Supplementary Information

Brønsted acid-catalyzed formal [5+2+1] cycloaddition of ynamides and isoxazoles with water: access to oxygen-bridged tetrahydro-1,4-oxazepines

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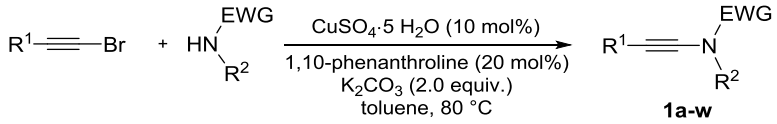
1. General information

Unless otherwise stated, all reactions were conducted under inert atmosphere using standard Schlenk techniques or in an argon-filled glove-box. All chemicals were obtained from commercial sources and were used directly without further purification. Solvents were treated prior to use according to the standard methods. Column chromatography was conducted on silica gel (300–400 mesh) using a forced flow of eluent at 0.3–0.5 bar pressure. NMR Spectra were recorded at room temperature in $CDCl_3$, DMSO-d_6 or acetone-d_6 on 400 MHz spectrometers. The chemical shifts for ^1H NMR were recorded in ppm downfield from tetramethylsilane (TMS) with $CDCl_3$ (7.26 ppm), DMSO-d_6 (2.50 ppm) or acetone-d_6 (2.05 ppm) as the internal standard. The chemical shifts for ^{13}C NMR were recorded in ppm downfield using the central peak of $CDCl_3$ (77.16 ppm), DMSO-d_6 (39.52 ppm) or acetone-d_6 (29.84 ppm) as the internal standard. Coupling constants (J) are reported in hertz and refer to apparent peak multiplications. The abbreviations *s*, *d*, *t*, *q* and *m* stand for singlet, doublet, triplet, quartet and multiplet in that order. HRMS data was obtained with Micromass HPLC-Q-TOF mass spectrometer (ESI) or Agilent 6540 Accurate-MS spectrometer (Q-TOF).

2. Synthesis and characterization data of ynamides

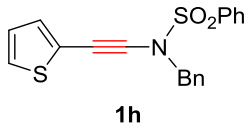


The ynamides were synthesized by copper-catalyzed cross-couplings of amides with the corresponding alkynyl bromides.[1] The substrates **1a–g** are known compounds.[2,3]

In a 25 mL flame-dried Schlenk tube, amides (2.5 mmol), $CuSO_4·5H_2O$ (10 mol%, 63.0 mg), 1,10-phenanthroline (20 mol%, 90.0 mg), K_2CO_3 (2.0 equiv, 0.69 g) and toluene (10 mL) were added in sequence under argon atmosphere. Then alkynyl bromide (6.0 mmol) was introduced and the resulting mixture was stirred at 80 °C for 12–24 h. After which time, the crude mixture was filtered through a short pad of celite and washed with ethyl acetate. Removal of the solvent and purification by silica gel column chromatography afforded the desired ynamides (eluent: petroleum ether/ethyl acetate = 10/1).

Characterization data of ynamides:

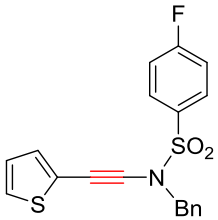
***N*-Benzyl-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (1h)**



1h

Brown solid; 592.9 mg; 67% yield; mp 98–99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.2 Hz, 2H), 7.66–7.58 (m, 1H), 7.53–7.46 (m, 2H), 7.32–7.25 (m, 5H), 7.22–7.18 (m, 1H), 7.10–7.05 (m, 1H), 6.91 (dd, *J* = 5.2, 3.6 Hz, 1H), 4.59 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 134.3, 133.8, 133.0, 129.2, 128.8, 128.6, 128.5, 127.9, 127.7, 127.1, 122.7, 86.1, 64.8, 56.0. HRMS (ESI) calcd for $C_{19}H_{16}NO_2S_2$ $[M + H]^+$ 354.0617, found 354.0614.

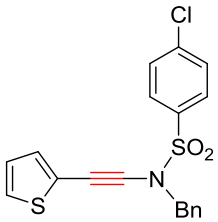
***N*-Benzyl-4-fluoro-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (1i)**



1i

Brown solid; 525.5 mg; 56% yield; mp 95–96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89–7.79 (m, 2H), 7.33–7.28 (m, 5H), 7.25–7.23 (m, 1H), 7.19–7.13 (m, 2H), 7.11–7.09 (m, 1H), 6.96–6.89 (m, 1H), 4.62 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (d, *J* = 256.4 Hz), 134.2, 133.8 (d, *J* = 3.3 Hz), 133.2, 130.6 (d, *J* = 9.6 Hz), 128.9, 128.7, 128.6, 128.1, 127.1, 122.5, 116.5 (d, *J* = 22.7 Hz), 86.0, 65.0, 56.2. HRMS (ESI) calcd for $C_{19}H_{15}FNO_2S_2$ $[M + H]^+$ 372.0523, found 372.0520.

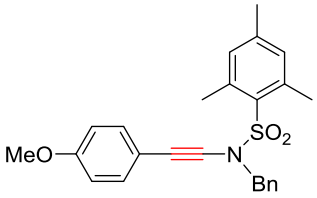
***N*-Benzyl-4-chloro-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (1j)**



1j

White solid; 409.1 mg; 42% yield; mp 117–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.74 (m, 2H), 7.53–7.43 (m, 2H), 7.36–7.25 (m, 5H), 7.26–7.24 (m, 1H), 7.13–7.09 (m, 1H), 6.97–6.91 (m, 1H), 4.62 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.4, 136.2, 134.2, 133.3, 129.5, 129.2, 128.9, 128.8, 128.7, 128.1, 127.1, 122.5, 85.9, 65.1, 56.3. HRMS (ESI) calcd for $C_{19}H_{15}ClNO_2S_2$ $[M + H]^+$ 388.0227, found 388.0216.

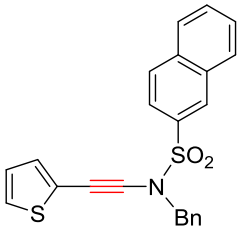
_N_-Benzyl-_N_-((4-methoxyphenyl)ethynyl)-2,4,6-trimethylbenzenesulfonamide (1k)



1k

Yellow oil; 725.8 mg; 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.29 (m, 5H), 7.09–7.04 (m, 2H), 6.97 (s, 2H), 6.76–6.71 (m, 2H), 4.67 (s, 2H), 3.75 (s, 3H), 2.68 (s, 6H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 143.7, 141.0, 135.1, 132.9, 132.1, 132.0, 129.0, 128.6, 128.3, 115.1, 113.9, 80.9, 72.4, 55.4, 54.3, 23.3, 21.2. HRMS (ESI) calcd for $C_{25}H_{26}NO_3S$ $[M + H]^+$ 420.1628, found 420.1621.

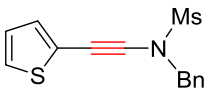
_N_-Benzyl-_N_-(thiophen-2-ylethynyl)naphthalene-2-sulfonamide (1l)



1l

Brown solid; 511.3 mg; 51% yield; mp 112–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.99–7.81 (m, 4H), 7.70–7.56 (m, 2H), 7.35–7.17 (m, 6H), 7.11–7.02 (m, 1H), 6.95–6.87 (m, 1H), 4.64 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.3, 134.6, 134.3, 133.0, 132.1, 129.6, 129.53, 129.51, 129.4, 128.9, 128.6, 128.5, 128.1, 127.9, 127.8, 127.1, 122.8, 122.6, 86.3, 64.9, 56.2. HRMS (ESI) calcd for $C_{23}H_{18}NO_2S_2$ $[M + H]^+$ 404.0773, found 404.0776.

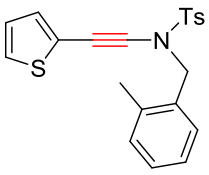
_N_-Benzyl-_N_-(thiophen-2-ylethynyl)methanesulfonamide (1m)



1m

Yellow solid; 3.0 mmol scale, 833.0 mg; 95% yield; mp 80–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.44 (m, 2H), 7.44–7.34 (m, 3H), 7.30–7.24 (m, 1H), 7.22–7.16 (m, 1H), 7.02–6.92 (m, 1H), 4.71 (s, 2H), 2.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5, 133.4, 129.1, 129.0, 128.9, 128.2, 127.2, 85.6, 65.0, 56.2, 39.3. HRMS (ESI) calcd for $C_{14}H_{14}NO_2S_2$ $[M + H]^+$ 292.0460, found 292.0439.

4-Methyl-_N_-(2-methylbenzyl)-_N_-(thiophen-2-ylethynyl)benzenesulfonamide (1n)

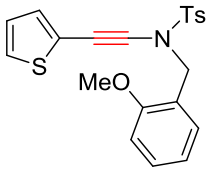


1n

Brown solid; 450.0 mg; 47% yield; mp 106–107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.26–7.08 (m, 5H), 7.03–7.00 (m, 1H), 6.91–6.88 (m, 1H), 4.55 (s, 2H), 2.46 (s, 3H),

2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 137.5, 134.3, 132.6, 132.1, 130.6, 130.4, 129.9, 128.7, 127.9, 127.5, 127.0, 126.1, 122.9, 86.3, 64.8, 53.7, 21.8, 19.3. HRMS (ESI) calcd for $C_{21}H_{20}NO_2S_2$ $[M + H]^+$ 382.0930, found 382.0934.

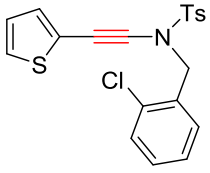
_N_-(2-Methoxybenzyl)-4-methyl-_N_-(thiophen-2-ylethynyl)benzenesulfonamide (1o)



1o

Brown solid; 438.7 mg; 44% yield; mp 101–102 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.84 (d, J = 8.3 Hz, 2H), 7.49 (d, J = 8.1 Hz, 2H), 7.45–7.40 (m, 1H), 7.32–7.27 (m, 2H), 7.11–7.06 (m, 1H), 7.01–6.97 (m, 1H), 6.96–6.88 (m, 2H), 4.66 (s, 2H), 3.74 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 158.7, 145.8, 135.8, 133.2, 131.4, 130.8, 130.7, 128.7, 128.5, 128.1, 123.6, 123.3, 121.1, 111.5, 87.6, 64.5, 55.8, 51.5, 21.5. HRMS (ESI) calcd for $C_{21}H_{20}NO_3S_2$ $[M + H]^+$ 398.0879, found 398.0889.

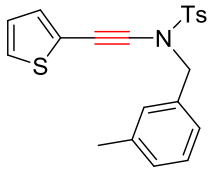
_N_-(2-Chlorobenzyl)-4-methyl-_N_-(thiophen-2-ylethynyl)benzenesulfonamide (1p)



1p

Brown solid; 381.7 mg; 38% yield; mp 96–97 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.91 (d, J = 8.4 Hz, 2H), 7.55–7.48 (m, 3H), 7.47–7.40 (m, 2H), 7.40–7.31 (m, 2H), 7.13–7.08 (m, 1H), 7.03–6.96 (m, 1H), 4.79 (s, 2H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 146.3, 135.3, 134.7, 133.6, 133.1, 132.1, 130.94, 130.92, 130.4, 129.0, 128.6, 128.10, 128.08, 123.1, 86.9, 65.1, 53.7, 21.6. HRMS (ESI) calcd for $C_{20}H_{17}ClNO_2S_2$ $[M + H]^+$ 402.0384, found 402.0386.

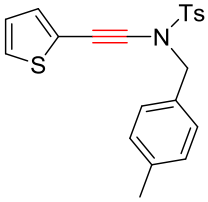
4-Methyl-_N_-(3-methylbenzyl)-_N_-(thiophen-2-ylethynyl)benzenesulfonamide (1q)



1q

Brown oil; 534.8 mg; 56% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.85 (d, J = 8.4 Hz, 2H), 7.53–7.41 (m, 3H), 7.26–7.19 (m, 1H), 7.17–7.09 (m, 4H), 7.05–6.97 (m, 1H), 4.61 (s, 2H), 2.47 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 146.0, 138.9, 135.8, 135.6, 133.5, 130.8, 130.2, 129.8, 129.2, 129.0, 128.5, 128.1, 126.7, 123.4, 87.7, 65.1, 56.4, 21.6, 21.3. HRMS (ESI) calcd for $C_{21}H_{20}NO_2S_2$ $[M + H]^+$ 382.0930, found 382.0927.

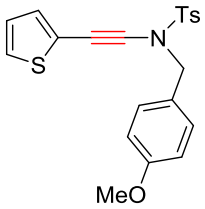
4-Methyl-*N*-(4-methylbenzyl)-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (1r)



1r

Brown solid; 464.0 mg; 49% yield; mp 85–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.23–7.15 (m, 3H), 7.13–7.04 (m, 3H), 6.92–6.88 (m, 1H), 4.52 (s, 2H), 2.43 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 138.2, 134.8, 132.8, 131.4, 129.8, 129.3, 128.9, 127.8, 127.7, 127.0, 122.9, 86.4, 64.8, 55.7, 21.8, 21.3. HRMS (ESI) calcd for $C_{21}H_{20}NO_2S_2$ $[M + H]^+$ 382.0930, found 382.0918.

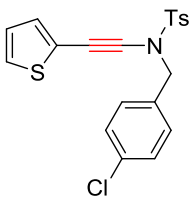
***N*-(4-methoxybenzyl)-4-methyl-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (1s)**



1s

Yellow solid; 425.7 mg; 43% yield; mp 97–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.25–7.19 (m, 3H), 7.10–7.05 (m, 1H), 6.95–6.89 (m, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 4.51 (s, 2H), 3.78 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 144.7, 134.9, 132.8, 130.5, 129.8, 127.9, 127.7, 127.0, 126.5, 123.0, 114.0, 86.4, 64.9, 55.5, 55.4, 21.8. HRMS (ESI) calcd for $C_{21}H_{20}NO_3S_2$ $[M + H]^+$ 398.0879, found 398.0888.

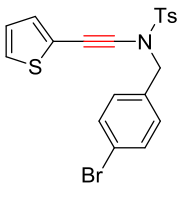
***N*-(4-chlorobenzyl)-4-methyl-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (1t)**



1t

Brown solid; 354.7 mg; 35% yield; mp 100–101 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.54–7.44 (m, 3H), 7.42–7.34 (m, 4H), 7.14 (d, *J* = 3.6 Hz, 1H), 7.04–6.96 (m, 1H), 4.66 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 146.2, 135.6, 134.8, 134.6, 133.8, 131.3, 130.9, 129.4, 129.1, 128.5, 128.1, 123.1, 87.0, 65.2, 55.6, 21.6. HRMS (ESI) calcd for $C_{20}H_{17}ClNO_2S_2$ $[M + H]^+$ 402.0384, found 402.0381.

***N*-(4-bromobenzyl)-4-methyl-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (1u)**

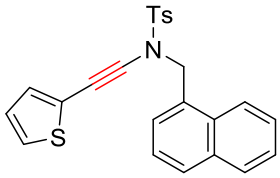


1u

Yellow solid; 605.4 mg; 54% yield; mp 91–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.7 Hz, 2H), 7.41 (d, *J* = 7.7 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 5.2 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 2H), 7.12–7.06 (m,

1H), 6.96–6.85 (m, 1H), 4.51 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 134.5, 133.5, 133.2, 131.8, 130.5, 129.9, 128.0, 127.8, 127.1, 122.6, 122.5, 86.0, 64.9, 55.3, 21.8. HRMS (ESI) calcd for $C_{20}H_{17}BrNO_2S_2$ $[M + H]^+$ 445.9879, found 445.9875.

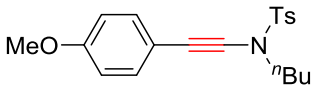
4-Methyl-*N*-(naphthalen-1-ylmethyl)-*N*-(thiophen-2-ylethynyl)benzenesulfonamide (1v)



1v

Brown solid; 443.3 mg; 42% yield; mp 107–108 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.29 (d, J = 8.0 Hz, 1H), 8.00–7.87 (m, 4H), 7.63–7.47 (m, 5H), 7.47–7.41 (m, 1H), 7.40–7.35 (m, 1H), 7.02–6.98 (m, 1H), 6.97–6.91 (m, 1H), 5.07 (s, 2H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 146.2, 134.9, 134.8, 133.3, 132.5, 130.9, 130.6, 130.3, 129.7, 129.6, 128.8, 128.6, 128.0, 127.5, 126.8, 126.0, 124.3, 123.1, 87.1, 65.6, 54.4, 21.6. HRMS (ESI) calcd for $C_{24}H_{20}NO_2S_2$ $[M + H]^+$ 418.0930, found 418.0928.

***N*-Butyl-*N*-((4-methoxyphenyl)ethynyl)-4-methylbenzenesulfonamide (1w)**



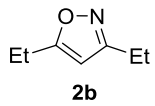
1w

Yellow oil; 741.1 mg; 83% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.87 (d, J = 8.2 Hz, 2H), 7.50 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H), 3.41 (t, J = 7.1 Hz, 2H), 2.46 (s, 3H), 1.72–1.61 (m, 2H), 1.42–1.36 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 160.6, 145.7, 135.6, 133.9, 130.7, 128.5, 115.6, 115.0, 82.0, 70.7, 55.7, 52.1, 27.5, 21.5, 20.1, 13.8. HRMS (ESI) calcd for $C_{20}H_{24}NO_3S$ $[M + H]^+$ 358.1471, found 358.1474.

3. Synthesis and characterization data of isoxazoles

3,5-Diethylisoxazole **2b** was prepared according to the known procedure.[4] Other isoxazoles were obtained from commercial sources.

3,5-Diethylisoxazole (2b)

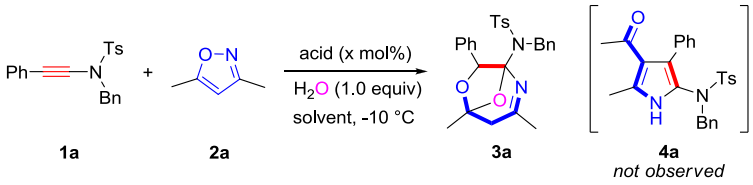


2b

Known compound;[4] ^{1}H NMR (400 MHz, Acetone-d_6) δ 6.02 (s, 1H), 2.71 (q, J = 7.6 Hz, 2H), 2.60 (q, J = 7.6 Hz, 2H), 1.45–1.08 (m, 6H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 175.0, 165.5, 100.2, 20.6, 20.0, 13.0, 12.1.

4. Optimization of the reaction conditions

Table S1. Optimization of the reaction conditions.[a]



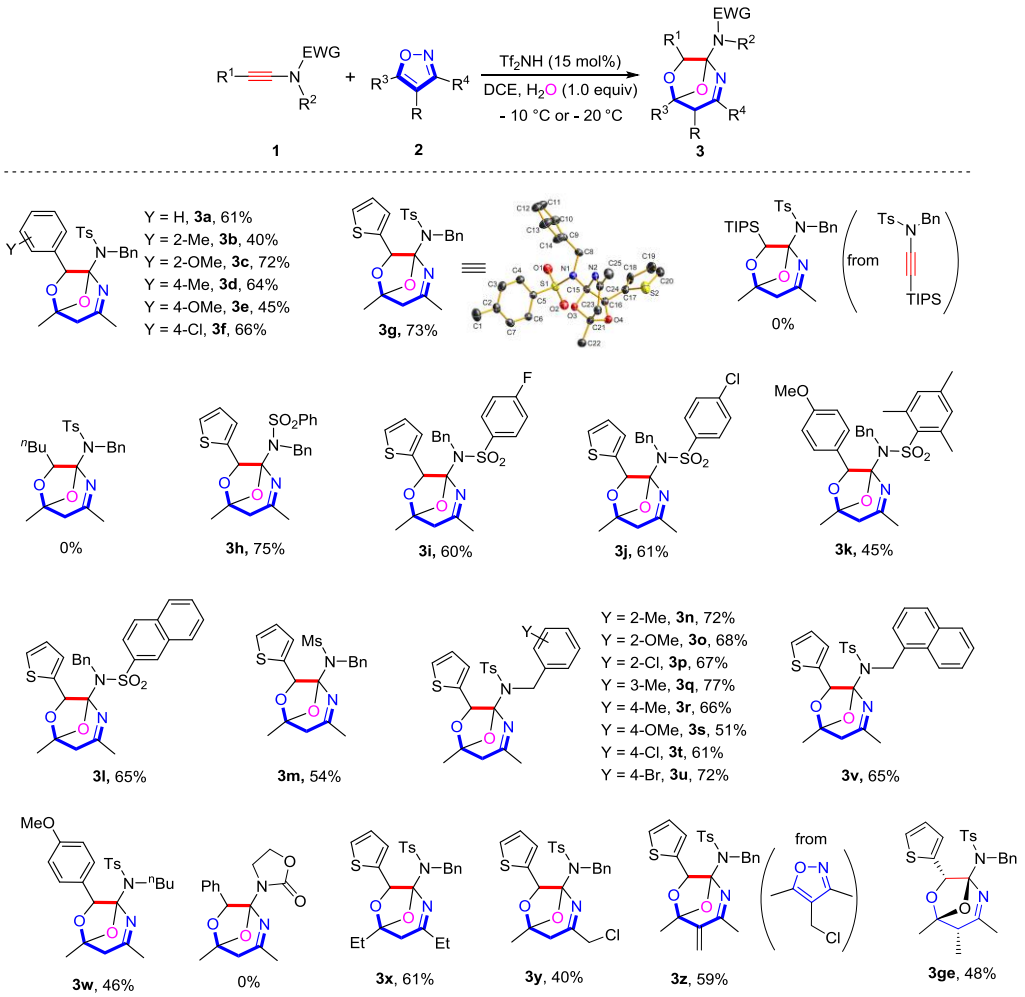
Entry	Acid	Solvent	x (mol%)	Yield (%)[b]
1	Tf_2NH	DCE	5	24
2	Tf_2NH	DCE	10	50
3	**Tf_2NH**	**DCE**	**15**	**70**
4	Tf_2NH	DCE	20	67
5[c]	Tf_2NH	DCE	15	62
6[d]	Tf_2NH	DCE	15	69
7[e]	Tf_2NH	DCE	15	59
8[f]	Tf_2NH	DCE	15	trace
9	-	DCE	-	0
10	Tf_2NH	DCM	15	50
11	Tf_2NH	THF	15	0
12	Tf_2NH	CH_3CN	15	21
13	Tf_2NH	Toluene	15	25
14	TfOH	DCE	15	28
15	TFA	DCE	15	0
16	TsOH	DCE	15	0
17	MsOH	DCE	15	0
18	TMSOTf	DCE	15	37

[a] The reaction was performed at 0.1 mmol scale with **1a** (1.5 equiv), **2a** (0.1 M), H_2O (1 equiv) and acid (x mol% based on **2a**) in DCE (1 mL) at -10 °C for 6 hours unless otherwise stated. [b] Yields were determined by HPLC using naphthalene as an internal standard. [c] **1a**/**2a** = 1.2/1. [d] **1a**/**2a** = 2/1. [e] **1a**/**2a** = 1/1.5. [f] In the absence of H_2O.

We commenced our investigation with the optimization of the reaction conditions by choosing ynamide **1a** and 3,5-dimethylisoxazole **2a** as the model substrates (Table S1). Submitting 5 mol% of Tf_2NH to the mixture of **1a**, **2a** and H_2O in DCE at -10 °C afforded the oxygen-bridged tetrahydro-1,4-oxazepine **3a** in 24% yield (entry 1). The structure of **3a** was unambiguously confirmed by single-crystal X-ray diffraction analysis of its analogue **3g** (CCDC 1561884). The product yield can be improved to 70% by increasing the amount of catalyst to 15 mol% (entries 1 to 3). However, further increasing the catalyst loading to 20 mol% did not provide better yield (entry 4). Subsequently, the ratio of the substrates was

examined. It was found that the best yield could be obtained with a ratio of **1a**/**2a** = 1.5/1 (entry 3 vs entries 5–7). Only a trace amount of **3a** was detected along with recovered starting material when the reaction was carried out in the absence of water (entry 8), suggesting that water is very crucial in the formation of **3a**. Remarkably, no reaction occurred in the absence of Tf_2NH (entry 9). The reaction in DCM gave a decreased yield (entry 10), since when adding Tf_2NH solution via syringe, the solution often spontaneously dropped out owing to the low boiling point of DCM. The reaction cannot take place in THF, while the poor solubility of ynamides in CH_3CN and toluene at low temperature resulted in low yields of **3a** (entries 11−13). The screening of other acids such as TfOH, TFA, TsOH and MsOH, as well as Lewis acid TMSOTf, revealed that only TfOH and TMSOTf could catalyze the cycloaddition, but gave inferior yields (entries 14−18). It is noteworthy that no 2-aminopyrrole product **4a** was formed during the optimization (including the one in the absence of water), revealing the distinct catalytic activity of acid catalysis from that of gold catalysis.

5. Tf_2NH-catalyzed [5+2+1] cycloaddition of ynamides and isoxazoles with water



*Representative procedure for the reactions of ynamides **1a–f** with 3,5-dimethylisoxazole **2a**:*

In a 10 mL flame-dried Schlenk flask, ynamide **1** (0.3 mmol, 1.5 equiv), **2a** (0.20 mmol, 20 μL), H_2O (0.20 mmol, 3.6 μL) and DCE (1.5 mL) were added in sequence and the resulting mixture were stirred at -10 °C for 20 min. Then a solution of Tf_2NH (15 mol%, 8.4 mg) in DCE (0.5 mL) was added quickly and further stirred for additional 6 hours. The reaction was quenched by Et_3N solution (10 vol% in pentane, 120 μL). The crude product was purified by silica gel column chromatography to yield the desired products (eluent: petroleum ether/ethyl acetate = 10/1).

