37.969
37.486
37.226
26.203
24.997
24.738
22.799
22.698
^{13}C NMR (150 MHz, C_6D_6)
Br
O
O
1l
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

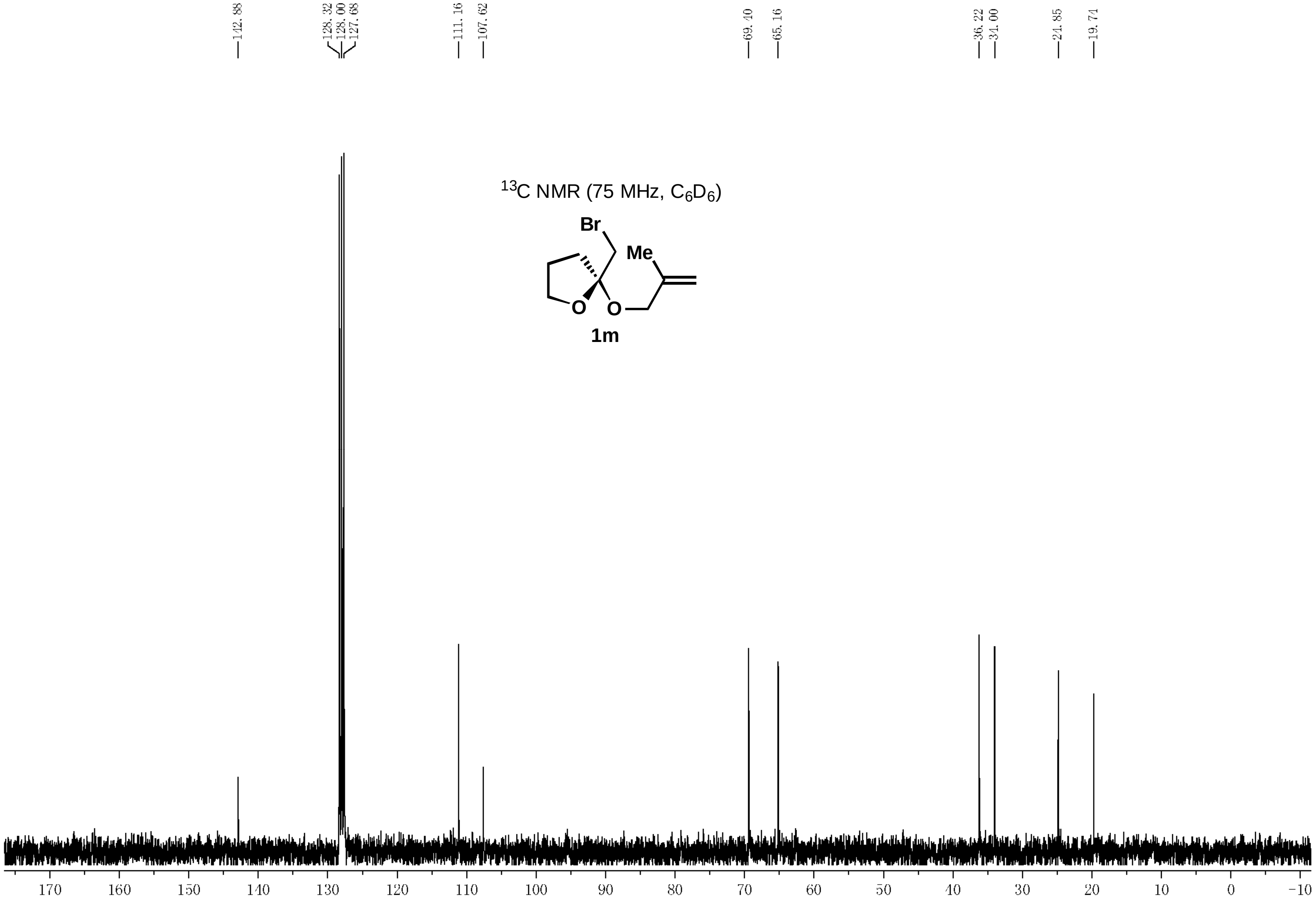

7.159
7.021
7.000
6.989
6.967
6.828
6.822
6.816
6.809
6.792
6.787
3.932
3.926
3.922
3.912
3.907
3.640
3.626
3.362
3.354
3.101
2.609
2.599
2.578
2.258
2.252
2.226
2.216
2.068
2.052
2.038
2.021
2.011
1.982
1.972
1.960
1.951
1.940
1.936
1.931
1.922
1.916
1.905
1.896
1.887
1.882
1.878
1.873
1.866
1.859
1.853
1.841
1.839
1.723
1.694
1.676
1.663
1.657
1.651
1.647
1.633
1.622
1.604
1.592
1.583
1.571
1.553
1.536
1.522
1.518
1.512
1.503
1.499
1.494
1.490
1.486
1.478
1.414
1.403
1.370
1.185
1.176
1.164
1.142
1.132
1.110
0.640
^{1}H NMR (400 MHz, C_6D_6)
H
OMe
O
O
2l
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
2.05
1.04
0.48
0.61
3.08
2.01
1.50
6.29
7.06
1.29
2.13


158.54
133.71
133.44
130.04
129.87
128.24
128.00
127.76
114.20
113.30
112.41
83.98
83.46
66.94
66.58
54.76
54.74
51.40
50.21
41.49
41.39
38.60
38.06
37.96
36.13
35.66
35.52
33.01
31.70
26.51
26.39
24.91
24.83
23.69
23.64
22.73
22.48
^{13}C NMR (100 MHz, C_6D_6)
H
O
O
OMe
2l
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



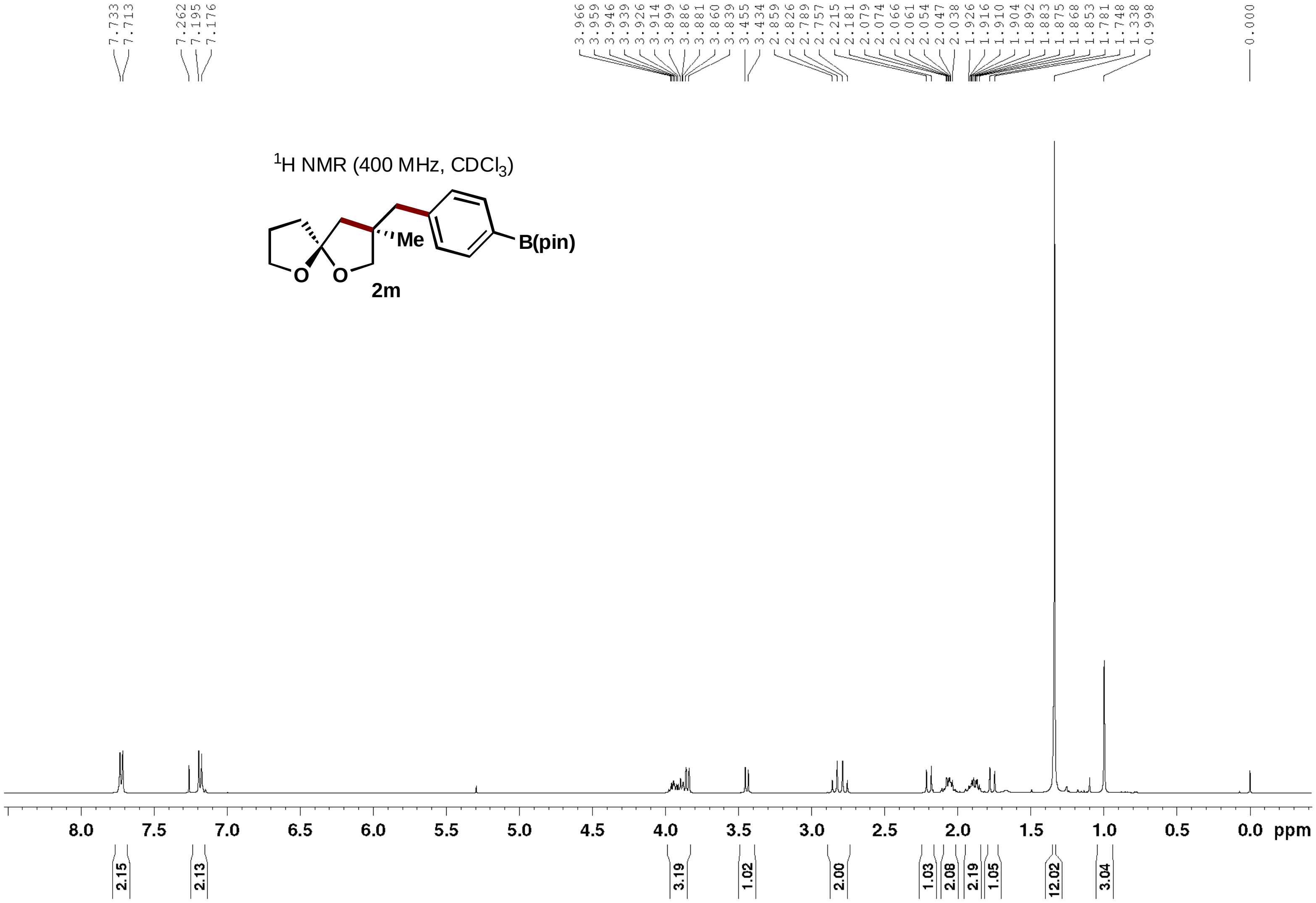
^{1}H NMR (300 MHz, C_6D_6)

1m



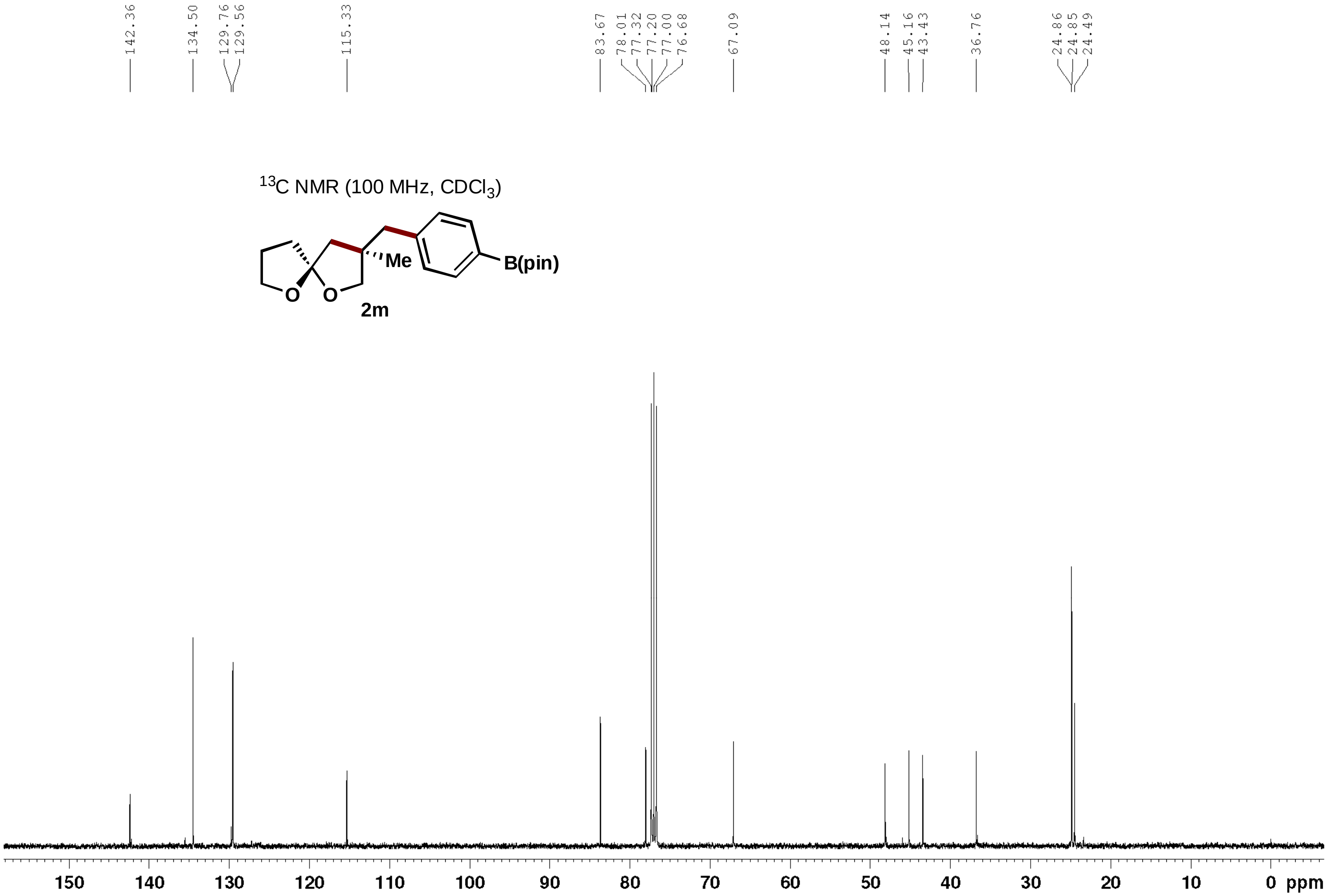
^{13}C NMR (75 MHz, C_6D_6)

1m



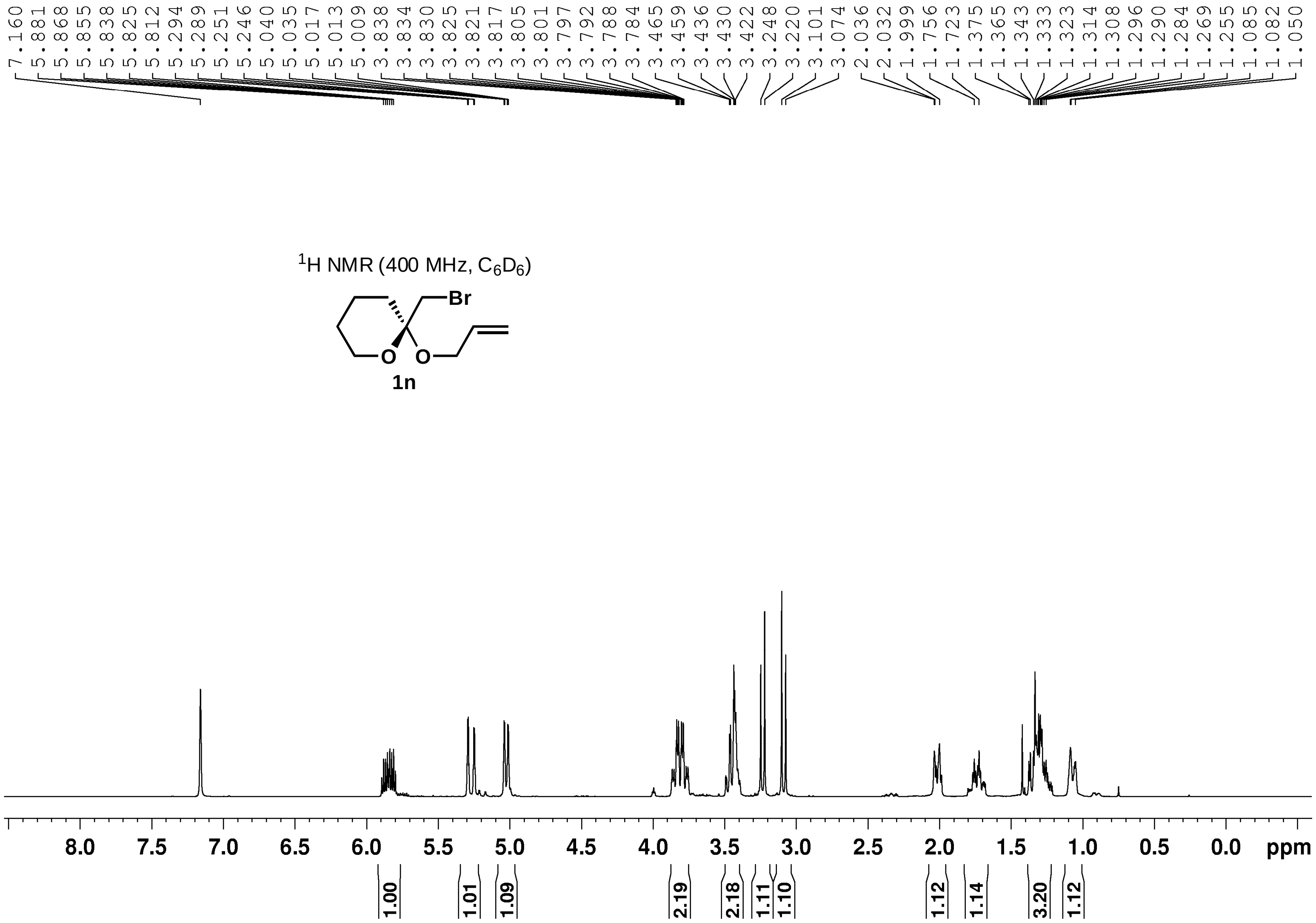
^{1}H NMR (400 MHz, $CDCl_3$)

2m



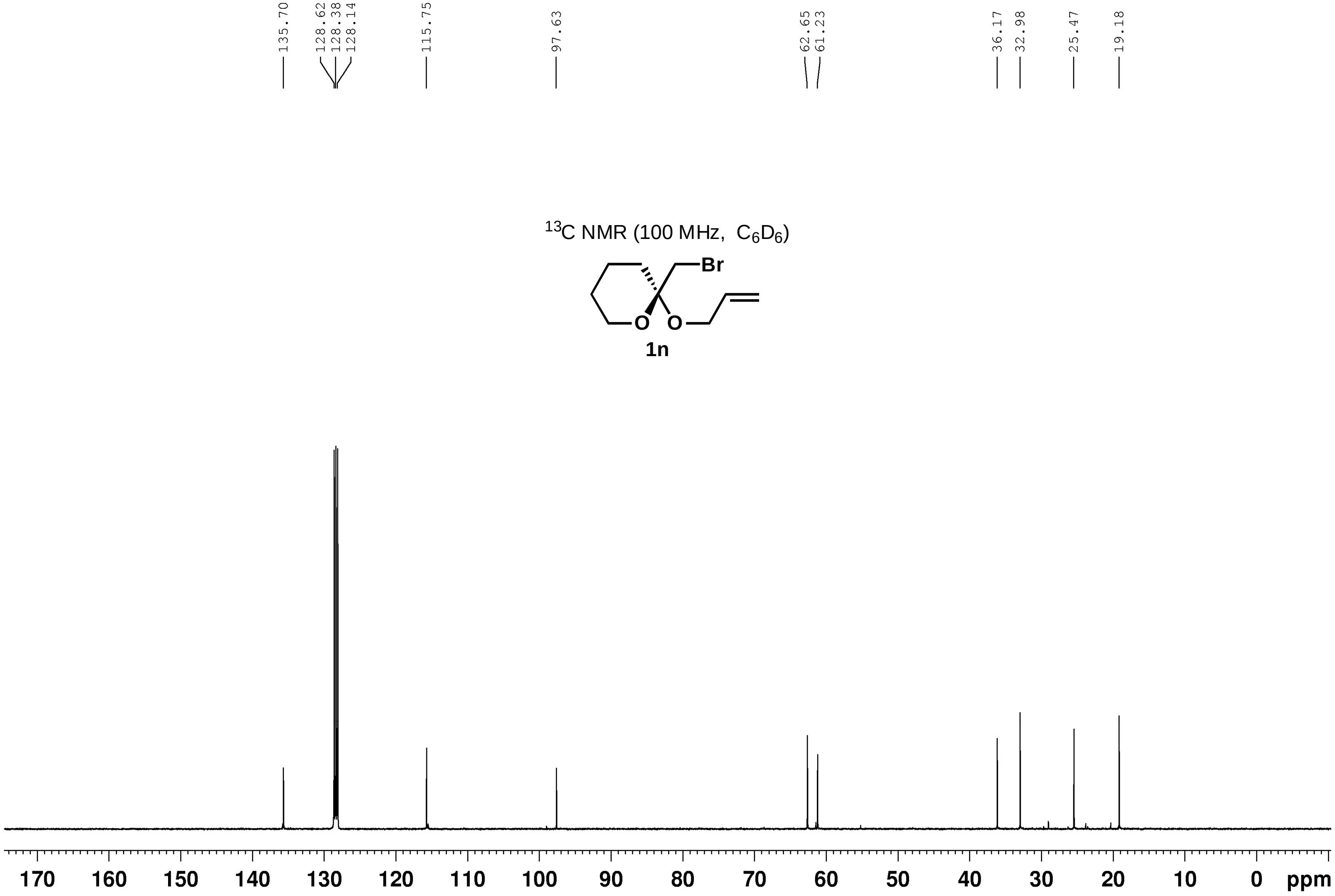
^{13}C NMR (100 MHz, CDCl$_3$)

2m



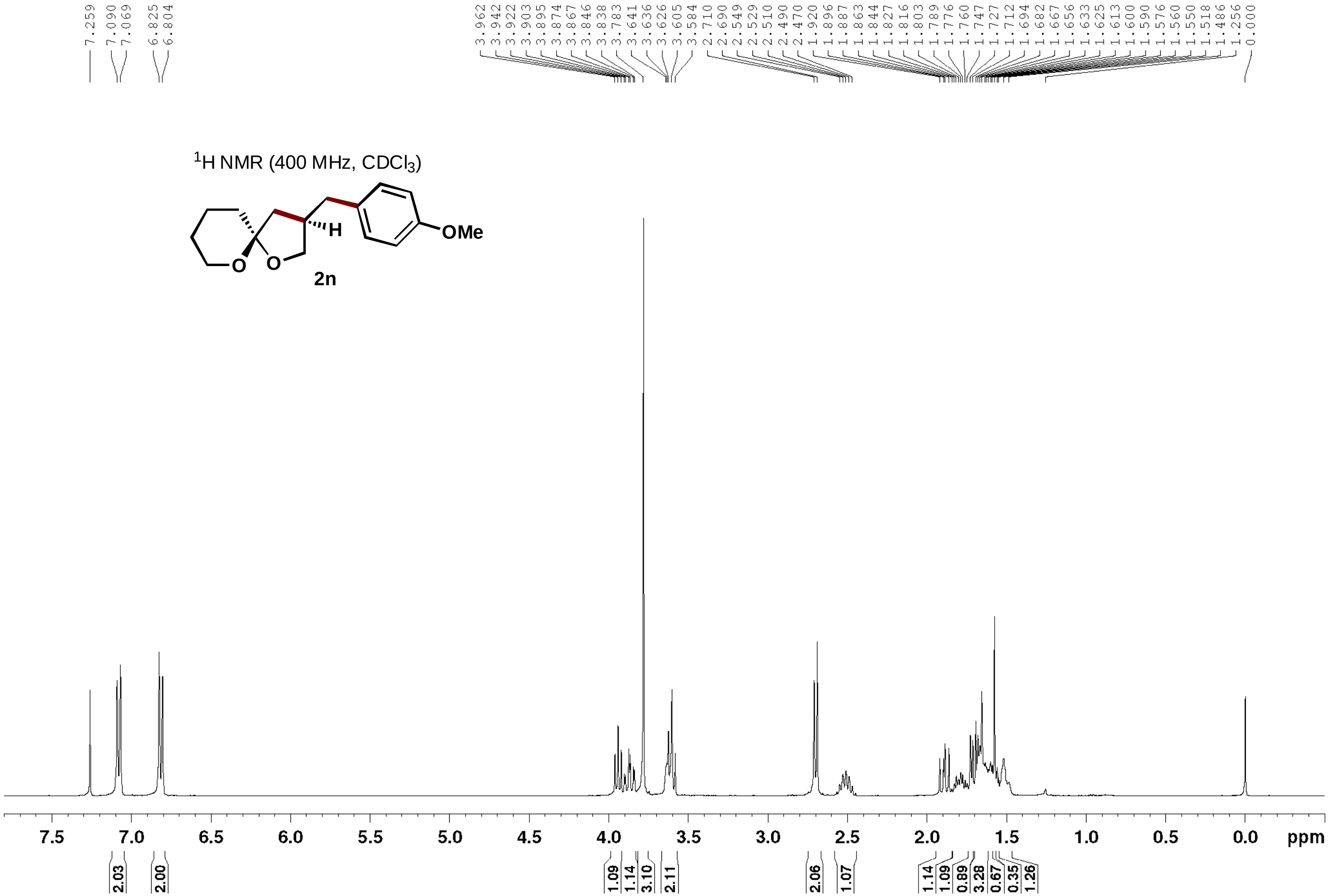
^{1}H NMR (400 MHz, C_6D_6)

1n



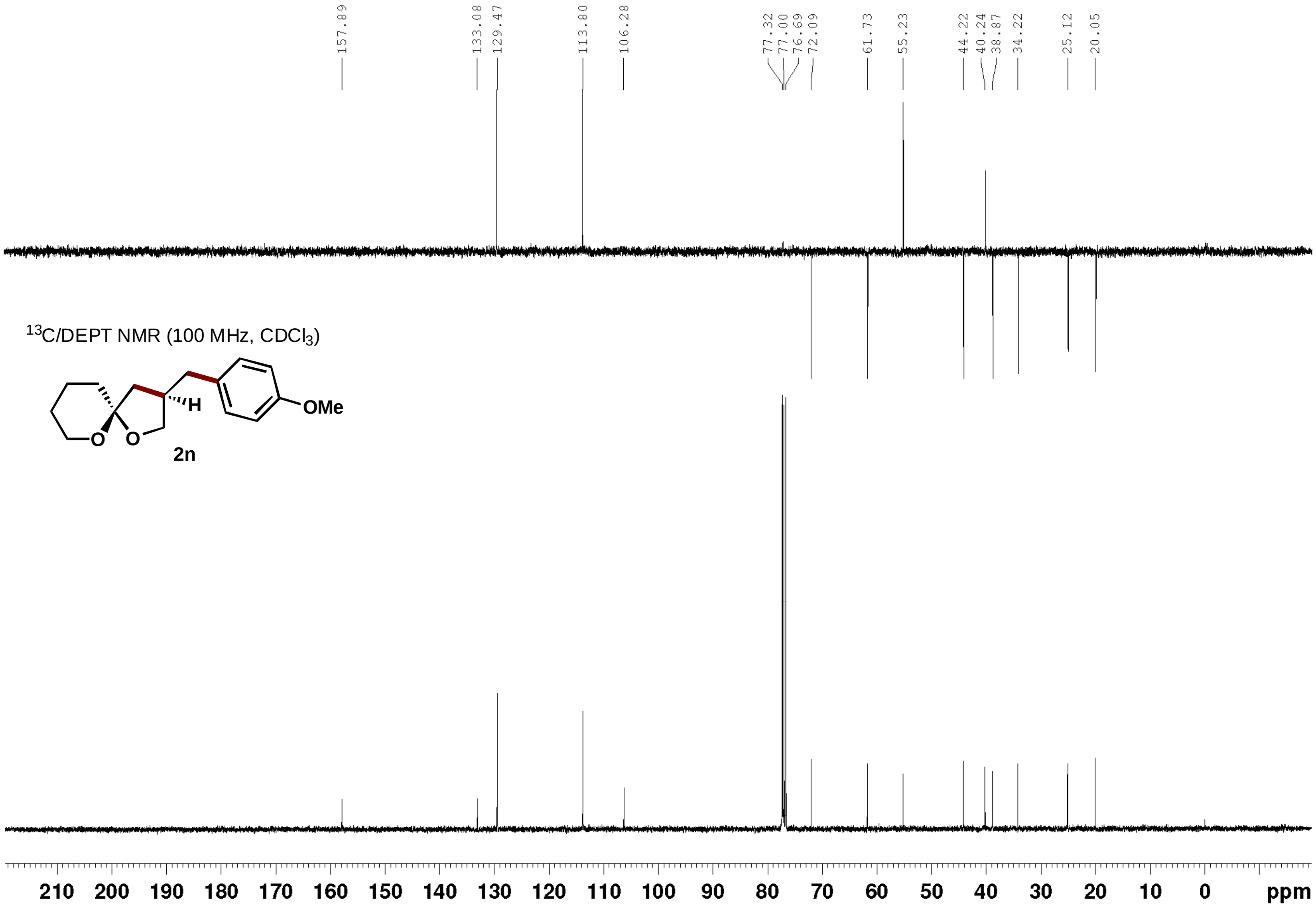
^{13}C NMR (100 MHz, C_6D_6)

1n

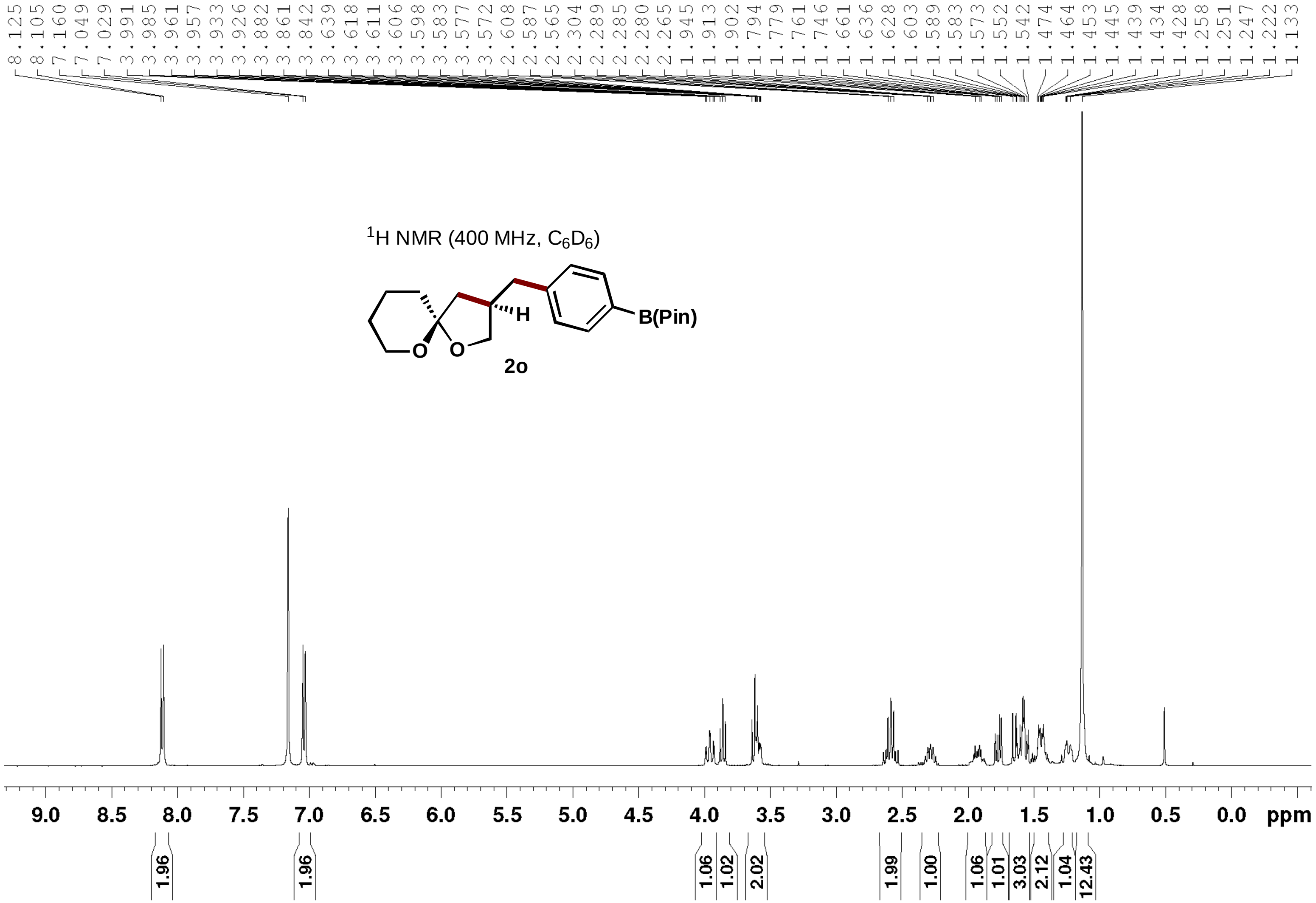


^{1}H NMR (400 MHz, $CDCl_3$)