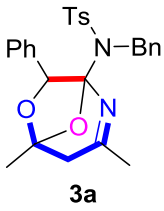
Representative procedure for the other reactions:

In a 10 mL flame-dried Schlenk flask, ynamides **1g–w** (0.2 mmol), isoxazoles **2** (0.24 mmol, 1.2 equiv), H_2O (0.20 mmol, 3.6 μL) and DCE (1.5 mL) were added in sequence and

the resulting mixture were stirred at - 20 °C for 20 min. Then a solution of Tf_2NH (15 mol%, 8.4 mg) in DCE (0.5 mL) was added quickly and further stirred for 12–24 h. The reaction was quenched by Et_3N solution (10 vol% in pentane, 120 μL). The crude product was purified by silica gel column chromatography to yield the desired products (eluent: petroleum ether/ethyl acetate 10/1).

6. Characterization data of *O*-bridged tetrahydro-1,4-oxazepines

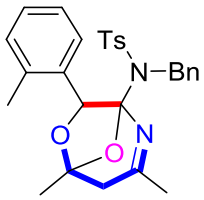
_N_-Benzyl-_N_-(3,5-dimethyl-7-phenyl-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methyl benzenesulfonamide (3a)



3a

White solid; 58.0 mg; 61% yield; mp 127–128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.28–7.12 (m, 12H), 6.06 (s, 1H), 4.87–4.66 (m, 2H), 2.52 (d, *J* = 18.0 Hz, 1H), 2.42–2.32 (m, 4H), 1.75 (s, 3H), 1.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 143.0, 139.1, 135.9, 129.9, 128.8, 128.6, 128.4, 127.90, 127.87, 127.6, 126.8, 126.3, 103.9, 103.8, 85.4, 49.7, 44.1, 25.4, 23.6, 21.6. HRMS (ESI) calcd for $C_{27}H_{29}N_2O_4S$ $[M + H]^+$ 477.1843, found 477.1841.

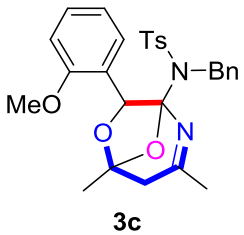
_N_-Benzyl-_N_-(3,5-dimethyl-7-(*o*-tolyl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methy lbenzenesulfonamide (3b)



3b

Colorless oil; 38.8 mg; 40% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.3 Hz, 2H), 7.33–7.27 (m, 1H), 7.17–7.06 (m, 10H), 6.26 (s, 1H), 4.78 (s, 2H), 2.61 (d, *J* = 18.1 Hz, 1H), 2.48–2.44 (m, 4H), 2.35 (s, 3H), 1.87 (s, 3H), 1.64 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 142.7, 139.6, 138.6, 137.0, 133.7, 130.6, 129.9, 128.8, 128.7, 128.6, 127.8, 127.0, 126.9, 125.1, 103.7, 103.2, 83.7, 49.0, 44.3, 25.5, 23.7, 21.6, 20.3. HRMS (ESI) calcd for $C_{28}H_{31}N_2O_4S$ $[M + H]^+$ 491.1999, found 491.1995.

_N_-Benzyl-_N_-(7-(2-methoxyphenyl)-3,5-dimethyl-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3c)

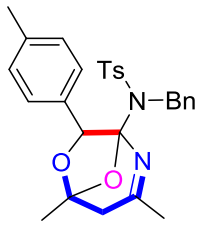


3c

White solid; 72.9 mg; 72% yield; mp 181–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.24–7.19 (m, 3H), 7.17–7.11 (m, 3H), 7.06–7.02 (m, 3H), 6.91–6.76 (m, 2H), 6.29 (s, 1H), 4.87–4.72 (m, 2H), 3.86 (s, 3H), 2.59 (d, *J* = 18.0 Hz, 1H), 2.41 (d, *J* = 18.0 Hz, 1H), 2.32 (s, 3H), 1.79 (s, 3H), 1.62 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 157.3, 142.3, 140.3, 139.4, 128.71, 128.66, 128.5, 128.3, 127.7, 126.9, 126.6, 124.6, 119.9, 110.0, 103.6, 103.3, 81.5, 55.2, 48.9, 44.3, 25.3, 23.8, 21.6. HRMS (ESI) calcd for

$C_{28}H_{31}N_2O_5S$ [M + H]$^+$ 507.1948, found 507.1945.

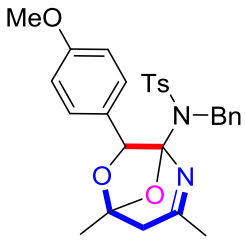
_N_-Benzyl-_N_-(3,5-dimethyl-7-(_p_-tolyl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3d)



3d

Colorless oil; 63.2 mg; 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, _J_ = 8.2 Hz, 2H), 7.27–7.24 (m, 2H), 7.18–7.15 (m, 3H), 7.12 (d, _J_ = 8.1 Hz, 2H), 7.08–7.01 (m, 4H), 5.99 (s, 1H), 4.83–4.70 (m, 2H), 2.52 (d, _J_ = 18.0 Hz, 1H), 2.41–2.31 (m, 4H), 2.31 (s, 3H), 1.77 (s, 3H), 1.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 142.9, 139.3, 139.2, 137.3, 132.7, 128.8, 128.7, 128.5, 128.4, 127.9, 126.8, 126.3, 103.9, 103.7, 85.5, 49.7, 44.1, 25.5, 23.7, 21.6, 21.3. HRMS (ESI) calcd for $C_{28}H_{31}N_2O_4S$ [M + H]$^+$ 491.1999, found 491.1996.

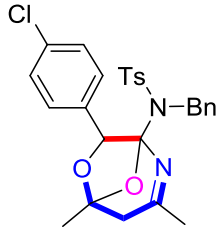
_N_-Benzyl-_N_-(7-(4-methoxyphenyl)-3,5-dimethyl-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3e)



3e

White solid; 45.0 mg; 45% yield; mp 175–176 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.76 (d, _J_ = 8.1 Hz, 2H), 7.36–7.27 (m, 4H), 7.24–7.11 (m, 5H), 6.80 (d, _J_ = 8.6 Hz, 2H), 6.01 (s, 1H), 4.74 (d, _J_ = 16.2 Hz, 1H), 4.65 (d, _J_ = 16.2 Hz, 1H), 3.77 (s, 3H), 2.60 (d, _J_ = 18.2 Hz, 1H), 2.49 (d, _J_ = 18.3 Hz, 1H), 2.40 (s, 3H), 1.78 (s, 3H), 1.49 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 170.6, 160.1, 144.0, 140.7, 140.1, 129.6, 129.4, 129.0, 128.9, 128.6, 128.2, 127.3, 113.9, 104.6, 104.6, 85.5, 55.4, 50.5, 44.3, 25.4, 23.7, 21.4. HRMS (ESI) calcd for $C_{28}H_{31}N_2O_5S$ [M + H]$^+$ 507.1948, found 507.1949.

_N_-Benzyl-_N_-(7-(4-chlorophenyl)-3,5-dimethyl-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3f)

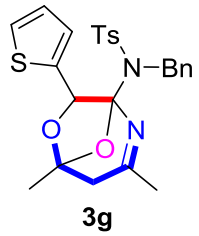


3f

White solid; 67.7 mg; 66% yield; mp 149–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, _J_ = 8.3 Hz, 2H), 7.31–7.23 (m, 2H), 7.22–7.12 (m, 7H), 7.10 (d, _J_ = 8.4 Hz, 2H), 6.03 (s, 1H), 4.80–4.65 (m, 2H), 2.52 (d, _J_ = 18.0 Hz, 1H), 2.38 (s, 3H), 2.33 (d, _J_ = 18.0 Hz, 1H), 1.76 (s, 3H), 1.56

(s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 143.2, 139.0, 138.9, 134.4, 133.3, 128.9, 128.6, 128.04, 127.97, 127.6, 127.0, 104.0, 103.7, 84.7, 49.8, 44.0, 25.5, 23.6, 21.7. HRMS (ESI) calcd for $C_{27}H_{28}ClN_2O_4S$ $[M + H]^+$ 511.1453, found 511.1455.

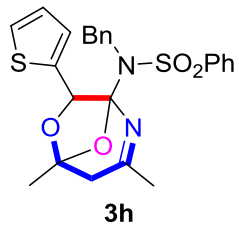
_N_-Benzyl-_N_-(3,5-dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3g)



3g

White solid; 70.7 mg; 73% yield; mp 135–136 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.71 (d, J = 8.4 Hz, 2H), 7.44 (dd, J = 4.9, 1.4 Hz, 1H), 7.37–7.28 (m, 4H), 7.27–7.18 (m, 3H), 6.96–6.86 (m, 2H), 5.96 (s, 1H), 4.69 (d, J = 16.7 Hz, 1H), 4.58 (d, J = 16.7 Hz, 1H), 2.62 (d, J = 18.4 Hz, 1H), 2.42–2.32 (m, 4H), 1.81 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.5, 143.3, 139.4, 138.2, 138.0, 129.1, 128.0, 127.7, 127.5, 127.1, 126.7, 126.6, 126.2, 103.9, 102.4, 81.4, 49.4, 43.2, 25.4, 23.0, 21.0. HRMS (ESI) calcd for $C_{25}H_{27}N_2O_4S_2$ $[M + H]^+$ 483.1407, found 483.1411.

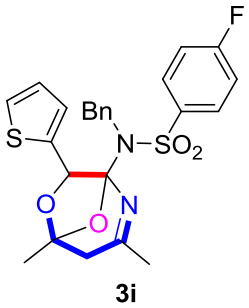
_N_-Benzyl-_N_-(3,5-dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)benzenesulfonamide (3h)



3h

Colorless oil; 70.1 mg; 75% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.87 (d, J = 7.4 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.41–7.31 (m, 3H), 7.25–7.16 (m, 3H), 6.96–6.87 (m, 2H), 6.11 (s, 1H), 4.85 (d, J = 16.4 Hz, 1H), 4.72 (d, J = 16.4 Hz, 1H), 2.60 (d, J = 18.3, 1H), 2.40 (d, J = 18.3 Hz, 1H), 1.86 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 171.9, 143.0, 140.5, 139.5, 133.3, 129.2, 129.0, 128.8, 128.5, 127.8, 127.4, 126.8, 126.7, 104.9, 103.8, 83.2, 50.5, 44.2, 25.8, 23.5. HRMS (ESI) calcd for $C_{24}H_{25}N_2O_4S_2$ $[M + H]^+$ 469.1250, found 469.1258.

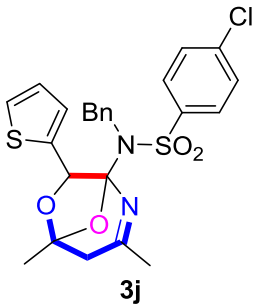
***N*-Benzyl-*N*-(3,5-dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-fluorobenzenesulfonamide (3i)**



3i

White solid; 58.2 mg; 60% yield; mp 109–110 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.94–7.85 (m, 2H), 7.41–7.31 (m, 3H), 7.27–7.14 (m, 5H), 6.96–6.88 (m, 2H), 6.07 (s, 1H), 4.87 (d, *J* = 16.4 Hz, 1H), 4.74 (d, *J* = 16.4 Hz, 1H), 2.64 (d, *J* = 18.3 Hz, 1H), 2.42 (d, *J* = 18.3 Hz, 1H), 1.89 (s, 3H), 1.46 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 172.1, 165.6 (d, *J* = 251.8 Hz), 140.2, 139.4 (d, *J* = 3.3 Hz), 139.4, 132.1 (d, *J* = 9.5 Hz), 128.8, 128.6, 127.9, 127.5, 126.9, 126.8, 116.1 (d, *J* = 22.7 Hz), 105.0, 103.8, 83.3, 50.4, 44.2, 25.8, 23.5. HRMS (ESI) calcd for $C_{24}H_{24}FN_2O_4S_2$ $[M + H]^+$ 487.1156, found 487.1162.

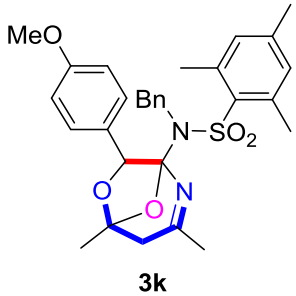
***N*-Benzyl-4-chloro-*N*-(3,5-dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)benzenesulfonamide (3j)**



3j

Colorless oil; 61.7 mg; 61% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.80 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.40–7.31 (m, 3H), 7.27–7.17 (m, 3H), 6.95–6.87 (m, 2H), 6.04 (s, 1H), 4.88 (d, *J* = 16.4 Hz, 1H), 4.75 (d, *J* = 16.4 Hz, 1H), 2.64 (d, *J* = 18.3 Hz, 1H), 2.43 (d, *J* = 18.3 Hz, 1H), 1.90 (s, 3H), 1.47 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 172.1, 141.9, 140.1, 139.2, 138.9, 130.8, 129.3, 128.9, 128.6, 128.0, 127.6, 126.9, 126.8, 105.1, 103.7, 83.3, 50.3, 44.2, 25.8, 23.5. HRMS (ESI) calcd for $C_{24}H_{24}ClN_2O_4S_2$ $[M + H]^+$ 503.0861, found 503.0862.

***N*-Benzyl-*N*-(7-(4-methoxyphenyl)-3,5-dimethyl-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-2,4,6-trimethylbenzenesulfonamide (3k)**

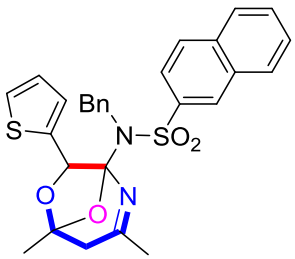


3k

Yellow oil; 48.1 mg; 45% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.57 (d, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.25 (t, *J* = 7.3 Hz, 1H), 6.96–6.88 (m, 4H), 6.74–6.68 (m, 2H), 5.17 (s, 1H), 5.07 (d, *J* = 16.7 Hz, 1H), 4.91 (d, *J* = 16.7 Hz, 1H), 3.73 (s, 3H), 2.47

(d, *J* = 18.3 Hz, 1H), 2.56 (s, 6H), 2.37 (d, *J* = 18.3 Hz, 1H), 2.24 (s, 3H), 1.62 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 170.2, 160.2, 142.5, 141.2, 140.2, 139.1, 132.4, 129.6, 129.4, 129.0, 128.5, 127.9, 113.7, 104.8, 104.1, 85.0, 55.5, 50.1, 44.7, 24.8, 23.8, 23.4, 20.9. HRMS (ESI) calcd for $C_{30}H_{35}N_2O_5S$ $[M + H]^+$ 535.2261, found 535.2258.

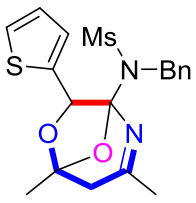
_N_-Benzyl-_N_-(3,5-dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)naphthalene-2-sulfonamide (3l)



3l

White solid; 67.2 mg; 65% yield; mp 120–121 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.41 (s, 1H), 8.05–7.95 (m, 3H), 7.90–7.85 (m, 1H), 7.71–7.61 (m, 2H), 7.44–7.39 (m, 2H), 7.31 (d, *J* = 5.1, 1H), 7.25–7.18 (m, 3H), 7.00–6.96 (m, 1H), 6.91–6.87 (m, 1H), 6.18 (s, 1H), 4.95 (d, *J* = 16.3 Hz, 1H), 4.76 (d, *J* = 16.3 Hz, 1H), 2.55 (d, *J* = 18.3 Hz, 1H), 2.37 (d, *J* = 18.3 Hz, 1H), 1.83 (s, 3H), 1.41 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 171.9, 140.4, 140.1, 139.5, 135.6, 132.8, 130.3, 130.1, 129.5, 129.0, 128.9, 128.59, 128.56, 128.1, 127.8, 127.5, 126.8, 126.7, 124.7, 104.9, 103.8, 83.3, 50.5, 44.1, 25.8, 23.5. HRMS (ESI) calcd for $C_{28}H_{27}N_2O_4S_2$ $[M + H]^+$ 519.1407, found 519.1413.

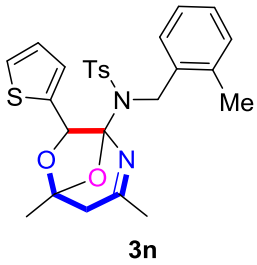
_N_-Benzyl-_N_-(3,5-dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)methanesulfonamide (3m)



3m

Colorless oil; 43.7 mg; 54% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.40–7.34 (m, 3H), 7.28–7.17 (m, 3H), 6.93–6.88 (m, 2H), 6.01 (s, 1H), 4.81–4.68 (m, 2H), 3.08 (s, 3H), 2.78 (d, *J* = 18.3 Hz, 1H), 2.52 (d, *J* = 18.3 Hz, 1H), 2.00 (s, 3H), 1.53 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 172.2, 140.3, 139.4, 128.8, 128.7, 127.58, 127.56, 126.9, 126.6, 104.9, 103.7, 82.8, 49.6, 44.2, 43.4, 26.0, 23.7. HRMS (ESI) calcd for $C_{19}H_{23}N_2O_4S_2$ $[M + H]^+$ 407.1094, found 407.1095.

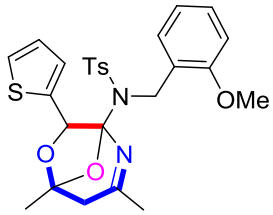
***N*-(3,5-Dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methyl-*N*-(2-methylbenzyl)benzenesulfonamide (3n)**



3n

White solid; 71.7 mg; 72% yield; mp 128–129 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.83 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 6.8 Hz, 1H), 7.38–7.31 (m, 3H), 7.07–7.00 (m, 3H), 6.95–6.88 (m, 2H), 6.05 (s, 1H), 4.76 (d, J = 17.4 Hz, 1H), 4.60 (d, J = 17.4 Hz, 1H), 2.59 (d, J = 18.2 Hz, 1H), 2.42 (s, 3H), 2.37 (d, J = 18.2 Hz, 1H), 2.17 (s, 3H), 1.80 (s, 3H), 1.46 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 171.9, 144.2, 139.8, 139.3, 138.5, 134.8, 130.1, 129.7, 129.3, 128.3, 128.2, 127.0, 126.9, 126.7, 126.2, 105.0, 103.7, 83.3, 48.2, 44.1, 25.8, 23.6, 21.4, 19.1. HRMS (ESI) calcd for $C_{26}H_{29}N_2O_4S_2$ $[M + H]^+$ 497.1563, found 497.1569.

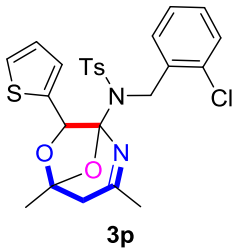
***N*-(3,5-Dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-*N*-(2-methoxybenzyl)-4-methylbenzenesulfonamide (3o)**



3o

White solid; 70.2 mg; 68% yield; mp 139–140 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.84 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 7.3 Hz, 1H), 7.36–7.33 (m, 3H), 7.15 (t, J = 7.7 Hz, 1H), 6.96–6.90 (m, 2H), 6.86 (d, J = 8.1 Hz, 1H), 6.79 (t, J = 7.5 Hz, 1H), 6.08 (s, 1H), 4.76 (d, J = 17.9 Hz, 1H), 4.64 (d, J = 17.9 Hz, 1H), 3.78 (s, 3H), 2.58 (d, J = 18.2 Hz, 1H), 2.41 (s, 3H), 2.36 (d, J = 18.2 Hz, 1H), 1.79 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 171.7, 156.8, 144.2, 139.6, 139.4, 129.7, 129.32, 129.28, 128.6, 128.1, 127.0, 126.7, 120.6, 110.4, 104.9, 103.8, 83.1, 55.6, 45.6, 44.0, 25.8, 23.6, 21.4. HRMS (ESI) calcd for $C_{26}H_{29}N_2O_5S_2$ $[M + H]^+$ 513.1512, found 513.1514.

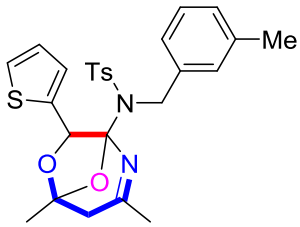
***N*-(2-Chlorobenzyl)-*N*-(3,5-dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3p)**



3p

White solid; 69.4 mg; 67% yield; mp 161–162 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.91 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 7.5 Hz, 1H), 7.41 (d, J = 8.1 Hz, 2H), 7.36 (dd, J = 5.1, 1.2 Hz, 1H), 7.28 (dd, J = 7.7, 1.5 Hz, 1H), 7.20–7.07 (m, 3H), 6.99–6.94 (m, 1H), 6.28 (s, 1H), 4.80 (d, J = 17.7 Hz, 1H), 4.65 (d, J = 17.6 Hz, 1H), 2.60 (d, J = 18.2 Hz, 1H), 2.44 (s, 3H), 2.39 (d, J = 18.2 Hz, 1H), 1.80 (s, 3H), 1.46 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 172.5, 144.7, 139.3, 138.9, 138.0, 131.8, 130.4, 130.0, 129.5, 129.2, 128.6, 128.2, 127.2, 127.1, 126.8, 105.0, 103.9, 82.9, 48.5, 44.0, 25.9, 23.5, 21.5. HRMS (ESI) calcd for $C_{25}H_{26}ClN_2O_4S_2$ $[M + H]^+$ 517.1017, found 517.1024.

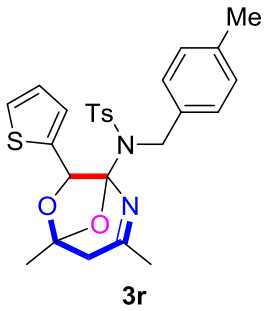
***N*-(3,5-Dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methyl-*N*-(3-methylbenzyl)benzenesulfonamide (3q)**



3q

Colorless oil; 76.9 mg; 77% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.77 (d, J = 8.3 Hz, 2H), 7.35–7.28 (m, 3H), 7.16–7.12 (m, 2H), 7.08 (t, J = 7.7 Hz, 1H), 7.00–6.89 (m, 3H), 6.14 (s, 1H), 4.76 (d, J = 16.4 Hz, 1H), 4.66 (d, J = 16.4 Hz, 1H), 2.60 (d, J = 18.2 Hz, 1H), 2.43–2.36 (m, 4H), 2.22 (s, 3H), 1.87 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 171.7, 144.0, 140.4, 140.1, 139.5, 137.8, 129.7, 129.4, 129.2, 128.4, 128.0, 127.8, 126.8, 126.7, 125.8, 104.9, 103.8, 83.2, 50.4, 44.2, 25.8, 23.6, 21.5, 21.4. HRMS (ESI) calcd for $C_{26}H_{29}N_2O_4S_2$ $[M + H]^+$ 497.1563, found 497.1564.

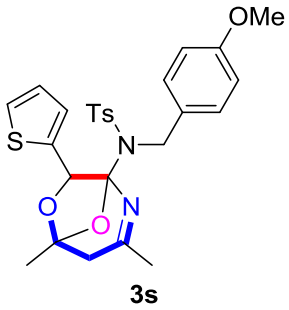
***N*-(3,5-Dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methyl-*N*-(4-methylbenzyl)benzenesulfonamide (3r)**



3r

Colorless oil; 65.1 mg; 66% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.74 (d, J = 8.3 Hz, 2H), 7.34–7.27 (m, 3H), 7.25 (d, J = 7.9 Hz, 2H), 7.02 (d, J = 7.9 Hz, 2H), 6.94–6.88 (m, 2H), 6.12 (s, 1H), 4.76 (d, J = 16.3 Hz, 1H), 4.64 (d, J = 16.3 Hz, 1H), 2.60 (d, J = 18.3 Hz, 1H), 2.43–2.36 (m, 4H), 2.28 (s, 3H), 1.88 (s, 3H), 1.44 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 171.7, 144.0, 140.2, 139.6, 137.5, 136.7, 129.7, 129.2, 129.1, 128.9, 127.7, 126.8, 126.6, 104.9, 103.9, 83.2, 50.2, 44.2, 25.8, 23.5, 21.4, 21.1. HRMS (ESI) calcd for $C_{26}H_{29}N_2O_4S_2$ $[M + H]^+$ 497.1563, found 497.1565.

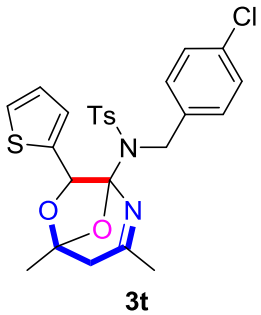
***N*-(3,5-Dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-*N*-(4-methoxybenzyl)-4-methylbenzenesulfonamide (3s)**



3s

White solid; 52.7 mg; 51% yield; mp 134–135 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.73 (d, J = 8.2 Hz, 2H), 7.35–7.25 (m, 5H), 6.95–6.86 (m, 2H), 6.76 (d, J = 8.6 Hz, 2H), 6.11 (s, 1H), 4.74 (d, J = 16.0 Hz, 1H), 4.62 (d, J = 16.0 Hz, 1H), 3.76 (s, 3H), 2.60 (d, J = 18.2 Hz, 1H), 2.45–2.36 (m, 4H), 1.90 (s, 3H), 1.44 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 171.7, 159.6, 143.9, 140.3, 139.6, 132.4, 130.4, 129.7, 129.1, 127.7, 126.9, 126.6, 113.9, 104.9, 103.9, 83.2, 55.4, 49.8, 44.2, 25.8, 23.6, 21.4. HRMS (ESI) calcd for $C_{26}H_{29}N_2O_5S_2$ $[M + H]^+$ 513.1512, found 513.1516.

***N*-(4-Chlorobenzyl)-*N*-(3,5-dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3t)**

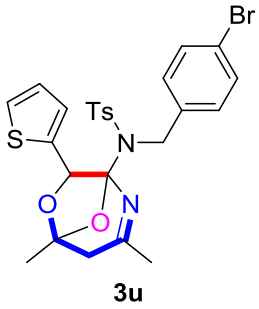


3t

White solid; 63.4 mg; 61% yield; mp 128–129 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.81 (d, J = 8.4 Hz, 2H), 7.39–7.31 (m, 5H), 7.23–7.16 (m, 2H), 6.98 (d, J = 3.5 Hz, 1H), 6.94–6.89 (m, 1H), 6.20 (s, 1H), 4.74 (d, J = 16.4 Hz, 1H), 4.60 (d, J = 16.4 Hz, 1H), 2.60 (d, J = 18.2 Hz, 1H), 2.45–2.37 (m, 4H), 1.88 (s, 3H), 1.44 (s, 3H). ^{13}C

NMR (100 MHz, Acetone-d_6) δ 172.2, 144.3, 139.6, 139.4, 132.6, 130.5, 129.8, 129.2, 128.4, 127.8, 126.8, 126.7, 104.9, 103.8, 83.1, 50.0, 44.1, 25.8, 23.5, 21.4. HRMS (ESI) calcd for $C_{25}H_{26}ClN_2O_4S_2$ $[M + H]^+$ 517.1017, found 517.1018.