2n

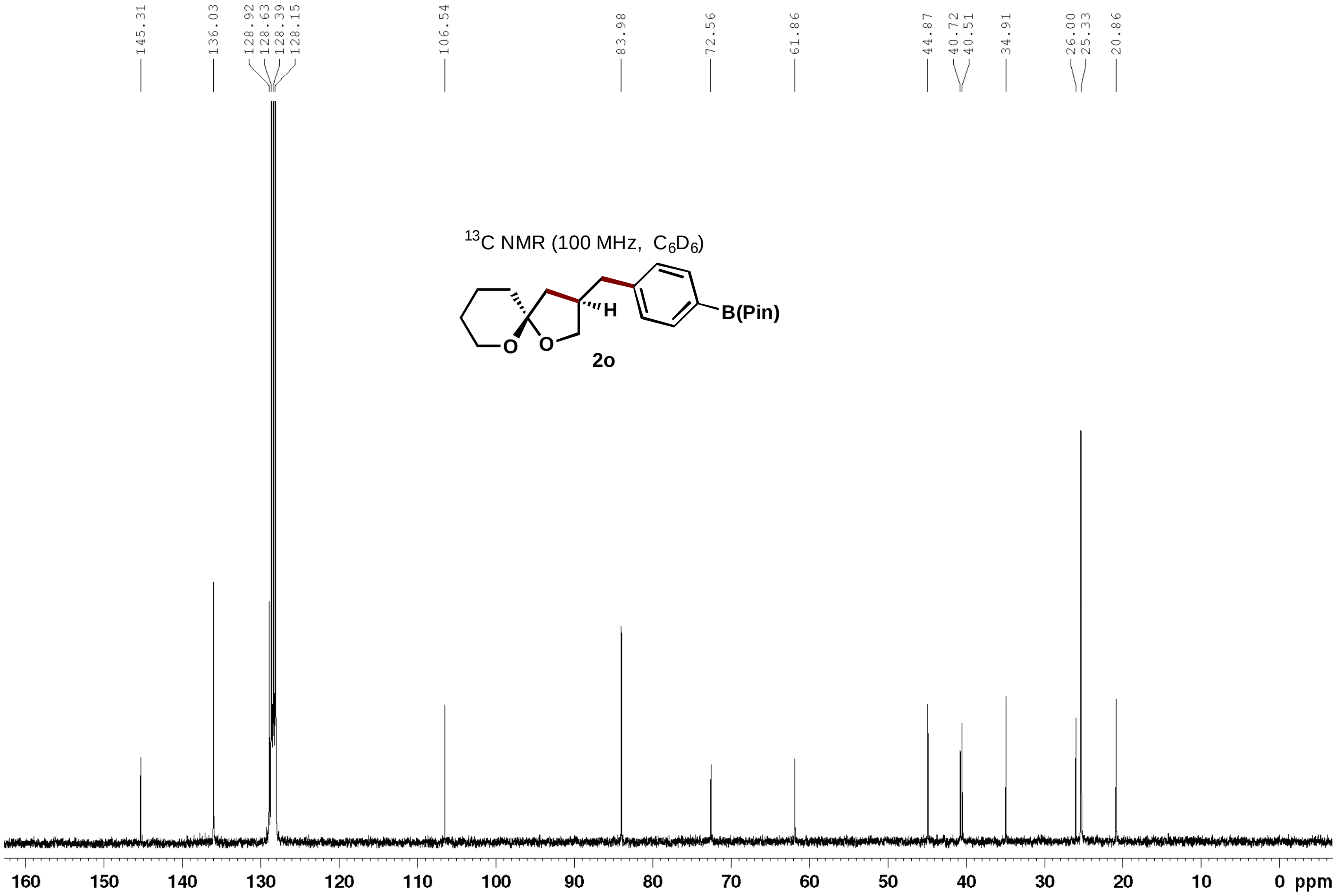

^{13}C/DEPT NMR (100 MHz, $CDCl_3$)

2n



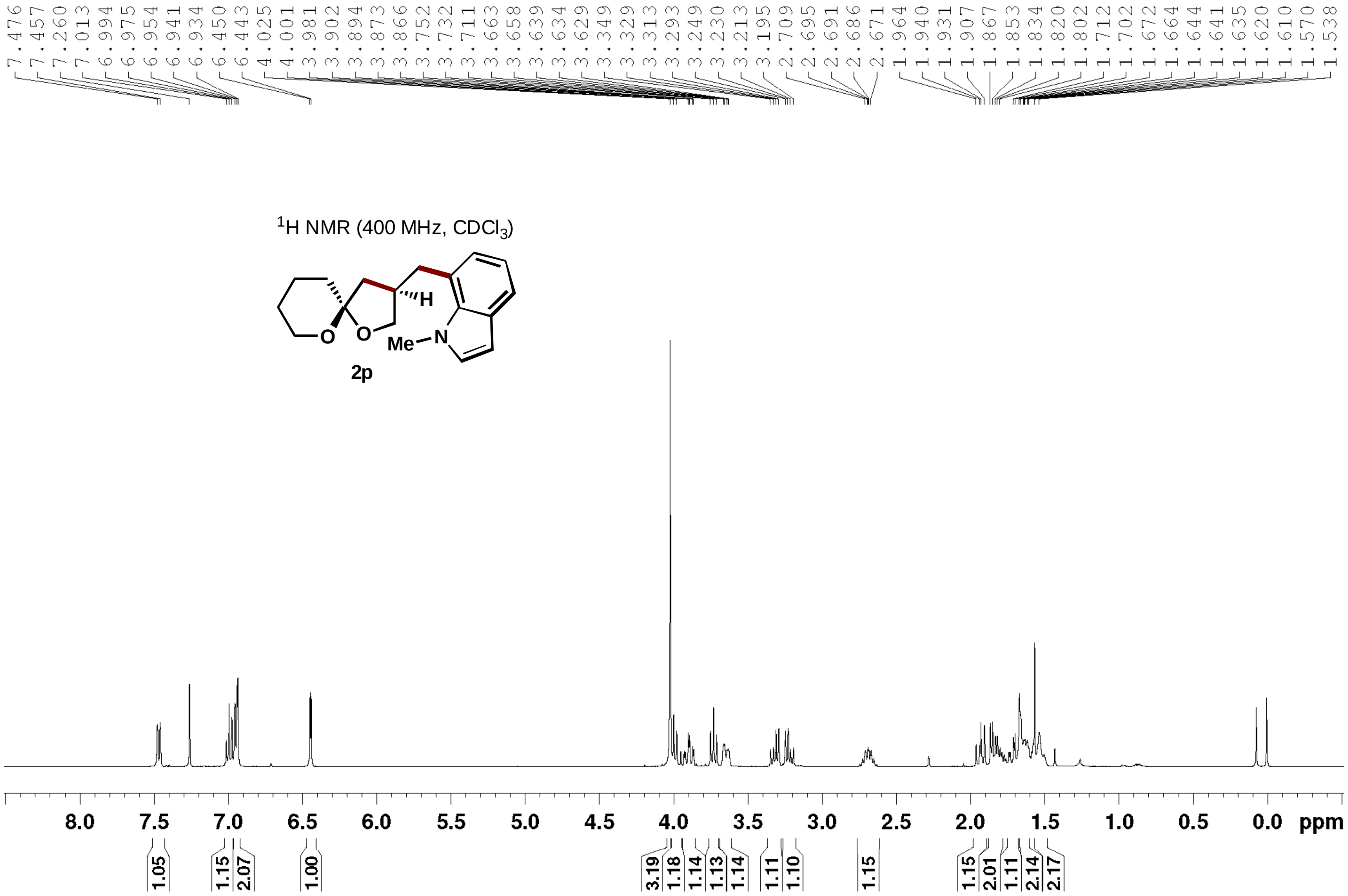
^{1}H NMR (400 MHz, C_6D_6)

2o

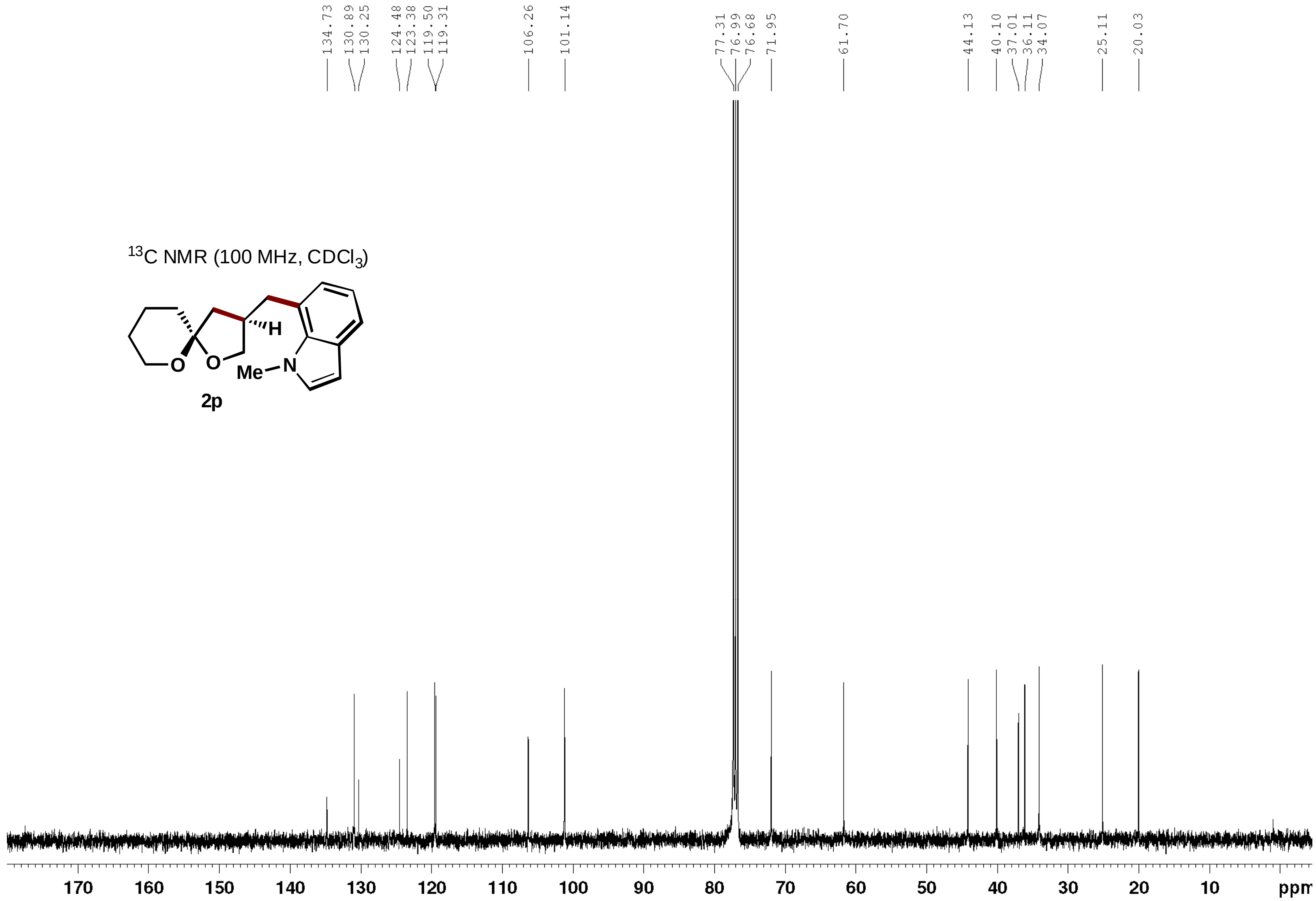


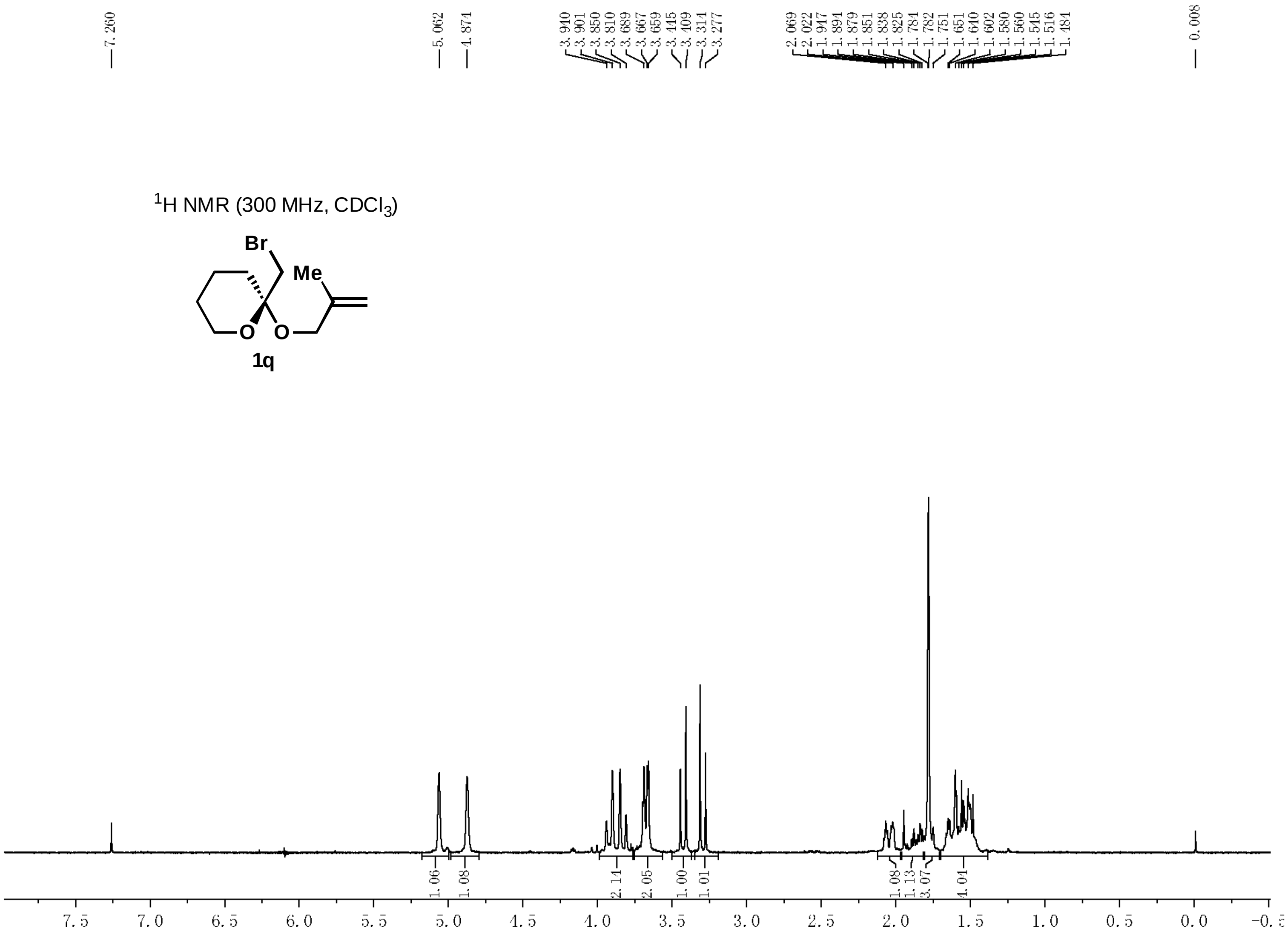
^{13}C NMR (100 MHz, C_6D_6)

2o

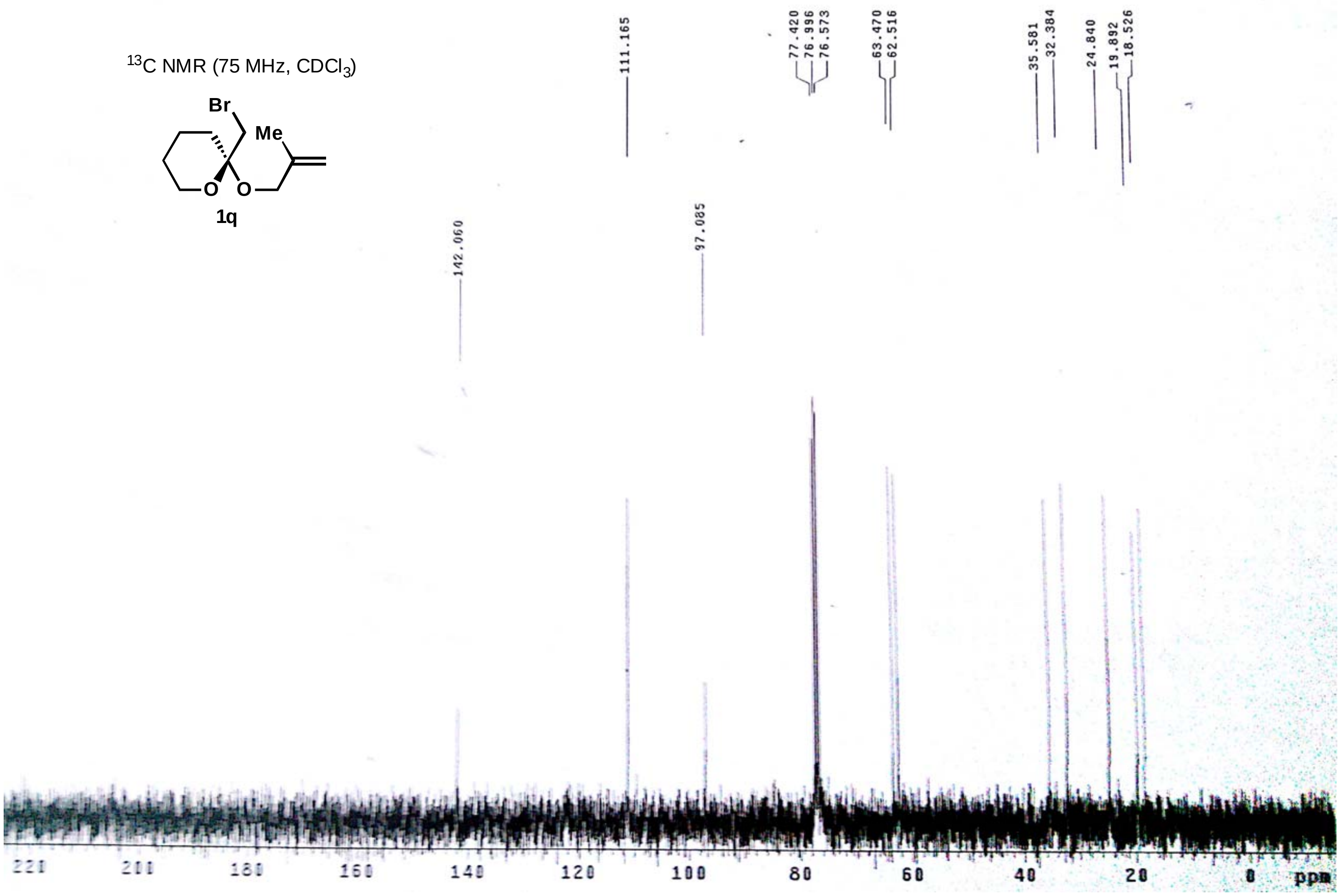

^{1}H NMR (400 MHz, $CDCl_3$)

2p

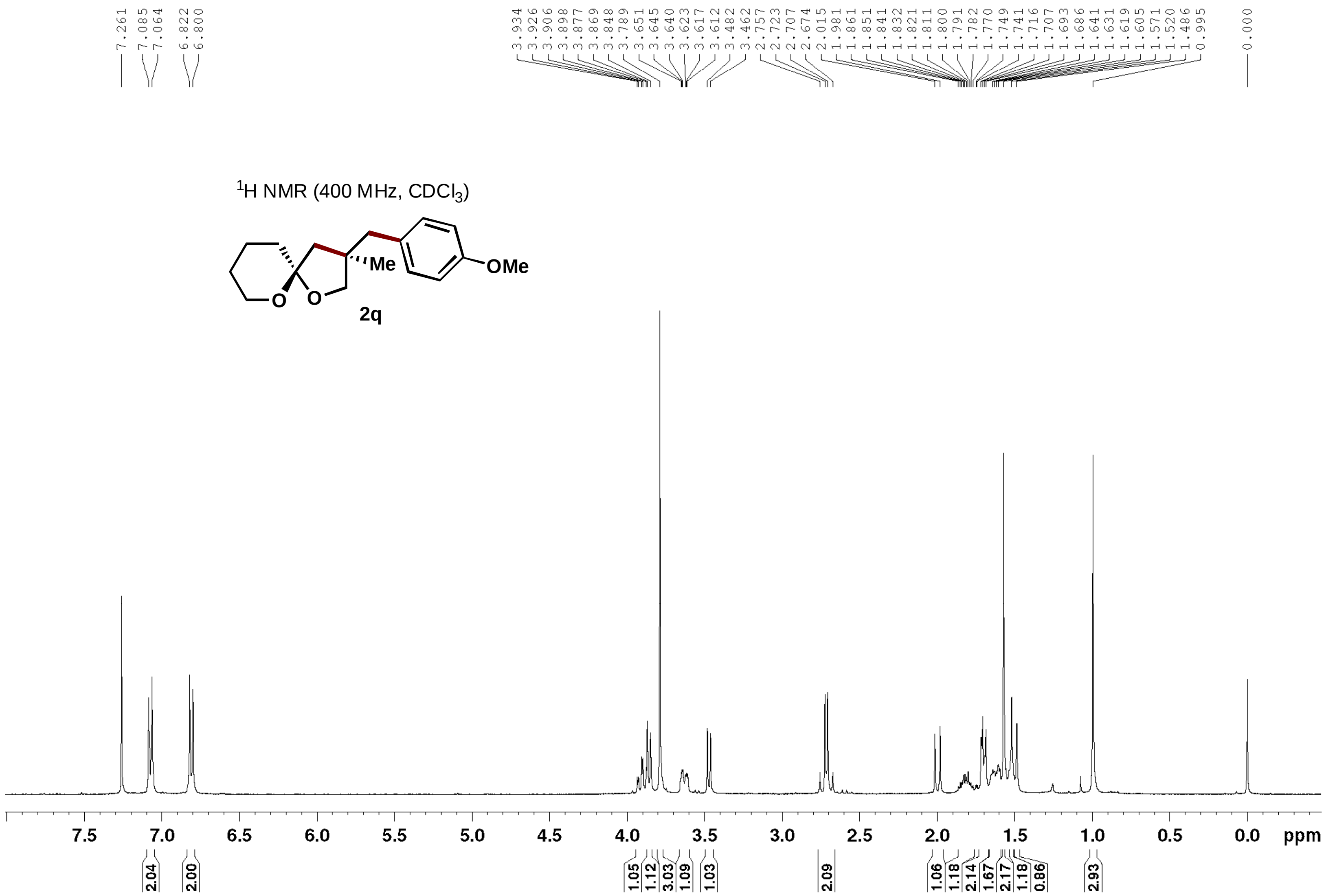

134.73
130.89
130.25
124.48
123.38
119.50
119.31
106.26
101.14
77.31
76.99
76.68
71.95
61.70
44.13
40.10
37.01
36.11
34.07
25.11
20.03
^{13}C NMR (100 MHz, $CDCl_3$)
O
O
H
Me
N
2p
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

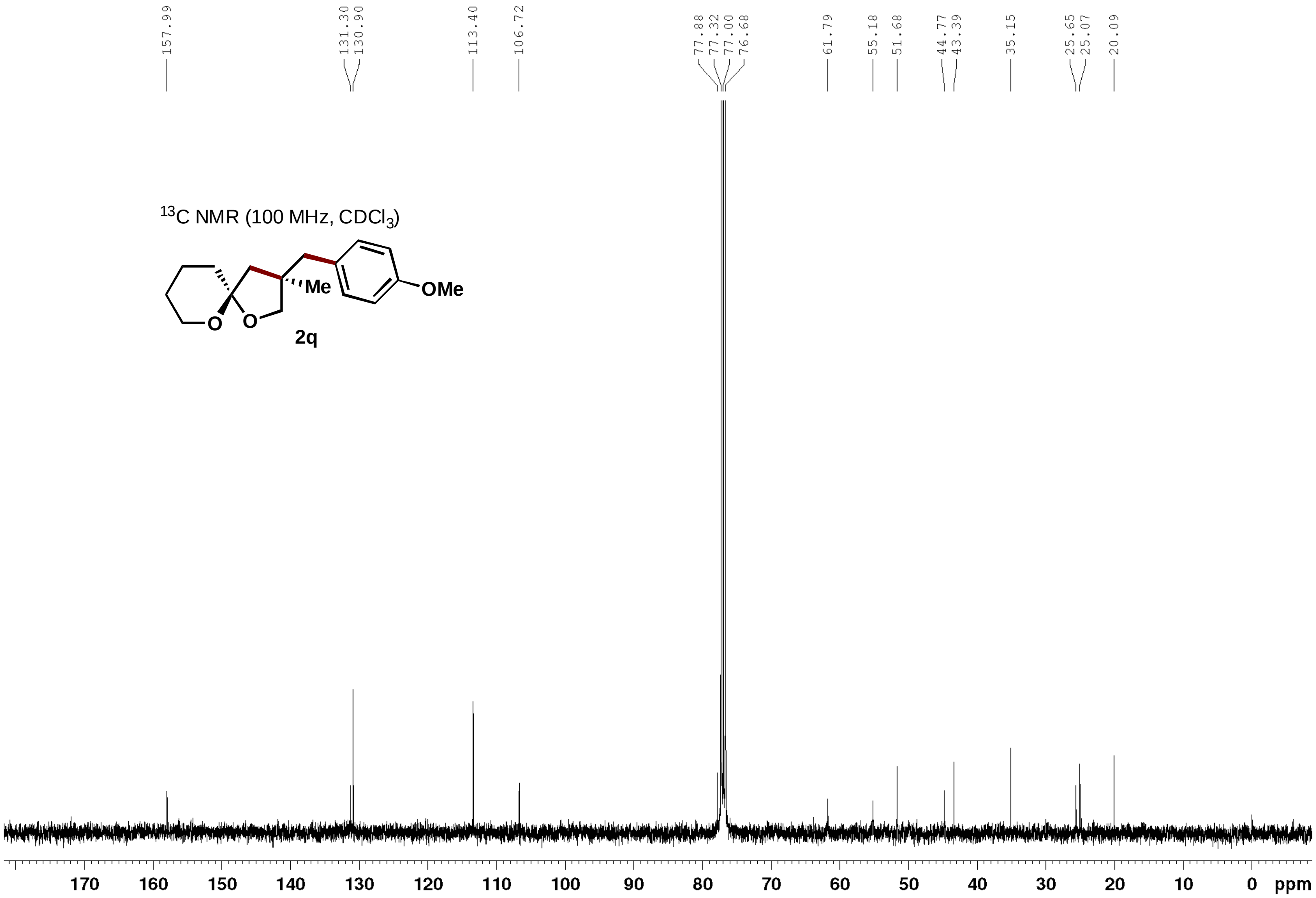

7.260
5.062
4.874
3.940
3.901
3.850
3.810
3.689
3.667
3.659
3.415
3.409
3.314
3.277
2.069
2.022
1.917
1.894
1.879
1.851
1.838
1.825
1.784
1.782
1.751
1.651
1.610
1.602
1.580
1.560
1.545
1.516
1.484
0.008
^{1}H NMR (300 MHz, $CDCl_3$)
Br
Me
O
O
1q
1.06
1.08
2.14
2.05
1.00
1.01
1.08
1.13
3.07
4.04
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

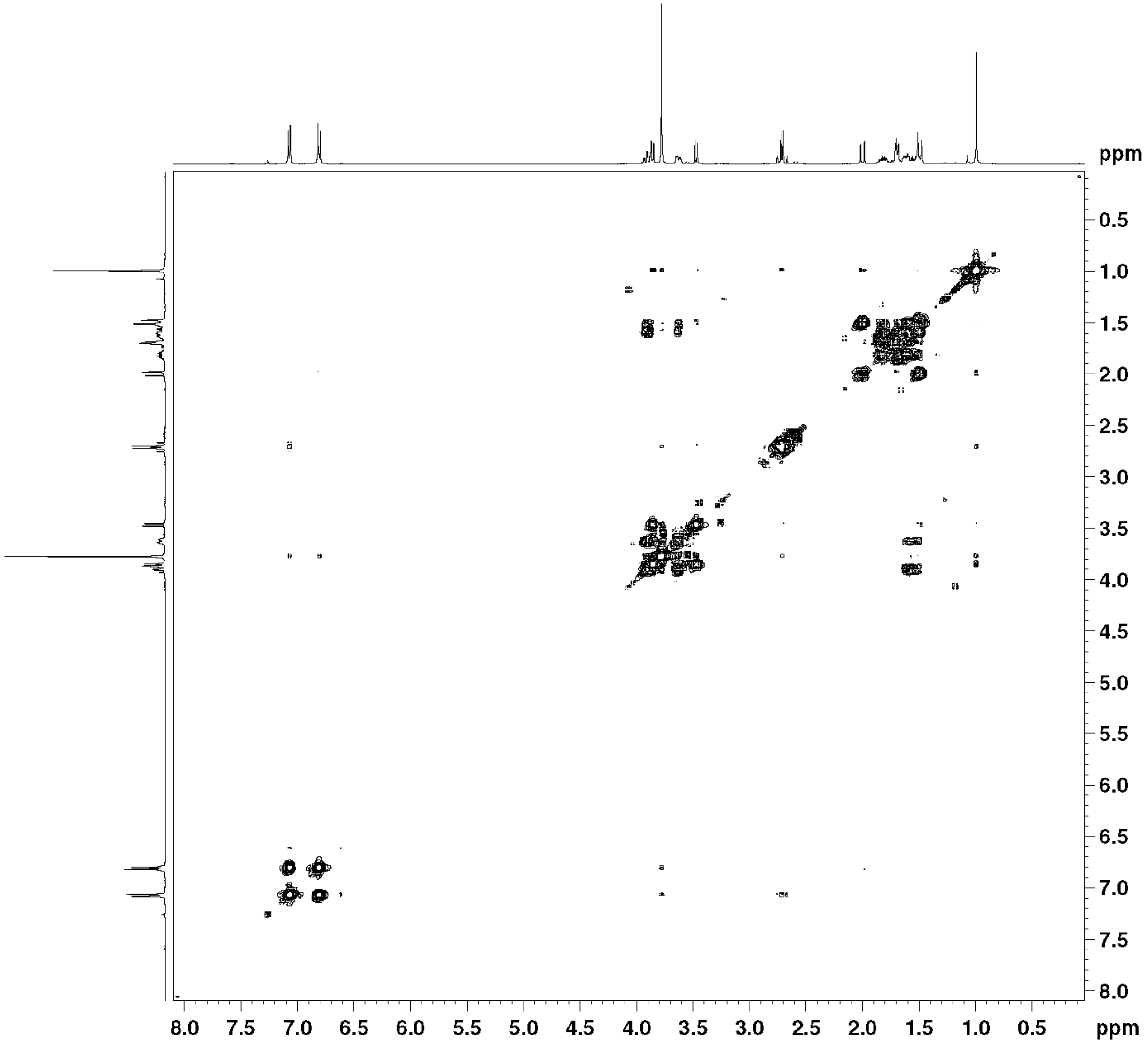
^{13}C NMR (75 MHz, $CDCl_3$)



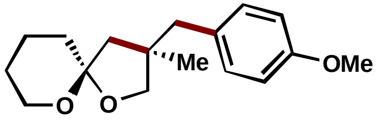
1q

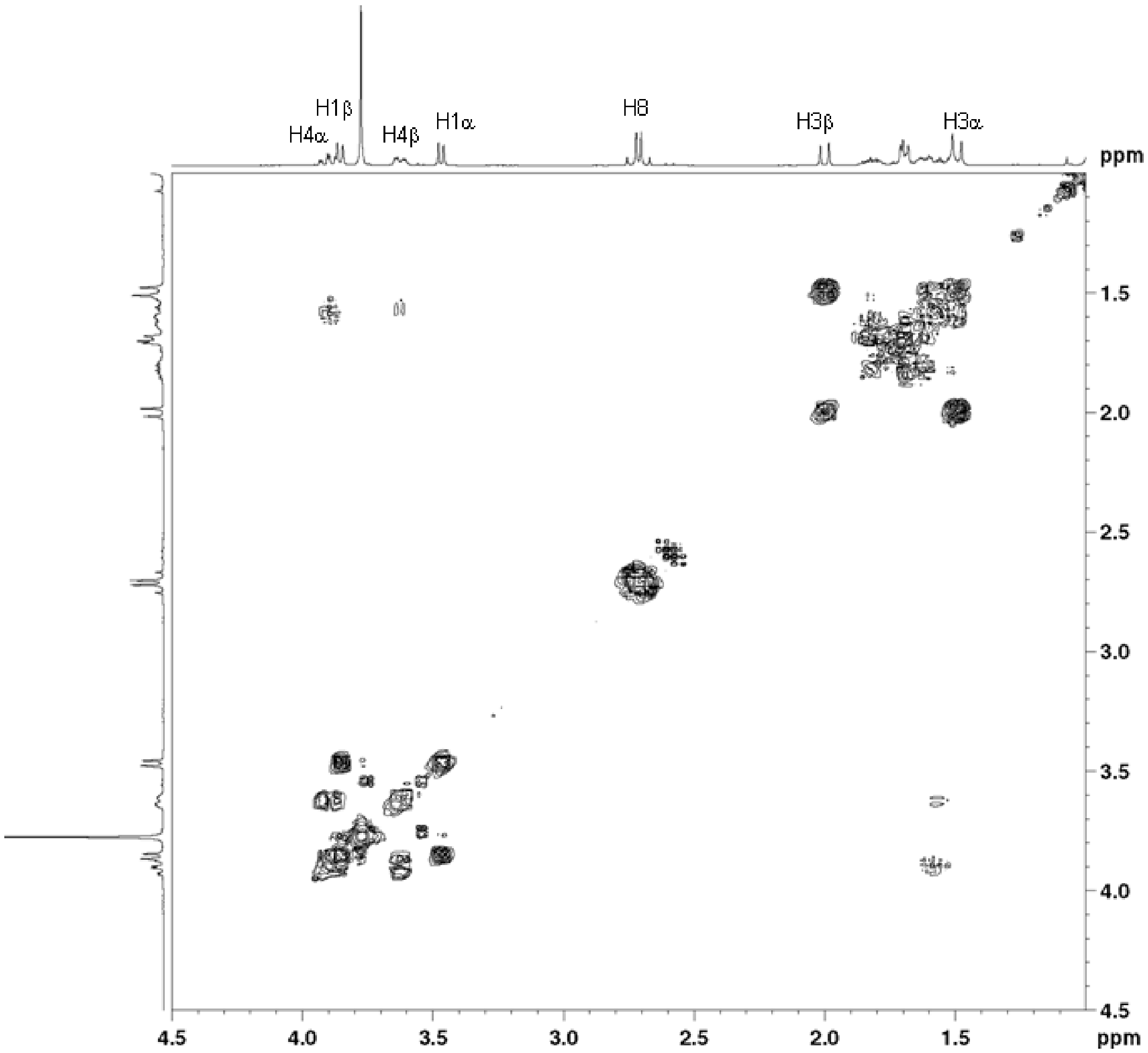

7.261
7.085
7.064
6.822
6.800
3.934
3.926
3.906
3.898
3.877
3.869
3.848
3.789
3.651
3.645
3.640
3.623
3.617
3.612
3.482
3.462
2.757
2.723
2.707
2.674
2.015
1.981
1.861
1.851
1.841
1.832
1.821
1.811
1.800
1.791
1.782
1.770
1.749
1.741
1.716
1.707
1.693
1.686
1.641
1.631
1.619
1.605
1.571
1.520
1.486
0.995
0.000
^{1}H NMR (400 MHz, CDCl$_3$)
Me
OMe
O
O
2q
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.04
2.00
1.05
1.12
3.03
1.09
1.03
2.09
1.06
1.18
2.14
1.67
2.17
1.18
0.86
2.93


157.99
131.30
130.90
113.40
106.72
77.88
77.32
77.00
76.68
61.79
55.18
51.68
44.77
43.39
35.15
25.65
25.07
20.09
13C NMR (100 MHz, CDCl3)
Me
OMe
O
O
2q
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

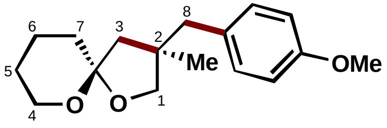


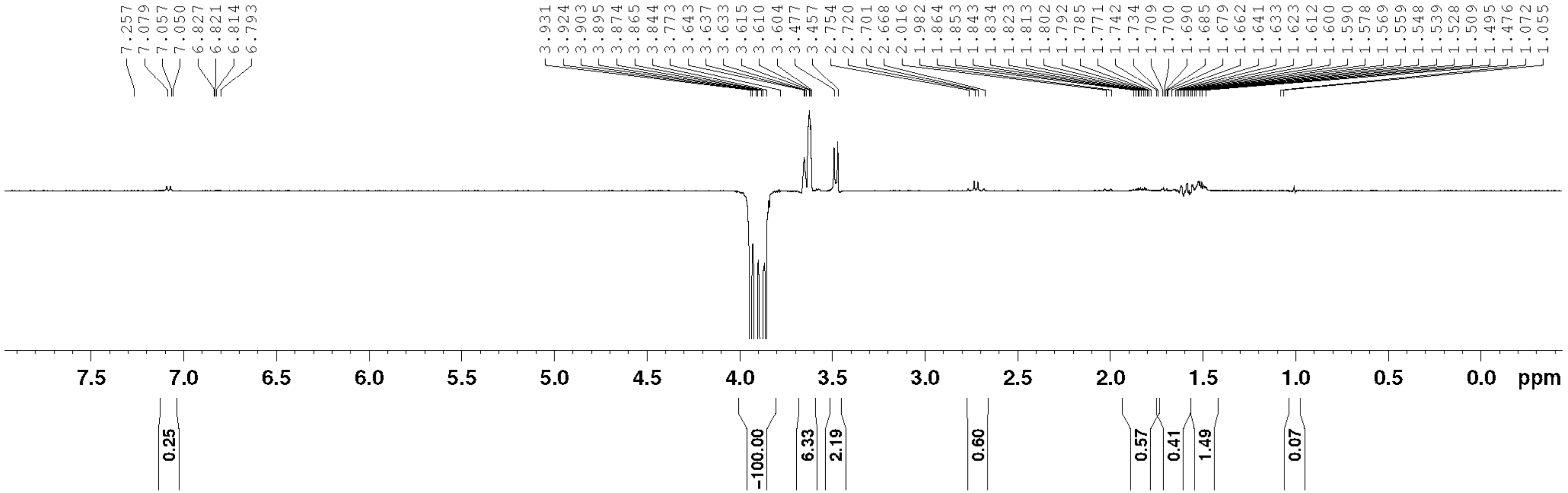
^{1}H –^{1}H COSY of **2q**



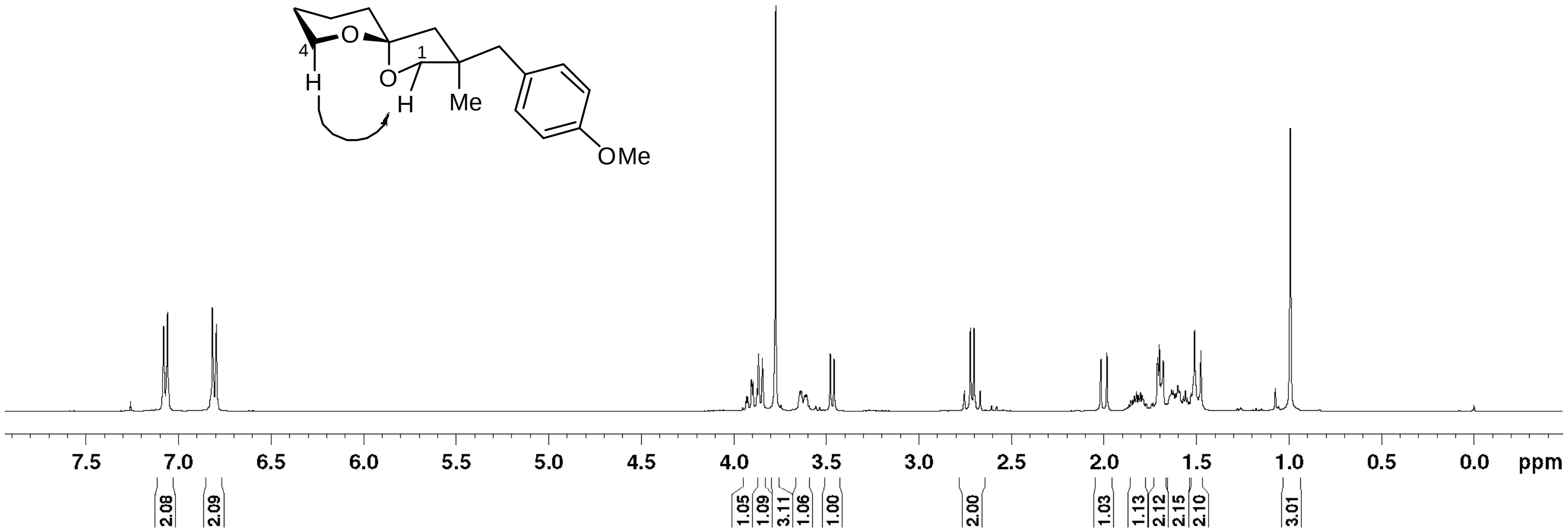


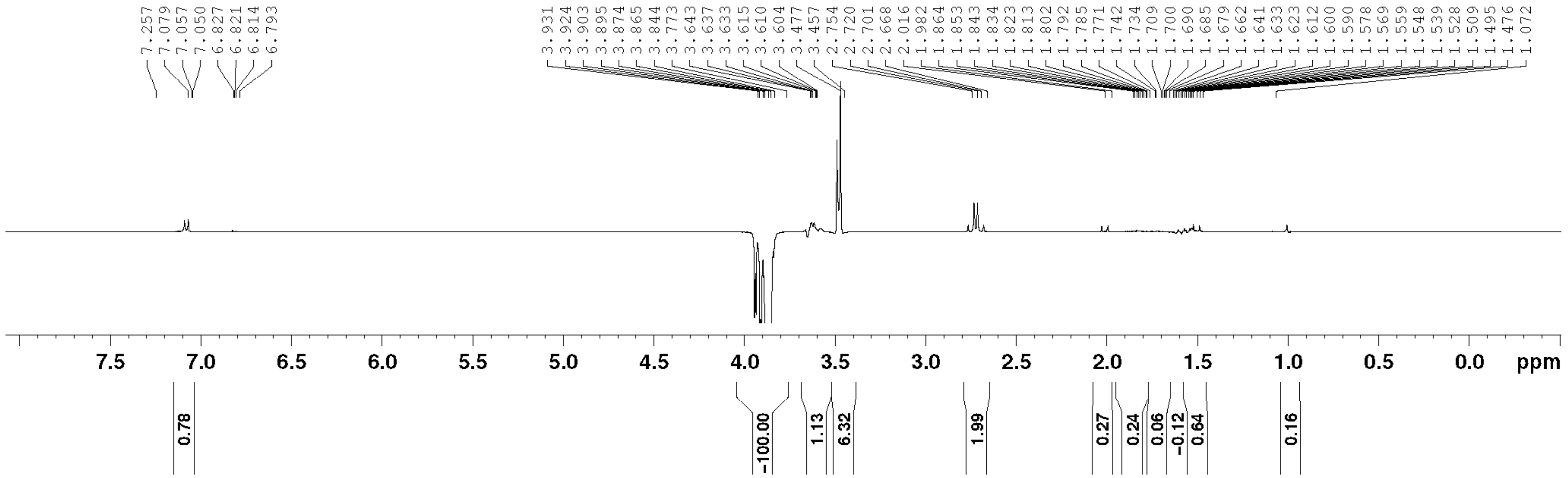
^{1}H –^{1}H COSY of **2q**

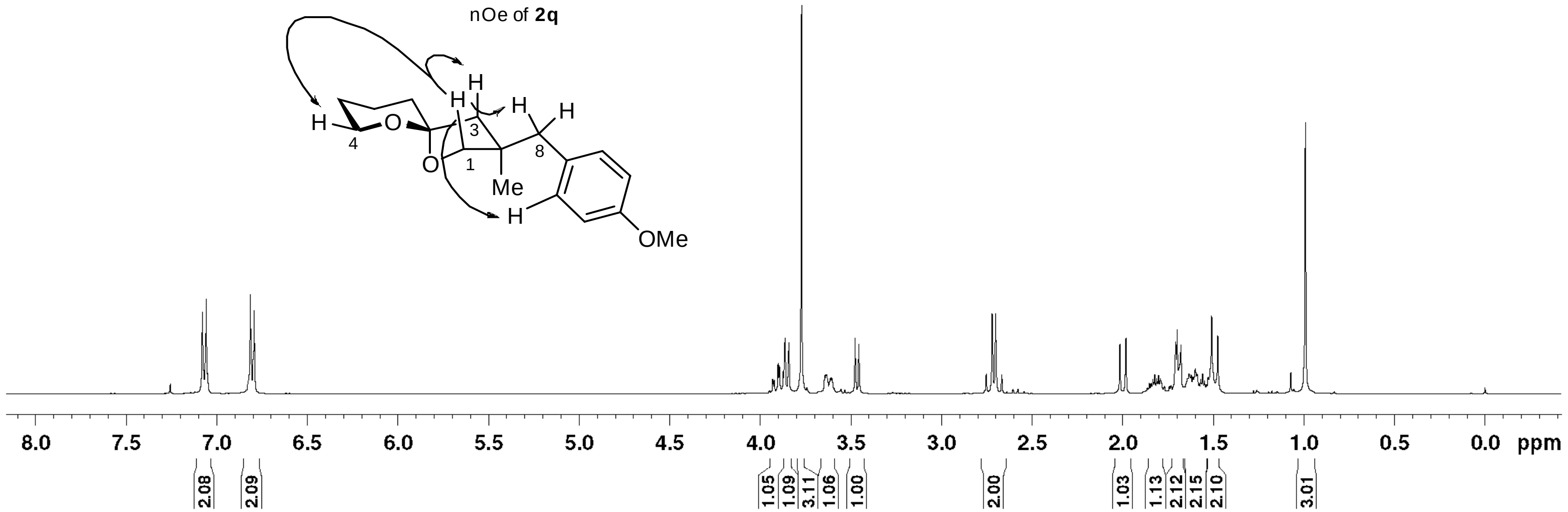


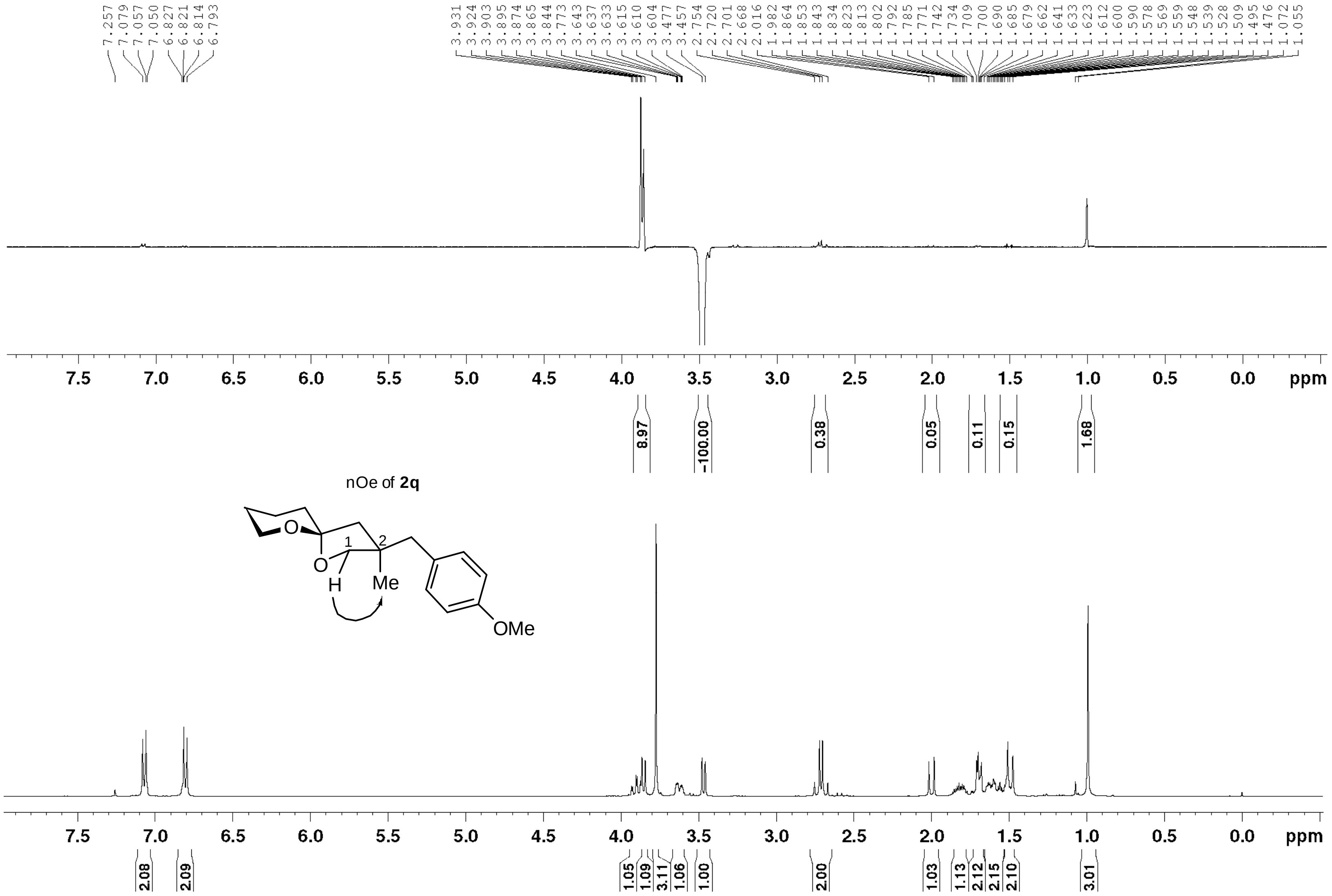

7.257
7.079
7.057
7.050
6.827
6.821
6.814
6.793
3.931
3.924
3.903
3.895
3.874
3.865
3.844
3.773
3.643
3.637
3.633
3.615
3.610
3.604
3.477
3.457
2.754
2.720
2.701
2.668
2.016
1.982
1.864
1.853
1.843
1.834
1.823
1.813
1.802
1.792
1.785
1.771
1.742
1.734
1.709
1.700
1.690
1.685
1.679
1.662
1.641
1.633
1.623
1.612
1.600
1.590
1.578
1.569
1.559
1.548
1.539
1.528
1.509
1.495
1.476
1.072
1.055
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.25
-100.00
6.33
2.19
0.60
0.57
0.41
1.49
0.07

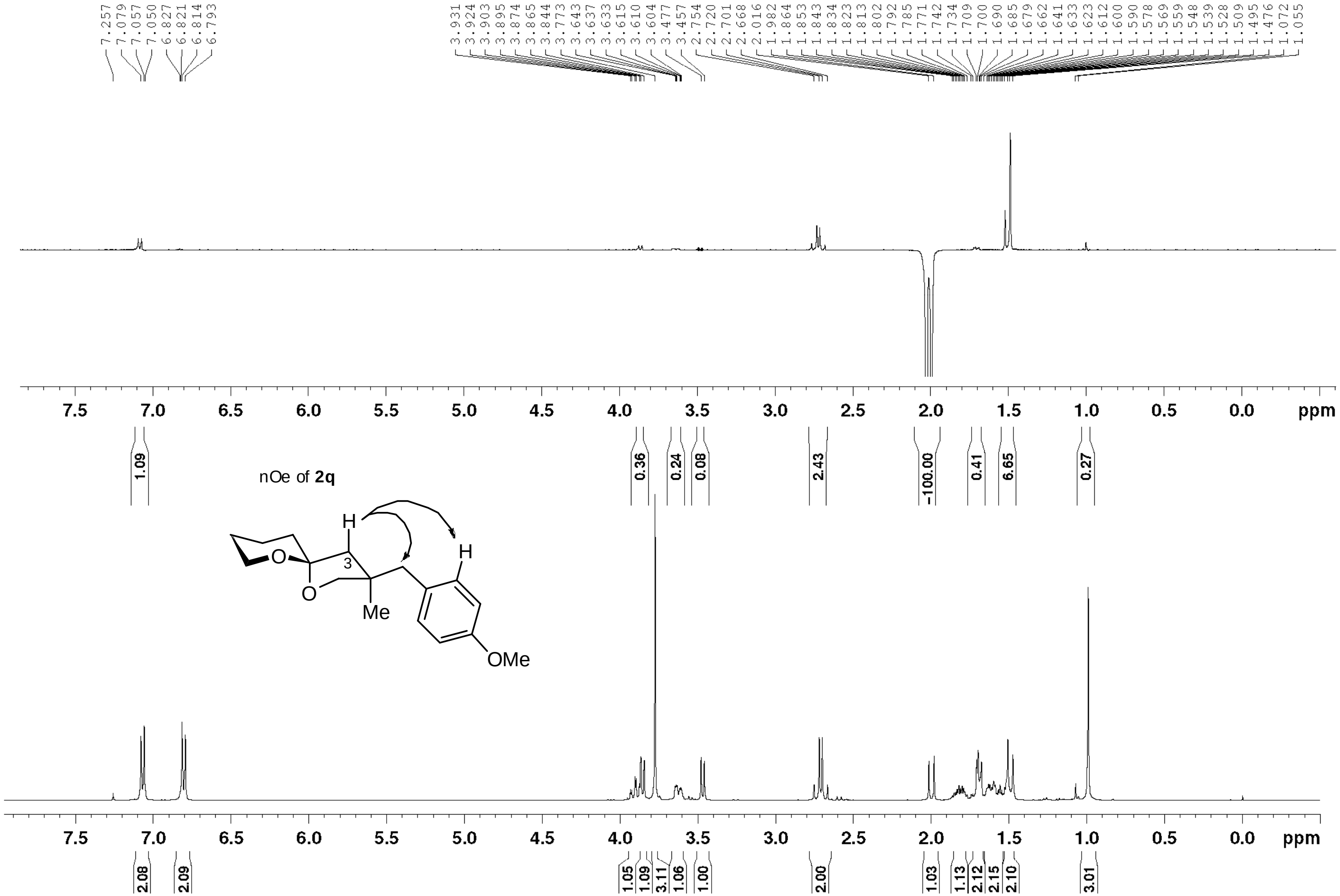
nOe of **2q**


O
4
H
1
O
H
Me
OMe
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.08
2.09
1.05
1.09
3.11
1.06
1.00
2.00
1.03
1.13
2.12
2.15
2.10
3.01


7.257
7.079
7.057
7.050
6.827
6.821
6.814
6.793
3.931
3.924
3.903
3.895
3.874
3.865
3.844
3.773
3.643
3.637
3.633
3.615
3.610
3.604
3.477
3.457
2.754
2.720
2.701
2.668
2.016
1.982
1.864
1.853
1.843
1.834
1.823
1.813
1.802
1.792
1.785
1.771
1.742
1.734
1.709
1.700
1.690
1.685
1.679
1.662
1.641
1.633
1.623
1.612
1.600
1.590
1.578
1.569
1.559
1.548
1.539
1.528
1.509
1.495
1.476
1.072
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.78
-100.00
1.13
6.32
1.99
0.27
0.24
0.06
-0.12
0.64
0.16

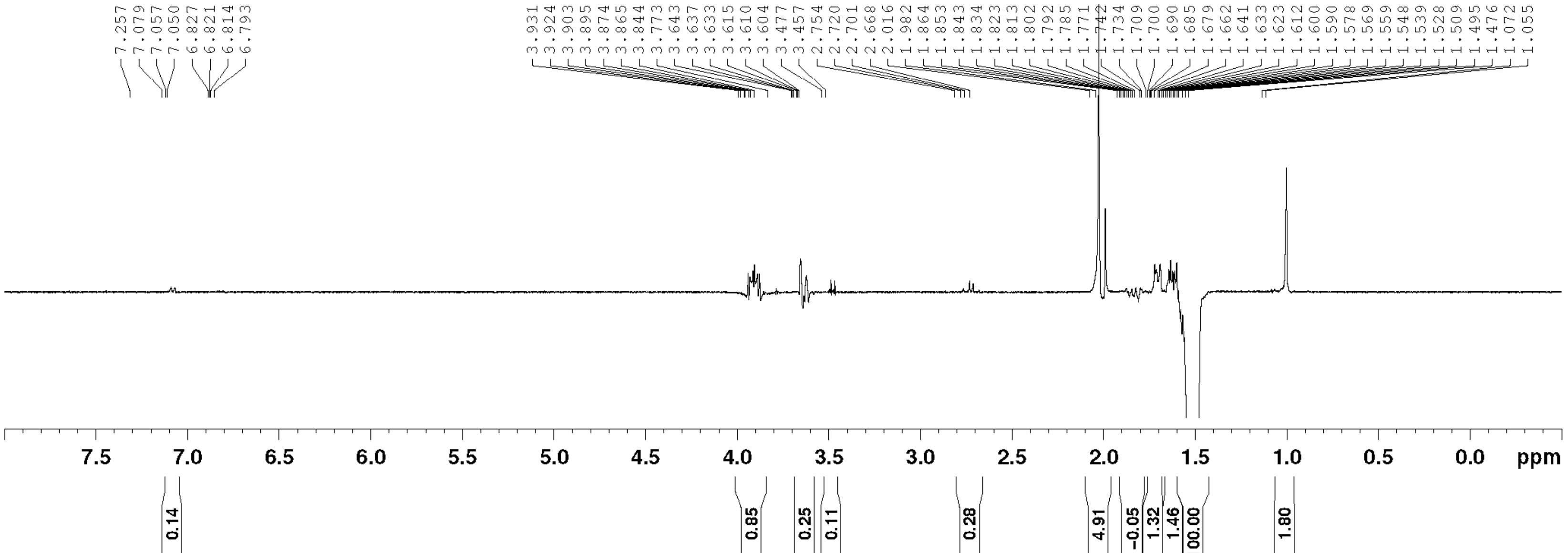

nOe of **2q**
H
O
4
O
1
3
H
H
H
H
8
Me
H
OMe
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.08
2.09
1.05
1.09
3.11
1.06
1.00
2.00
1.03
1.13
2.12
2.15
2.10
3.01


7.257
7.079
7.057
7.050
6.827
6.821
6.814
6.793
3.931
3.924
3.903
3.895
3.874
3.865
3.844
3.773
3.643
3.637
3.633
3.615
3.610
3.604
3.477
3.457
2.754
2.720
2.701
2.668
2.016
1.982
1.864
1.853
1.843
1.834
1.823
1.813
1.802
1.792
1.785
1.771
1.742
1.734
1.709
1.700
1.690
1.685
1.679
1.662
1.641
1.633
1.623
1.612
1.600
1.590
1.578
1.569
1.559
1.548
1.539
1.528
1.509
1.495
1.476
1.072
1.055
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
8.97
-100.00
0.38
0.05
0.11
0.15
1.68
nOe of **2q**
O
O
1
2
H
Me
OMe
2.08
2.09
1.05
1.09
3.11
1.06
1.00
2.00
1.03
1.13
2.12
2.15
2.10
3.01



nOe of **2q**

7.257
7.079
7.057
7.050
6.827
6.821
6.814
6.793
3.931
3.924
3.903
3.895
3.874
3.865
3.844
3.773
3.643
3.637
3.633
3.615
3.610
3.604
3.477
3.457
2.754
2.720
2.701
2.668
2.016
1.982
1.864
1.853
1.843
1.834
1.823
1.813
1.802
1.792
1.785
1.771
1.742
1.734
1.709
1.700
1.690
1.685
1.679
1.662
1.641
1.633
1.623
1.612
1.600
1.590
1.578
1.569
1.559
1.548
1.539
1.528
1.509
1.495
1.476
1.072
1.055
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.09
0.36
0.24
0.08
2.43
-100.00
0.41
6.65
0.27
H
H
O
3
O
Me
OMe
2.08
2.09
1.05
1.09
3.11
1.06
1.00
2.00
1.03
1.13
2.12
2.15
2.10
3.01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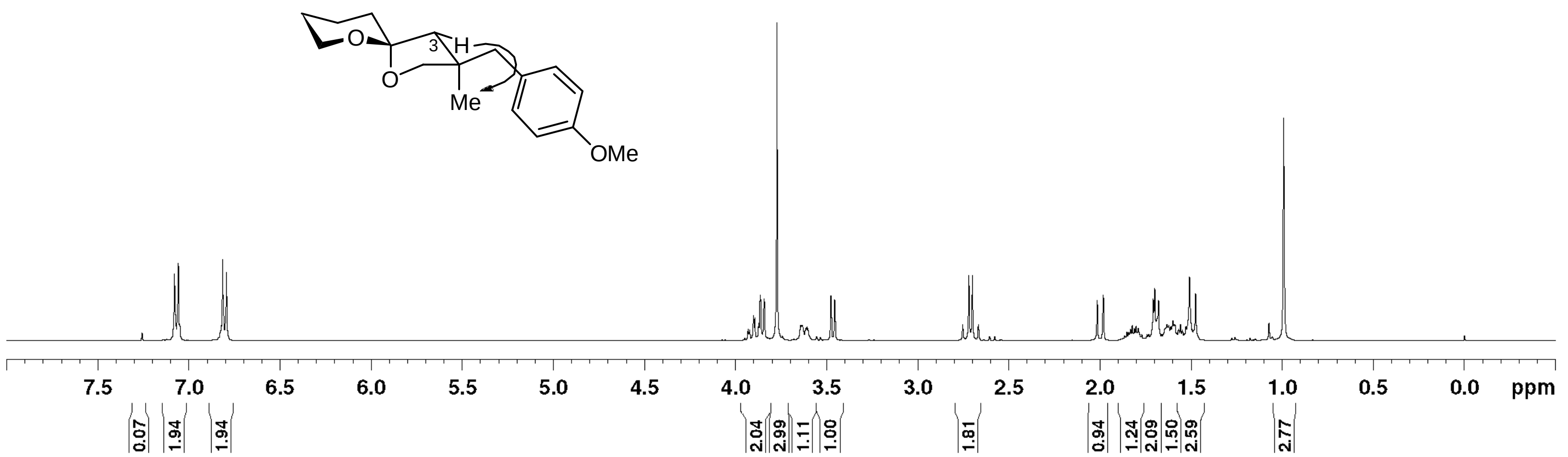
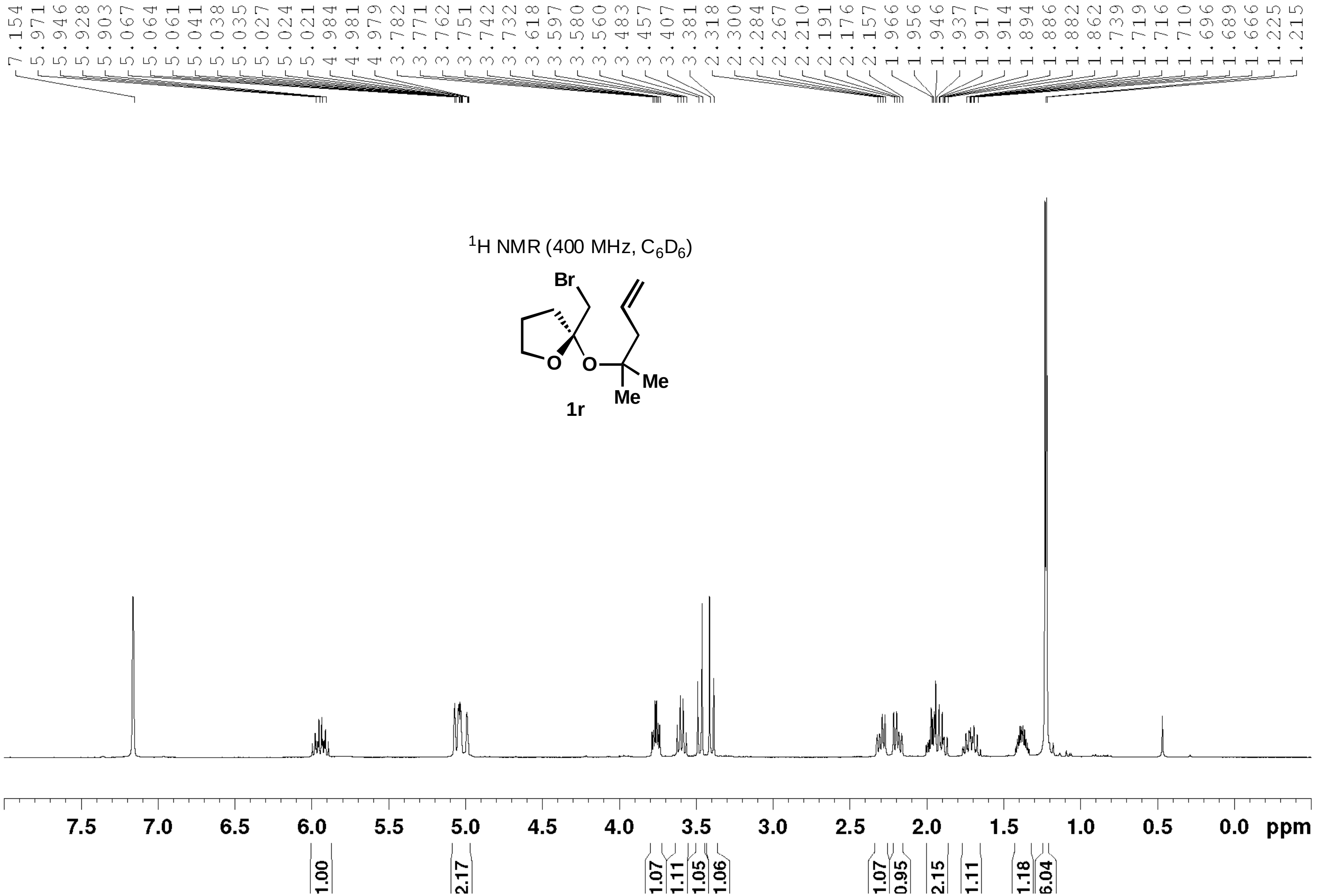
7.079
7.057
7.050
6.827
6.821
6.814
6.793
3.931
3.924
3.903
3.895
3.874
3.865
3.844
3.773
3.643
3.637
3.633
3.615
3.610
3.604
3.477
3.457
2.754
2.720
2.701
2.668
2.016
1.982
1.864
1.853
1.843
1.834
1.823
1.813
1.802
1.792
1.785
1.771
1.742
1.734
1.709
1.700
1.690
1.685
1.679
1.662
1.641
1.633
1.623
1.612
1.600
1.590
1.578
1.569
1.559
1.548
1.539
1.528
1.509
1.495
1.476
1.072
1.055
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.14
0.85
0.25
0.11
0.28
4.91
-0.05
1.32
1.46
-100.00
1.80