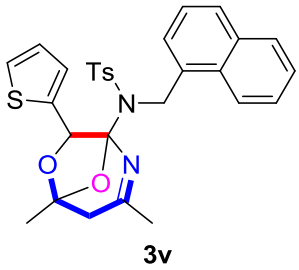
_N_-(4-Bromobenzyl)-_N_-(3,5-dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3u)



3u

White solid; 80.5 mg; 72% yield; mp 133–134 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.83 (d, J = 7.8 Hz, 2H), 7.38–7.32 (m, 5H), 7.32–7.26 (m, 2H), 7.02–6.97 (m, 1H), 6.95–6.90 (m, 1H), 6.22 (s, 1H), 4.72 (d, J = 16.4 Hz, 1H), 4.57 (d, J = 16.5 Hz, 1H), 2.60 (d, J = 18.3 Hz, 1H), 2.46–2.38 (m, 4H), 1.88 (s, 3H), 1.44 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 172.2, 144.3, 140.1, 139.42, 139.36, 131.3, 130.8, 129.8, 129.2, 127.7, 126.8, 126.7, 120.7, 104.9, 103.7, 83.0, 50.0, 44.1, 25.8, 23.4, 21.4. HRMS (ESI) calcd for $C_{25}H_{26}BrN_2O_4S_2$ $[M + H]^+$ 561.0512, found 561.0513.

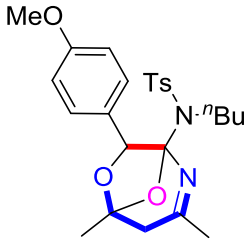
_N_-(3,5-Dimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methyl-_N_-(naphthalen-1-ylmethyl)benzenesulfonamide (3v)



3v

White solid; 69.0 mg; 65% yield; mp 150–151 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 8.00–7.94 (m, 1H), 7.92–7.86 (m, 3H), 7.77–7.65 (m, 2H), 7.51–7.44 (m, 2H), 7.39–7.30 (m, 4H), 7.01–6.97 (m, 1H), 6.91–6.86 (m, 1H), 6.16 (s, 1H), 5.30–5.17 (m, 2H), 2.59 (d, J = 18.1 Hz, 1H), 2.42 (s, 3H), 2.37 (d, J = 18.2 Hz, 1H), 1.71 (s, 3H), 1.47 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 172.0, 144.3, 139.7, 139.4, 135.7, 134.2, 131.2, 129.8, 129.4, 128.3, 127.6, 127.0, 126.7, 126.6, 126.1, 126.0, 123.4, 105.0, 103.9, 83.2, 48.4, 44.1, 25.8, 23.6, 21.4. HRMS (ESI) calcd for $C_{29}H_{29}N_2O_4S_2$ $[M + H]^+$ 533.1563, found 533.1570.

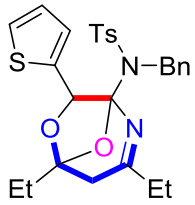
***N*-Butyl-*N*-(7-(4-methoxyphenyl)-3,5-dimethyl-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3w)**



3w

White solid; 43.1 mg; 46% yield; mp 129–130 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.03 (s, 1H), 3.77 (s, 3H), 3.46–3.25 (m, 2H), 2.59 (d, *J* = 18.2 Hz, 1H), 2.46 (d, *J* = 18.2 Hz, 1H), 2.42 (s, 3H), 1.82 (s, 3H), 1.56–1.39 (m, 5H), 1.24–1.07 (m, 2H), 0.78 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 170.1, 160.0, 143.9, 140.1, 129.8, 129.3, 129.2, 128.4, 113.8, 104.6, 104.4, 85.3, 55.4, 47.8, 44.2, 34.1, 25.5, 23.8, 21.4, 20.5, 14.0. HRMS (ESI) calcd for $C_{25}H_{33}N_2O_5S$ $[M + H]^+$ 473.2105, found 473.2104.

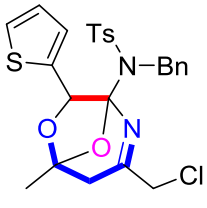
***N*-Benzyl-*N*-(3,5-diethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3x)**



3x

Colorless oil; 62.8 mg; 61% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.39–7.34 (m, 2H), 7.34–7.28 (m, 4H), 7.17–7.14 (m, 2H), 7.02–6.99 (m, 1H), 6.94–6.91 (m, 1H), 6.16 (s, 1H), 4.83 (d, *J* = 16.5 Hz, 1H), 4.70 (d, *J* = 16.5 Hz, 1H), 2.61 (d, *J* = 18.1 Hz, 1H), 2.39 (s, 3H), 2.33 (d, *J* = 18.1 Hz, 1H), 2.27–2.18 (m, 2H), 1.80–1.71 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H), 0.76 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 175.2, 144.0, 140.5, 140.1, 139.5, 129.8, 128.9, 128.5, 128.4, 128.0, 127.2, 126.8, 126.7, 106.9, 103.9, 83.6, 50.6, 41.7, 32.7, 21.4, 9.2, 6.9. HRMS (ESI) calcd for $C_{27}H_{31}N_2O_4S_2$ $[M + H]^+$ 511.1720, found 511.1726.

***N*-Benzyl-*N*-(3-(chloromethyl)-5-methyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3y)**

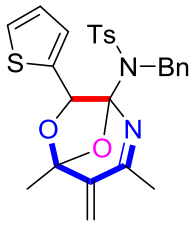


3y

Colorless oil; 41.6 mg; 40% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.45–7.28 (m, 5H), 7.26–7.11 (m, 3H), 7.02–6.92 (m, 1H), 6.94–6.82 (m, 1H), 6.19 (s, 1H), 4.81 (d, *J* = 16.5 Hz, 1H), 4.63 (d, *J* = 16.5 Hz, 1H), 4.12 (d, *J* = 12.9 Hz, 1H), 4.05 (d, *J* = 12.9 Hz, 1H),

2.77 (d, J = 18.4 Hz, 1H), 2.64 (d, J = 18.4 Hz, 1H), 2.41 (s, 3H), 1.51 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 169.6, 144.4, 140.3, 139.7, 138.6, 129.9, 129.2, 128.8, 128.6, 127.9, 127.5, 127.0, 126.8, 105.2, 104.0, 83.3, 50.8, 47.4, 40.7, 23.5, 21.4. HRMS (ESI) calcd for $C_{25}H_{26}ClN_2O_4S_2$ $[M + H]^+$ 517.1017, found 517.1008.

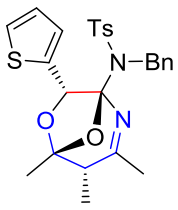
_N_-Benzyl-_N_-(3,5-dimethyl-4-methylene-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)-4-methylbenzenesulfonamide (3z)



3z

Colorless oil; 58.1 mg; 59% yield; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.74 (d, J = 8.3 Hz, 2H), 7.43–7.27 (m, 5H), 7.27–7.13 (m, 3H), 6.95–6.84 (m, 2H), 6.21 (s, 1H), 5.70 (s, 1H), 5.65 (s, 1H), 4.84 (d, J = 16.4 Hz, 1H), 4.71 (d, J = 16.4 Hz, 1H), 2.40 (s, 3H), 2.06 (s, 3H), 1.64 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 166.9, 144.2, 141.3, 140.5, 140.0, 139.2, 129.8, 129.1, 128.8, 128.6, 128.0, 127.5, 127.0, 126.9, 115.8, 105.1, 104.2, 82.2, 50.7, 21.4, 20.1. HRMS (ESI) calcd for $C_{26}H_{27}N_2O_4S_2$ $[M + H]^+$ 495.1407, found 495.1405.

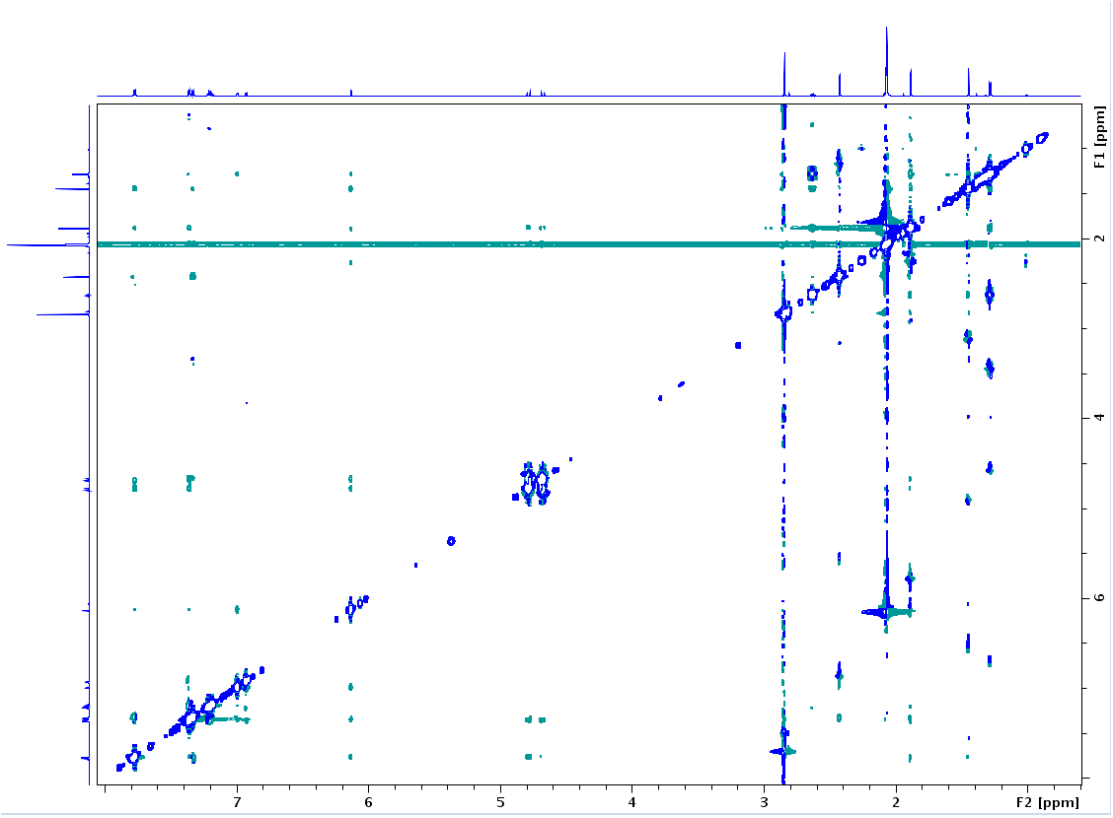
_N_-Benzyl-4-methyl-_N_-(3,4,5-trimethyl-7-(thiophen-2-yl)-6,8-dioxa-2-azabicyclo[3.2.1]oct-2-en-1-yl)benzenesulfonamide (3ge)



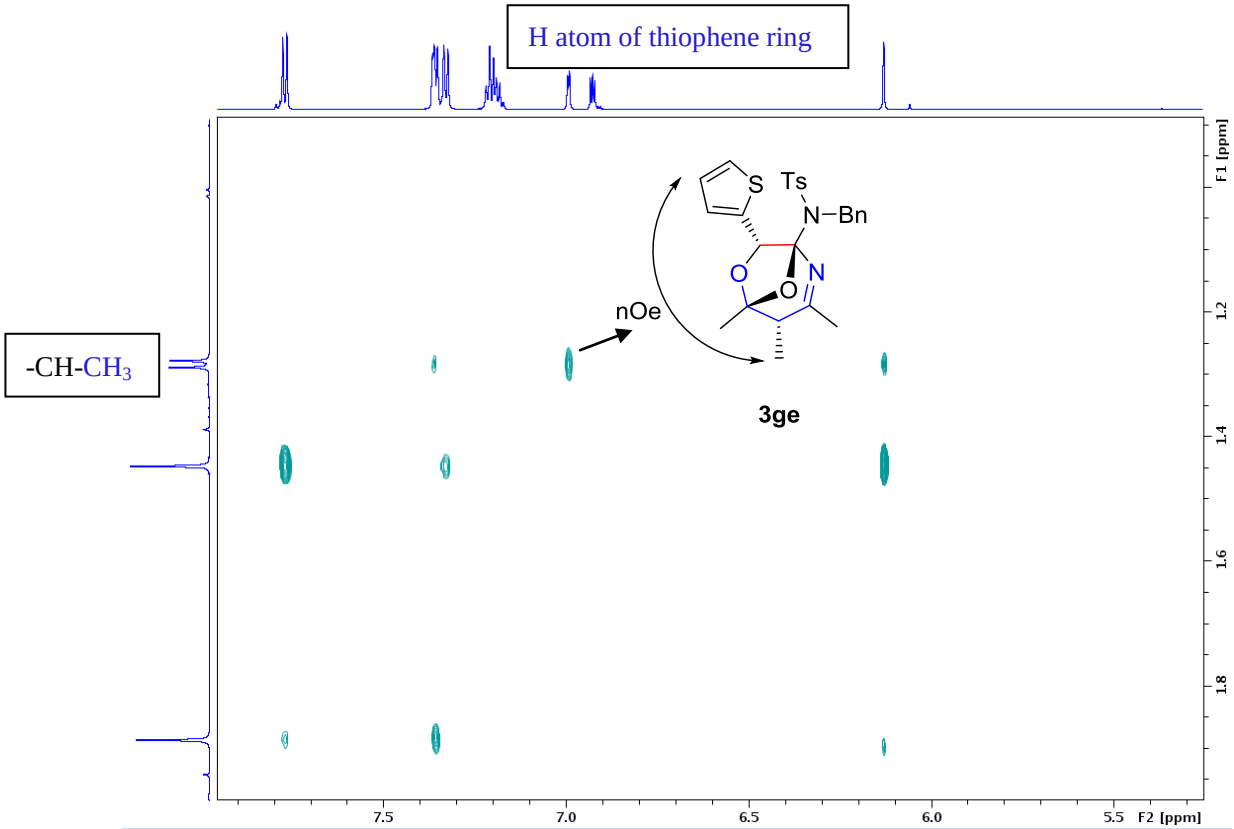
3ge

White solid; 47.4 mg; 48% yield; mp 118–119 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.75 (d, J = 8.0 Hz, 2H), 7.37–7.29 (m, 5H), 7.23–7.14 (m, 3H), 7.00–6.95 (m, 1H), 6.91 (t, J = 4.3 Hz, 1H), 6.11 (s, 1H), 4.77 (d, J = 16.5 Hz, 1H), 4.66 (d, J = 16.4 Hz, 1H), 2.61 (q, J = 7.5 Hz, 1H), 2.41 (s, 3H), 1.87 (s, 3H), 1.43 (s, 3H), 1.26 (d, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, Acetone) δ175.0, 144.1, 140.6, 140.1, 139.1, 129.7, 129.2, 128.7, 128.5, 128.3, 127.3, 126.9, 126.7, 107.2, 103.4, 82.5, 50.5, 46.5, 23.6, 21.5, 21.4, 11.3. HRMS (ESI) calcd for $C_{26}H_{29}N_2O_4S_2$ $[M + H]^+$ 497.1563, found 497.1562.

The relative stereochemistry of compound **3ge** was determined by nOe.

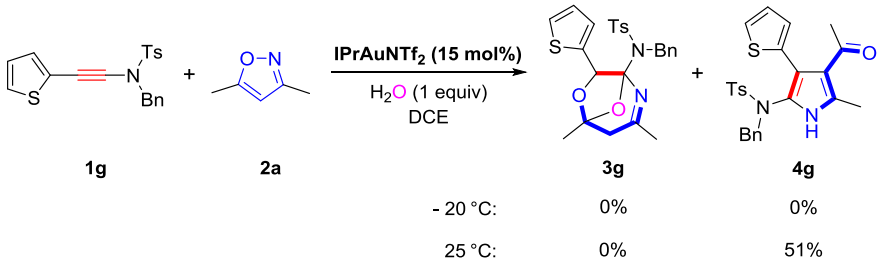


2D ^{1}H–^{1}H nOe NMR spectrum of compound **3ge** (700 MHz, Acetone-d_6).



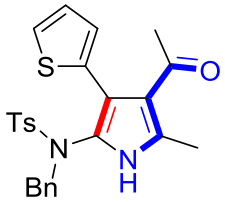
Expanded regions of 2D ^{1}H–^{1}H nOe NMR spectrum of compound **3ge**.

7. Gold-catalyzed cycloaddition in the presence of water



In a 10 mL flame-dried Schlenk flask, ynamide **1g** (0.2 mmol, 73.4 mg), 3,5-dimethylisoxazole **2a** (0.24 mmol, 24 μL), H_2O (0.20 mmol, 3.6 μL) and DCE (1.5 mL) were added in sequence and the resulting mixture was stirred at indicated temperature for 20 min. Then a solution of $IPrAuNTf_2$ (15 mol%, 26 mg) in DCE (0.5 mL) was added quickly and further stirred for 6 hours. Direct purification by silica gel column chromatography yielded the pyrrole **4g** in 51% yield (47.2 mg, eluent: petroleum ether/ethyl acetate = 5/1).

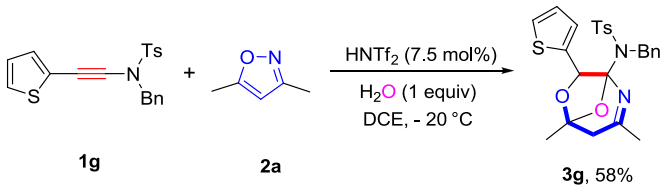
***N*-(4-Acetyl-5-methyl-3-(thiophen-2-yl)-1H-pyrrol-2-yl)-*N*-benzyl-4-methylbenzenesulfonamide (4g)**



4g

Yellow oil; 47.2 mg; 51% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.33–7.22 (m, 5H), 7.24–7.14 (m, 3H), 6.81 (dd, *J* = 5.2, 3.5 Hz, 1H), 6.04 (d, *J* = 3.5 Hz, 1H), 4.45 (s, 2H), 2.47 (s, 3H), 2.37 (s, 3H), 1.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 144.1, 136.5, 136.0, 134.2, 133.7, 129.8, 128.70, 128.66, 128.4, 128.1, 127.8, 127.0, 126.6, 122.1, 121.4, 113.6, 54.1, 30.0, 21.8, 14.3. HRMS (ESI) calcd. for $C_{25}H_{25}N_2O_3S_2$ $[M + H]^+$ 465.1301, found 465.1295.

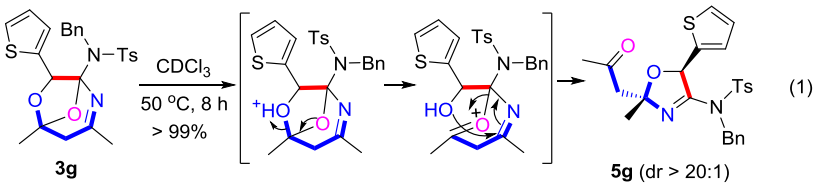
8. Scale-up experiment

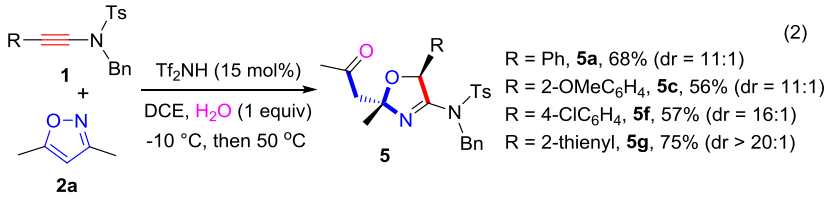


1g **2a** **3g**, 58%

In a 10 mL flame-dried Schlenk flask, ynamide **1g** (1.36 mmol, 0.5 g), 3,5-dimethylisoxazole **2a** (1.2 equiv, 147 μL), H_2O (1.0 equiv, 24.5 μL) and DCE (13 mL) were added in sequence and the resulting mixture was stirred at -20 °C for 20 min. Then a solution of $HNTf_2$ (7.5 mol%, 28.7 mg) in DCE (1.0 mL) was added quickly and further stirred for 16 hours. The reaction was quenched by Et_3N solution (10 vol% in pentane, 0.45 mL). Purification by silica gel column chromatography afforded the desired product **3g** in 58% yield (0.38 g, eluent: petroleum ether/ethyl acetate = 10/1).

9. Further transformations to dihydrooxazoles

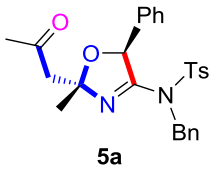




Procedure for eqn 1: In a 10 mL flame-dried Schlenk flask, ynamide **1g** (0.1 mmol, 48.2 mg) and $CDCl_3$ (0.5 mL) were added and the resulting mixture was stirred at 50 °C for 8 hours. Purification by silica gel column chromatography afforded dihydrooxazole **5g** in a nearly quantitative yield. The dr value was determined by NMR analysis of crude reaction mixture.

Procedure for eqn 2: In a 10 mL flame-dried Schlenk flask, ynamides **1** (0.2 mmol), 3,5-dimethylisoxazole **2a** (1.2 equiv, 24 μL), H_2O (1.0 equiv, 4 μL) and DCE (1.5 mL) were added in sequence and the resulting mixture was stirred at -10 °C for 20 min. Then a solution of $HNTf_2$ (15 mol%, 8.4 mg) in DCE (0.5 mL) was added quickly and stirred at this temperature for 6 hours. Subsequently, the mixture was further stirred at 50 °C for 8 hours. The reaction was quenched by Et_3N solution (10 vol% in pentane, 120 μL). Purification by silica gel column chromatography yielded the dihydrooxazoles **5**. The configuration of the product was confirmed by single-crystal X-ray diffraction analysis of **5a** (CCDC 1819934). The dr value was determined by NMR analysis of crude reaction mixture.

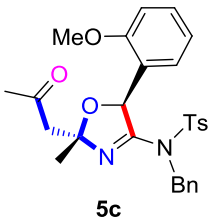
_N_-Benzyl-4-methyl-_N_-(2-methyl-2-(2-oxopropyl)-5-phenyl-2,5-dihydrooxazol-4-yl)benzenesulfonamide (5a)



Yellow solid; 64.5 mg; 68% yield; mp 109–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61–7.57 (m, 2H), 7.30–7.27 (m, 3H), 7.25–7.16 (m, 5H), 7.10–7.05 (m, 2H), 6.90–6.85 (m, 2H), 6.18 (s, 1H), 4.63 (d, J = 14.2 Hz, 1H), 4.52 (d, J = 14.2 Hz, 1H), 2.87–2.76 (m, 2H), 2.43 (s, 3H), 2.15 (s,

3H), 1.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.0, 159.2, 144.7, 137.8, 135.3, 135.0, 129.9, 129.4, 128.7, 128.6, 128.5, 128.1, 128.0, 127.9, 105.2, 86.4, 53.4, 51.7, 32.1, 28.8, 21.8. HRMS (ESI) calcd for $C_{27}H_{29}N_2O_4S$ $[M + H]^+$ 477.1843, found 477.1841.

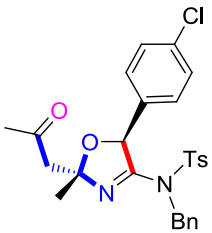
_N_-Benzyl-_N_-(5-(2-methoxyphenyl)-2-methyl-2-(2-oxopropyl)-2,5-dihydrooxazol-4-yl)-4-methylbenzenesulfonamide (5c)



5c

Yellow solid; 57.0 mg; 56% yield; mp 132–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.3 Hz, 2H), 7.30–7.21 (m, 8H), 6.85–6.79 (m, 1H), 6.70–6.61 (m, 1H), 6.48 (s, 1H), 6.40–6.32 (m, 1H), 4.79 (d, *J* = 14.9 Hz, 1H), 4.66 (d, *J* = 14.9 Hz, 1H), 3.70 (s, 3H), 2.85–2.72 (m, 2H), 2.42 (s, 3H), 2.10 (s, 3H), 1.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 159.0, 157.5, 144.5, 135.8, 135.7, 130.1, 129.6, 129.6, 129.2, 128.1, 128.1, 127.8, 126.3, 120.6, 111.0, 105.3, 79.8, 55.5, 54.1, 51.5, 32.0, 28.1, 21.7. HRMS (ESI) calcd for $C_{28}H_{31}N_2O_5S$ $[M + H]^+$ 507.1948, found 507.1948.

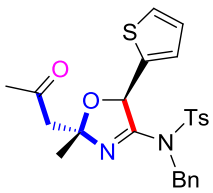
_N_-Benzyl-_N_-(5-(4-chlorophenyl)-2-methyl-2-(2-oxopropyl)-2,5-dihydrooxazol-4-yl)-4-methylbenzenesulfonamide (5f)



5f

White solid; 58.5 mg; 57% yield; mp 122–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.29–7.16 (m, 3H), 7.16–7.08 (m, 4H), 6.79 (d, *J* = 8.4 Hz, 2H), 6.19 (s, 1H), 4.60 (d, *J* = 13.8 Hz, 1H), 4.49 (d, *J* = 13.9 Hz, 1H), 2.90–2.76 (m, 2H), 2.44 (s, 3H), 2.13 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.6, 159.1, 144.8, 136.5, 135.2, 134.7, 134.2, 130.0, 129.9, 129.6, 128.6, 128.0, 127.9, 127.9, 105.3, 85.8, 52.8, 51.9, 32.0, 29.0, 21.7. HRMS (ESI) calcd for $C_{27}H_{28}ClN_2O_4S$ $[M + H]^+$ 511.1453, found 511.1477.