nOe of **2q**


O
O
3
H
Me
OMe
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.07
1.94
1.94
2.04
2.99
1.11
1.00
1.81
0.94
1.24
2.09
1.50
2.59
2.77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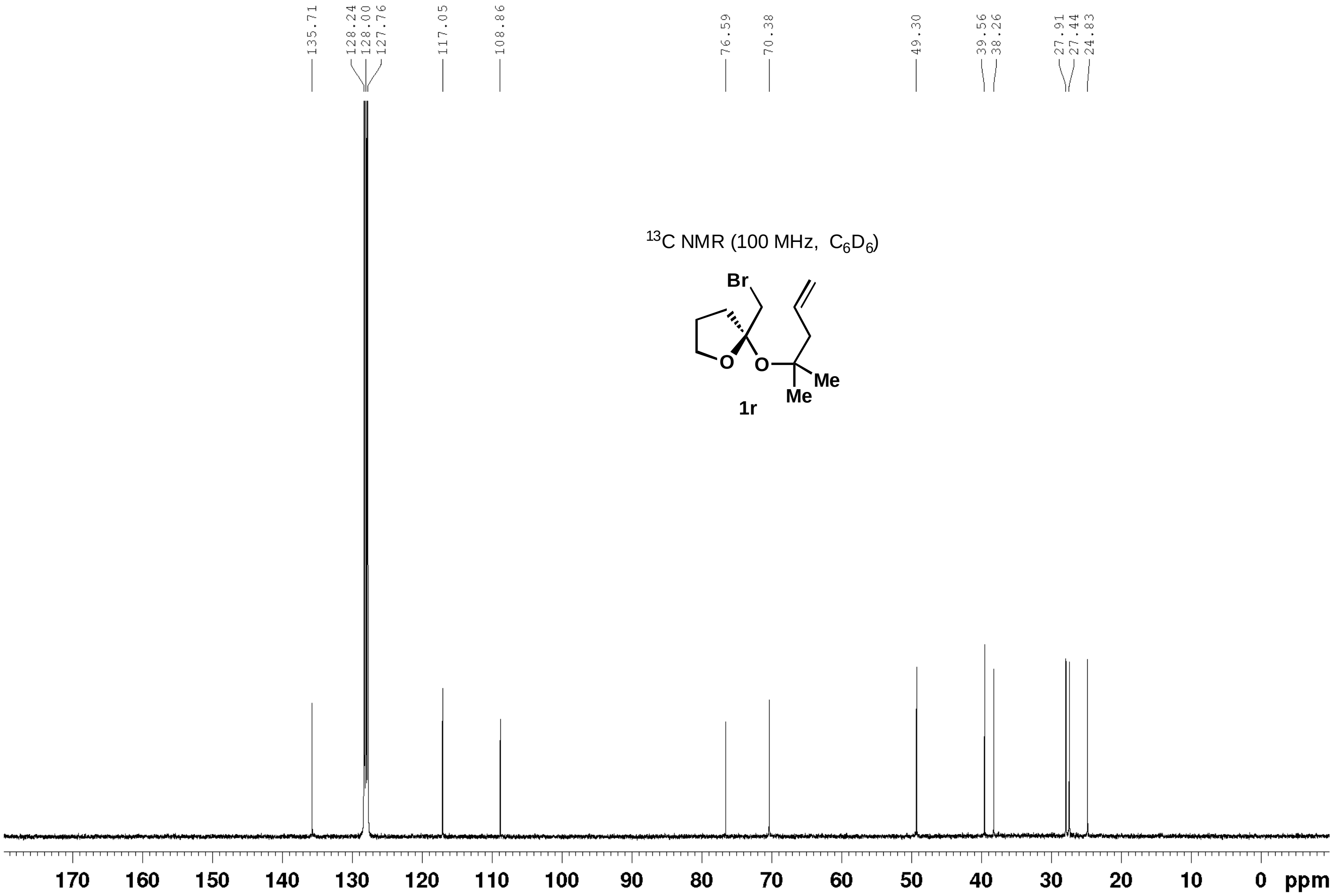
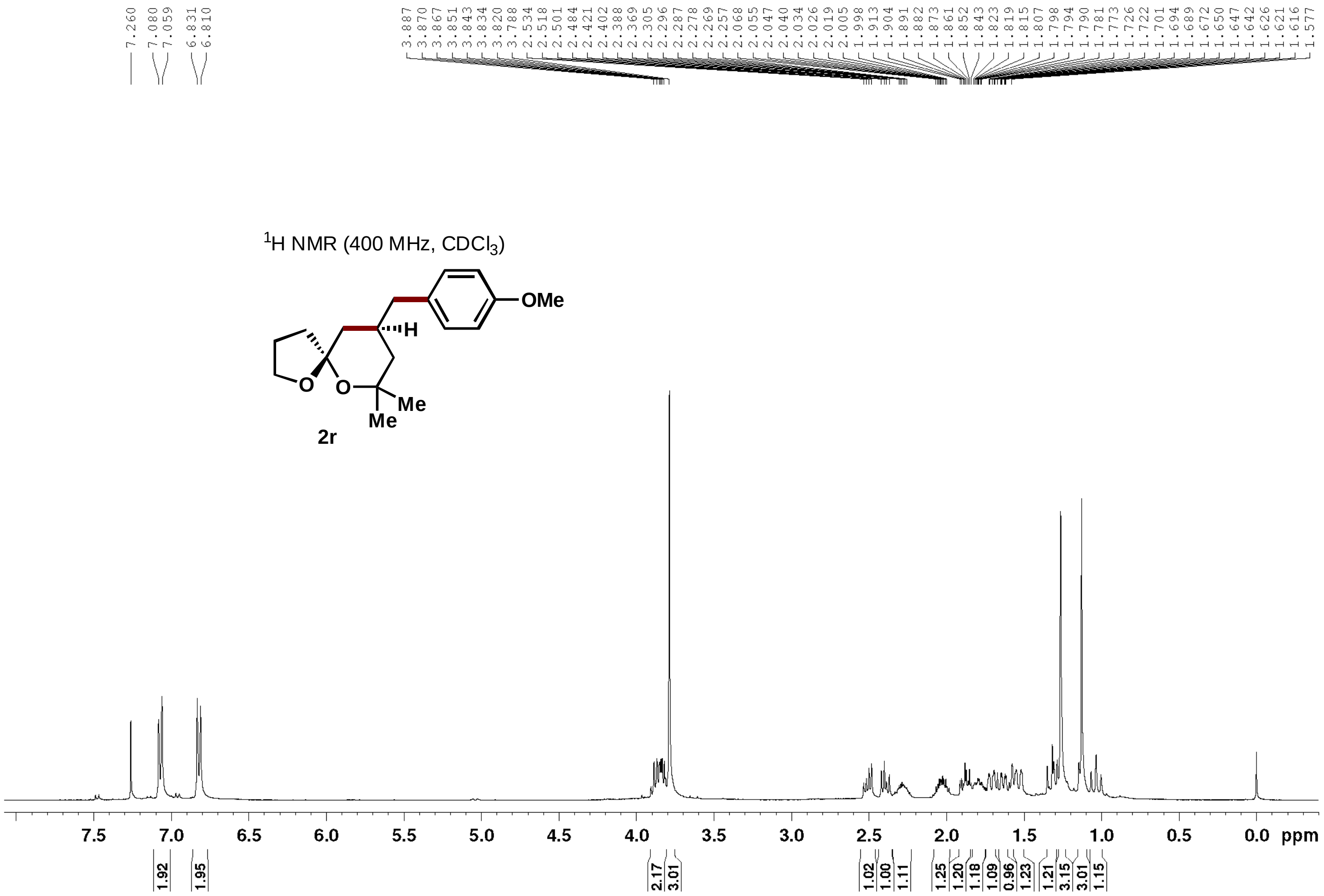
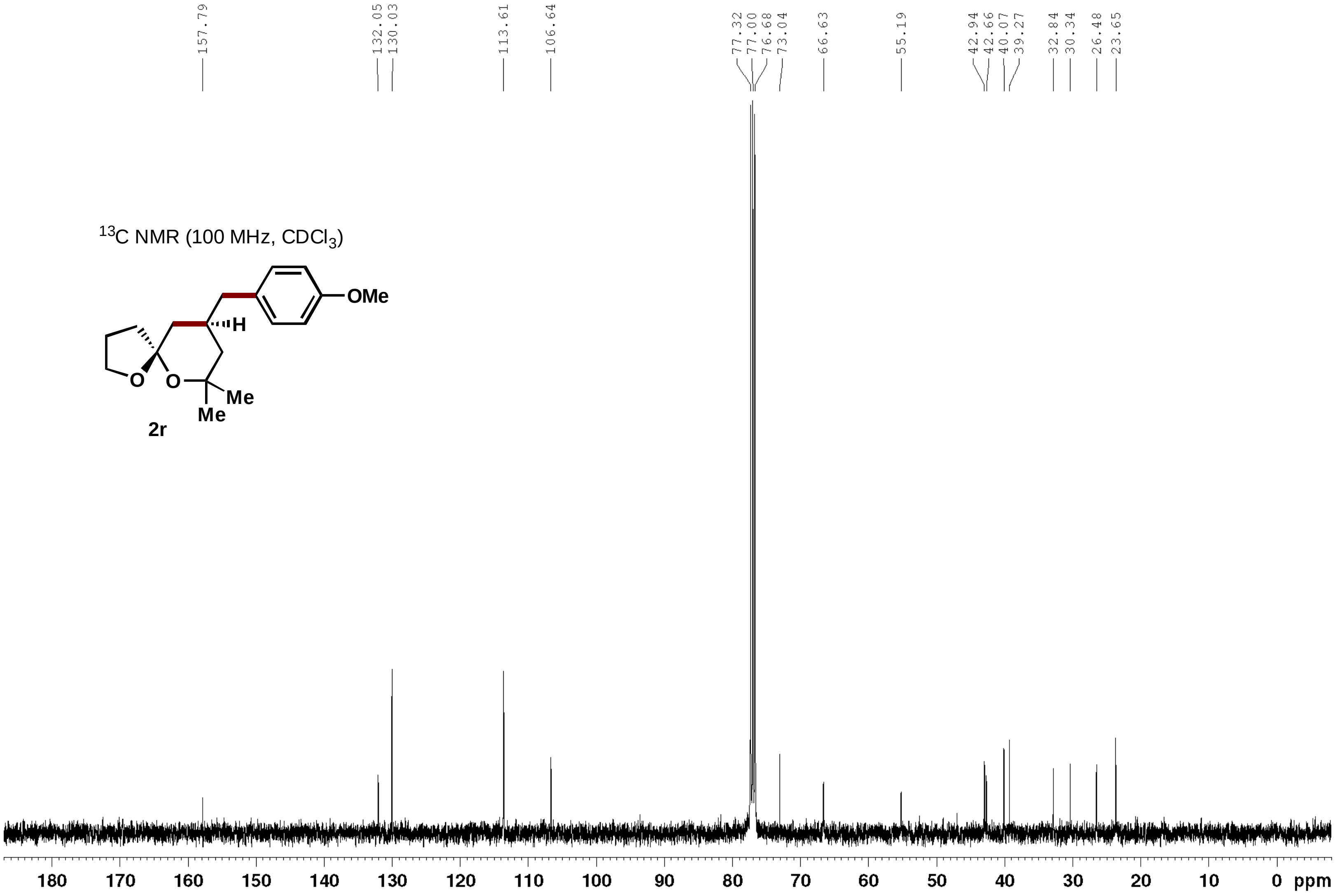
5.946
5.928
5.903
5.067
5.064
5.061
5.041
5.038
5.035
5.027
5.024
5.021
4.984
4.981
4.979
3.782
3.771
3.762
3.751
3.742
3.732
3.618
3.597
3.580
3.560
3.483
3.457
3.407
3.381
2.318
2.300
2.284
2.267
2.210
2.191
2.176
2.157
1.966
1.956
1.946
1.937
1.917
1.914
1.894
1.886
1.882
1.862
1.739
1.719
1.716
1.710
1.696
1.689
1.666
1.225
1.215
^{1}H NMR (400 MHz, C_6D_6)
Br
O
O
Me
Me
1r
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
2.17
1.07
1.11
1.05
1.06
1.07
0.95
2.15
1.11
1.18
6.04

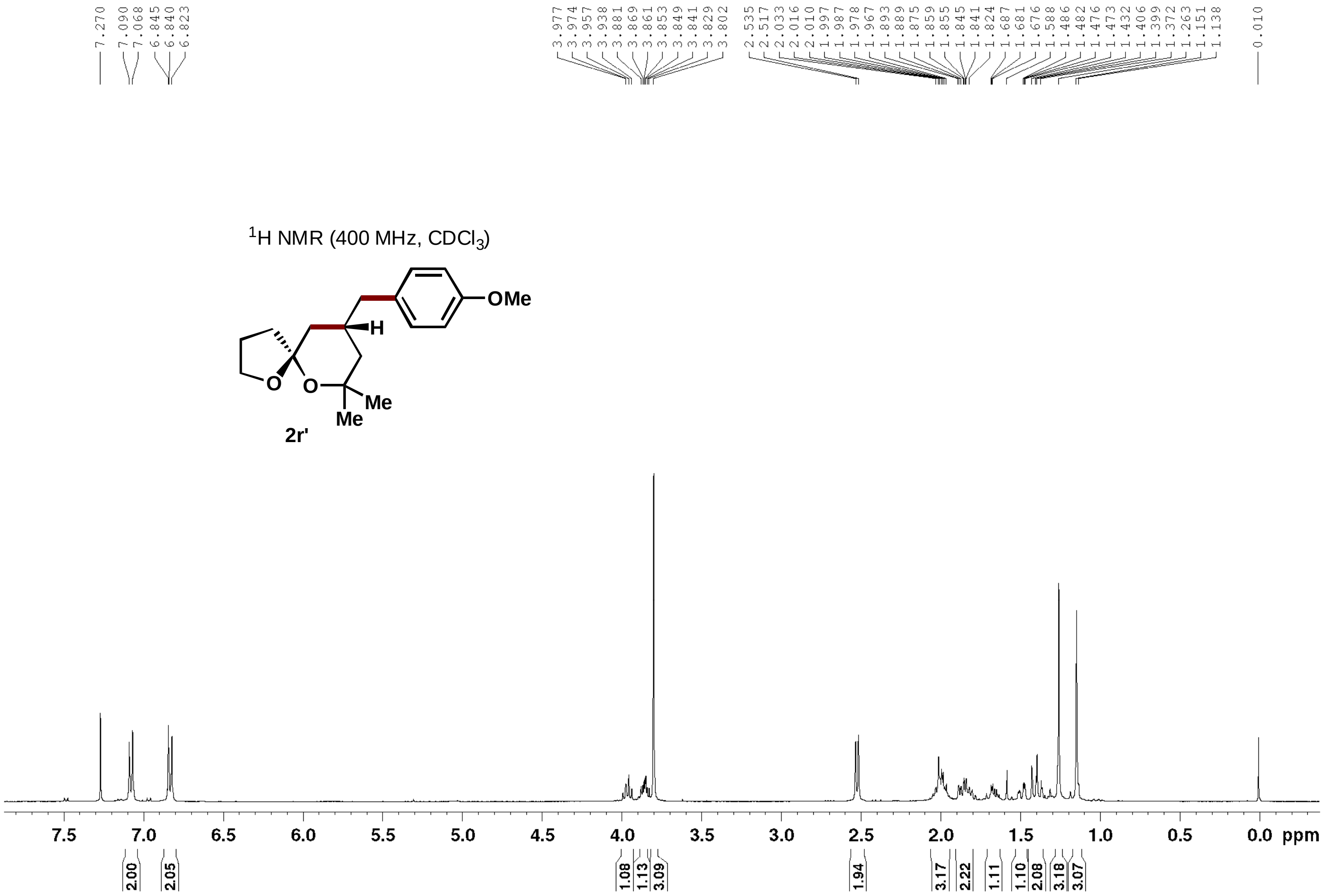

135.71
128.24
128.00
127.76
117.05
108.86
76.59
70.38
49.30
39.56
38.26
27.91
27.44
24.83
13C NMR (100 MHz, C6D6)
Br
O
O
Me
Me
1r
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.260
7.080
7.059
6.831
6.810
3.887
3.870
3.867
3.851
3.843
3.834
3.820
3.788
2.534
2.518
2.501
2.484
2.421
2.402
2.388
2.369
2.305
2.296
2.287
2.278
2.269
2.257
2.068
2.055
2.047
2.040
2.034
2.026
2.019
2.005
1.998
1.913
1.904
1.891
1.882
1.873
1.861
1.852
1.843
1.823
1.819
1.815
1.807
1.798
1.794
1.790
1.781
1.773
1.726
1.722
1.701
1.694
1.689
1.672
1.650
1.647
1.642
1.626
1.621
1.616
1.577
^{1}H NMR (400 MHz, CDCl$_3$)
OMe
H
O
O
Me
Me
2r
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.92
1.95
2.17
3.01
1.02
1.00
1.11
1.25
1.20
1.18
1.09
0.96
1.23
1.21
3.15
3.01
1.15

^{13}C NMR (100 MHz, CDCl$_3$)

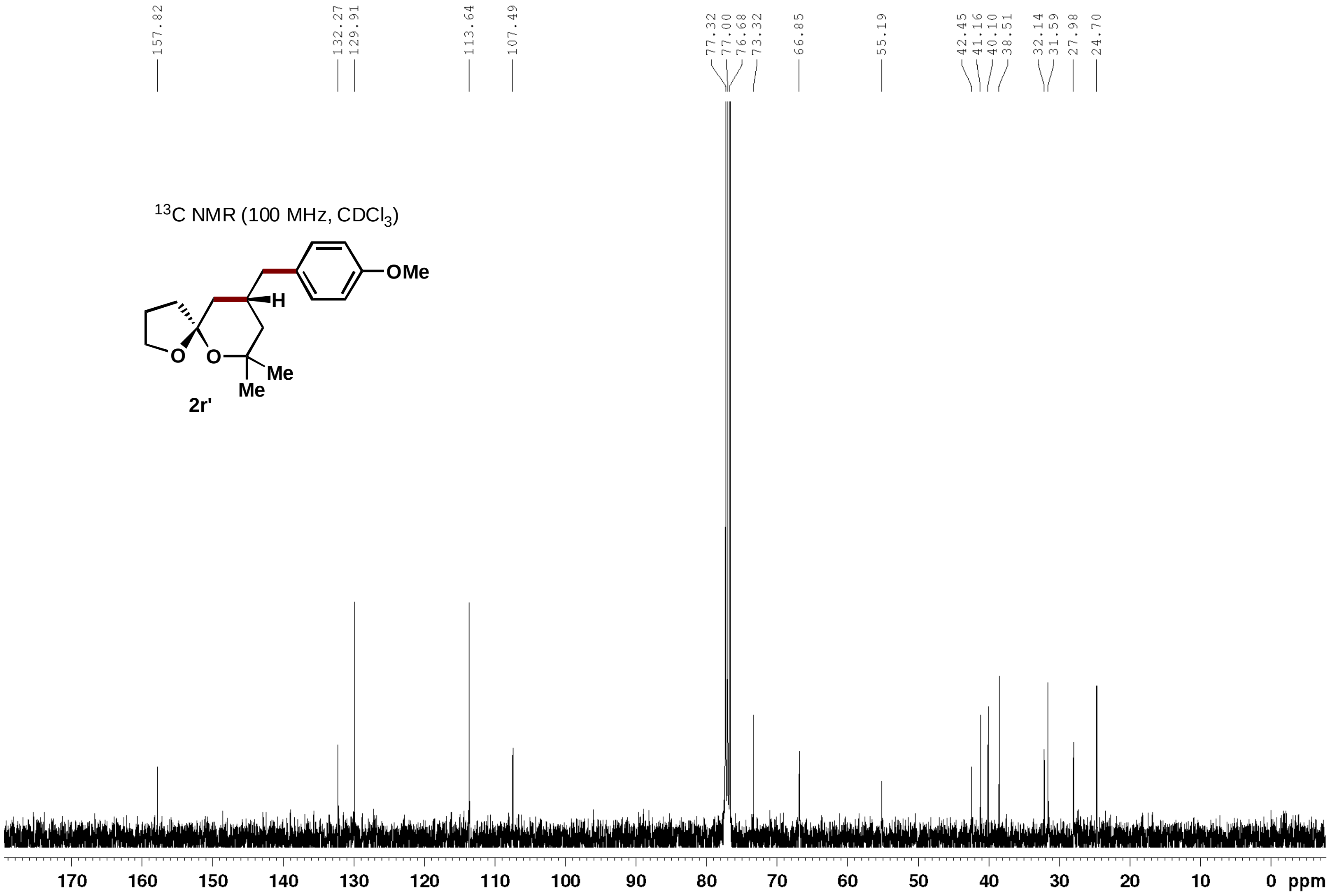


2r

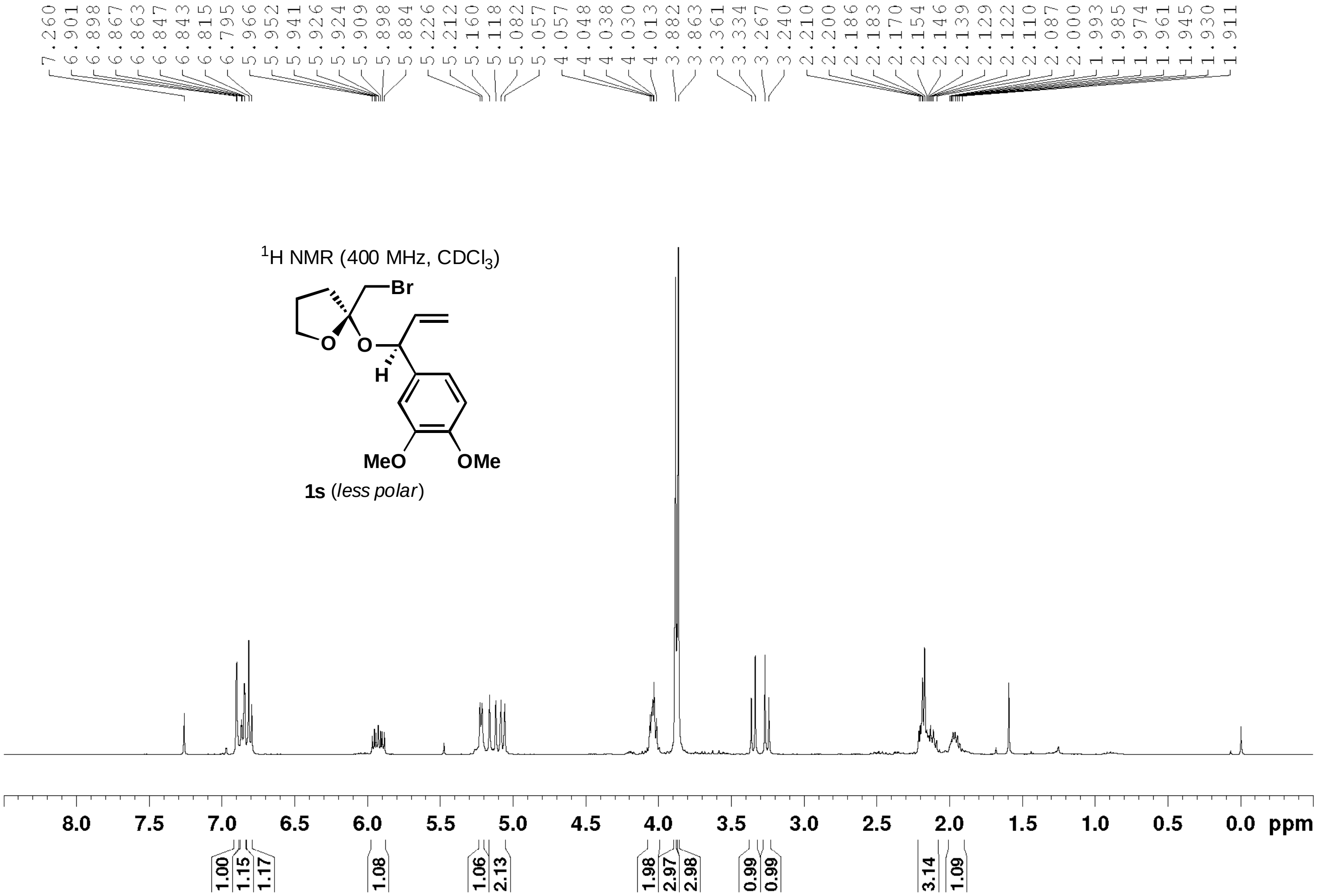


^{1}H NMR (400 MHz, CDCl$_3$)

2r'

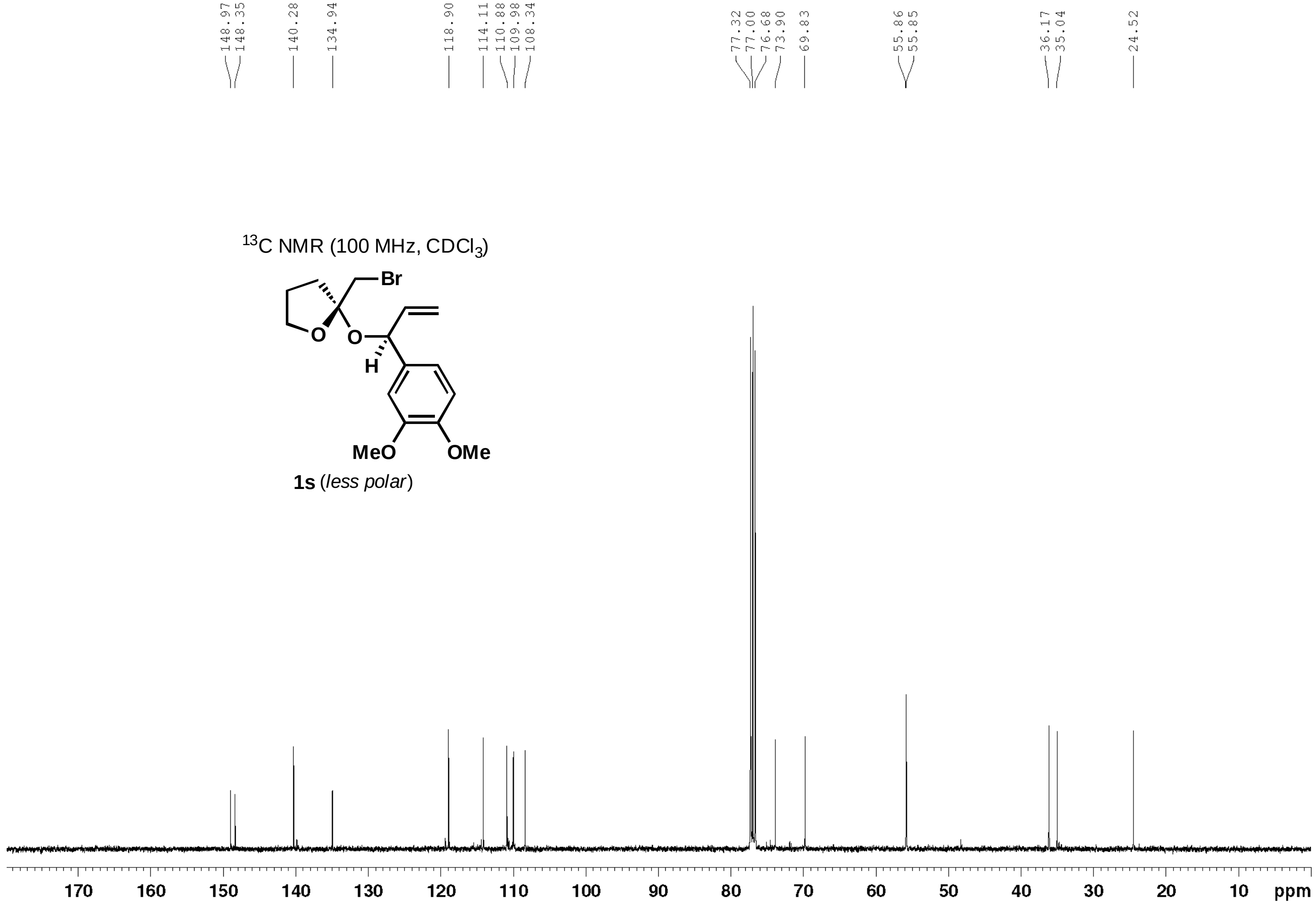

157.82
132.27
129.91
113.64
107.49
77.32
77.00
76.68
73.32
66.85
55.19
42.45
41.16
40.10
38.51
32.14
31.59
27.98
24.70
^{13}C NMR (100 MHz, CDCl$_3$)
OMe
H
O
O
Me
Me
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

2r'

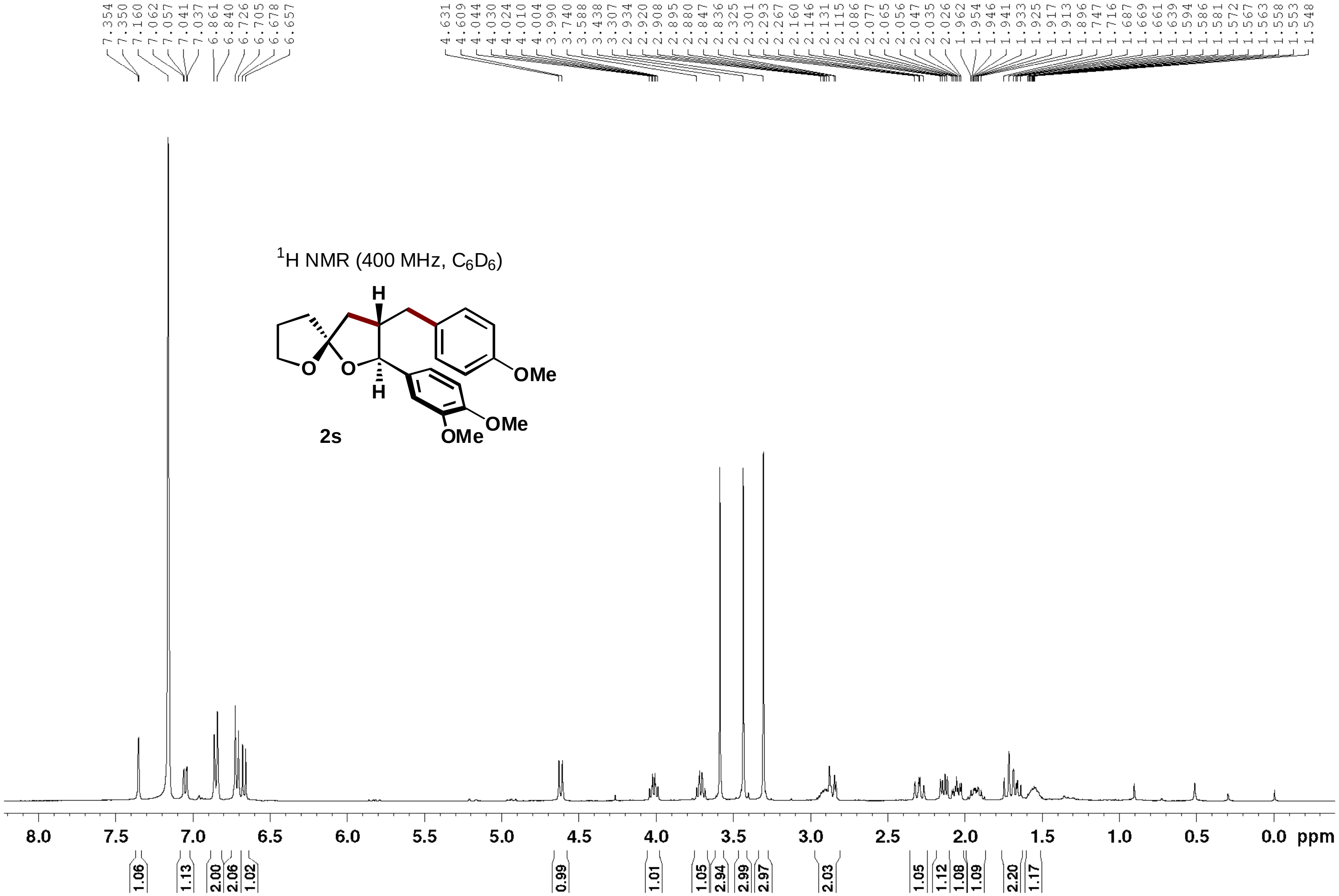


1s (*less polar*)

^{13}C NMR (100 MHz, $CDCl_3$)

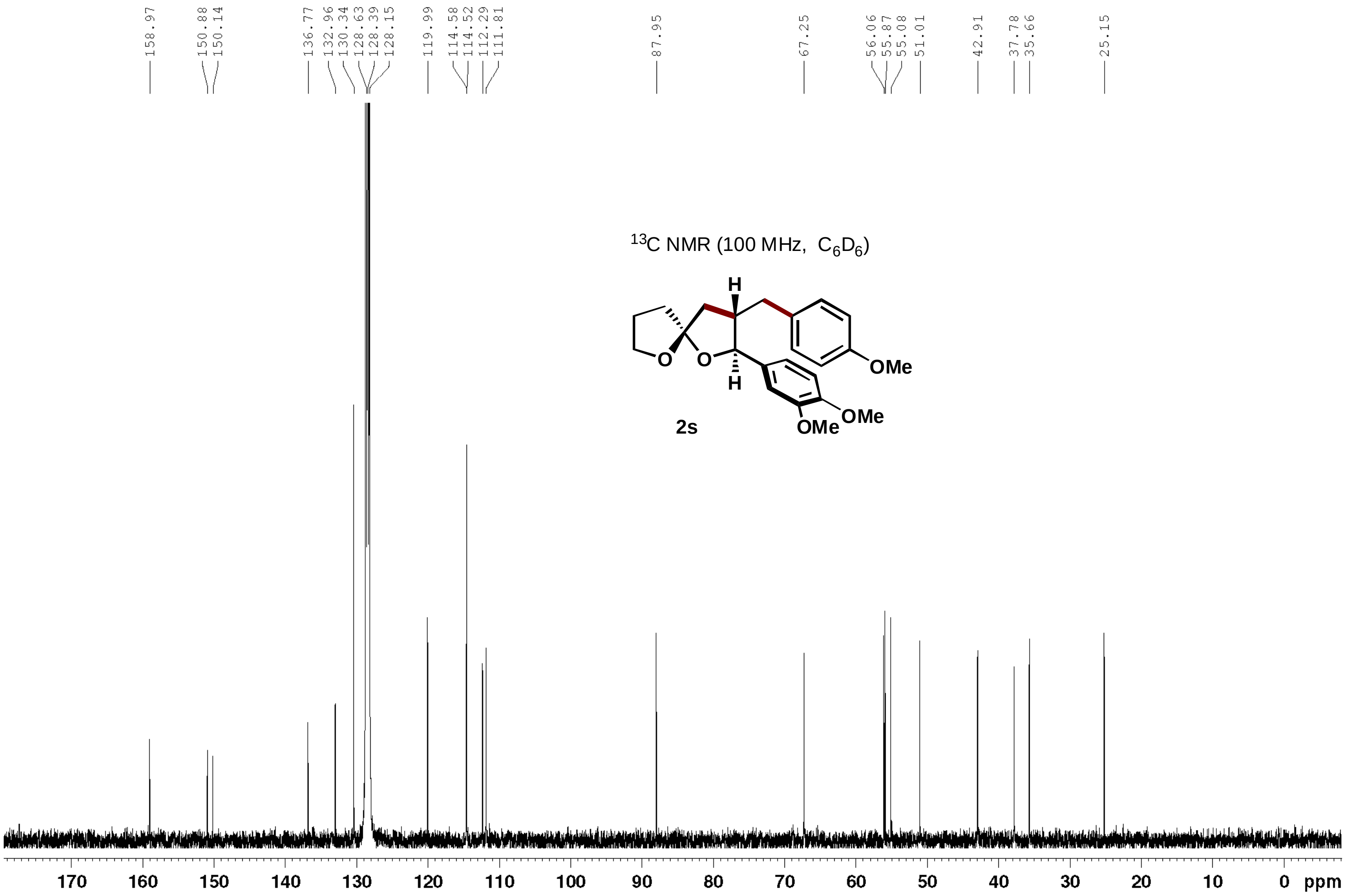


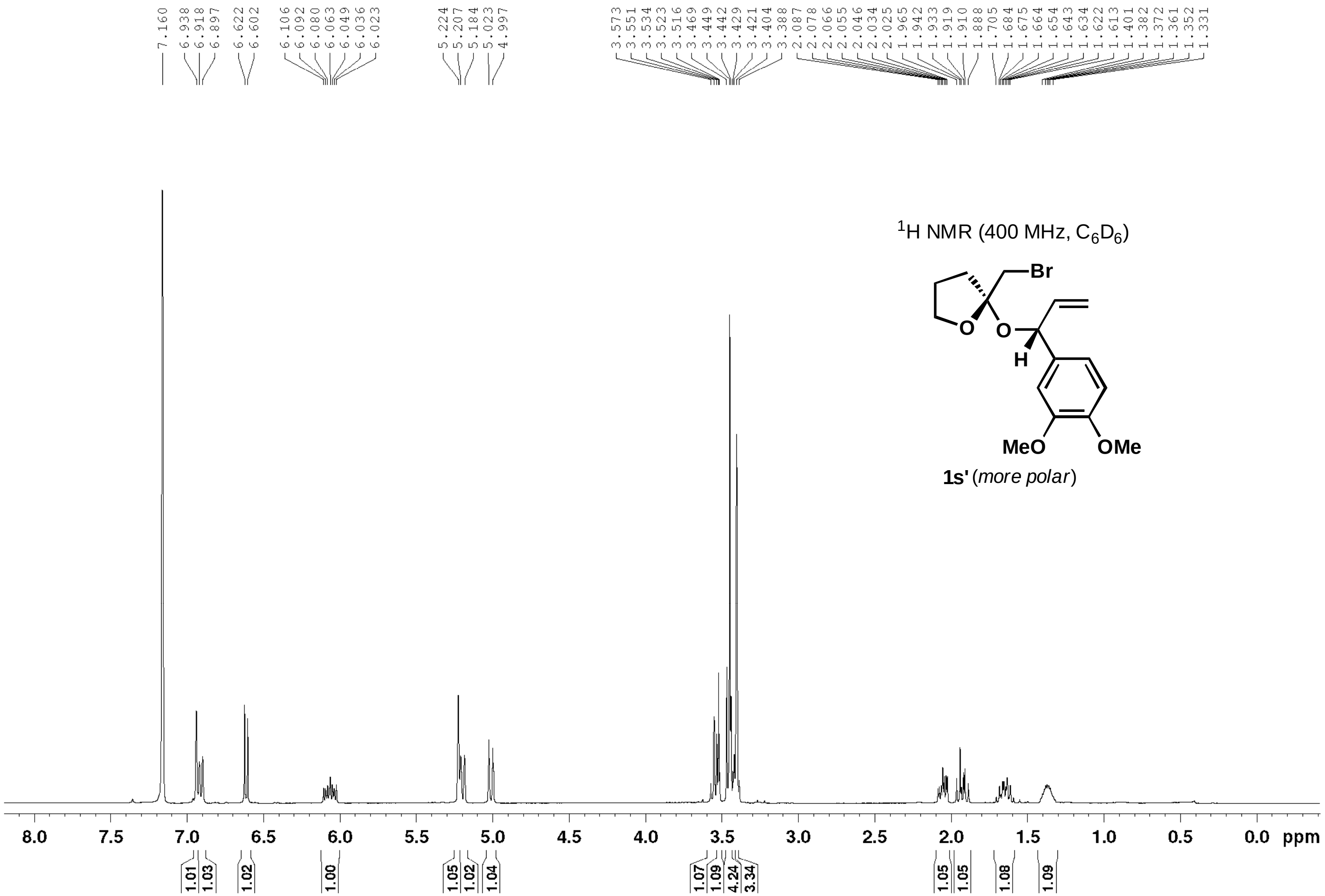
1s (*less polar*)



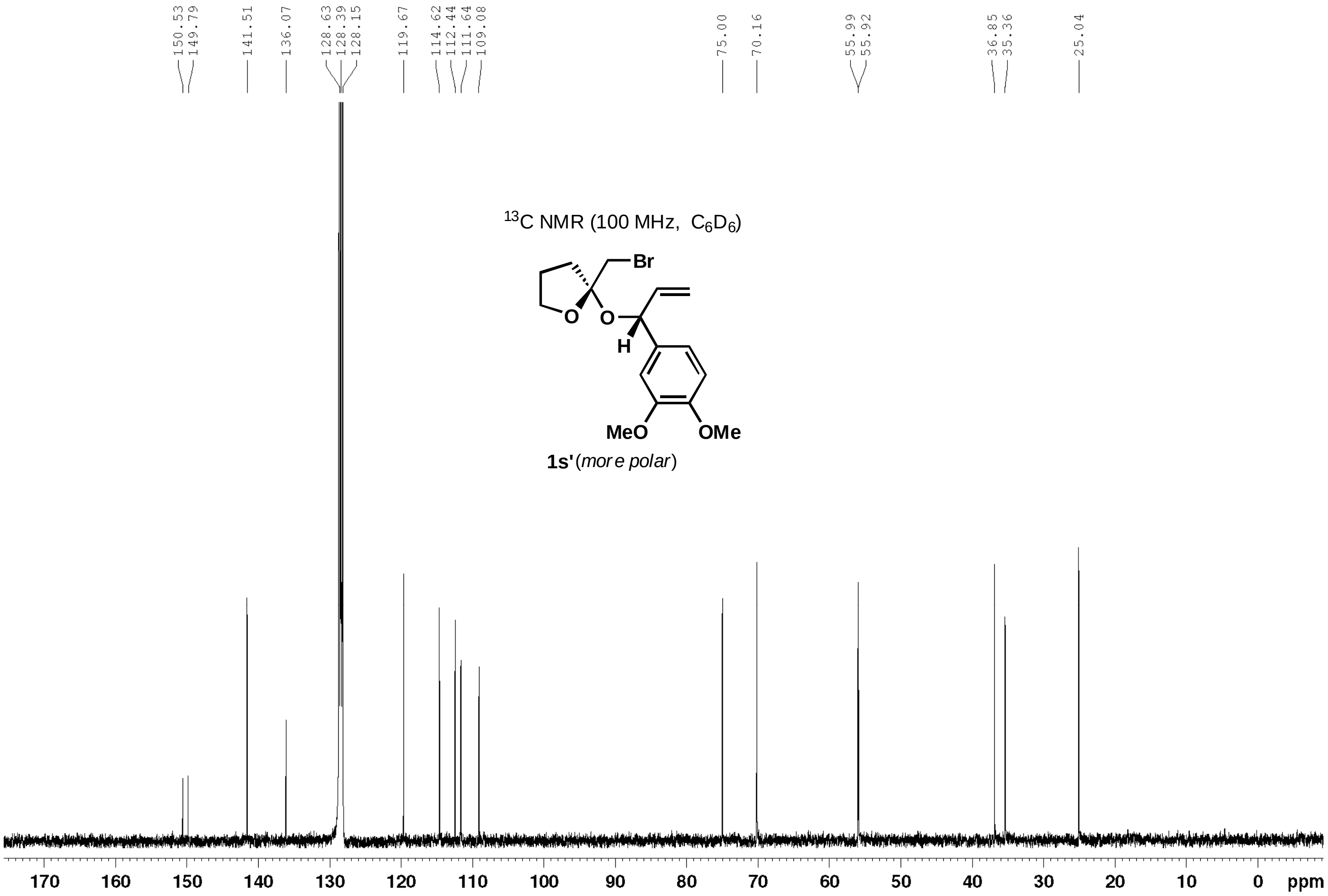
^{1}H NMR (400 MHz, C_6D_6)

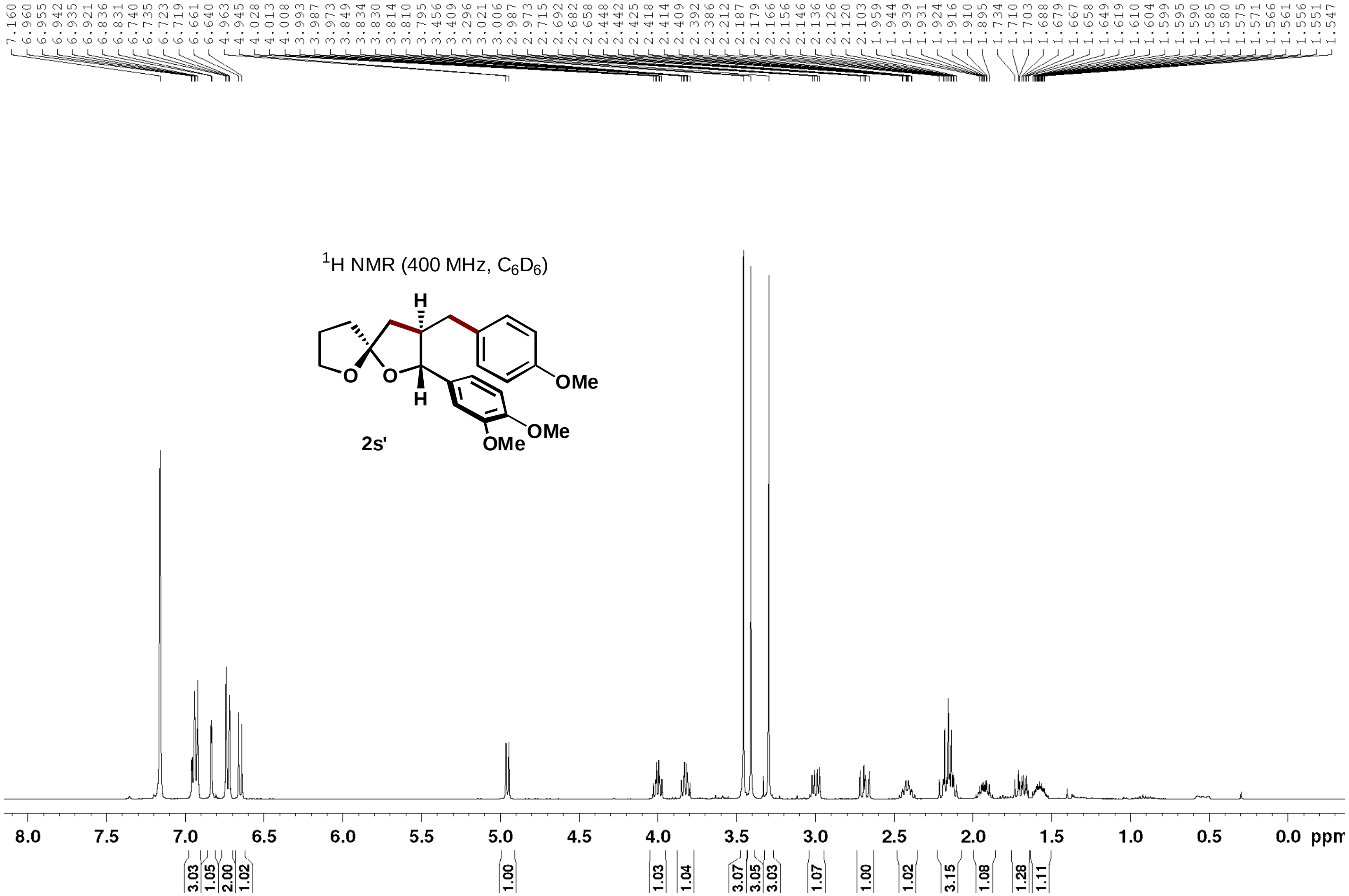
2s

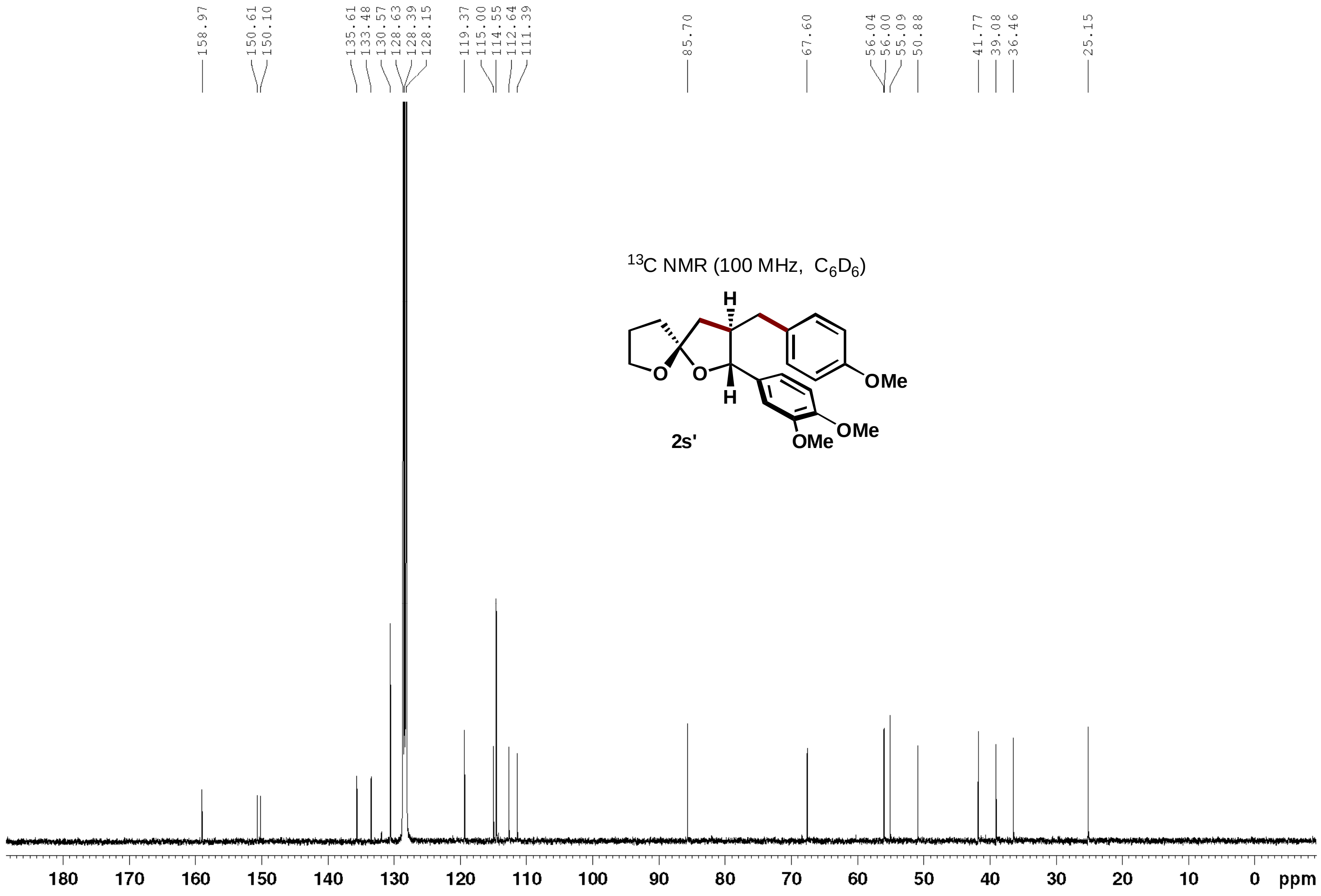

158.97
150.88
150.14
136.77
132.96
130.34
128.63
128.39
128.15
119.99
114.58
114.52
112.29
111.81
87.95
67.25
56.06
55.87
55.08
51.01
42.91
37.78
35.66
25.15
^{13}C NMR (100 MHz, C_6D_6)
H
O
O
H
OMe
OMe
OMe
2s
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

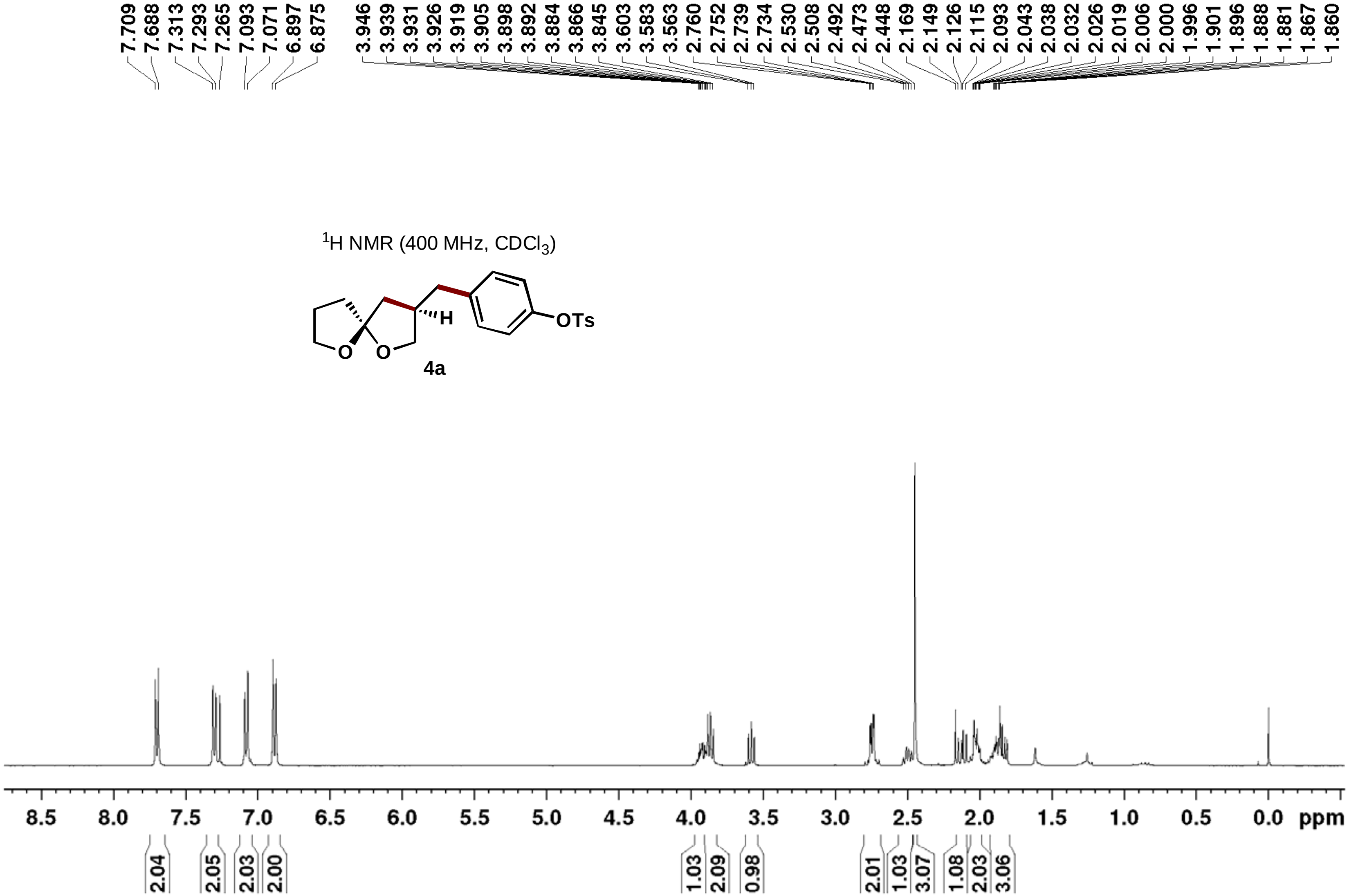


1s' (*more polar*)


150.53
149.79
141.51
136.07
128.63
128.39
128.15
119.67
114.62
112.44
111.64
109.08
75.00
70.16
55.99
55.92
36.85
35.36
25.04
^{13}C NMR (100 MHz, C_6D_6)
Br
O
O
H
MeO
OMe
1s' (more polar)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

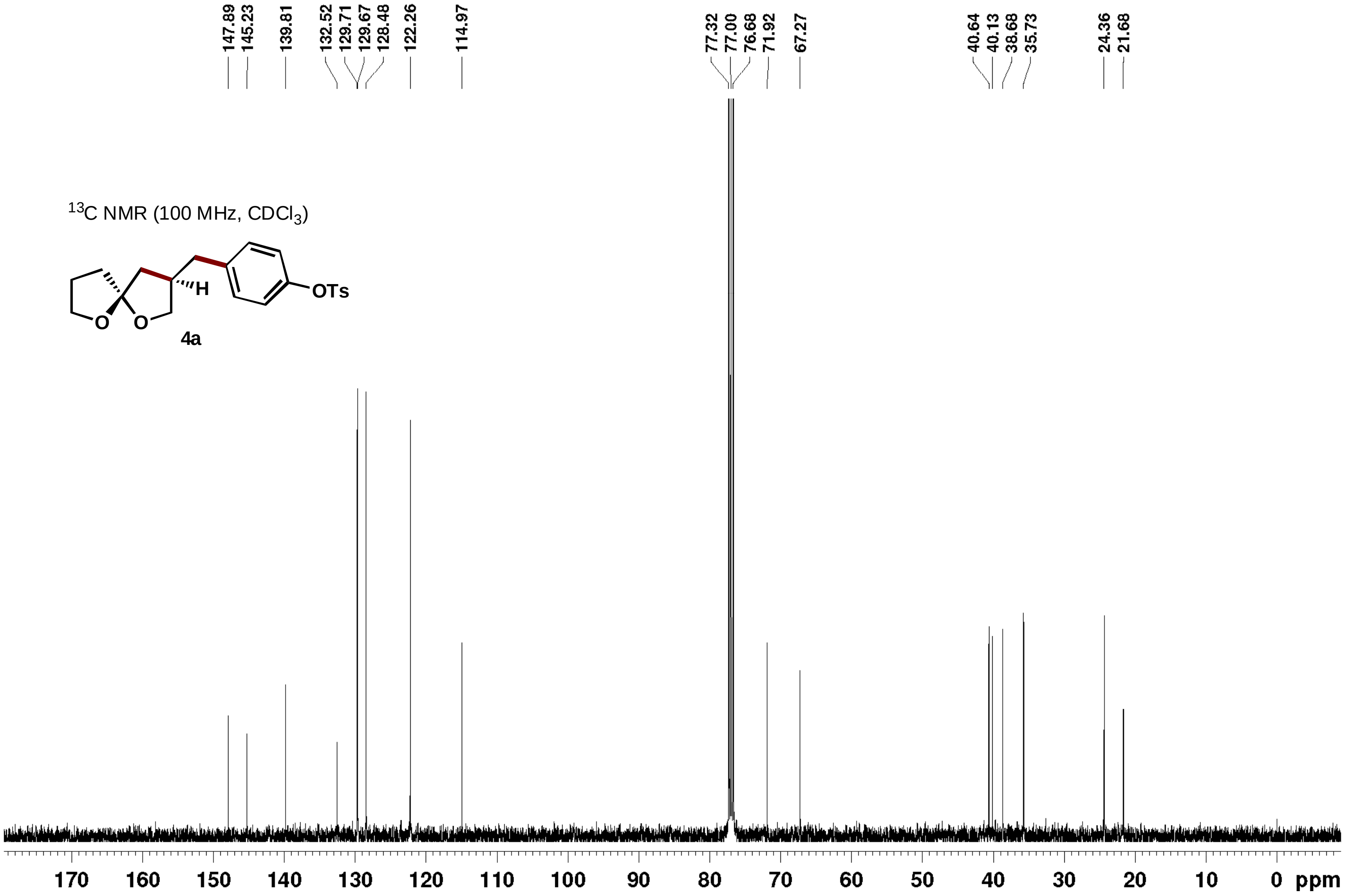

7.160
6.960
6.955
6.942
6.935
6.921
6.836
6.831
6.740
6.735
6.723
6.719
6.661
6.640
4.963
4.945
4.028
4.013
4.008
3.993
3.987
3.973
3.849
3.834
3.830
3.814
3.810
3.795
3.456
3.409
3.296
3.021
3.006
2.987
2.973
2.715
2.692
2.682
2.658
2.448
2.442
2.425
2.418
2.414
2.409
2.392
2.386
2.212
2.187
2.179
2.166
2.156
2.146
2.136
2.126
2.120
2.103
1.959
1.944
1.939
1.931
1.924
1.916
1.910
1.895
1.734
1.710
1.703
1.688
1.679
1.667
1.658
1.649
1.619
1.610
1.604
1.599
1.595
1.590
1.585
1.580
1.575
1.571
1.566
1.561
1.556
1.551
1.547
^{1}H NMR (400 MHz, C_6D_6)
H
O
O
H
OMe
OMe
OMe
2s'
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3.03
1.05
2.00
1.02
1.00
1.03
1.04
3.07
3.05
3.03
1.07
1.00
1.02
3.15
1.08
1.28
1.11