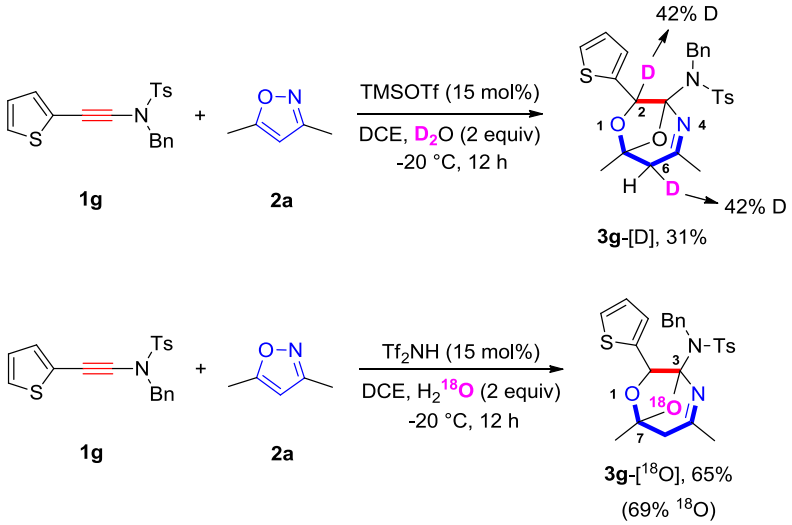
***N*-Benzyl-4-methyl-*N*-(2-methyl-2-(2-oxopropyl)-5-(thiophen-2-yl)-2,5-dihydrooxazol-4-yl)benzenesulfonamide (5g)**



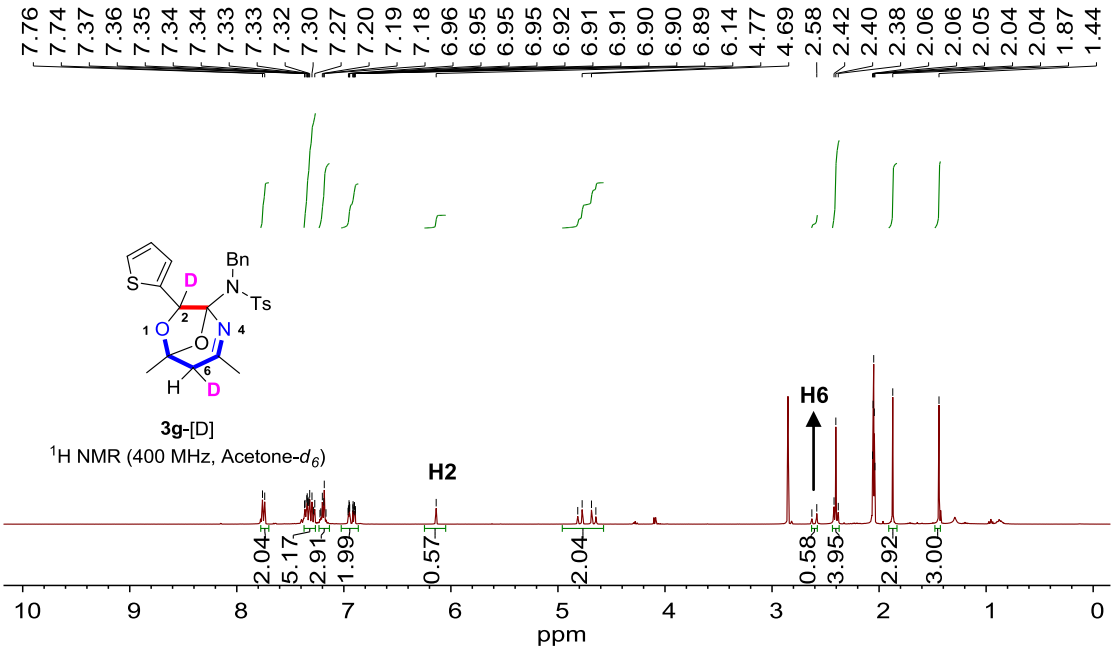
5g

White solid; 72.2 mg; 75% yield; mp 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.23–7.13 (m, 4H), 7.08 (d, *J* = 6.9 Hz, 2H), 6.94–6.88 (m, 2H), 6.51 (s, 1H), 4.65 (d, *J* = 14.2 Hz, 1H), 4.49 (d, *J* = 14.2 Hz, 1H), 2.90–2.76 (m, 2H), 2.44 (s, 3H), 2.14 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.7, 158.7, 144.7, 141.3, 135.2, 135.0, 130.0, 129.0, 128.07, 128.05, 127.7, 127.3, 127.0, 126.0, 105.4, 81.7, 52.9, 51.9, 32.1, 28.8, 21.8. HRMS (ESI) calcd for $C_{25}H_{27}N_2O_4S_2$ $[M + H]^+$ 483.1407, found 483.1409.

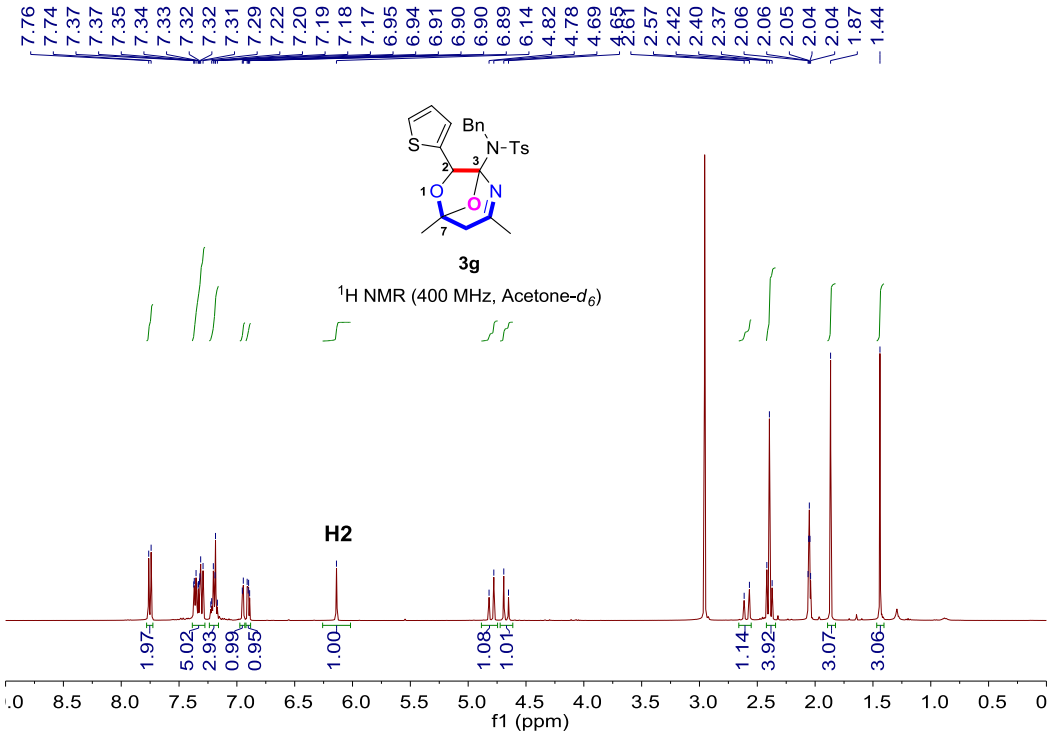
10. Mechanistic studies

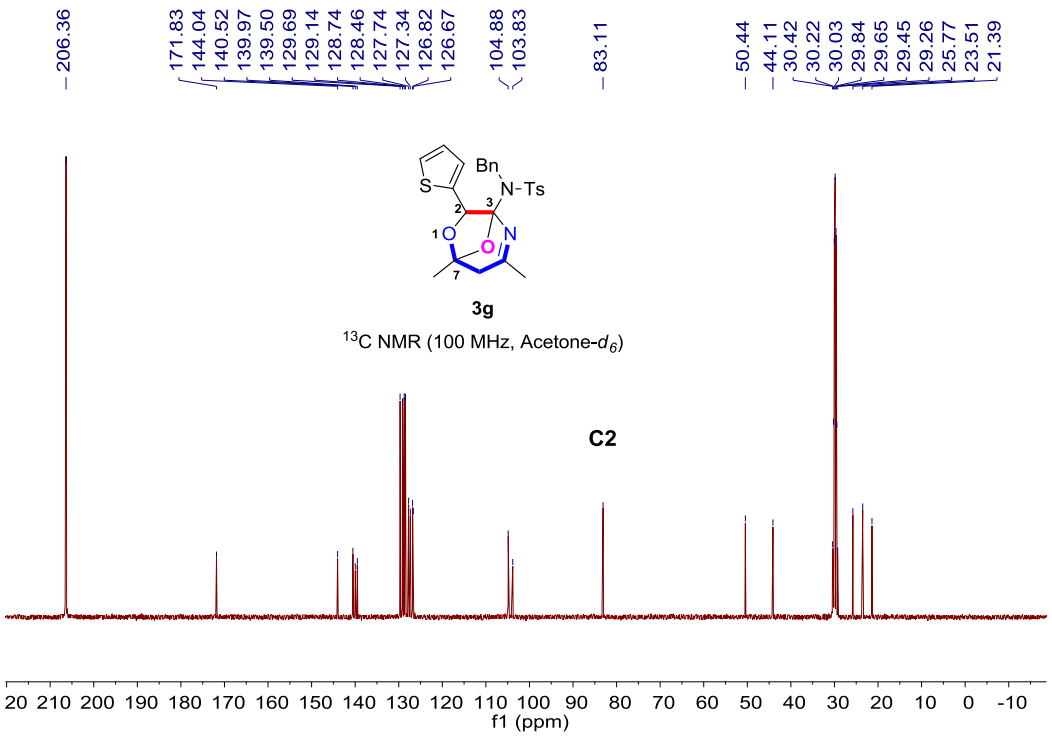


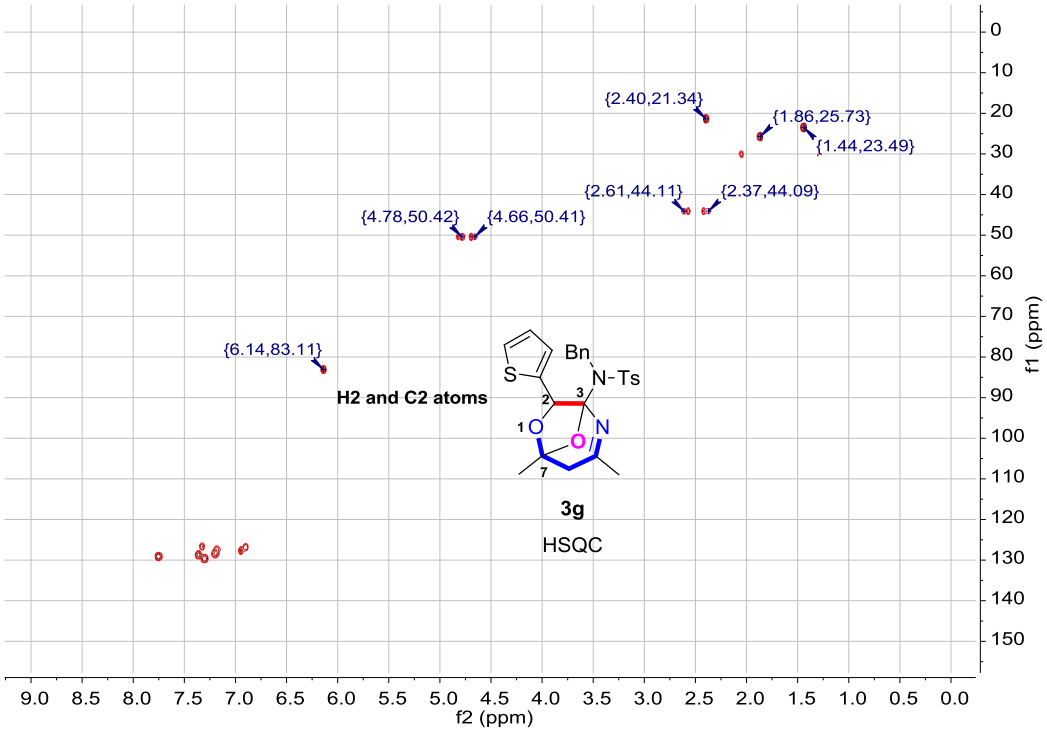
In a 10 mL flame-dried Schlenk flask, ynamide **1g** (0.2 mmol, 73.4 mg), 3,5-dimethylisoxazole **2a** (0.24 mmol, 24 μL), D_2O or $H_2{}^{18}O$ (0.40 mmol, 8.0 μL) and DCE (1.5 mL) were added in sequence and the resulting mixture was stirred at -20 °C for 20 min. Then a solution of TMSOTf (15 mol%, 5.5 μL) or Tf_2NH (15 mol%, 8.4 mg) in DCE (0.5 mL) was added quickly and further stirred for 12 hours. The reaction was quenched by Et_3N solution (10 vol% in pentane, 120 μL). Purification by silica gel column chromatography afforded the desired product.



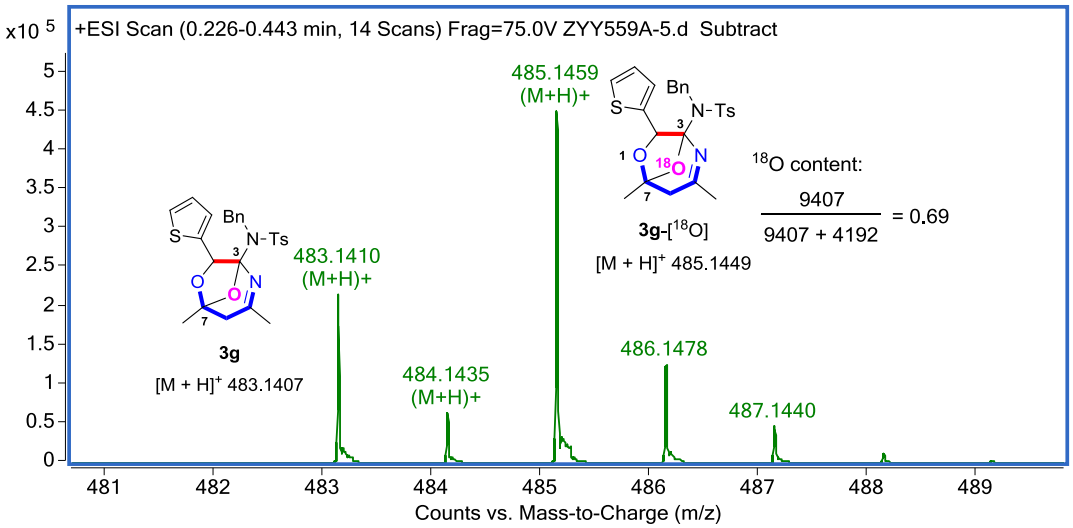
From ^{1}H, ^{13}C NMR, and HSQC of compound **3g**, we conclude that 6.14 ppm in ^{1}H NMR and 83.1 ppm in ^{13}C NMR were assigned to H2 and C2 atoms, respectively. Therefore, a splitting of the carbon signal (104.9 and 103.8 ppm) in ^{13}C NMR of **3g**-[^{18}O] (69% ^{18}O) suggests that the ^{18}O atom bridges 3 and 7 positions, rather than 2 and 7 positions of the tetrahydro-1,4-oxazepine ring.



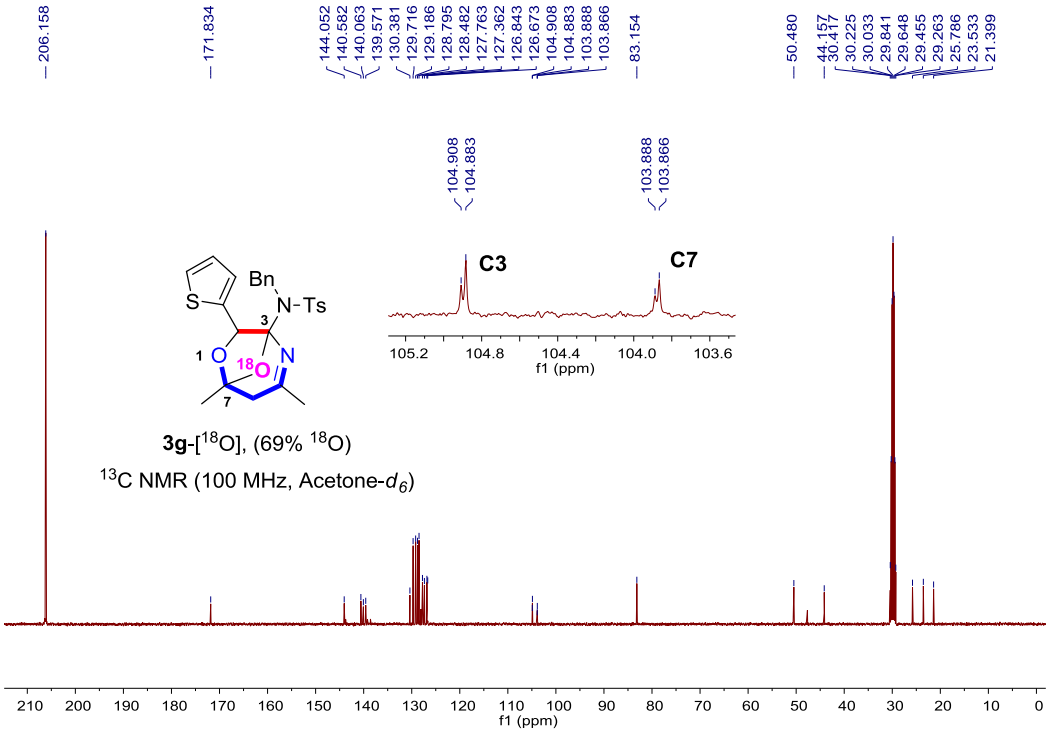


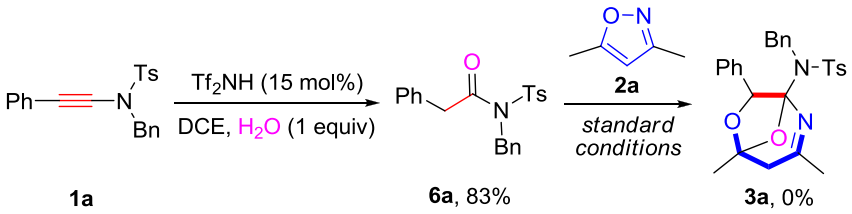


HRMS of compound **3g**-[^{18}O]



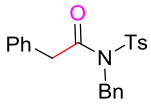
m/z	Abund	Area	Formula	Ion
483.141	217509	4192	$C_{25}H_{27}N_2O_4S_2$	$(M+H)^+$
484.1435	64346.5	1358	$C_{25}H_{27}N_2O_4S_2$	$(M+H)^+$
485.1459	454623.3	9407	$C_{25}H_{27}N_2O_3[^{18}O]S_2$	$(M+H)^+$
486.1478	128649.8	2653		
487.144	46496.4	1214		





In a 10 mL flame-dried Schlenk flask, ynamide **1a** (0.2 mmol, 72.2 mg), H_2O (0.20 mmol, 3.6 μL) and DCE (1.5 mL) were added in sequence. Then a solution of Tf_2NH (15 mol%, 8.4 mg) in DCE (0.5 mL) was added quickly and stirred at room temperature for 12 hours. The reaction was quenched by Et_3N solution (10 vol.% in pentane, 120 μL). Purification by silica gel column chromatography afforded the amide **6a** (62 mg, 83%).

N-Benzyl-2-phenyl-*N*-tosylacetamide (6a)



6a

Colorless oil; 62 mg; 83% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.4 Hz, 2H), 7.46–7.01 (m, 9H), 7.12–6.76 (m, 2H), 5.07 (s, 2H), 3.87 (s, 2H), 2.42 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 145.0, 136.7, 133.3, 129.8, 129.4, 128.8, 128.7, 128.1, 127.9, 127.8, 127.3, 49.8, 43.0, 21.8. HRMS (ESI) calcd. for $C_{22}H_{22}NO_3S$ $[M + H]^+$ 380.1315, found 380.1323.

11. References

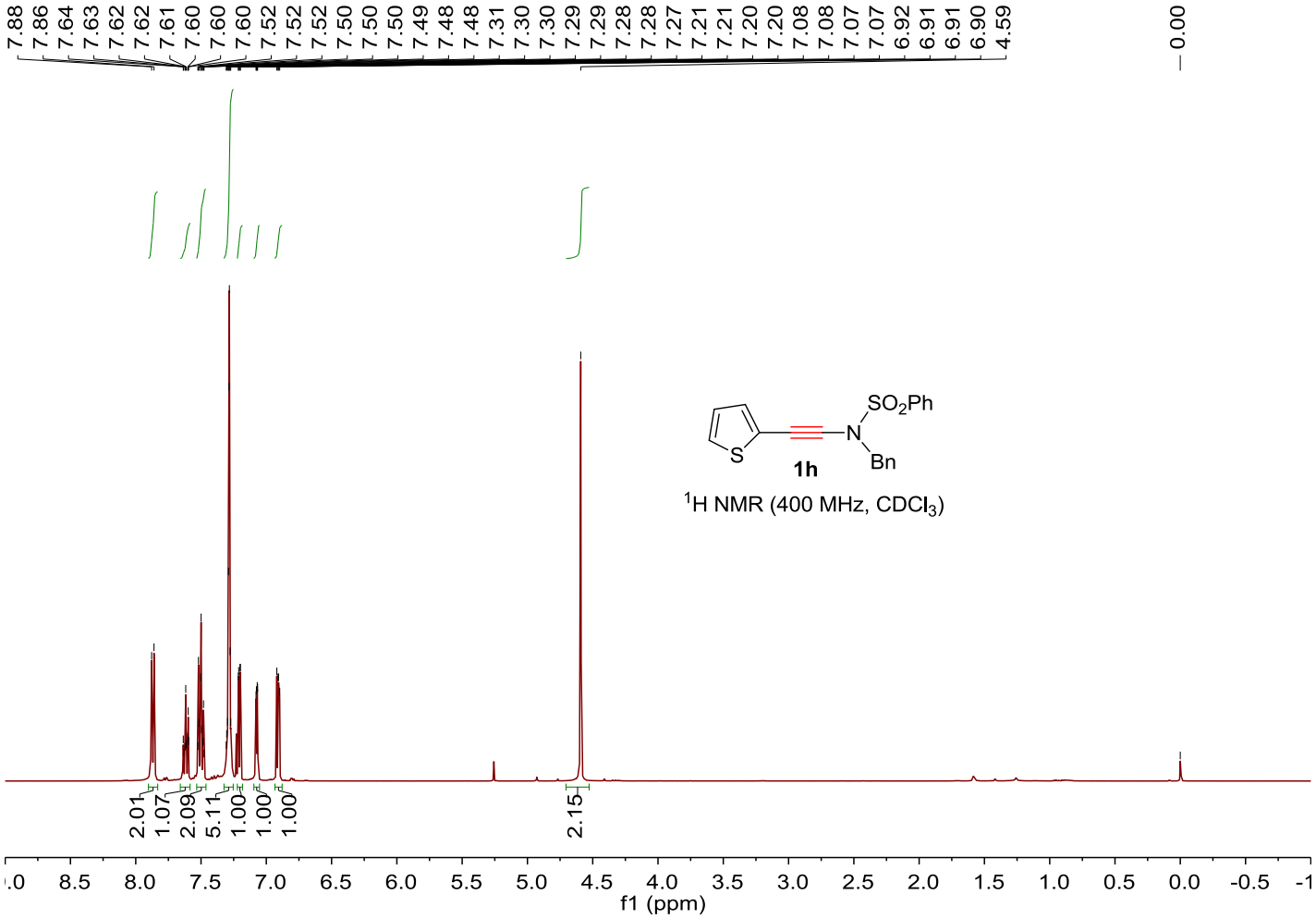
(1) Y. S. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz and E. L. Vera, *Org. Lett.*, 2004, **6**, 1151.

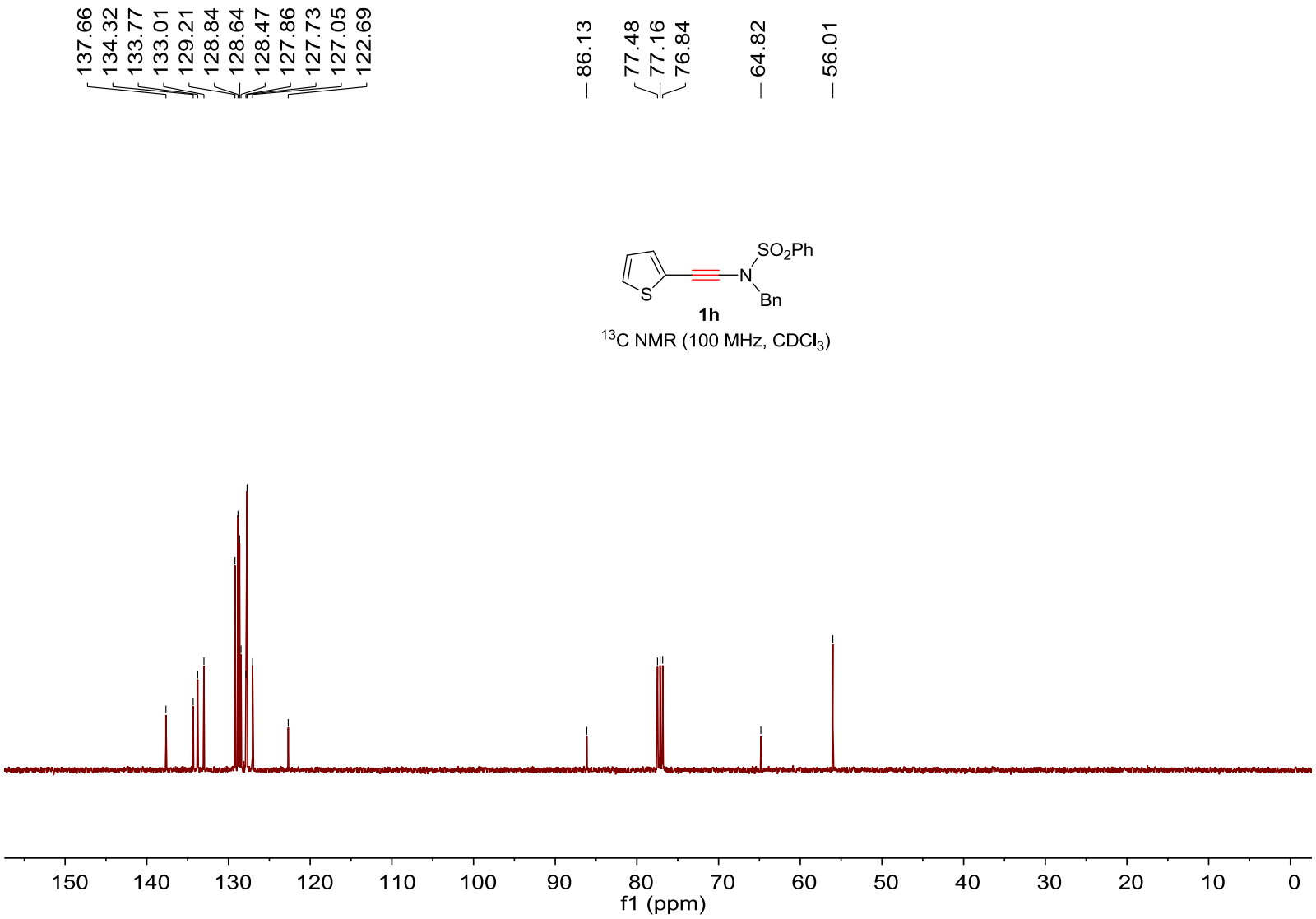
(2) Y. Zhao, Y. Hu, C. Wang, X. Li and B. Wan, *J. Org. Chem.*, 2017, **82**, 3935.

(3) Y. Zhao, Y. Hu, X. Li and B. Wan, *Org. Biomol. Chem.*, 2017, **15**, 3413.

(4) R. L. Sahani and R.-S. Liu, *Angew. Chem. Int. Ed.*, 2017, **56**, 1026.

12. NMR spectroscopy of ynamides

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128.64
128.47
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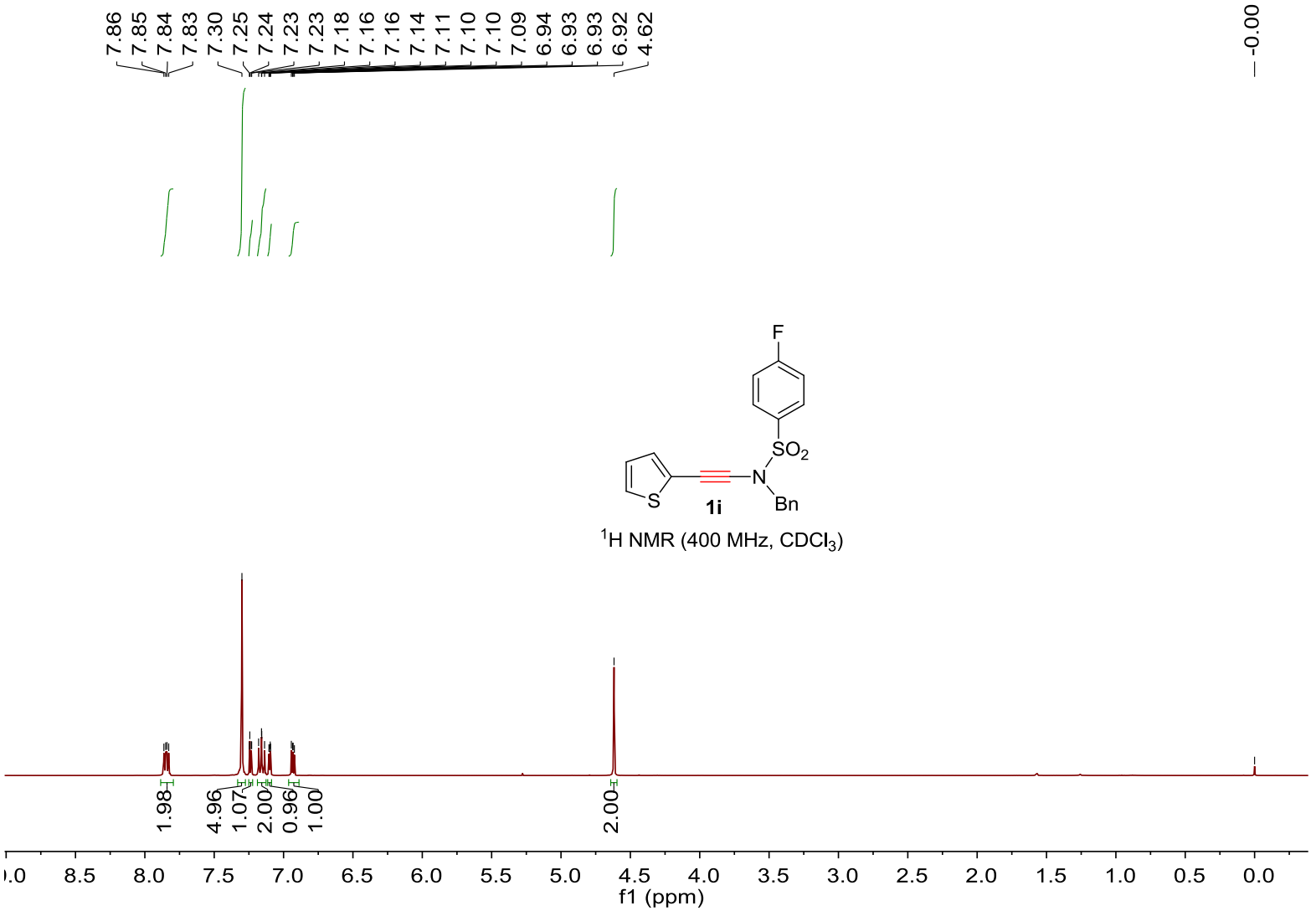
127.73
127.05
122.69
86.13
77.48
77.16
76.84
64.82
56.01
SO2Ph
N
S
Bn
1h
13C NMR (100 MHz, CDCl3)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.85
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7.83
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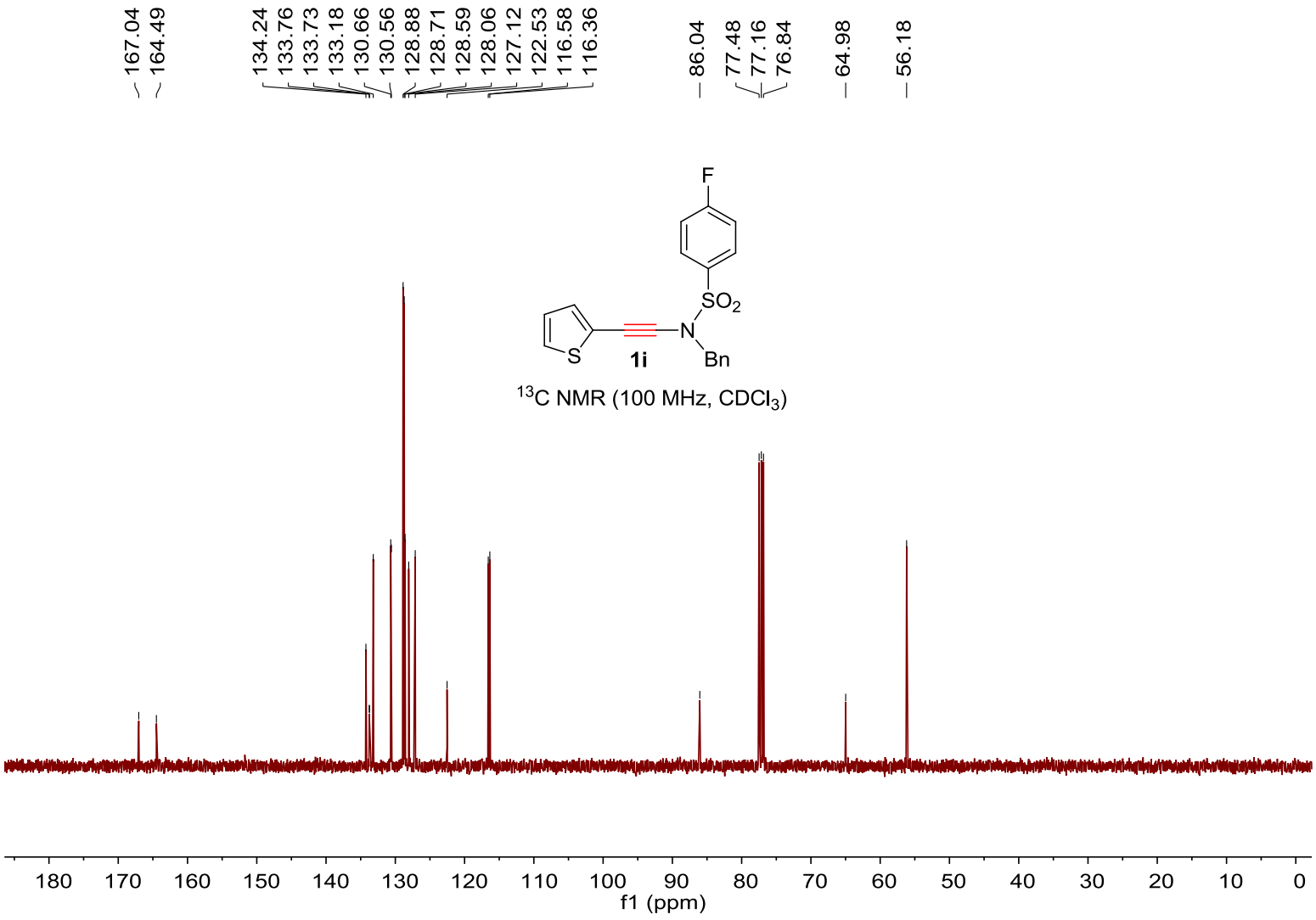
7.25
7.24
7.23
7.23
7.18
7.16
7.16
7.14
7.11
7.10
7.10
7.09
6.94
6.93
6.93
6.92
4.62
-0.00
F
SO2
N
S
Bn
1i
1H NMR (400 MHz, CDCl3)
1.98
4.96
1.07
2.00
0.96
1.00
2.00
f1 (ppm)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164.49
134.24
133.76
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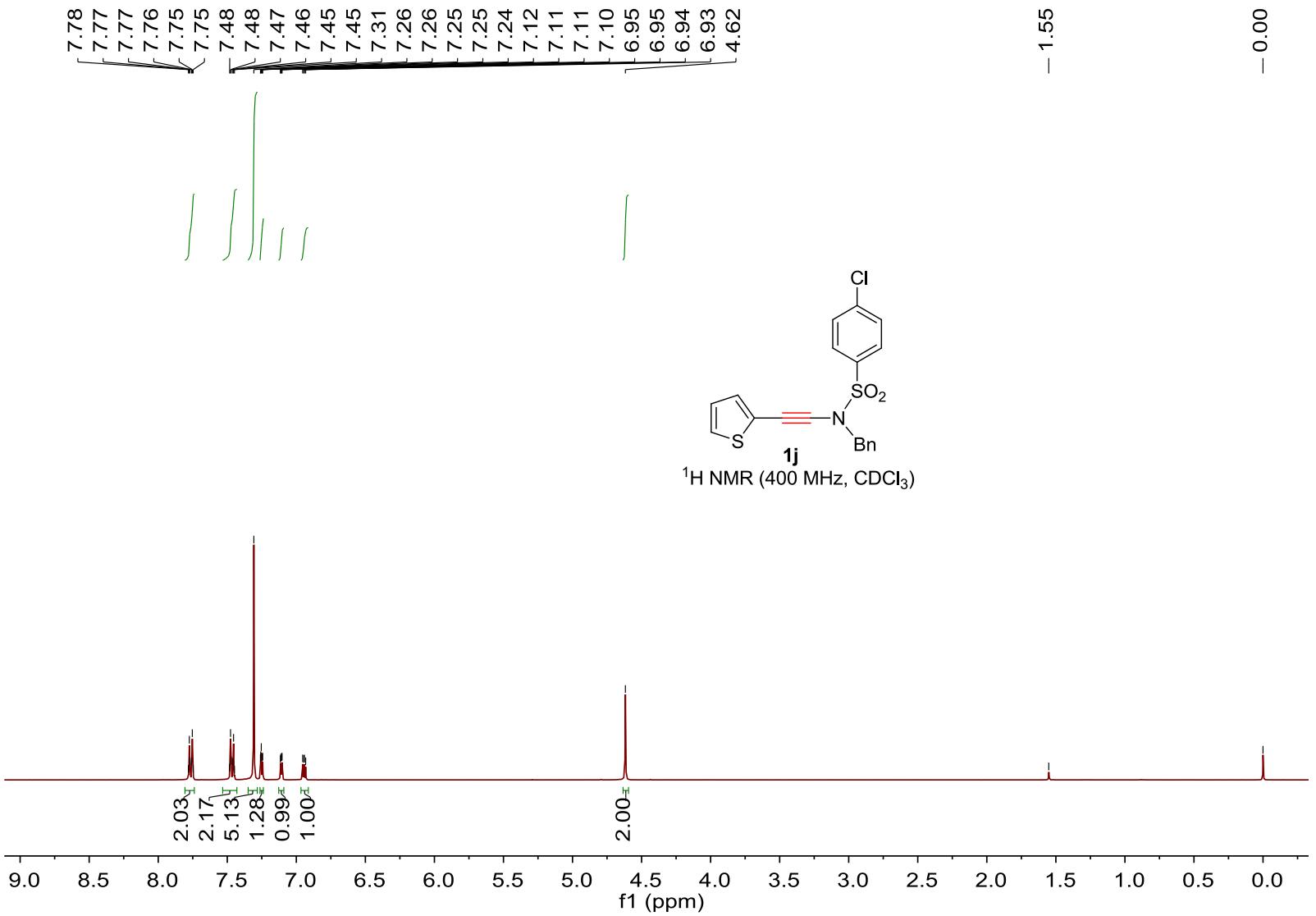
133.18
130.66
130.56
128.88
128.71
128.59
128.06
127.12
122.53
116.58
116.36
86.04
77.48
77.16
76.84
64.98
56.18
F
SO2
N
S
Bn
1i
13C NMR (100 MHz, CDCl3)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.77
7.77
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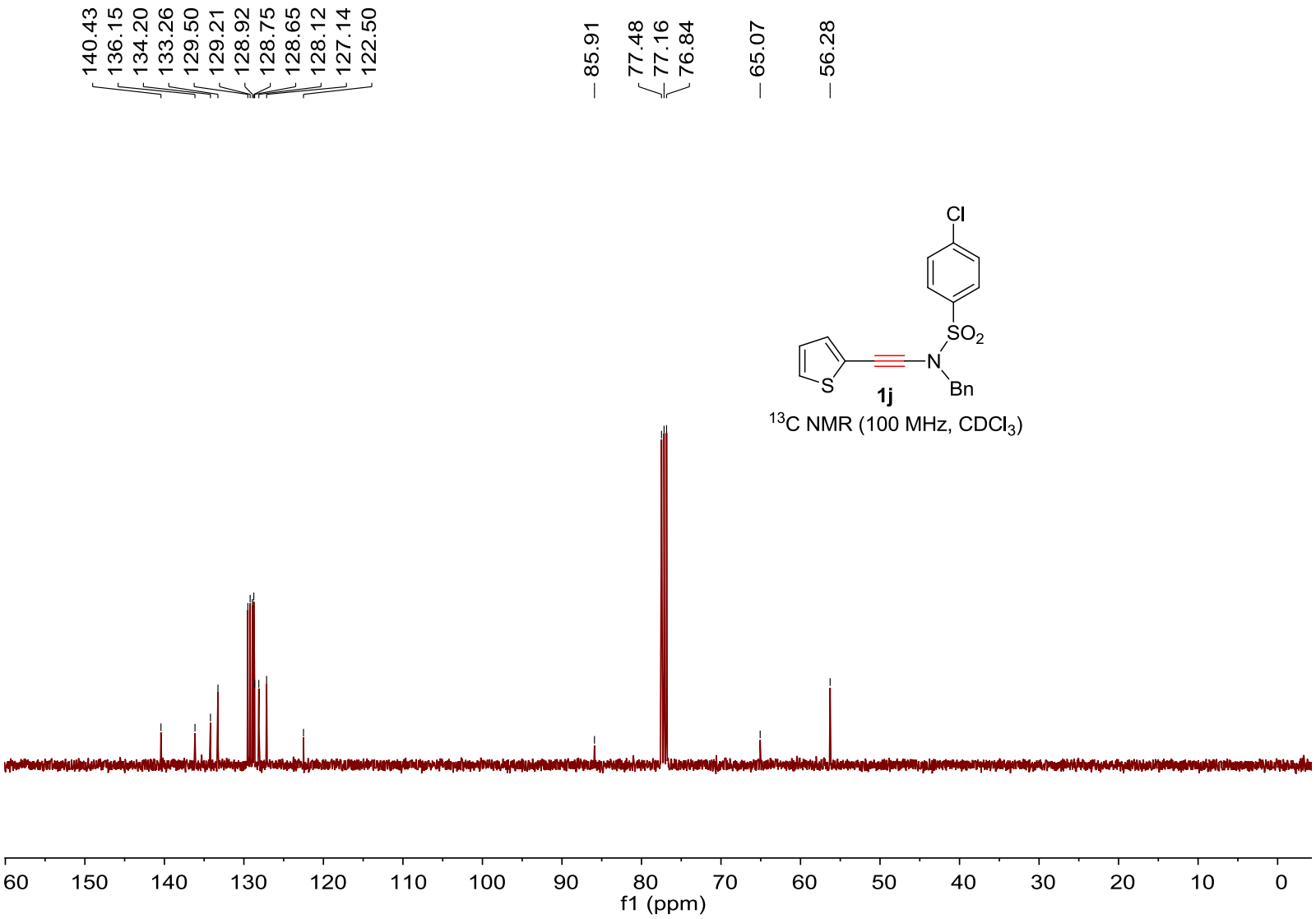
7.75
7.75
7.48
7.48
7.47
7.46
7.45
7.45
7.31
7.26
7.26
7.25
7.25
7.24
7.12
7.11
7.11
7.10
6.95
6.95
6.94
6.93
4.62
1.55
0.00
Cl
SO2
N
Bn
S
1j
1H NMR (400 MHz, CDCl3)
2.03
2.17
5.13
1.28
0.99
1.00
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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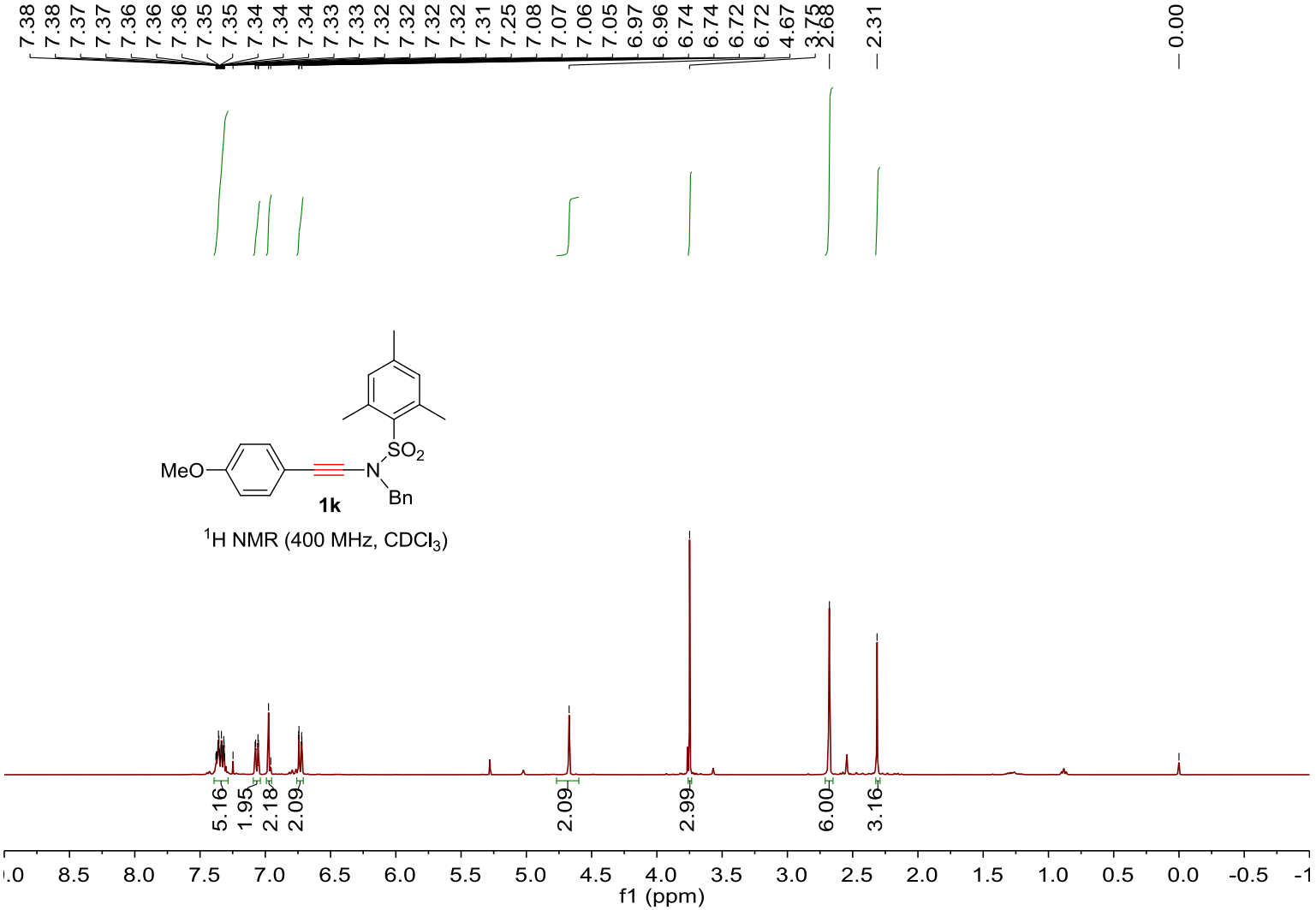
136.15
134.20
133.26
129.50
129.21
128.92
128.75
128.65
128.12
127.14
122.50
85.91
77.48
77.16
76.84
65.07
56.28
Cl
SO2
N
S
Bn
1j
13C NMR (100 MHz, CDCl3)
60
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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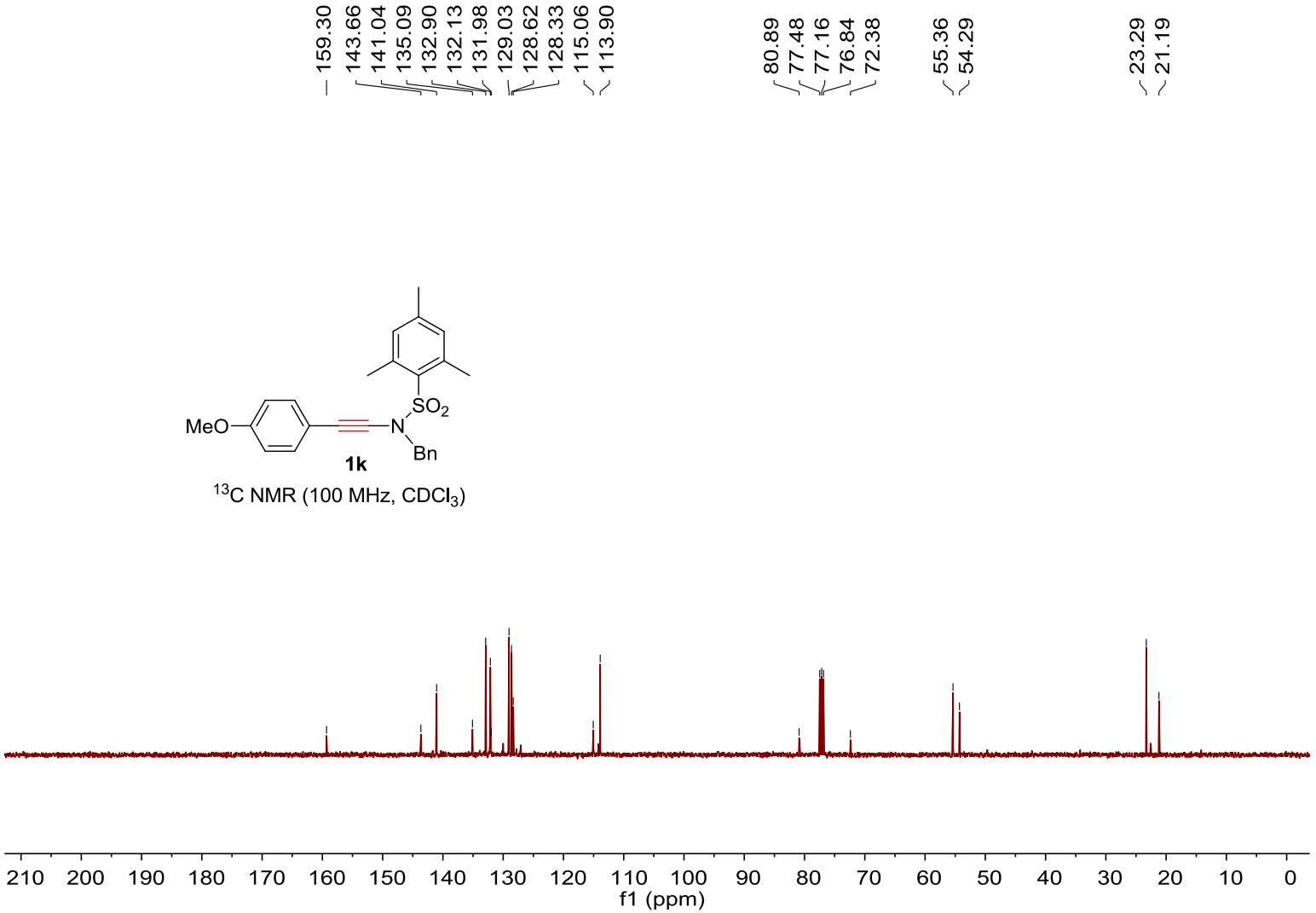
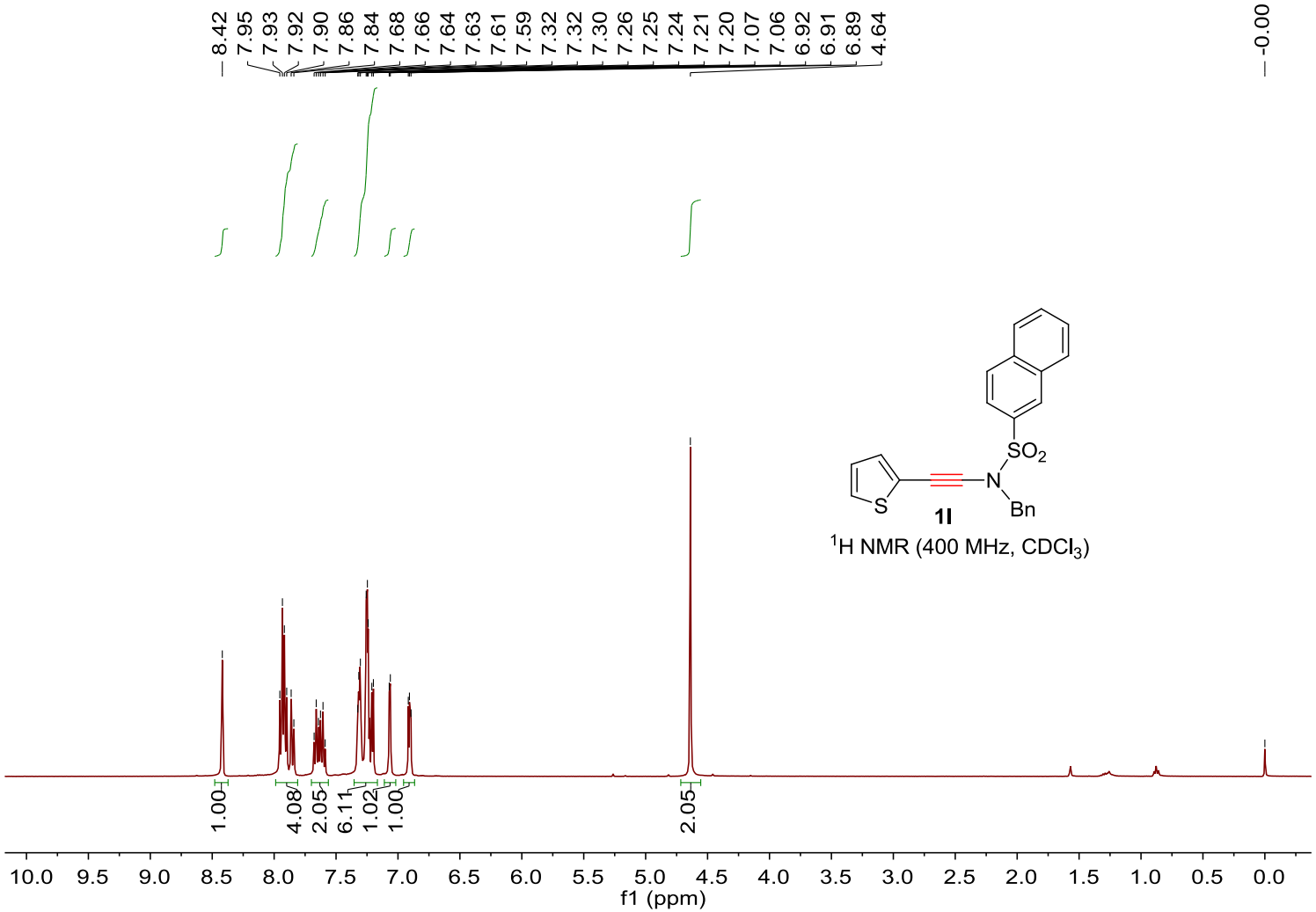
7.38
7.37
7.37
7.36
7.36
7.36
7.35
7.35
7.34
7.34
7.34
7.33
7.33
7.32
7.32
7.32
7.32
7.31
7.25
7.08
7.07
7.06
7.05
6.97
6.96
6.74
6.74
6.72
6.72
4.67
3.75
2.68
2.31
0.00
MeO
SO2
N
Bn
1k
1H NMR (400 MHz, CDCl3)
5.16
1.95
2.18
2.09
2.09
2.99
6.00
3.16
f1 (ppm)