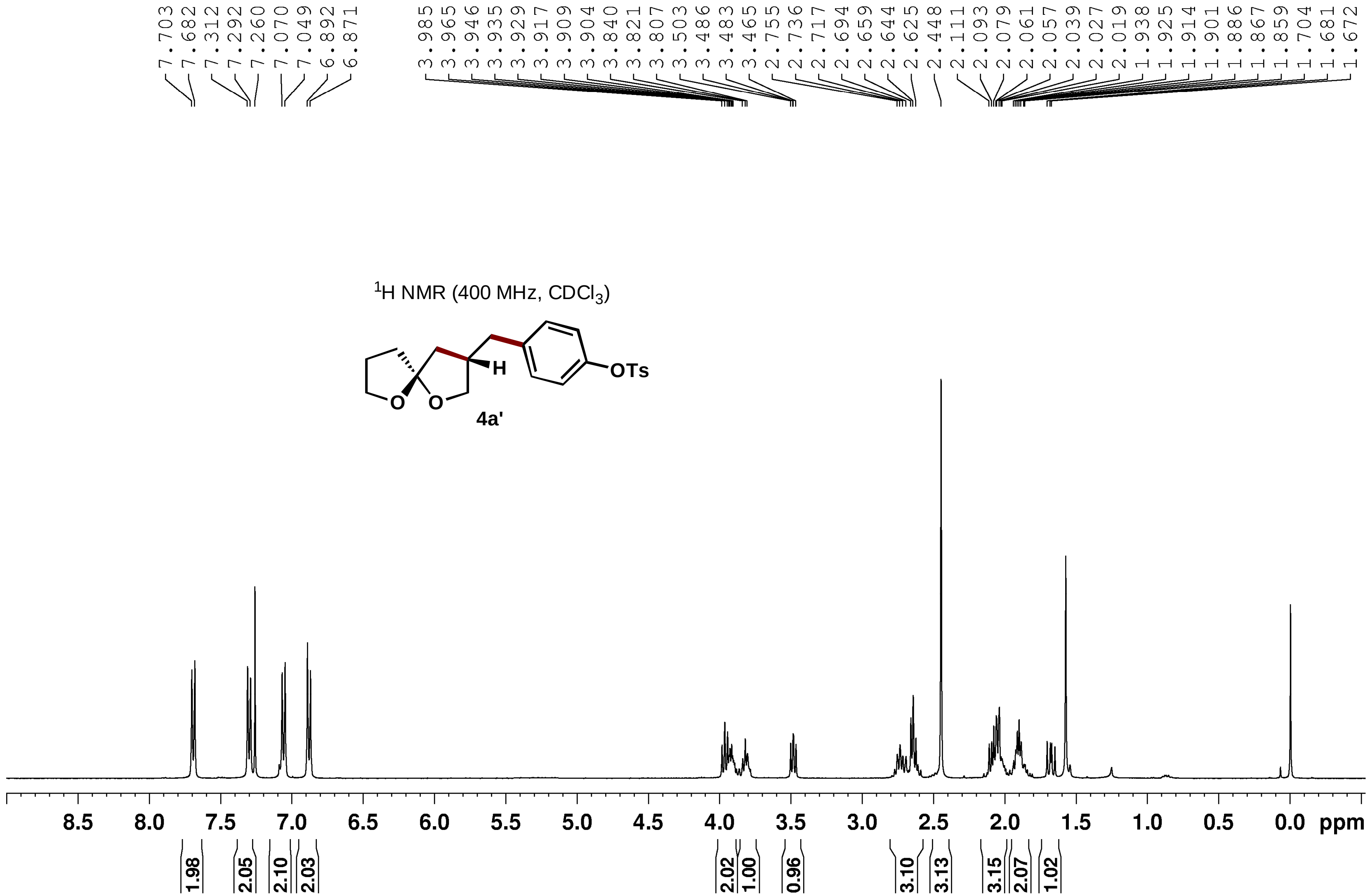

158.97
150.61
150.10
135.61
133.48
130.57
128.63
128.39
128.15
119.37
115.00
114.55
112.64
111.39
85.70
67.60
56.04
56.00
55.09
50.88
41.77
39.08
36.46
25.15
^{13}C NMR (100 MHz, C_6D_6)
H
O
O
H
OMe
OMe
OMe
2s'
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

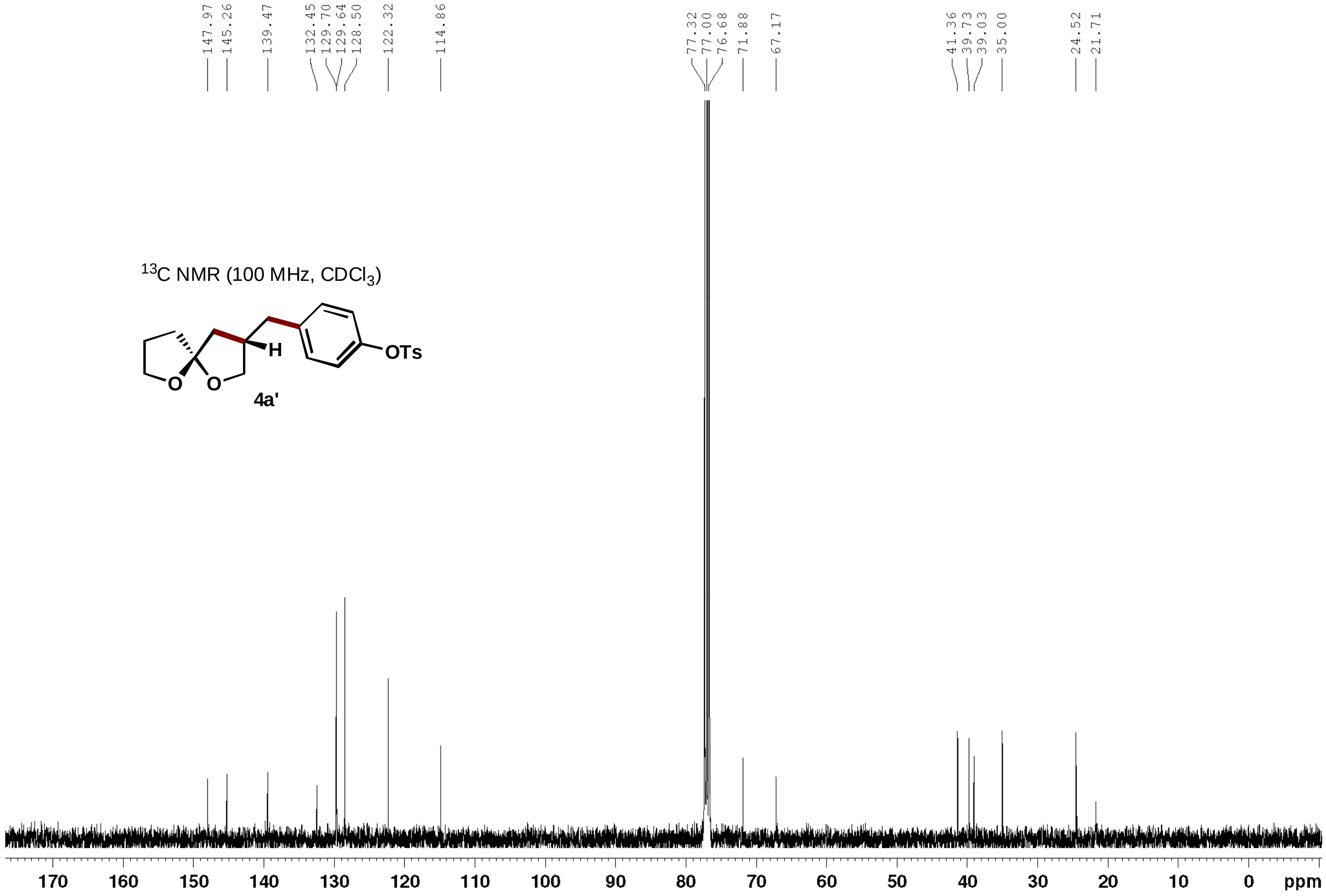


^{1}H NMR (400 MHz, $CDCl_3$)

4a

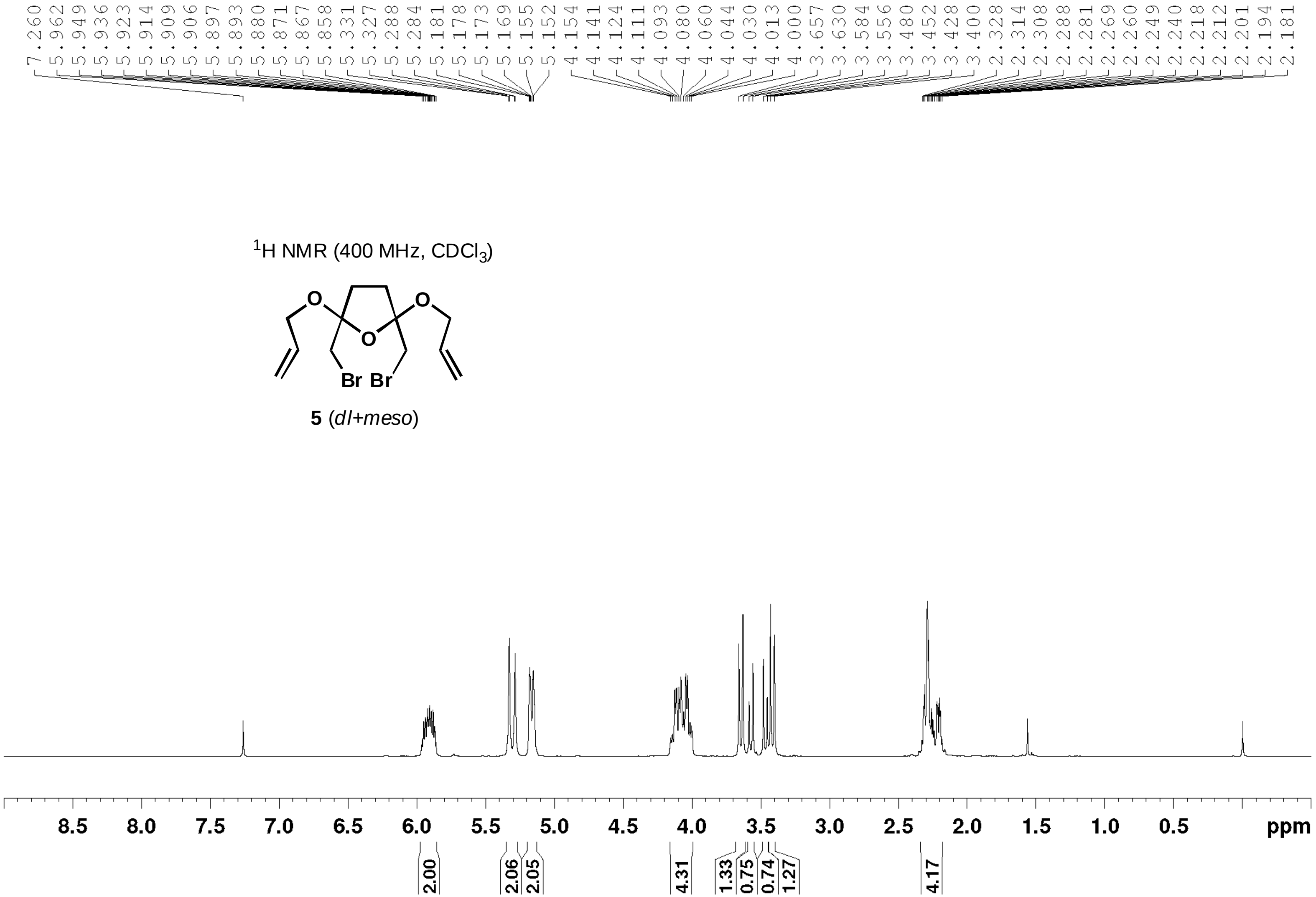

147.89
145.23
139.81
132.52
129.71
129.67
128.48
122.26
114.97
77.32
77.00
76.68
71.92
67.27
40.64
40.13
38.68
35.73
24.36
21.68
^{13}C NMR (100 MHz, CDCl$_3$)
H
OTs
O
O
4a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.703
7.682
7.312
7.292
7.260
7.070
7.049
6.892
6.871
3.985
3.965
3.946
3.935
3.929
3.917
3.909
3.904
3.840
3.821
3.807
3.503
3.486
3.483
3.465
2.755
2.736
2.717
2.694
2.659
2.644
2.625
2.448
2.111
2.093
2.079
2.061
2.057
2.039
2.027
2.019
1.938
1.925
1.914
1.901
1.886
1.867
1.859
1.704
1.681
1.672
^{1}H NMR (400 MHz, CDCl$_3$)
H
O
O
OTs
4a'
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.98
2.05
2.10
2.03
2.02
1.00
0.96
3.10
3.13
3.15
2.07
1.02



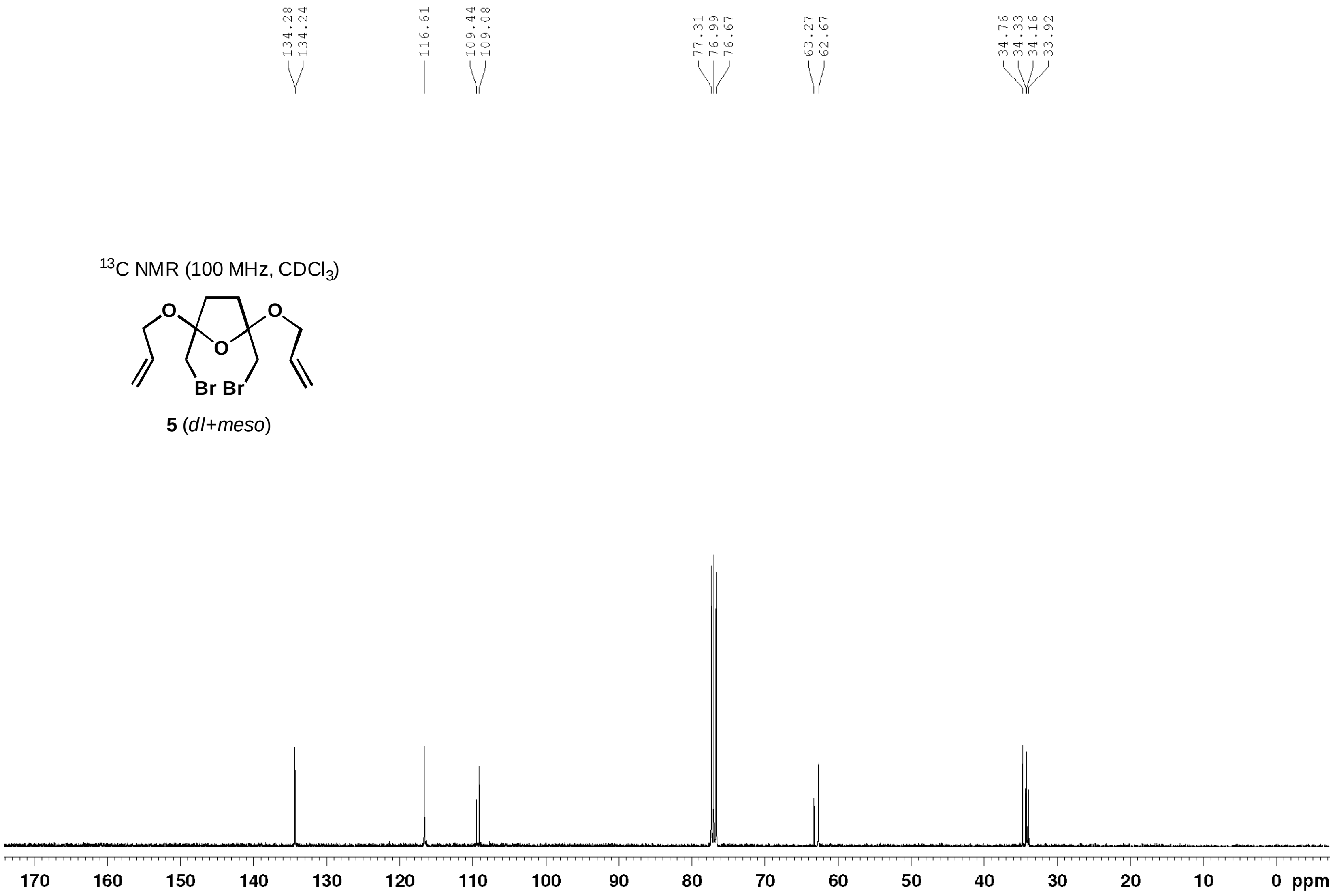
^{13}C NMR (100 MHz, $CDCl_3$)

4a'



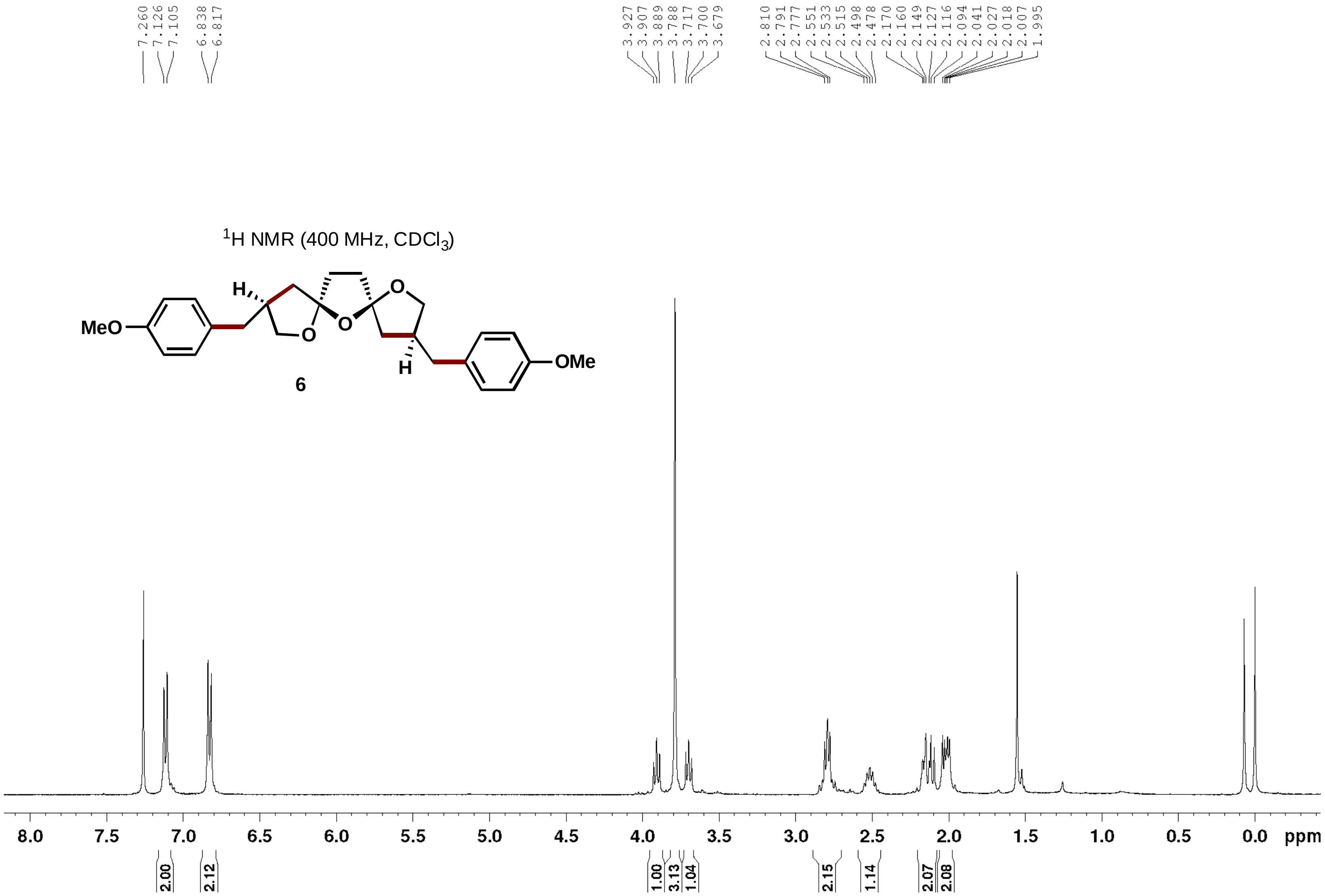
^{1}H NMR (400 MHz, $CDCl_3$)

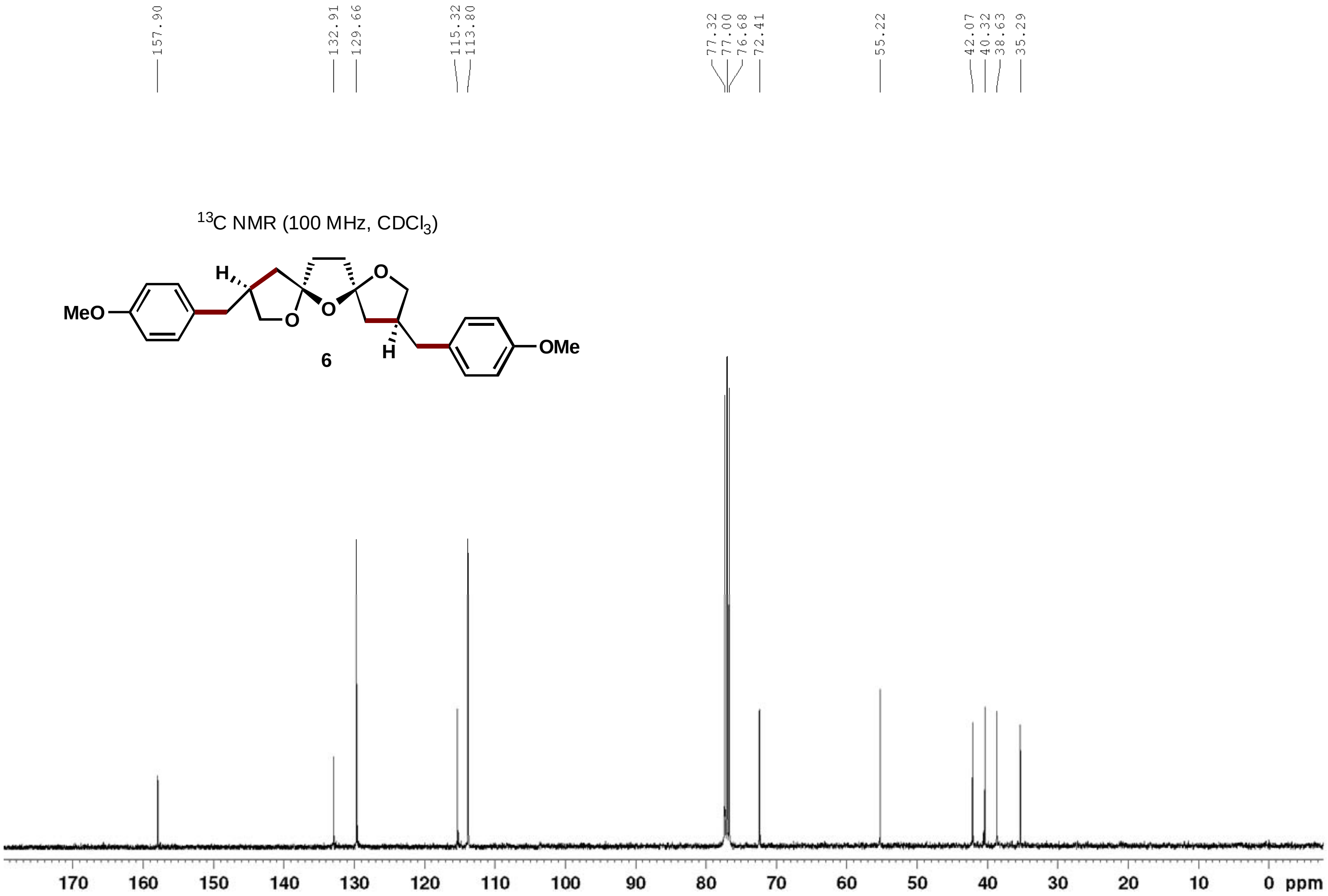
5 (*dl*+*meso*)

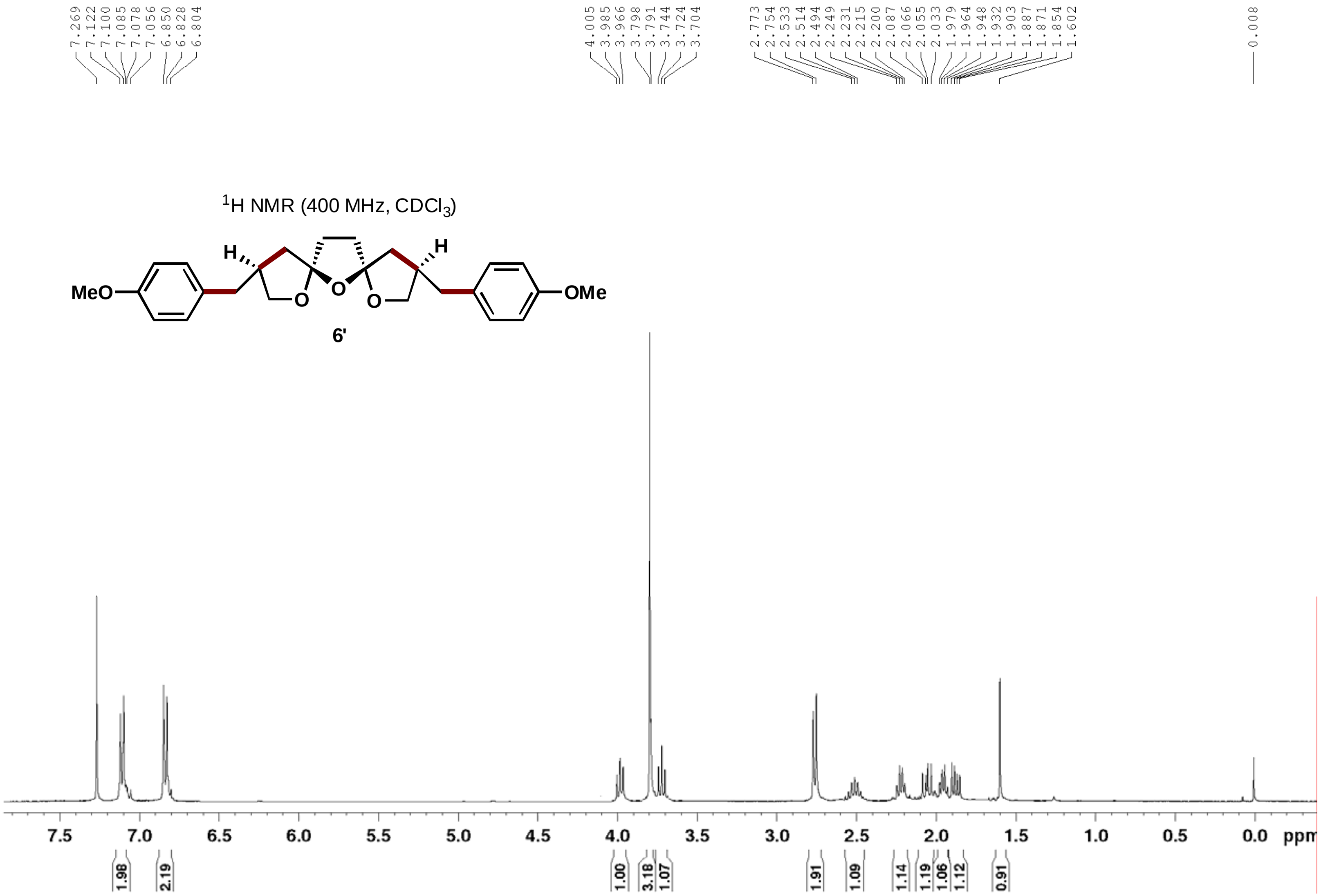


^{13}C NMR (100 MHz, $CDCl_3$)

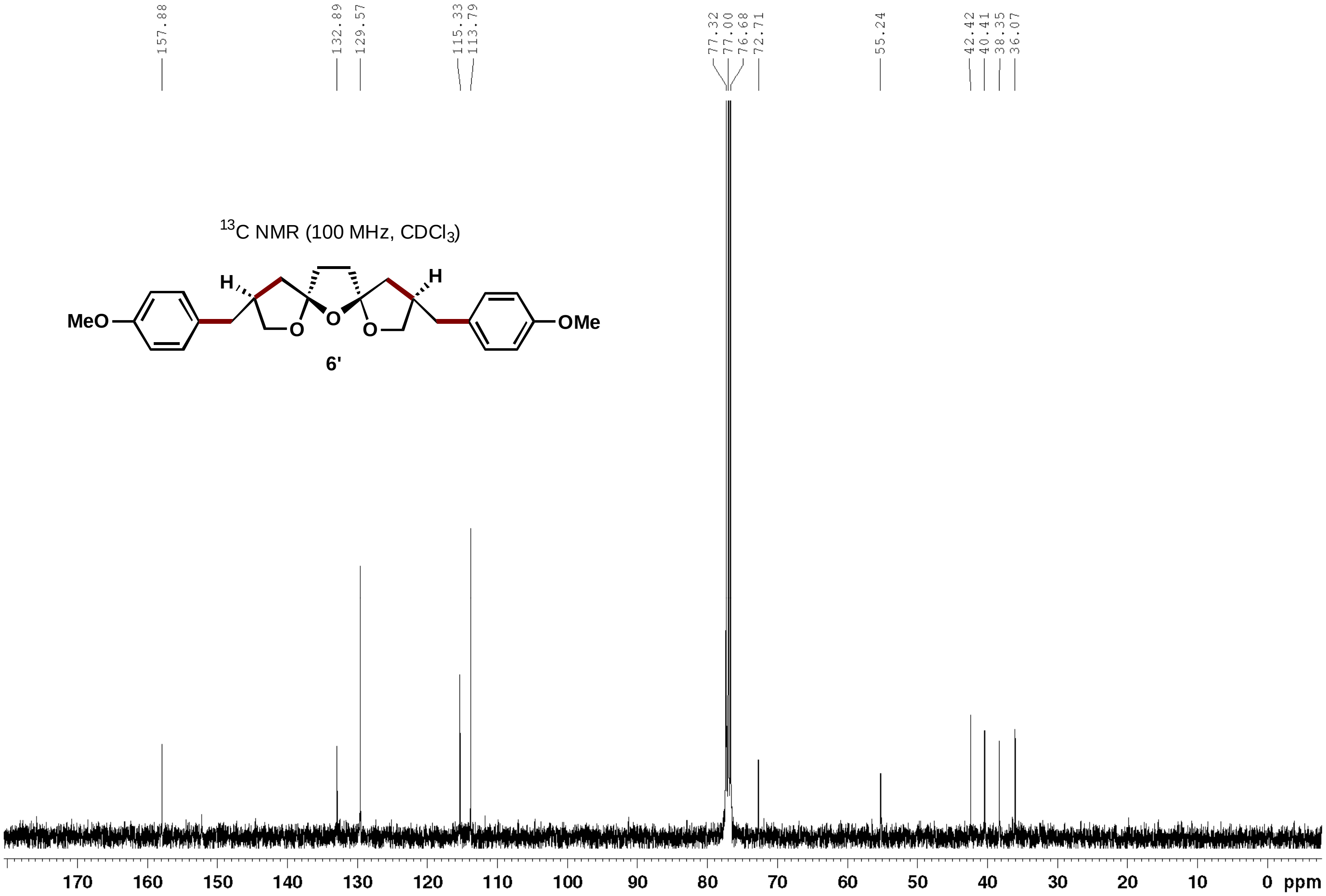
5 (*dl*+*meso*)