159.30
143.66
141.04
135.09
132.90
132.13
131.98
129.03
128.62
128.33
115.06
113.90
80.89
77.48
77.16
76.84
72.38
55.36
54.29
23.29
21.19
MeO
SO2
N
Bn
1k
13C NMR (100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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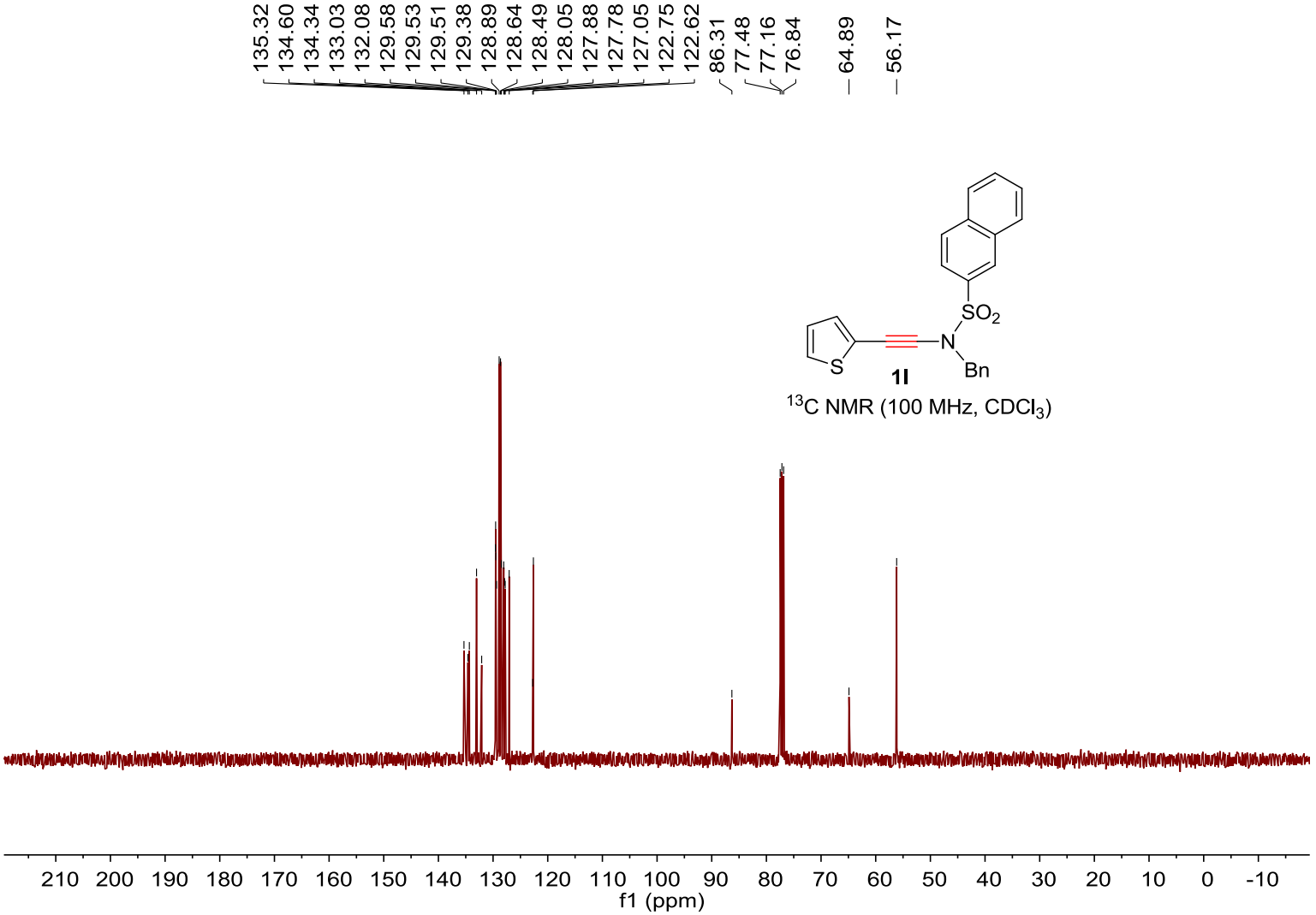
7.92
7.90
7.86
7.84
7.68
7.66
7.64
7.63
7.61
7.59
7.32
7.32
7.30
7.26
7.25
7.24
7.21
7.20
7.07
7.06
6.92
6.91
6.89
4.64
-0.00
SO2
N
S
Bn
1l
1H NMR (400 MHz, CDCl3)
1.00
4.08
2.05
6.11
1.02
1.00
2.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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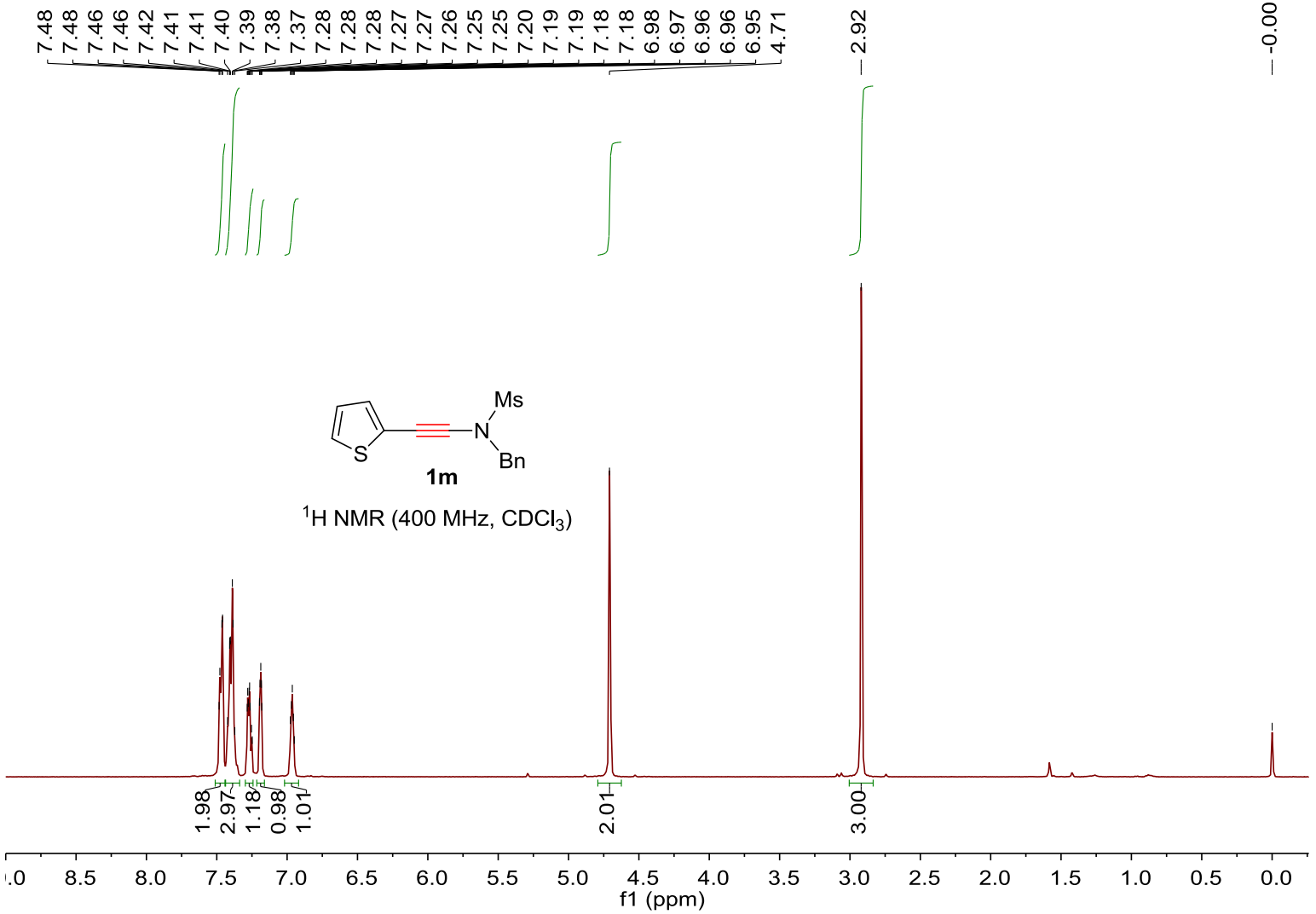
134.60
134.34
133.03
132.08
129.58
129.53
129.51
129.38
128.89
128.64
128.49
128.05
127.88
127.78
127.05
122.75
122.62
86.31
77.48
77.16
76.84
64.89
56.17
SO2
N
S
Bn
1l
13C NMR (100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.42
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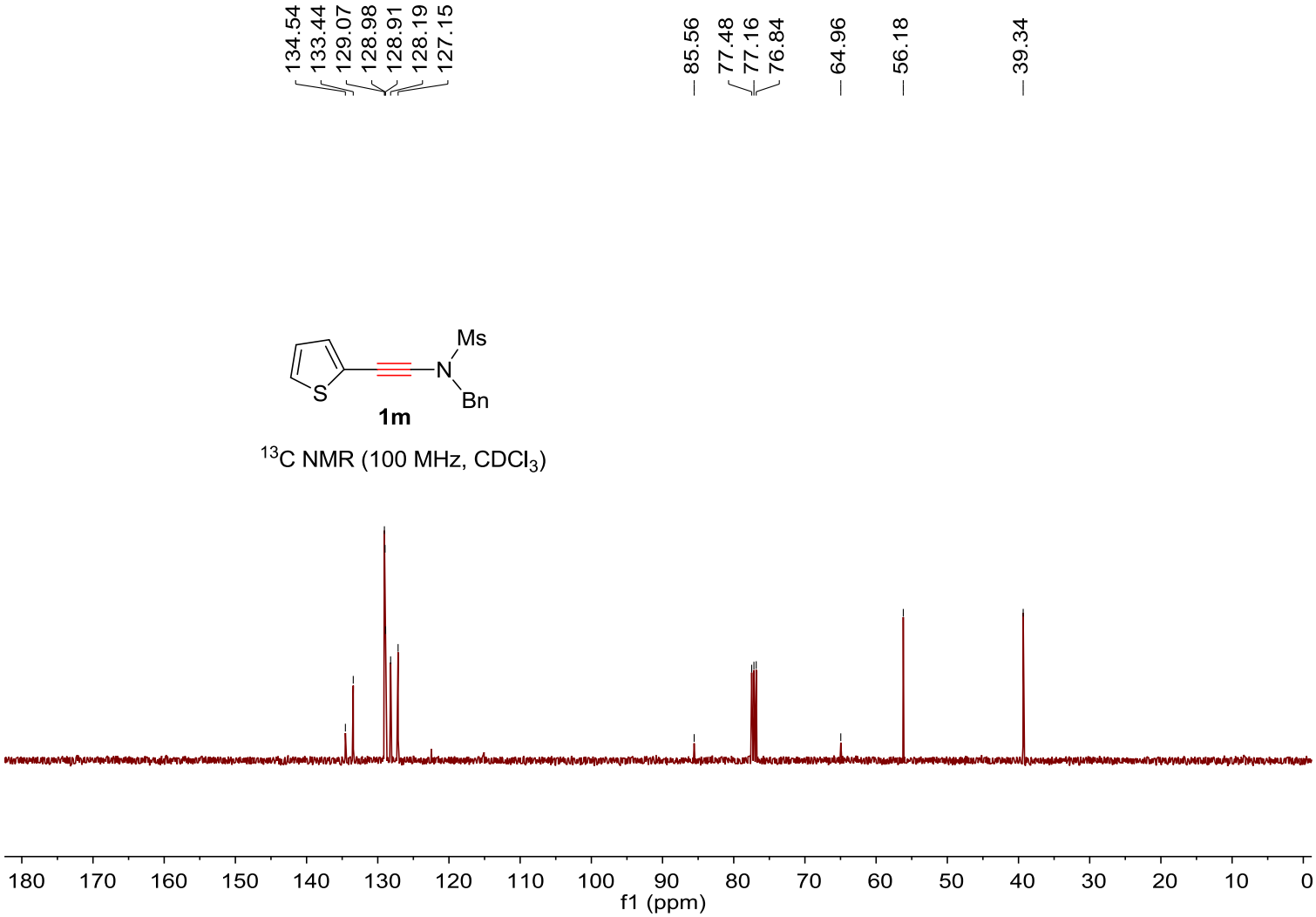
7.41
7.40
7.39
7.38
7.37
7.28
7.28
7.28
7.27
7.27
7.26
7.25
7.25
7.20
7.19
7.19
7.18
7.18
6.98
6.97
6.96
6.96
6.95
4.71
2.92
-0.00
Ms
N
Bn
S
1m
1H NMR (400 MHz, CDCl3)
1.98
2.97
1.18
0.98
1.01
2.01
3.00
f1 (ppm)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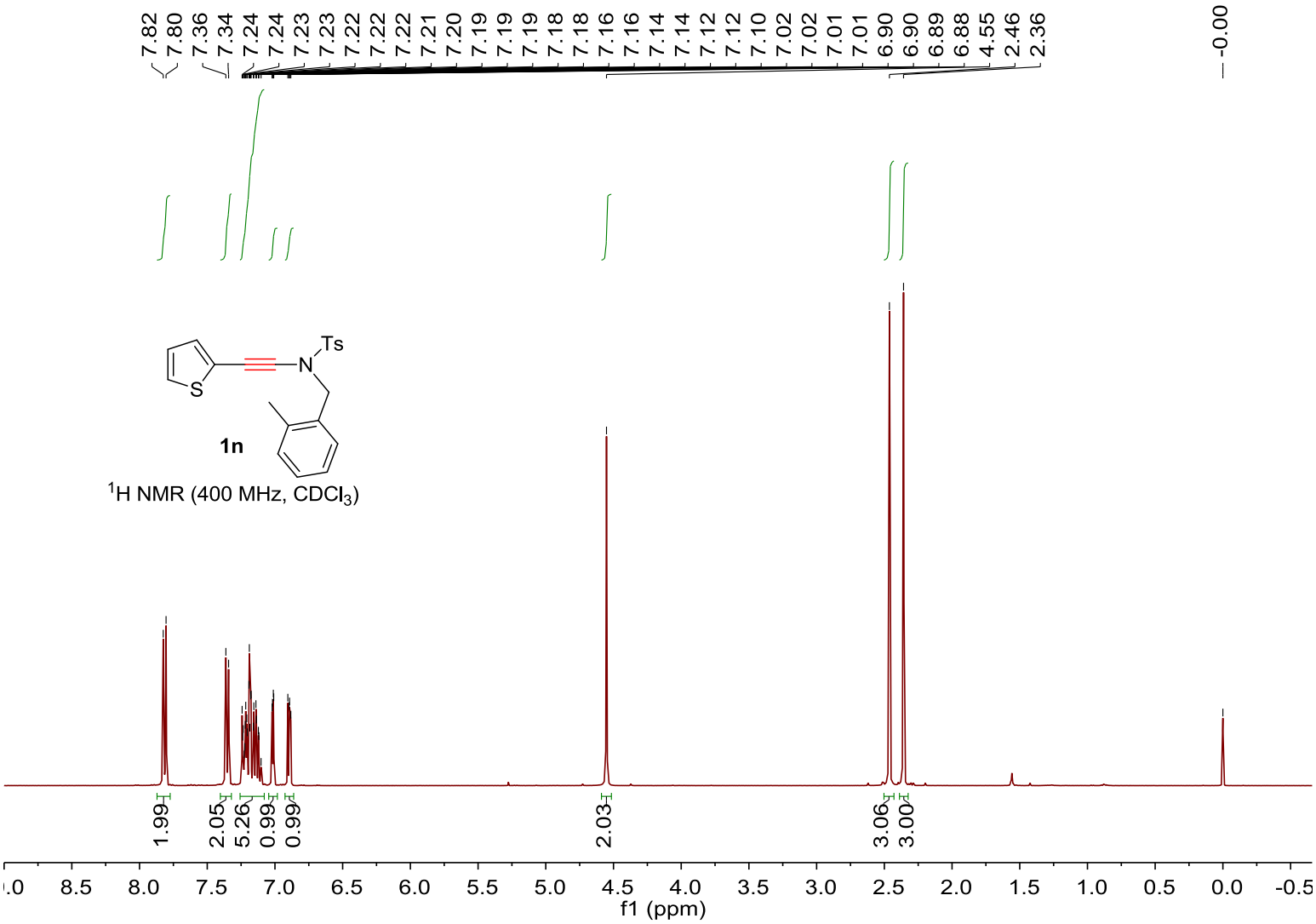
133.44
129.07
128.98
128.91
128.19
127.15
85.56
77.48
77.16
76.84
64.96
56.18
39.34
Ms
N
Bn
S
1m
13C NMR (100 MHz, CDCl3)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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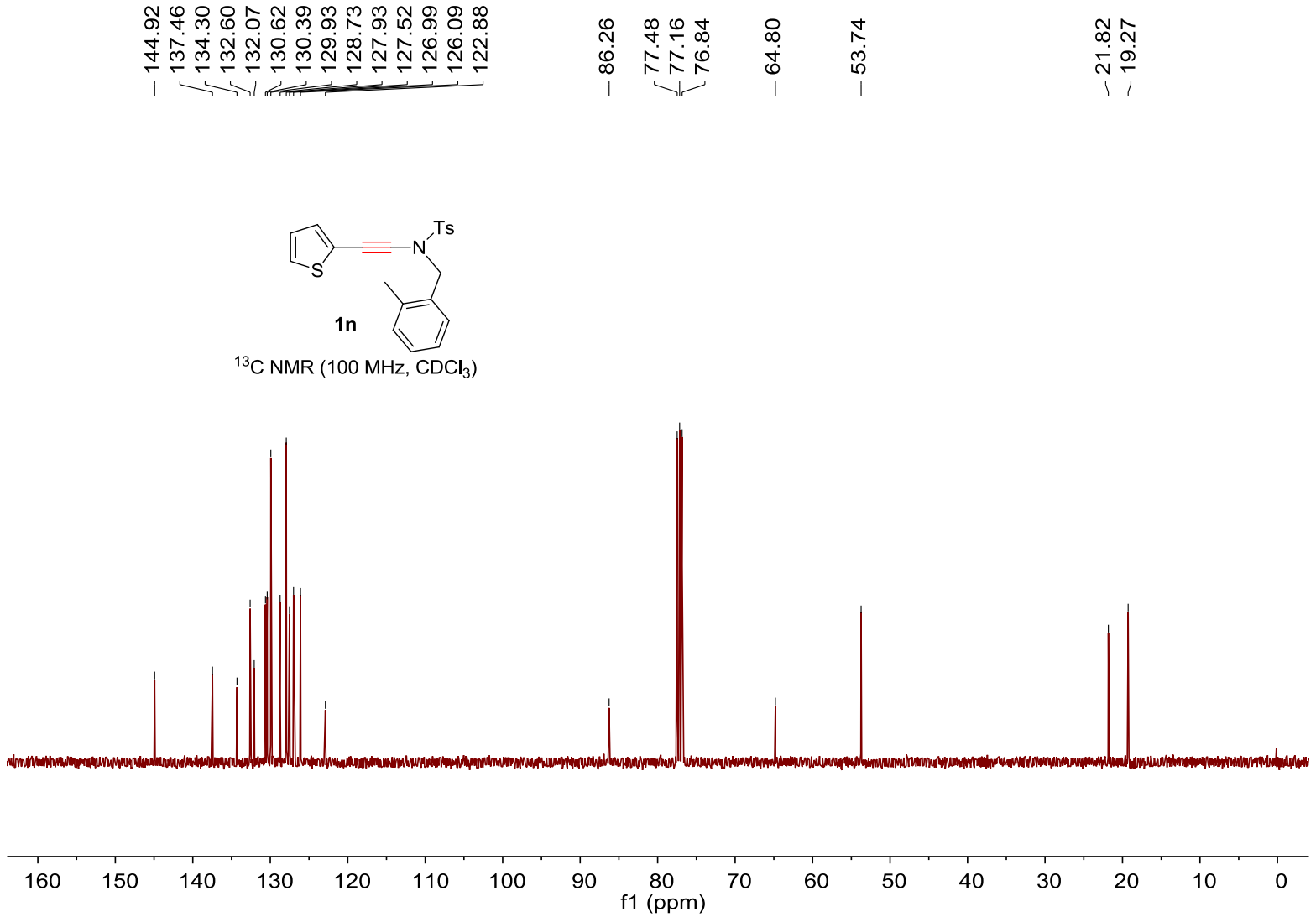
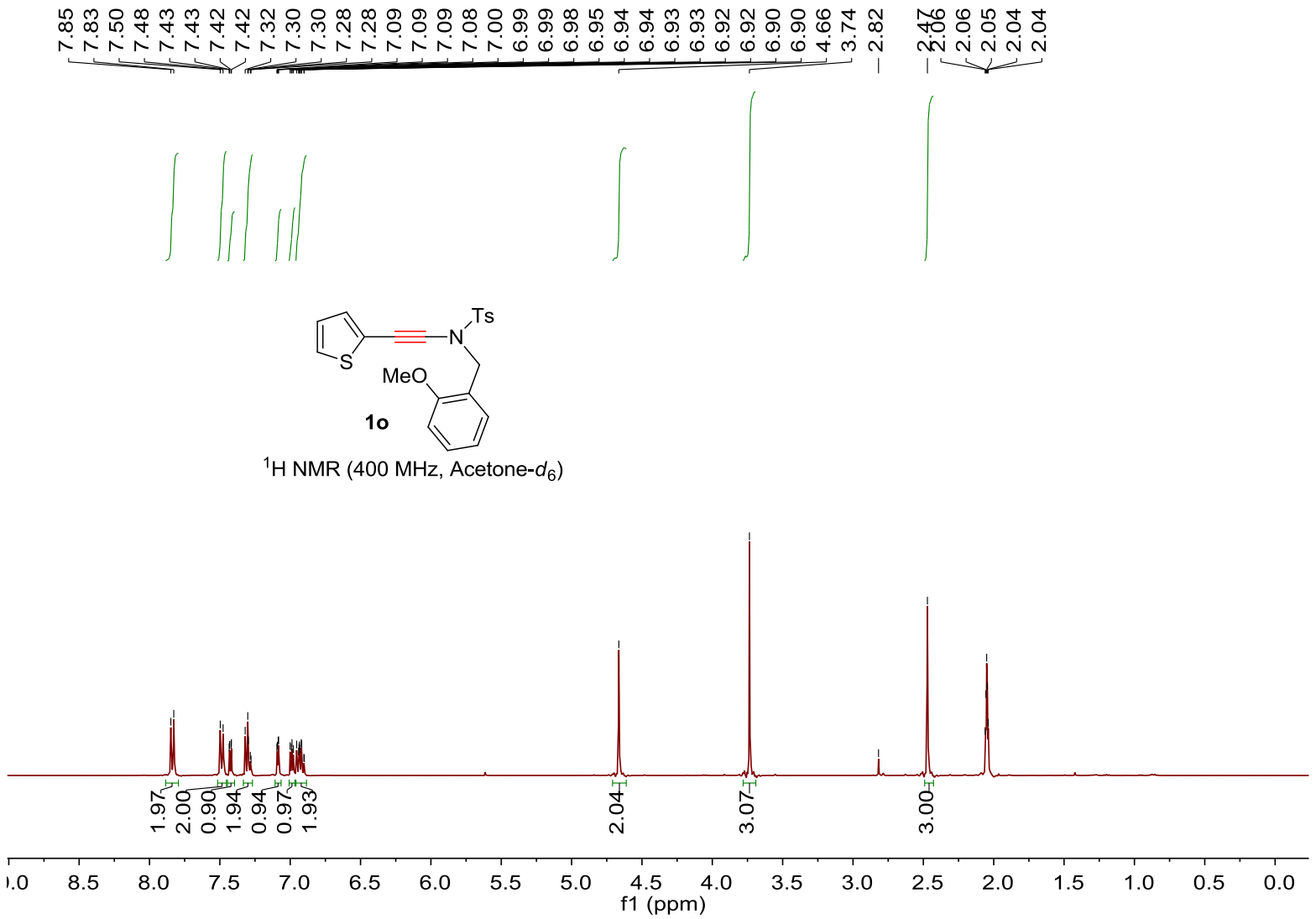
7.24
7.23
7.23
7.22
7.22
7.22
7.21
7.20
7.19
7.19
7.19
7.18
7.18
7.16
7.16
7.14
7.14
7.12
7.12
7.10
7.02
7.02
7.01
7.01
6.90
6.90
6.89
6.88
4.55
2.46
2.36
-0.00
Ts
N
S
1n
1H NMR (400 MHz, CDCl3)
1.99
2.05
5.26
0.99
0.99
2.03
3.06
3.00
f1 (ppm)


144.92
137.46
134.30
132.60
132.07
130.62
130.39
129.93
128.73
127.93
127.52
126.99
126.09
122.88
86.26
77.48
77.16
76.84
64.80
53.74
21.82
19.27
Ts
N
S
1n
13C NMR (100 MHz, CDCl3)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.85
7.83
7.50
7.48
7.43
7.43
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7.42
7.32
7.30
7.30
7.28
7.28
7.09
7.09
7.09
7.08
7.00
6.99
6.99
6.98
6.95
6.94
6.94
6.93
6.93
6.92
6.92
6.90
6.90
4.66
3.74
2.82
2.47
2.06
2.06
2.05
2.04
2.04
Ts
N
S
MeO
1o
1H NMR (400 MHz, Acetone-d6)
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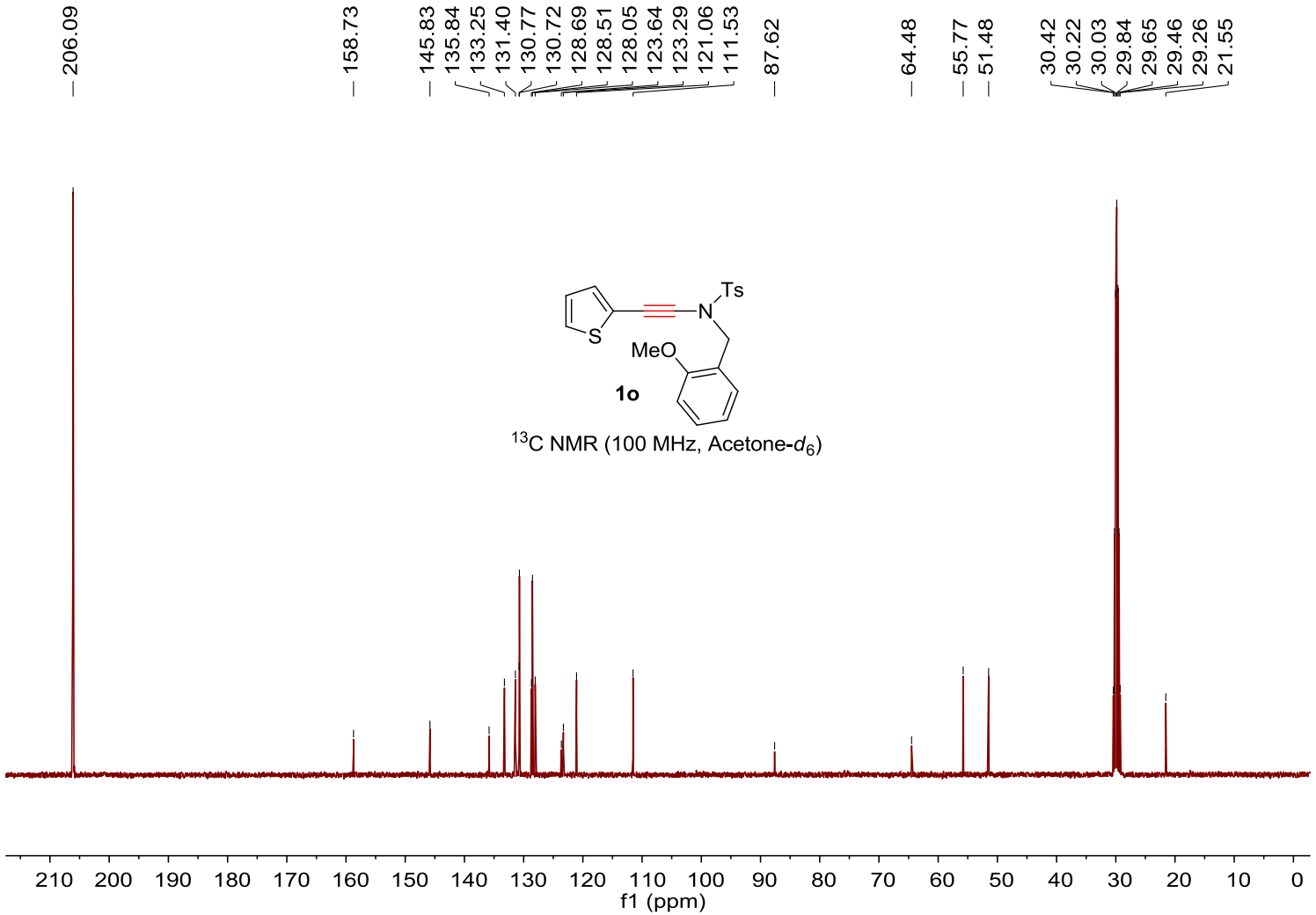
2.00
0.90
1.94
0.94
0.97
1.93
2.04
3.07
3.00
f1 (ppm)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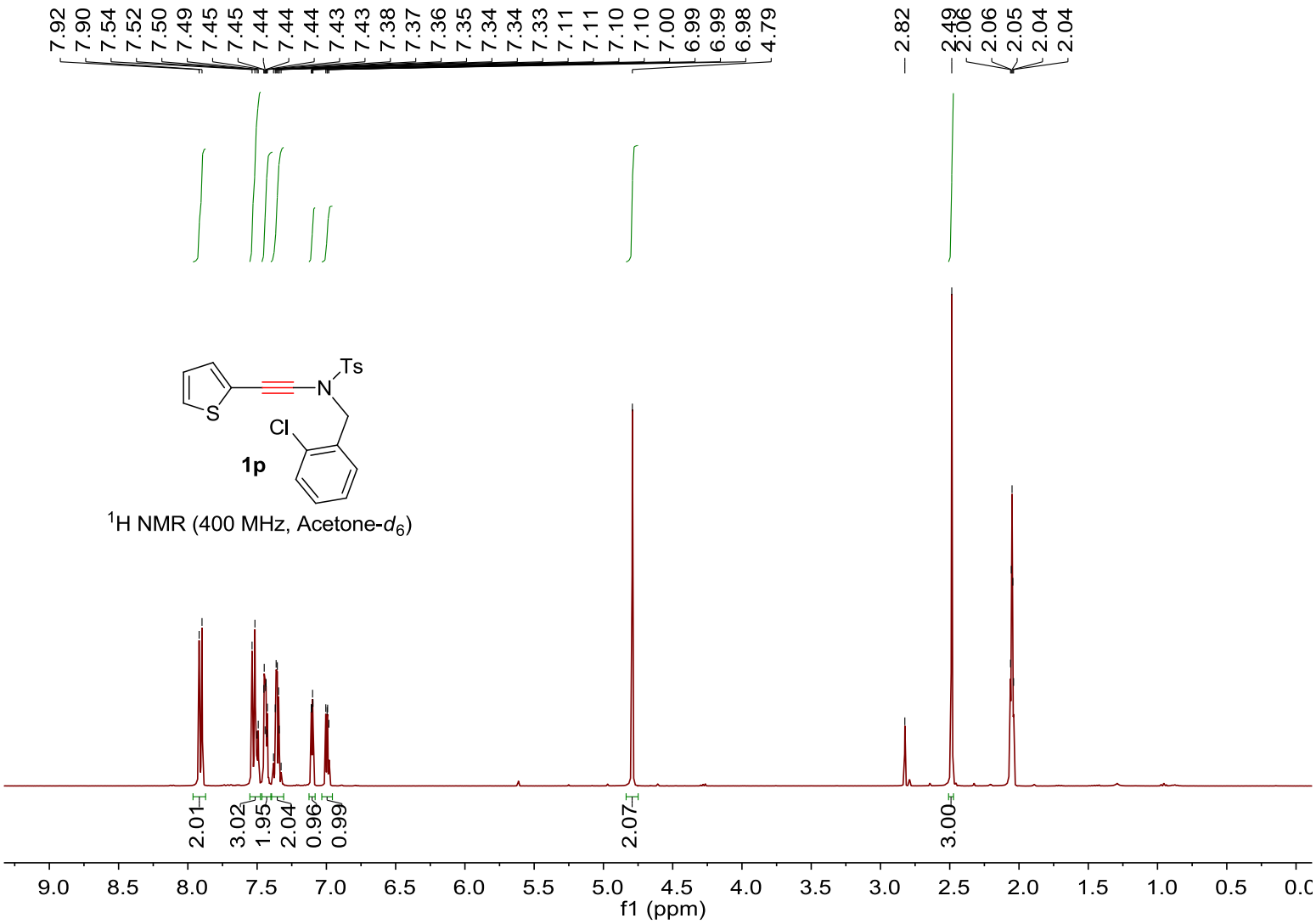
131.40
130.77
130.72
128.69
128.51
128.05
123.64
123.29
121.06
111.53
87.62
64.48
55.77
51.48
30.42
30.22
30.03
29.84
29.65
29.46
29.26
21.55
Ts
N
S
MeO
1o
13C NMR (100 MHz, Acetone-d6)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.50
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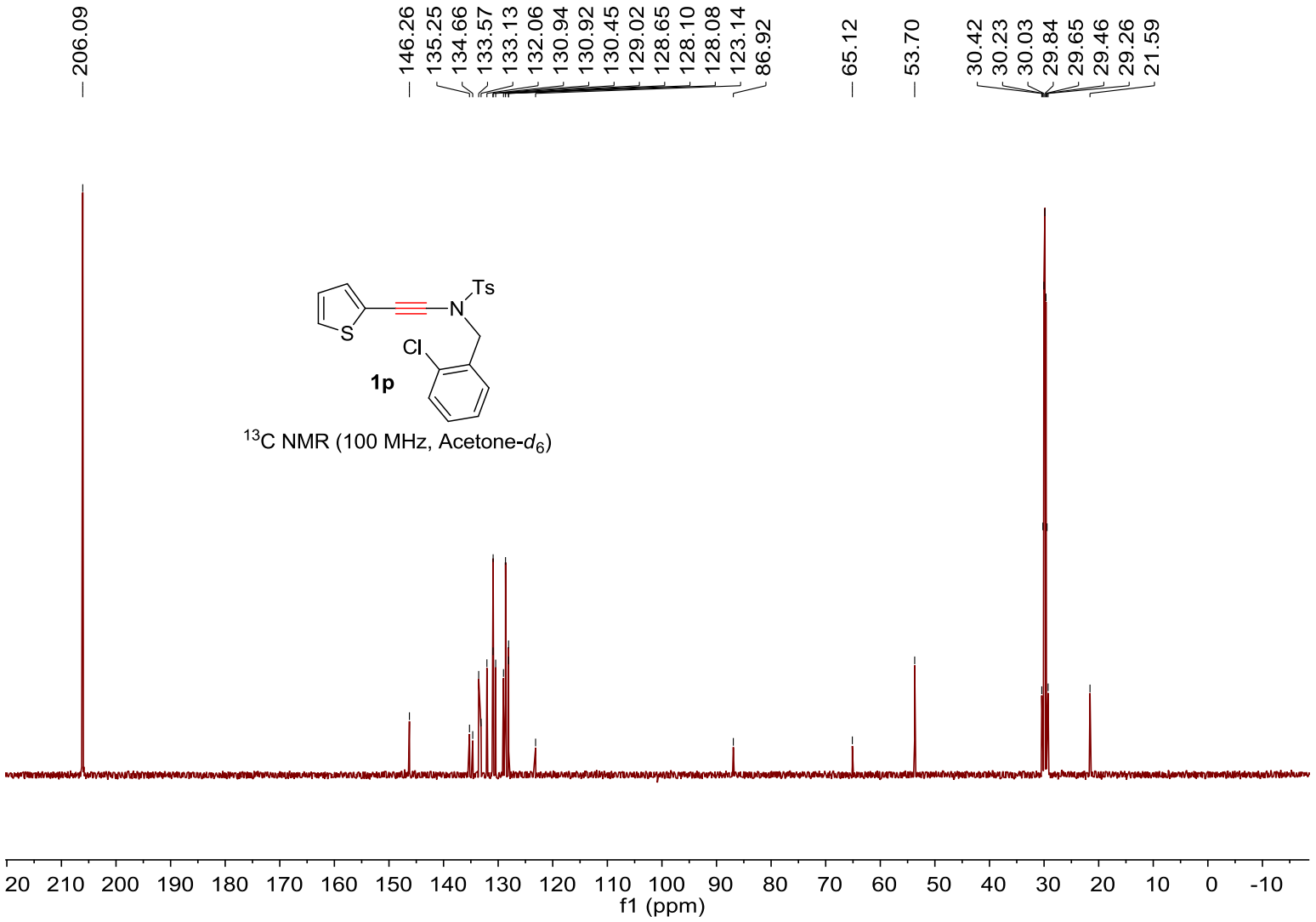
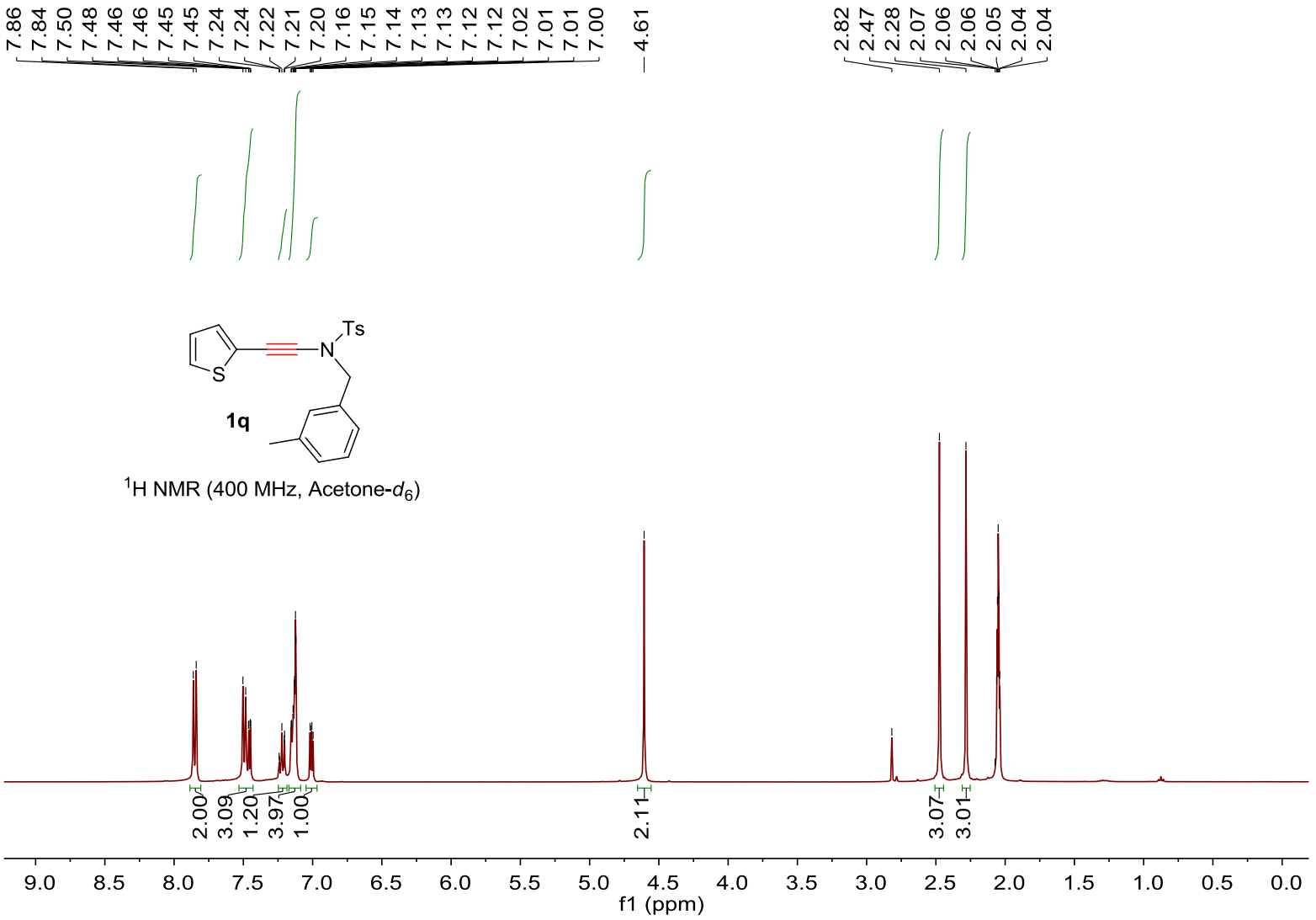
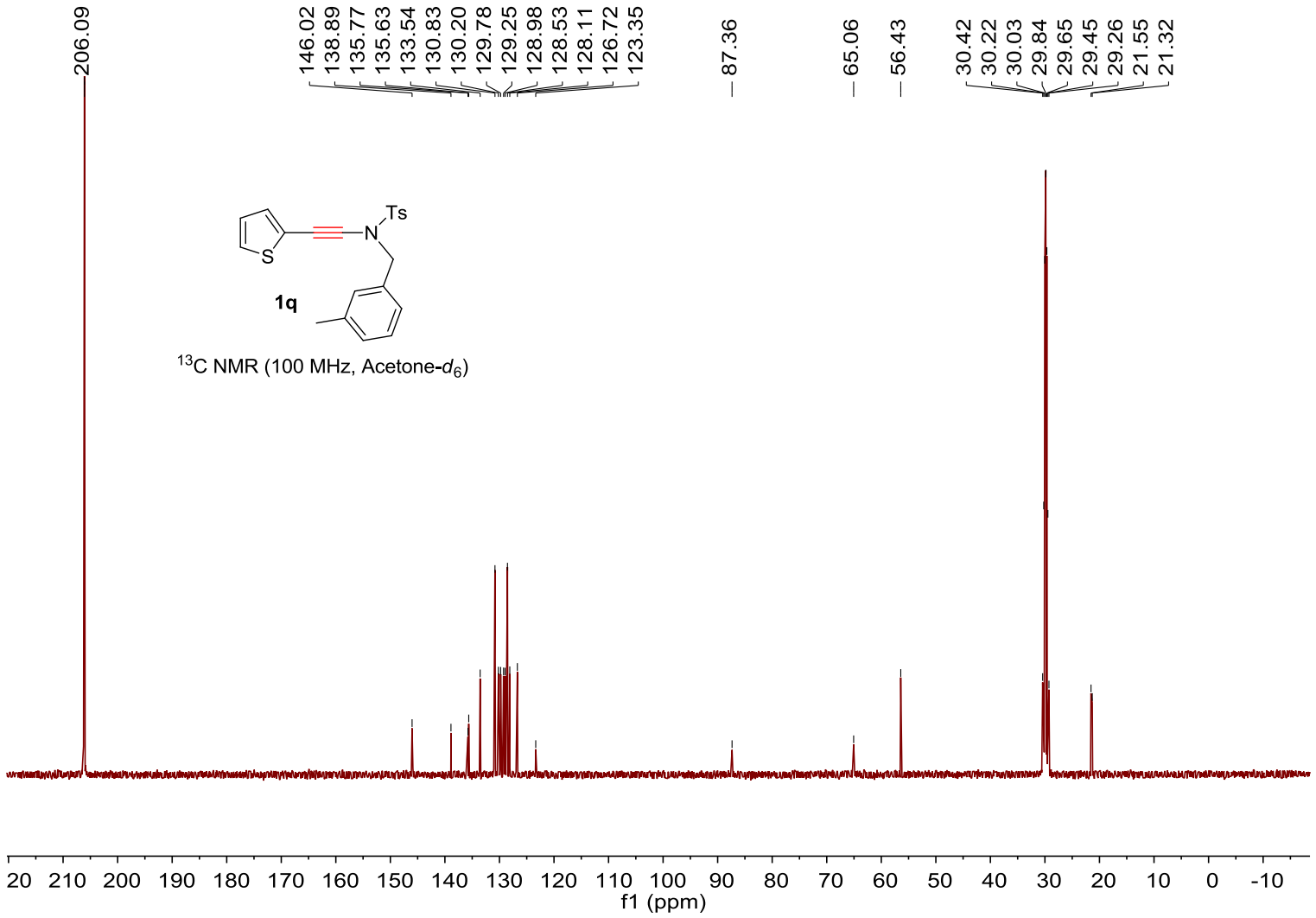
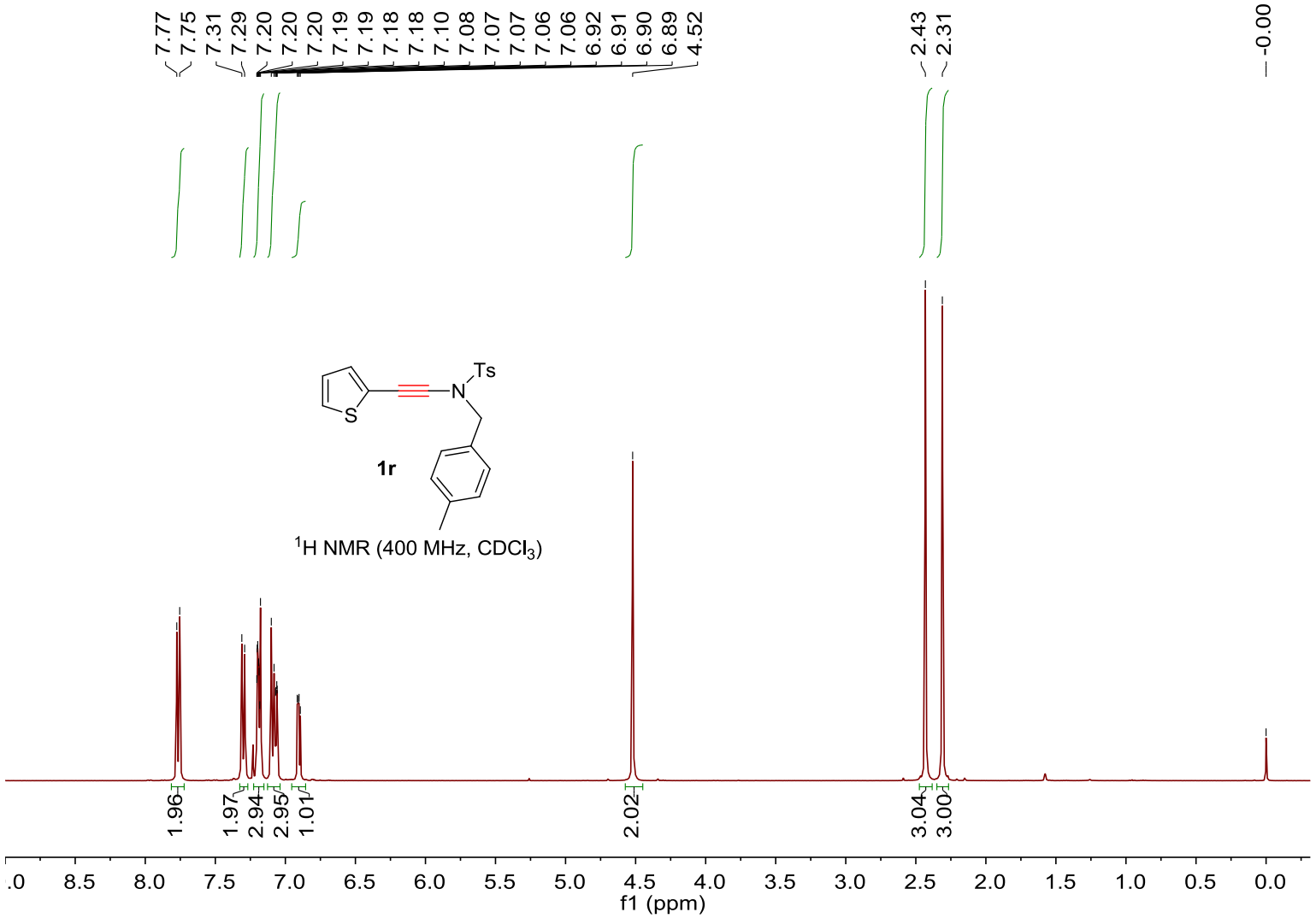
7.45
7.44
7.44
7.44
7.43
7.43
7.38
7.37
7.36
7.35
7.34
7.34
7.33
7.11
7.11
7.10
7.10
7.00
6.99
6.99
6.98
4.79
2.82
2.49
2.08
2.06
2.05
2.04
2.04
Ts
N
S
Cl
1p
1H NMR (400 MHz, Acetone-d6)
2.01
3.02
1.95
2.04
0.96
0.99
2.07
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