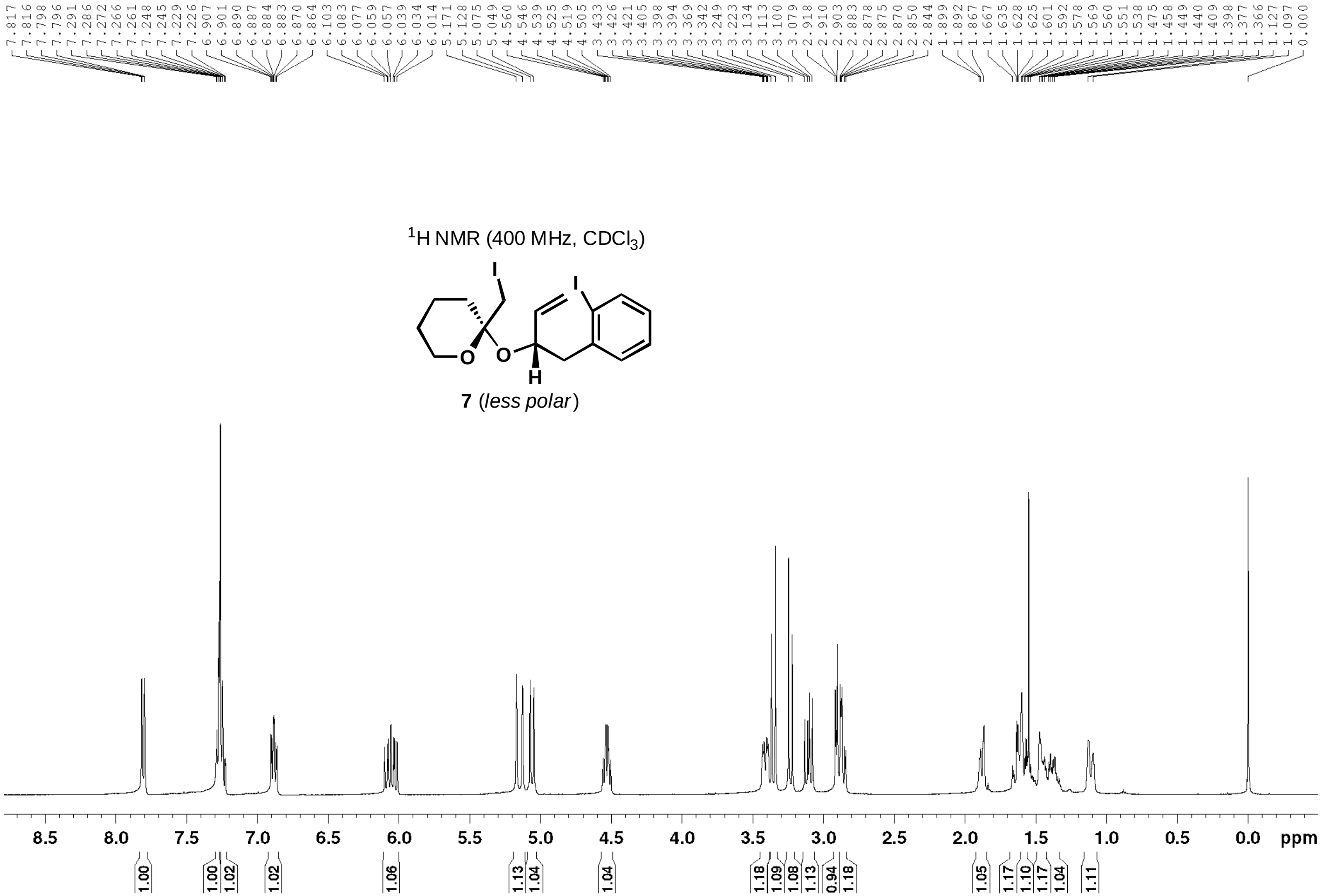

7.260
7.126
7.105
6.838
6.817
3.927
3.907
3.889
3.788
3.717
3.700
3.679
2.810
2.791
2.777
2.551
2.533
2.515
2.498
2.478
2.170
2.160
2.149
2.127
2.116
2.094
2.041
2.027
2.018
2.007
1.995
^{1}H NMR (400 MHz, CDCl$_3$)
H
O
O
O
MeO
OMe
H
6
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
2.12
1.00
3.13
1.04
2.15
1.14
2.07
2.08


157.90
132.91
129.66
115.32
113.80
77.32
77.00
76.68
72.41
55.22
42.07
40.32
38.63
35.29
^{13}C NMR (100 MHz, CDCl$_3$)
MeO
H
O
O
O
H
OMe
6
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm


^{1}H NMR (400 MHz, $CDCl_3$)

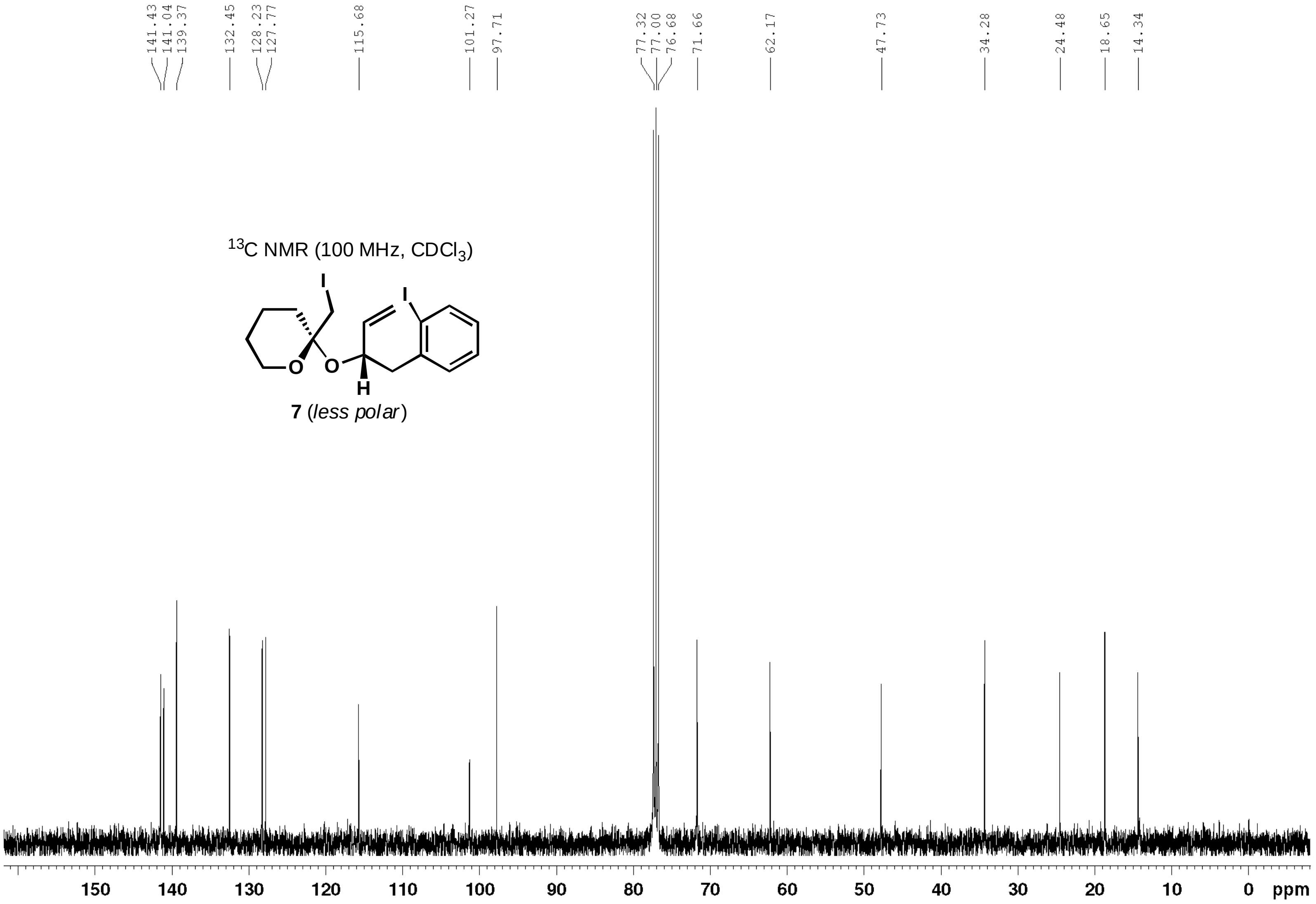
6'


157.88
132.89
129.57
115.33
113.79
77.32
77.00
76.68
72.71
55.24
42.42
40.41
38.35
36.07
^{13}C NMR (100 MHz, CDCl$_3$)
MeO
OMe
H
H
O
O
O
6'
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm



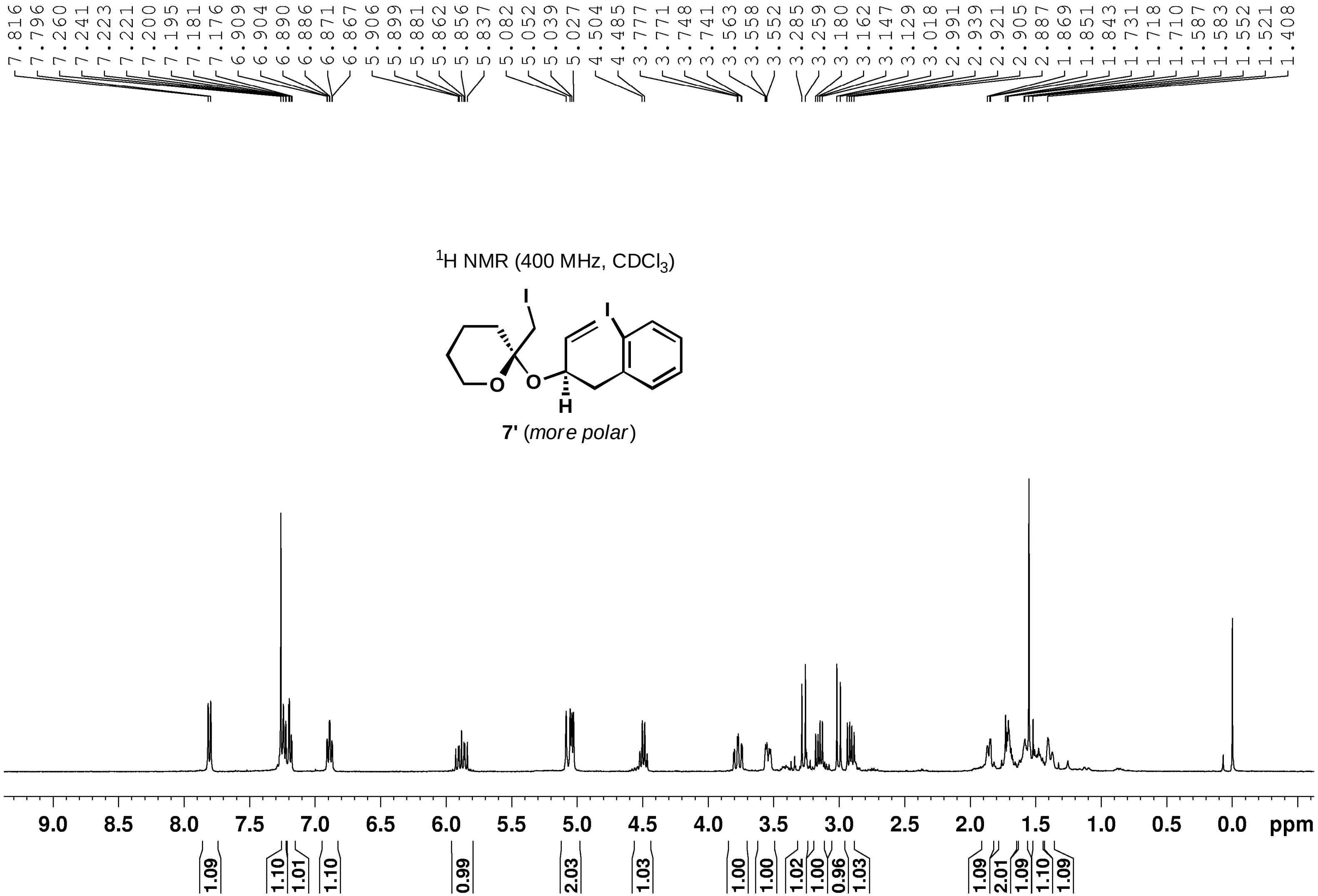
^{1}H NMR (400 MHz, CDCl$_3$)

7 (*less polar*)



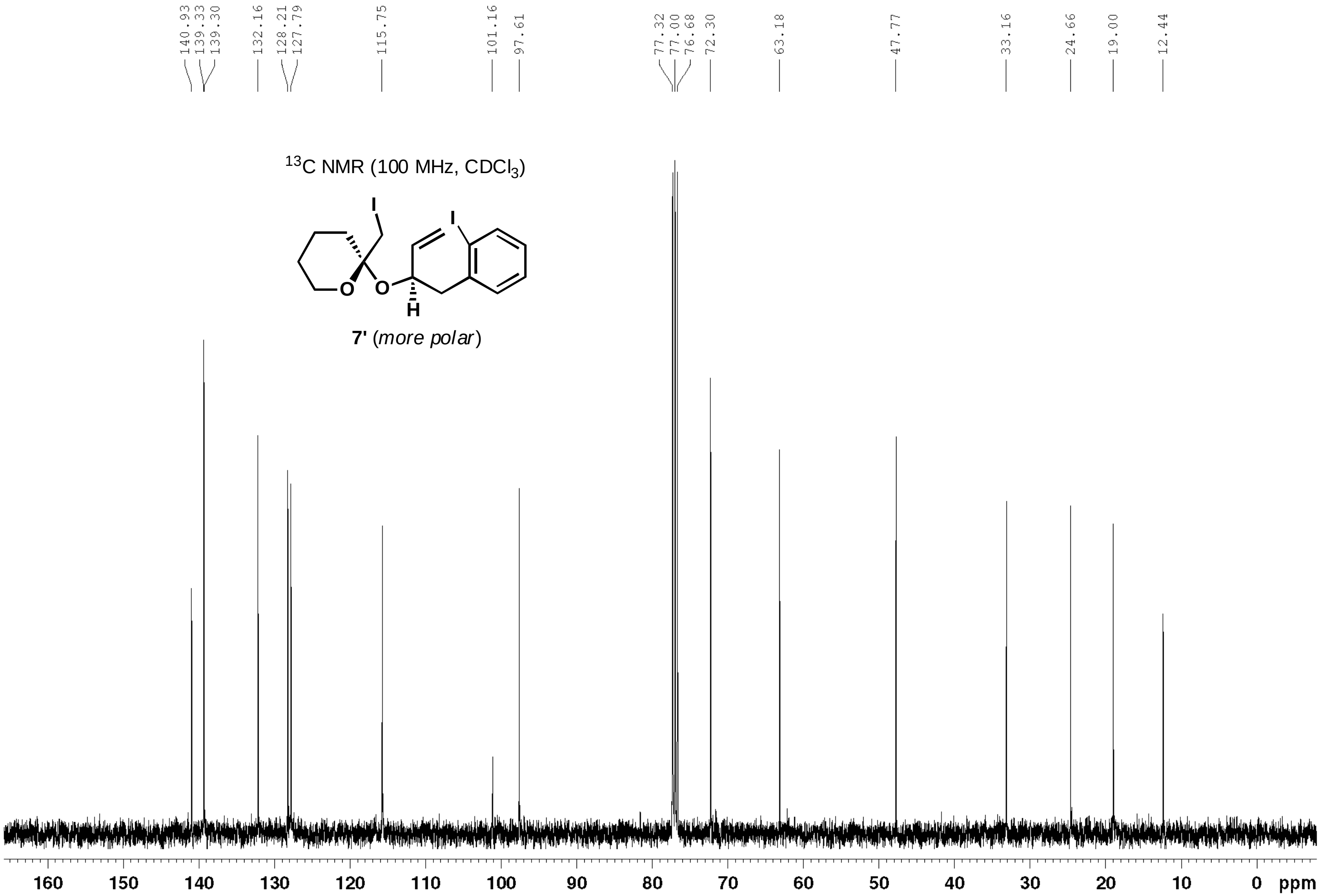
^{13}C NMR (100 MHz, CDCl$_3$)

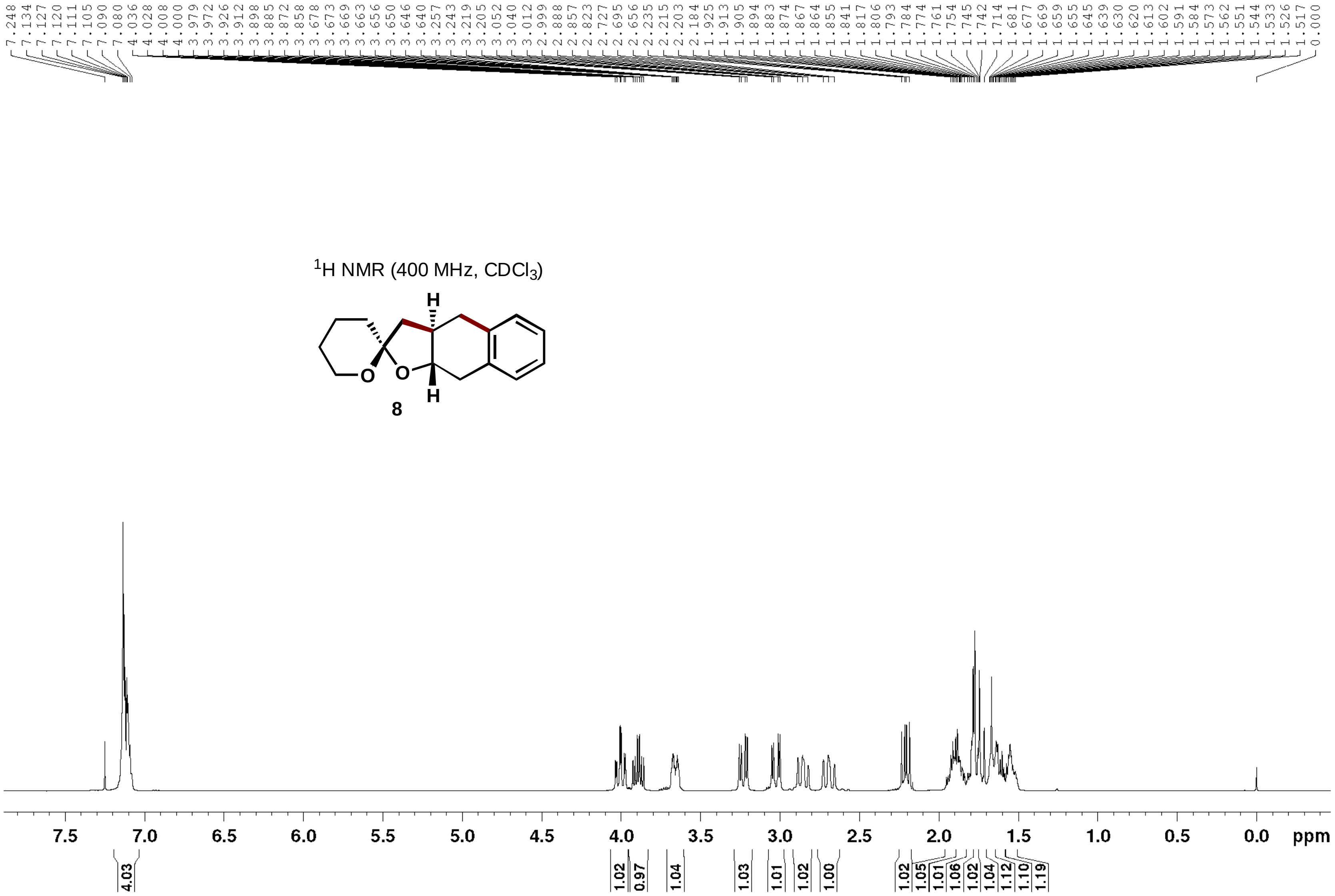
7 (*less polar*)

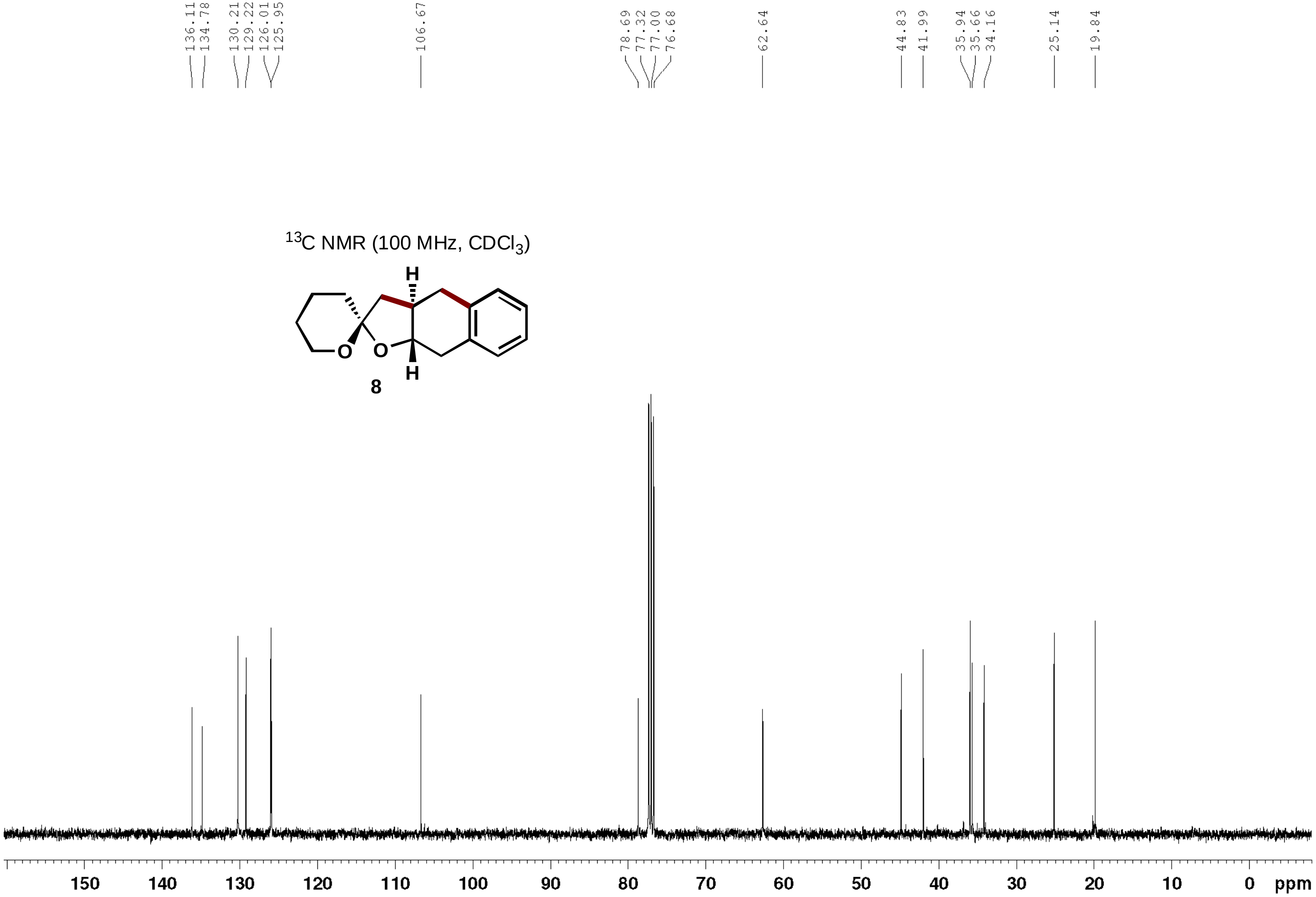


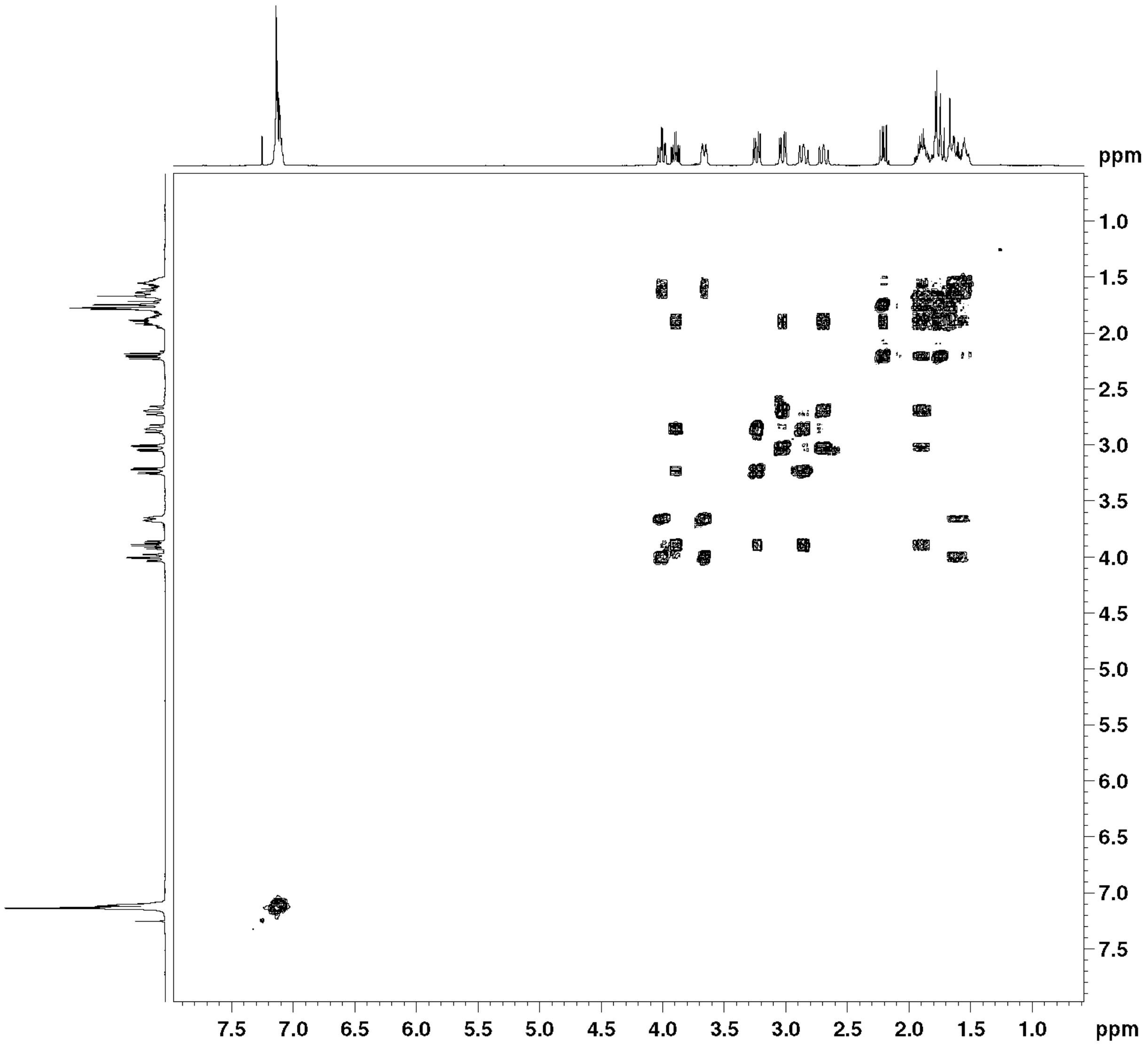
^{1}H NMR (400 MHz, CDCl$_3$)

7' (*more polar*)

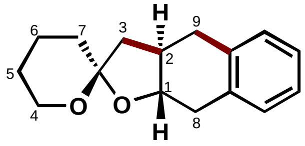

140.93
139.33
139.30
132.16
128.21
127.79
115.75
101.16
97.61
77.32
77.00
76.68
72.30
63.18
47.77
33.16
24.66
19.00
12.44
^{13}C NMR (100 MHz, CDCl$_3$)
I
I
O
O
H
7' (*more polar*)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

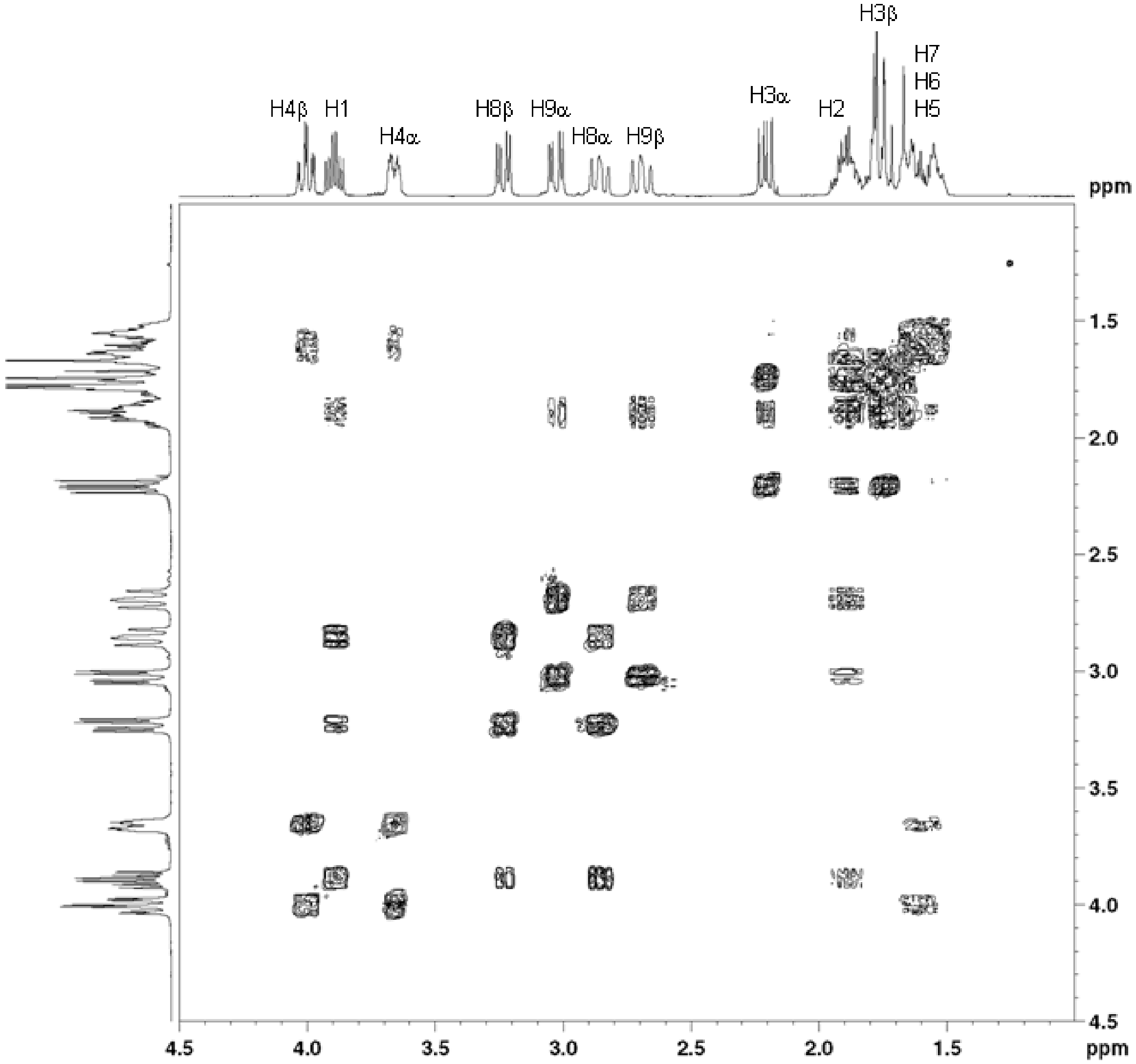

7.248
7.134
7.127
7.120
7.111
7.105
7.090
7.080
4.036
4.028
4.008
4.000
3.979
3.972
3.926
3.912
3.898
3.885
3.872
3.858
3.678
3.673
3.669
3.663
3.656
3.650
3.646
3.640
3.257
3.243
3.219
3.205
3.052
3.040
3.012
2.999
2.888
2.857
2.823
2.727
2.695
2.656
2.235
2.215
2.203
2.184
1.925
1.913
1.905
1.894
1.883
1.874
1.867
1.864
1.855
1.841
1.817
1.806
1.793
1.784
1.774
1.761
1.754
1.745
1.742
1.714
1.681
1.677
1.669
1.659
1.655
1.645
1.639
1.630
1.620
1.613
1.602
1.591
1.584
1.573
1.562
1.551
1.544
1.533
1.526
1.517
0.000
^{1}H NMR (400 MHz, CDCl$_3$)
H
O
O
H
8
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
4.03
1.02
0.97
1.04
1.03
1.01
1.02
1.00
1.02
1.05
1.01
1.06
1.02
1.04
1.12
1.10
1.19


136.11
134.78
130.21
129.22
126.01
125.95
106.67
78.69
77.32
77.00
76.68
62.64
44.83
41.99
35.94
35.66
34.16
25.14
19.84
^{13}C NMR (100 MHz, CDCl$_3$)
H
O
O
H
8
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

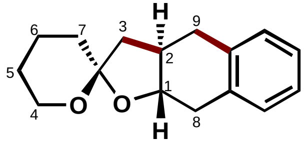


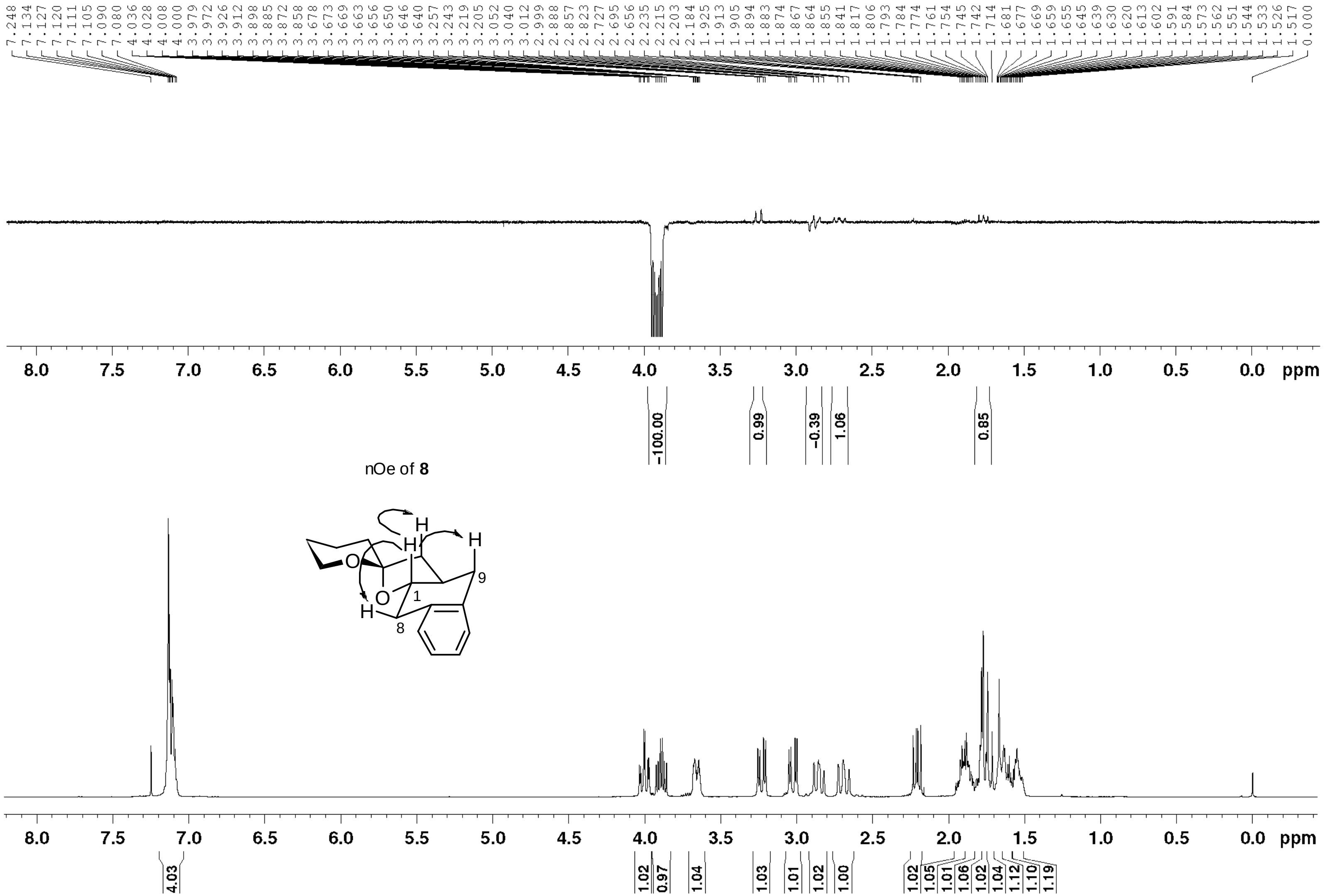
^{1}H –^{1}H COSY of **8**





^{1}H –^{1}H COSY of **8**




7.248
7.134
7.127
7.120
7.111
7.105
7.090
7.080
4.036
4.028
4.008
4.000
3.979
3.972
3.926
3.912
3.898
3.885
3.872
3.858
3.678
3.673
3.669
3.663
3.656
3.650
3.646
3.640
3.257
3.243
3.219
3.205
3.052
3.040
3.012
2.999
2.888
2.857
2.823
2.727
2.695
2.656
2.235
2.215
2.203
2.184
1.925
1.913
1.905
1.894
1.883
1.874
1.867
1.864
1.855
1.841
1.817
1.806
1.793
1.784
1.774
1.761
1.754
1.745
1.742
1.714
1.681
1.677
1.669
1.659
1.655
1.645
1.639
1.630
1.620
1.613
1.602
1.591
1.584
1.573
1.562
1.551
1.544
1.533
1.526
1.517
0.000
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
-100.00
0.99
-0.39
1.06
0.85
H
H
H
O
O
H
1
9
8
4.03
1.02
0.97
1.04
1.03
1.01
1.02
1.00
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1.02
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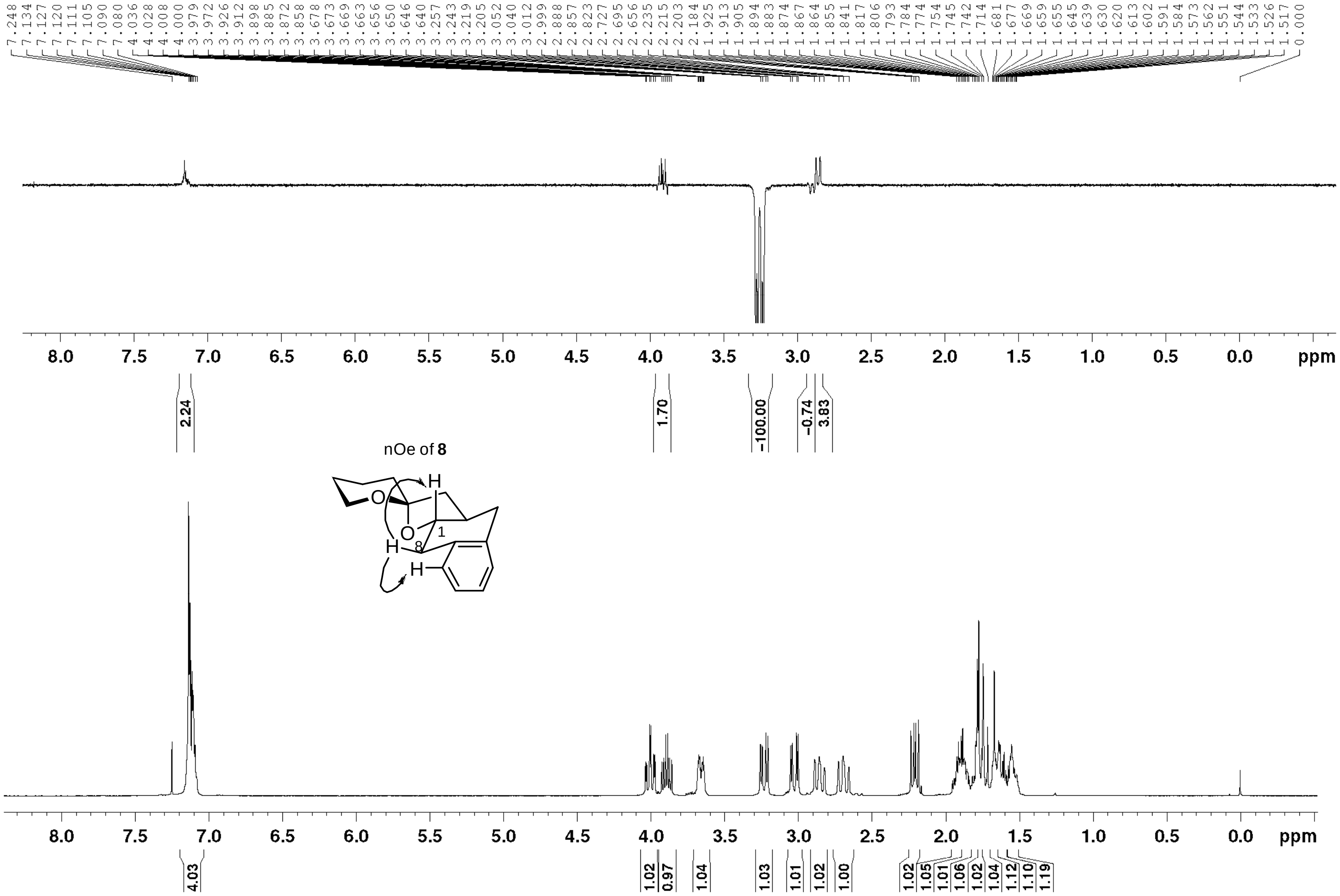
1.12
1.10
1.19

nOe of **8**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3.912
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3.885
3.872
3.858
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3.663
3.656
3.650
3.646
3.640
3.257
3.243
3.219
3.205
3.052
3.040
3.012
2.999
2.888
2.857
2.823
2.727
2.695
2.656
2.235
2.215
2.203
2.184
1.925
1.913
1.905
1.894
1.883
1.874
1.867
1.864
1.855
1.841
1.817
1.806
1.793
1.784
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1.745
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1.620
1.613
1.602
1.591
1.584
1.573
1.562
1.551
1.544
1.533
1.526
1.517
0.000
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.24
1.70
-100.00
-0.74
3.83
nOe of **8**
O
H
O
1
H
8
H
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
4.03
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0.97
1.04
1.03
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1.02
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1.04
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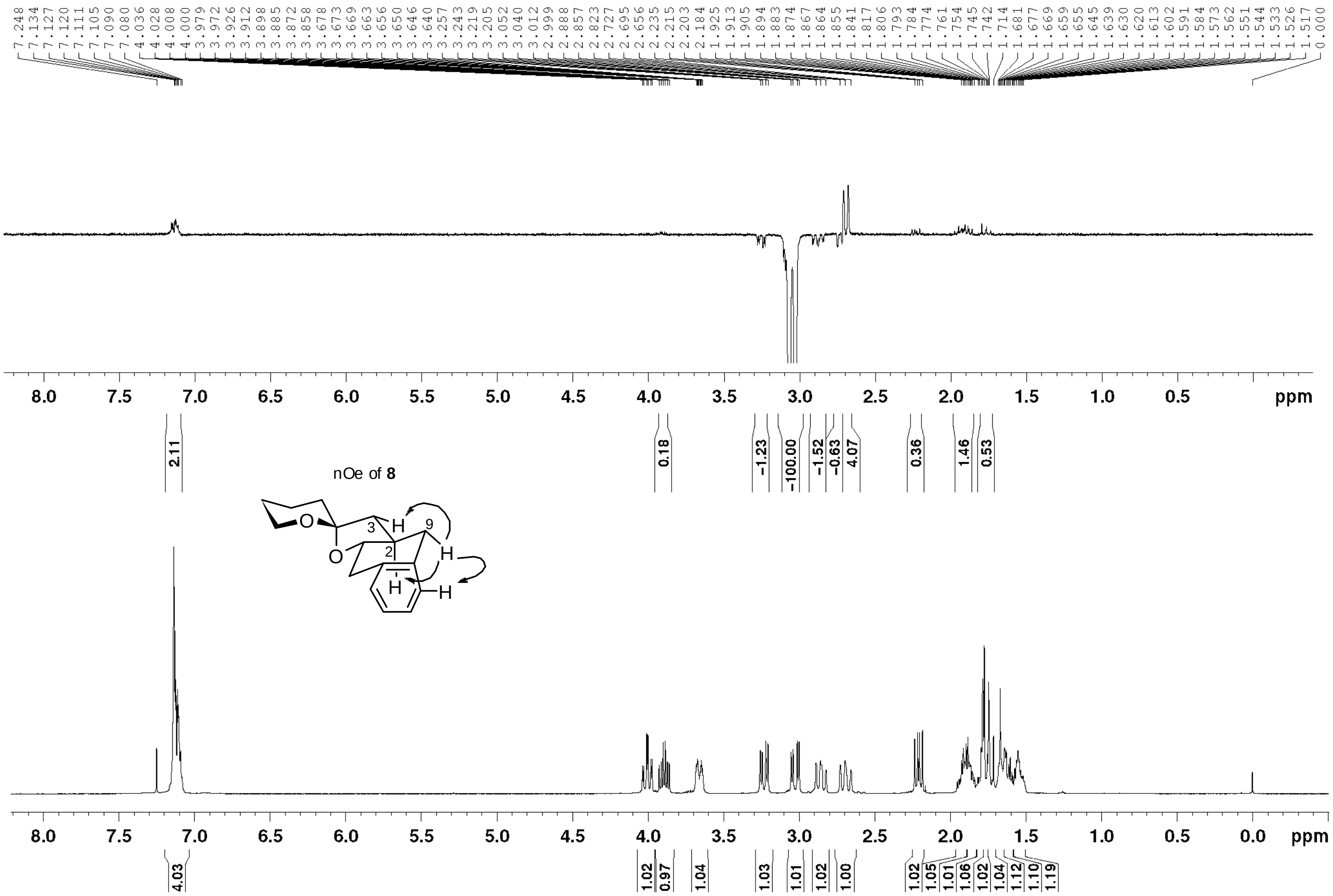
1.19


nOe of **8**
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4.000
3.979
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3.912
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3.885
3.872
3.858
3.678
3.673
3.669
3.663
3.656
3.650
3.646
3.640
3.257
3.243
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3.205
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2.888
2.857
2.823
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1.883
1.874
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1.864
1.855
1.841
1.817
1.806
1.793
1.784
1.774
1.761
1.754
1.745
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1.714
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1.655
1.645
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1.630
1.620
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1.602
1.591
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1.573
1.562
1.551
1.544
1.533
1.526
1.517
0.000
8.0
7.5
7.0
6.5
6.0
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5.0
4.5
4.0
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3.0
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ppm
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0.53
O
O
3
H
9
2
H
H
H
0.0
4.03
1.02
0.97
1.04
1.03
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1.02
1.05
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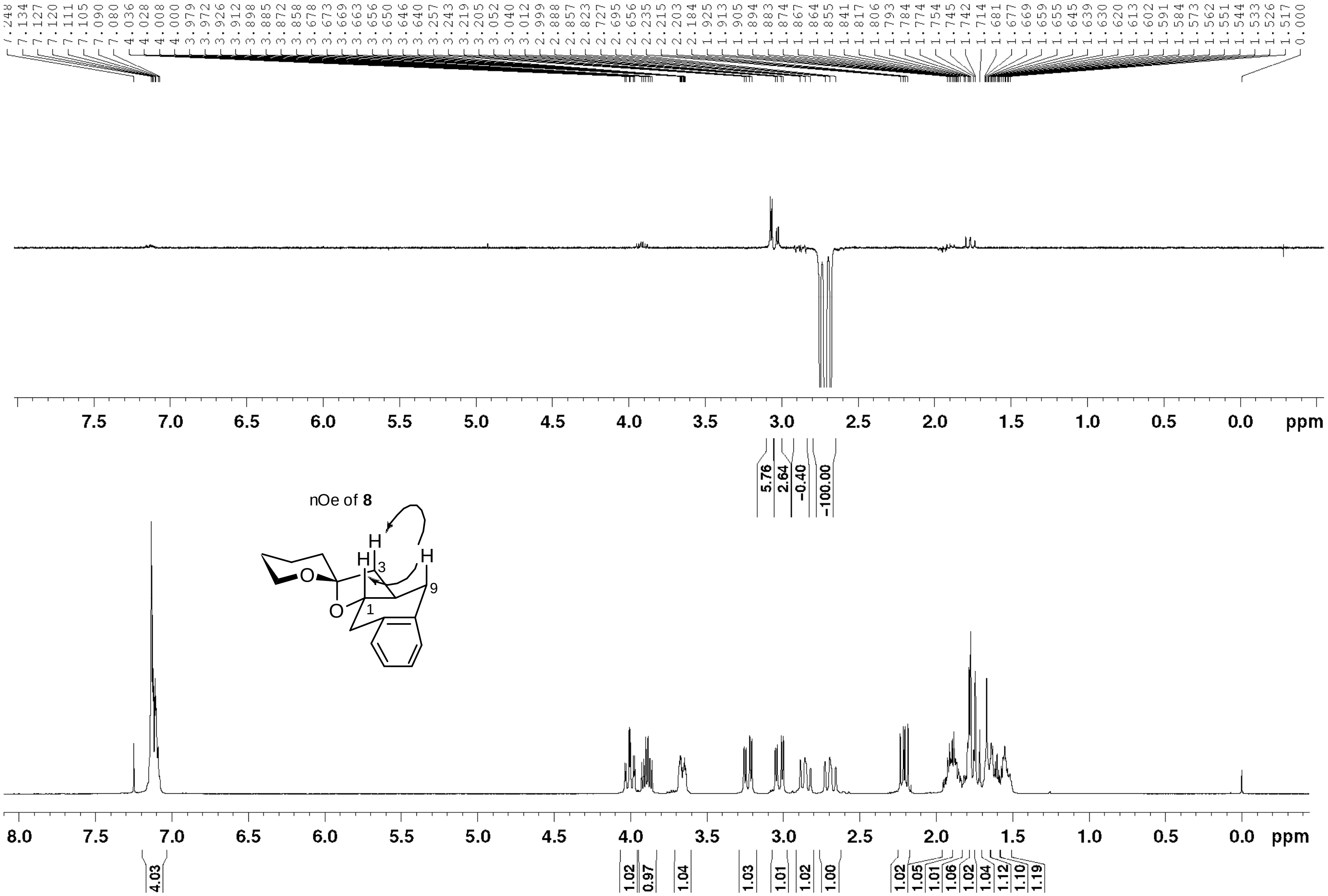
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3.912
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3.872
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0.0
ppm
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−0.40
−100.00
nOe of **8**
H
H
3
H
9
O
O
1
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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0.5
0.0
ppm
4.03
1.02
0.97
1.04
1.03
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1.02
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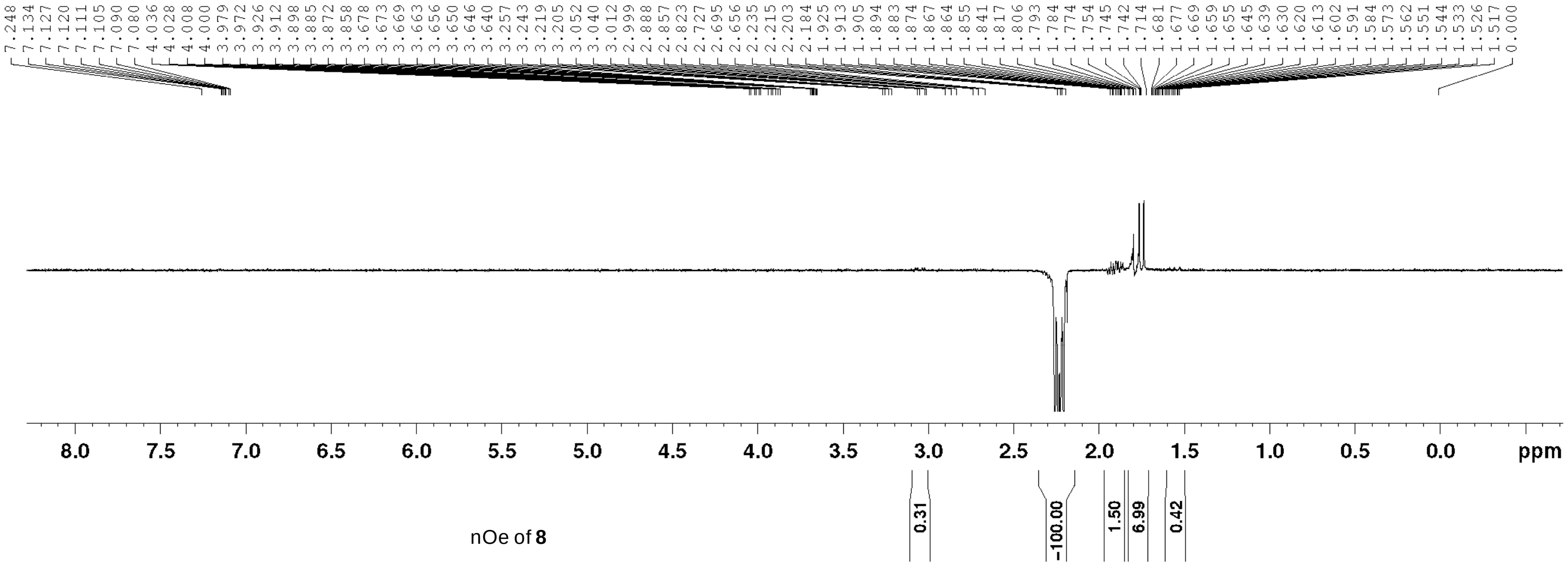
1.12
1.10
1.19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3.872
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6.5
6.0
5.5
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3.0
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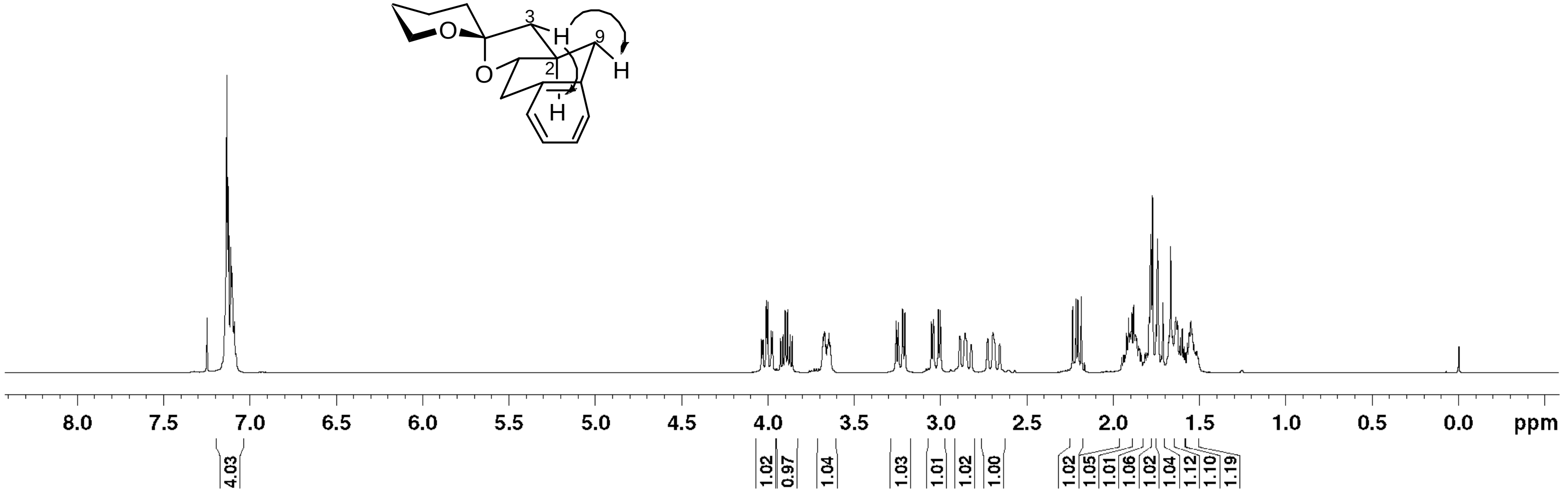
nOe of **8**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H
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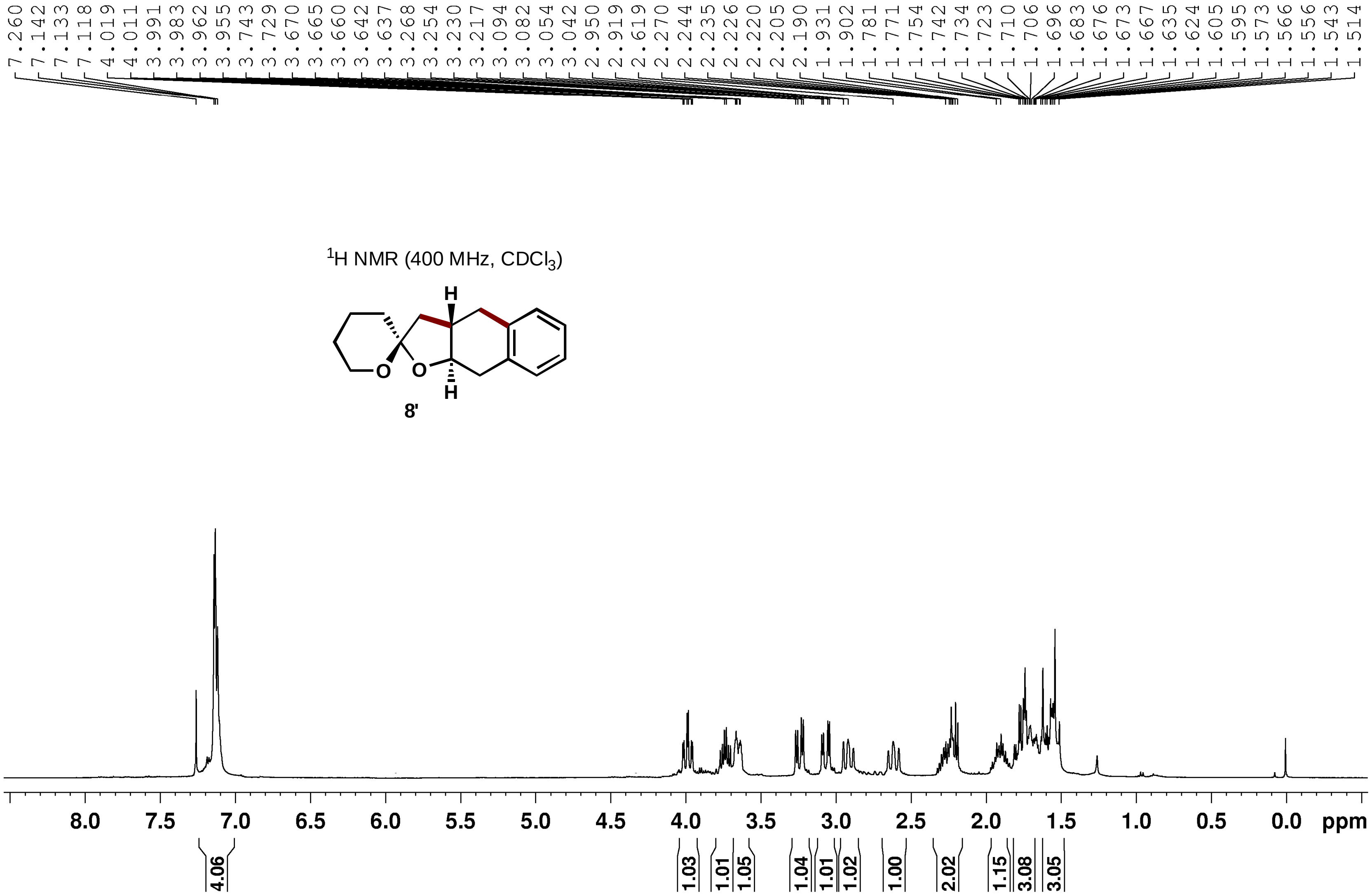
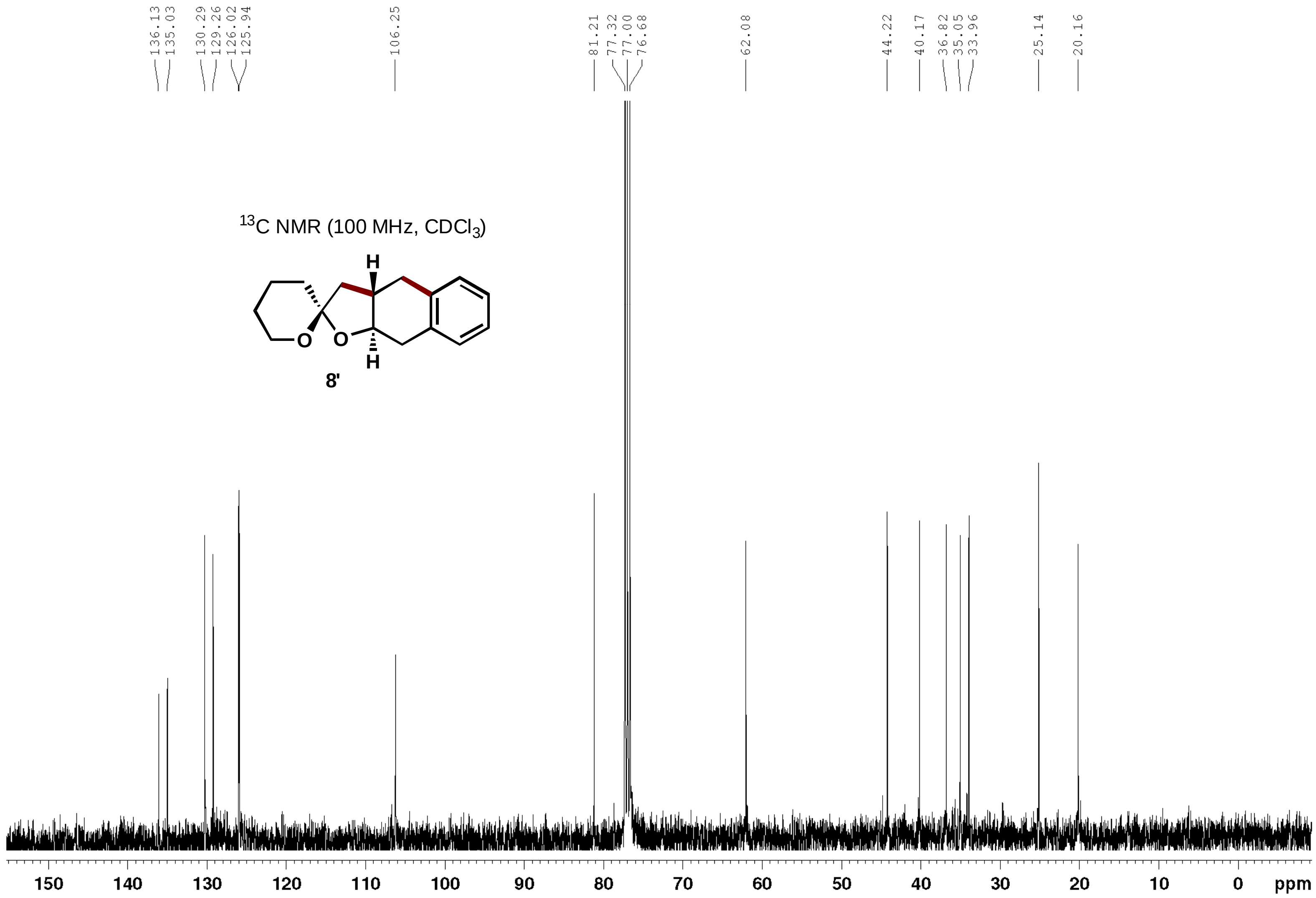
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
4.03
1.02
0.97
1.04
1.03
1.01
1.02
1.00
1.02
1.05
1.01
1.06
1.02
1.04
1.12
1.10
1.19



^{1}H NMR (400 MHz, $CDCl_3$)

8'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129.26
126.02
125.94
106.25
81.21
77.32
77.00
76.68
62.08
44.22
40.17
36.82
35.05
33.96
25.14
20.16
^{13}C NMR (100 MHz, $CDCl_3$)
H
O
O
H
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

8'