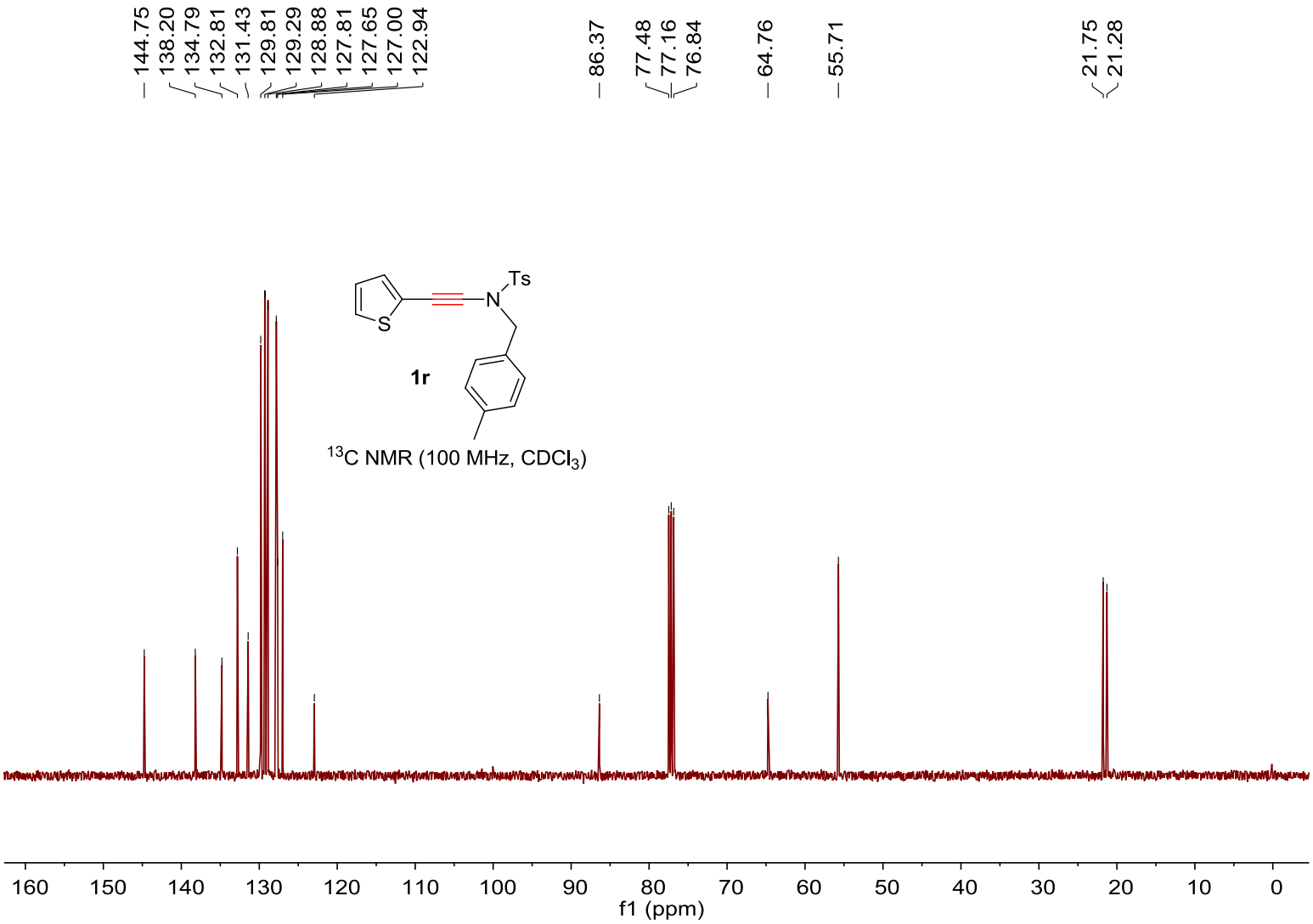


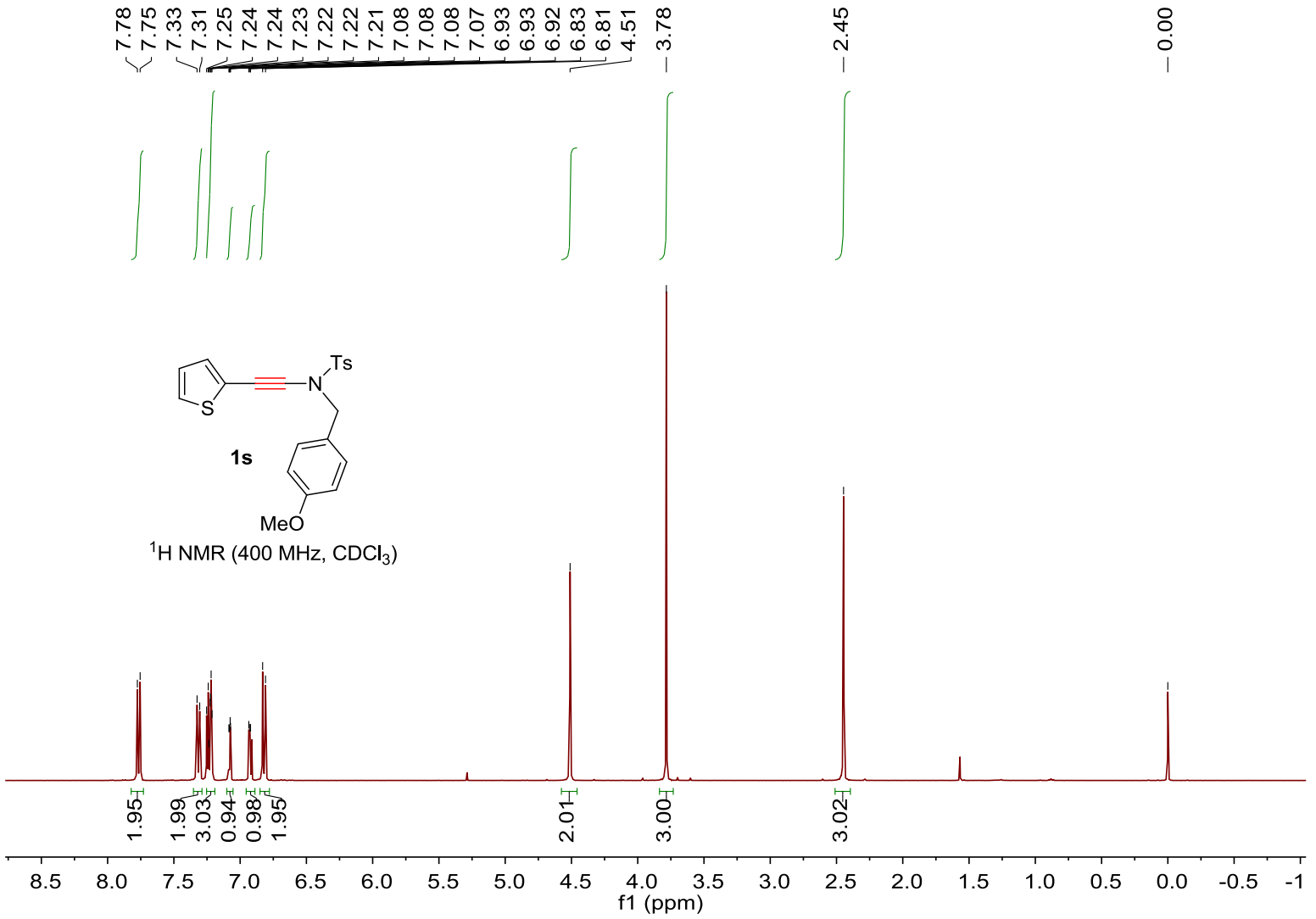
^{13}C NMR (100 MHz, Acetone-d_6)

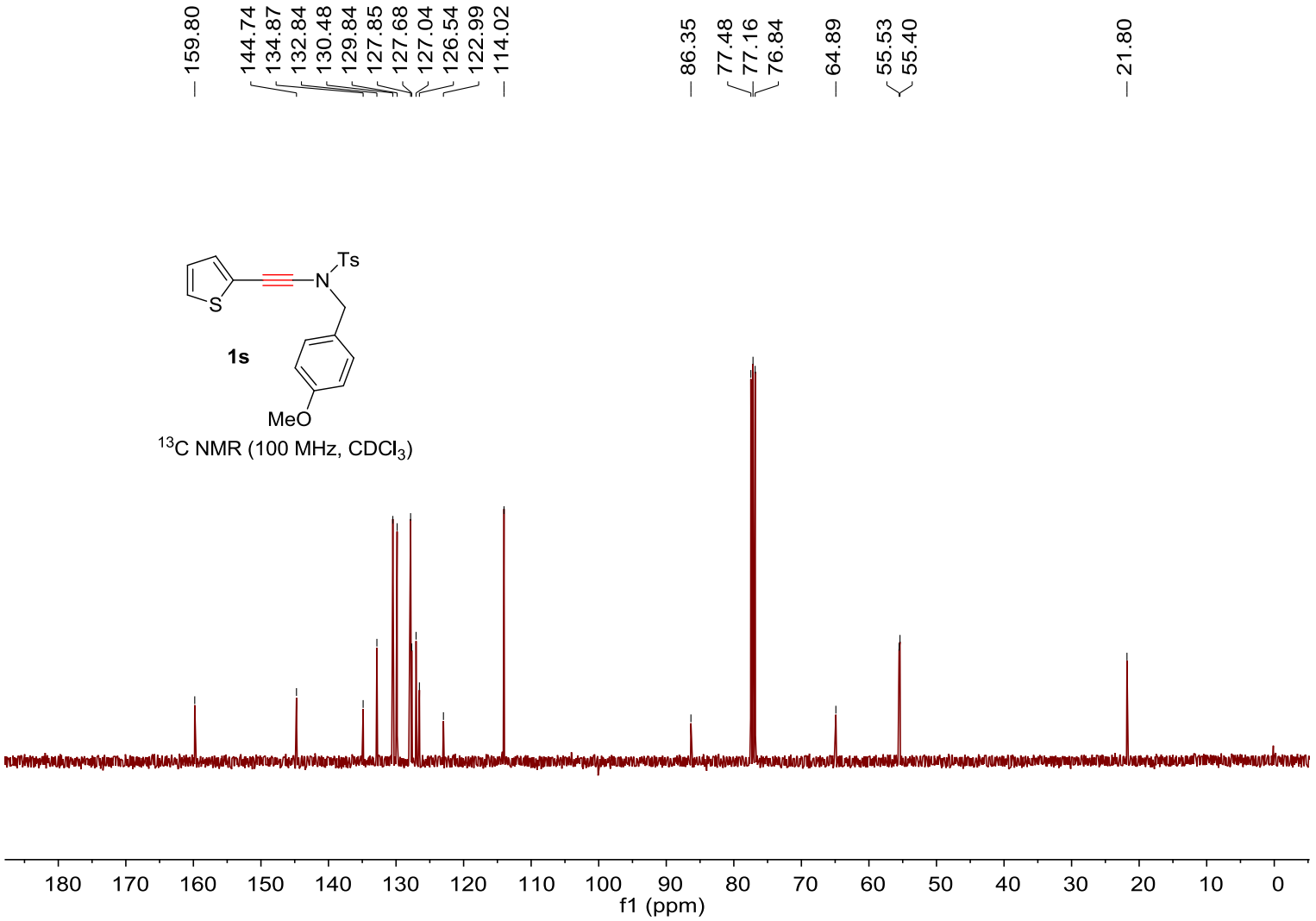

7.86
7.84
7.50
7.48
7.46
7.46
7.45
7.45
7.24
7.24
7.22
7.21
7.20
7.16
7.15
7.14
7.13
7.13
7.12
7.12
7.02
7.01
7.01
7.00
4.61
2.82
2.47
2.28
2.07
2.06
2.06
2.05
2.04
2.04
Ts
N
S
1q
1H NMR (400 MHz, Acetone-d6)
2.00
3.09
1.20
3.97
1.00
2.11
3.07
3.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


206.09
146.02
138.89
135.77
135.63
133.54
130.83
130.20
129.78
129.25
128.98
128.53
128.11
126.72
123.35
87.36
65.06
56.43
30.42
30.22
30.03
29.84
29.65
29.45
29.26
21.55
21.32
Ts
N
S
1q
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.77
7.75
7.31
7.29
7.20
7.20
7.20
7.19
7.19
7.18
7.18
7.10
7.08
7.07
7.07
7.06
7.06
6.92
6.91
6.90
6.89
4.52
2.43
2.31
-0.00
Ts
N
S
1r
1H NMR (400 MHz, CDCl3)
1.96
1.97
2.94
2.95
1.01
2.02
3.04
3.00
f1 (ppm)


144.75
138.20
134.79
132.81
131.43
129.81
129.29
128.88
127.81
127.65
127.00
122.94
86.37
77.48
77.16
76.84
64.76
55.71
21.75
21.28
Ts
N
S
1r
13C NMR (100 MHz, CDCl3)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.78
7.75
7.33
7.31
7.25
7.24
7.24
7.23
7.22
7.22
7.21
7.08
7.08
7.08
7.07
6.93
6.93
6.92
6.83
6.81
4.51
3.78
2.45
0.00
Ts
N
S
1s
MeO
1H NMR (400 MHz, CDCl3)
1.95
1.99
3.03
0.94
0.98
1.95
2.01
3.00
3.02
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
-0.5
-1
f1 (ppm)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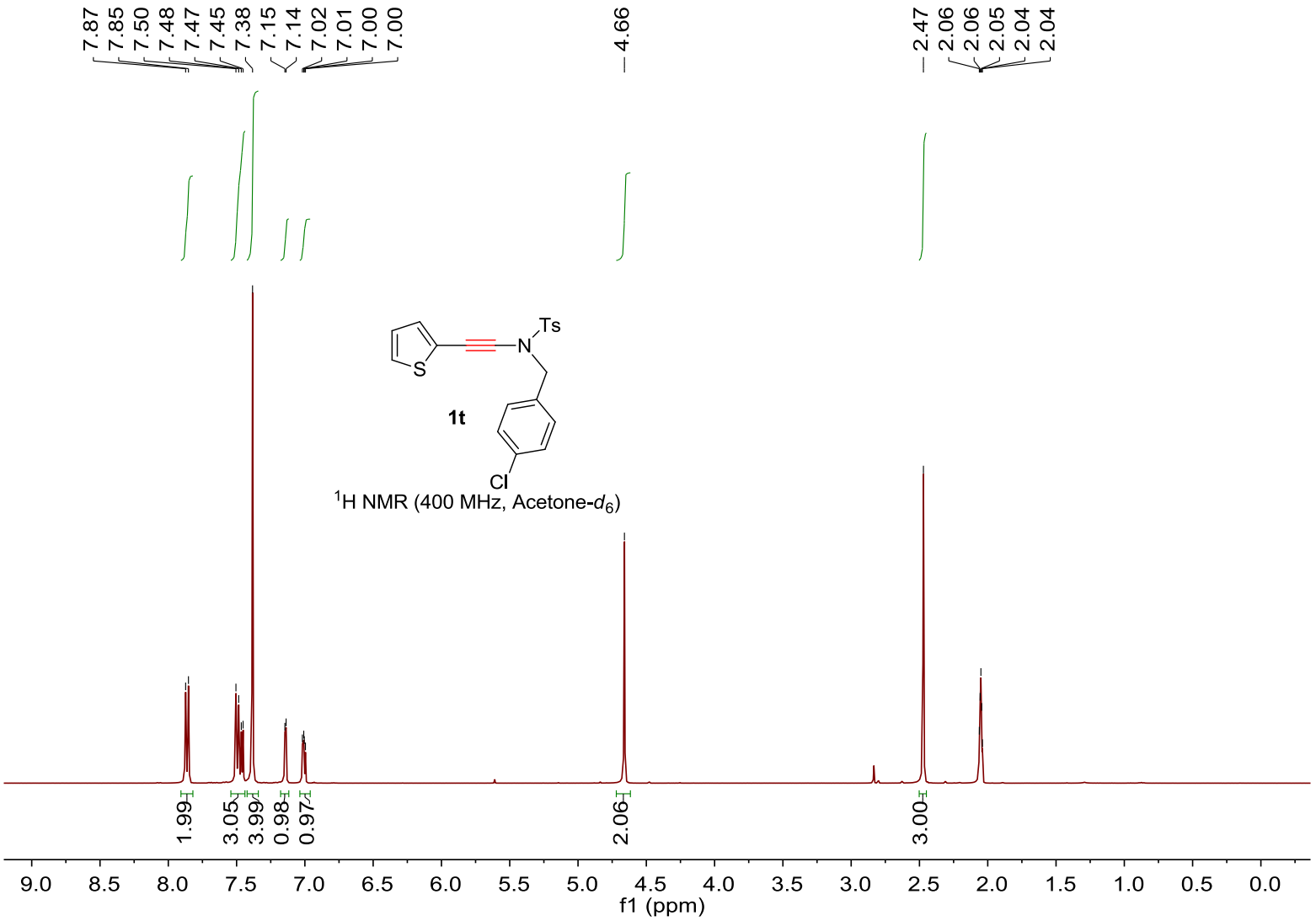
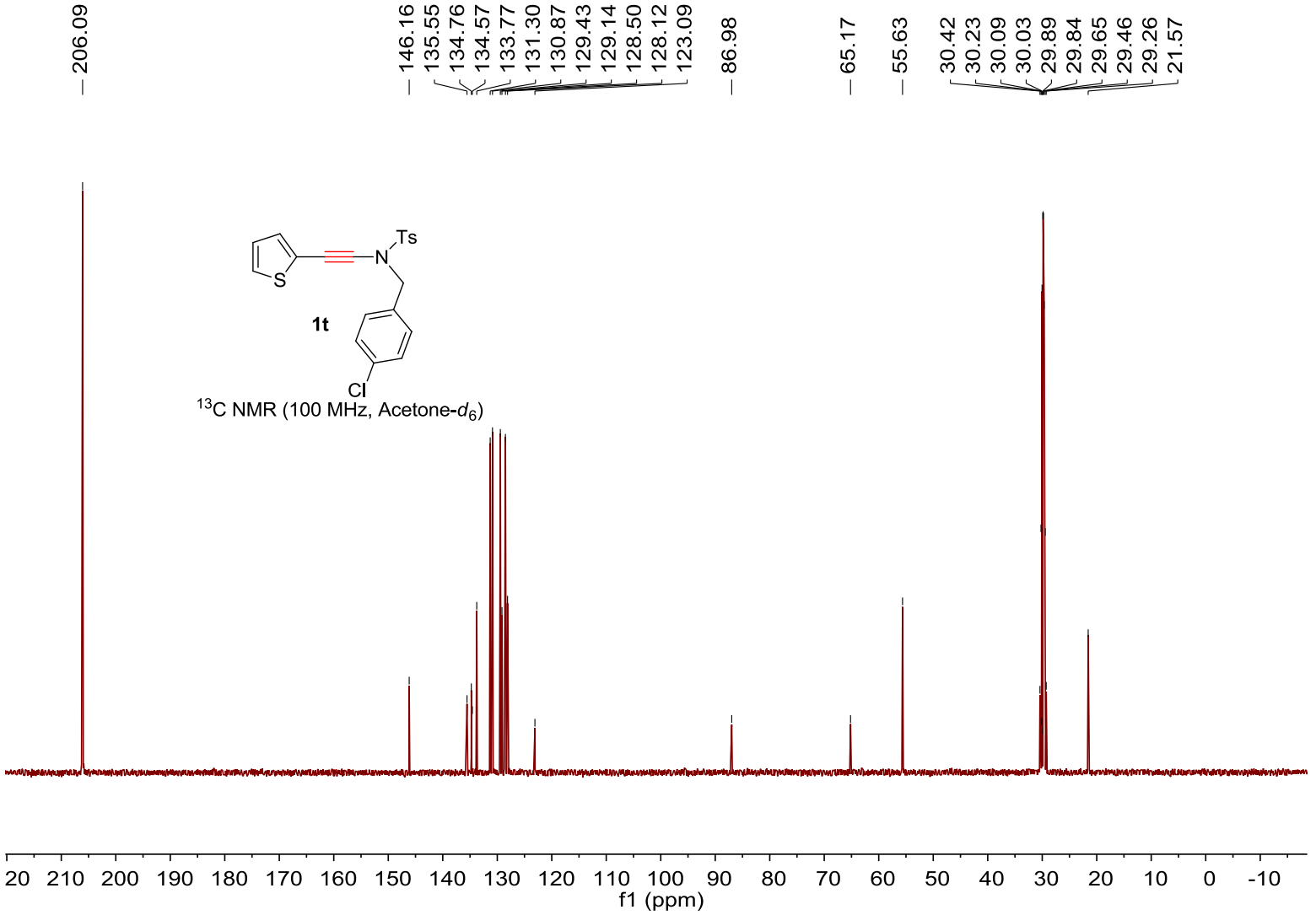
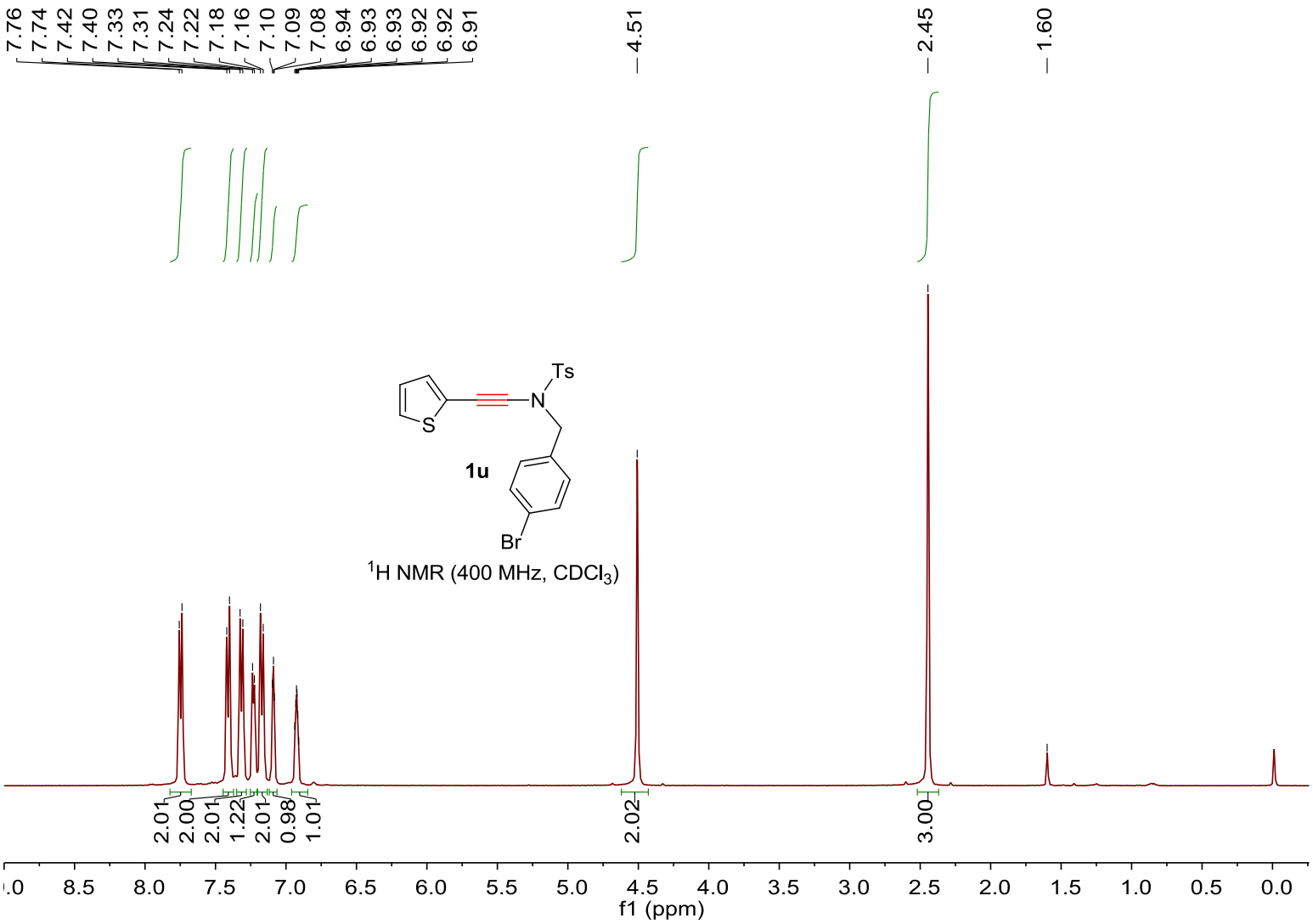
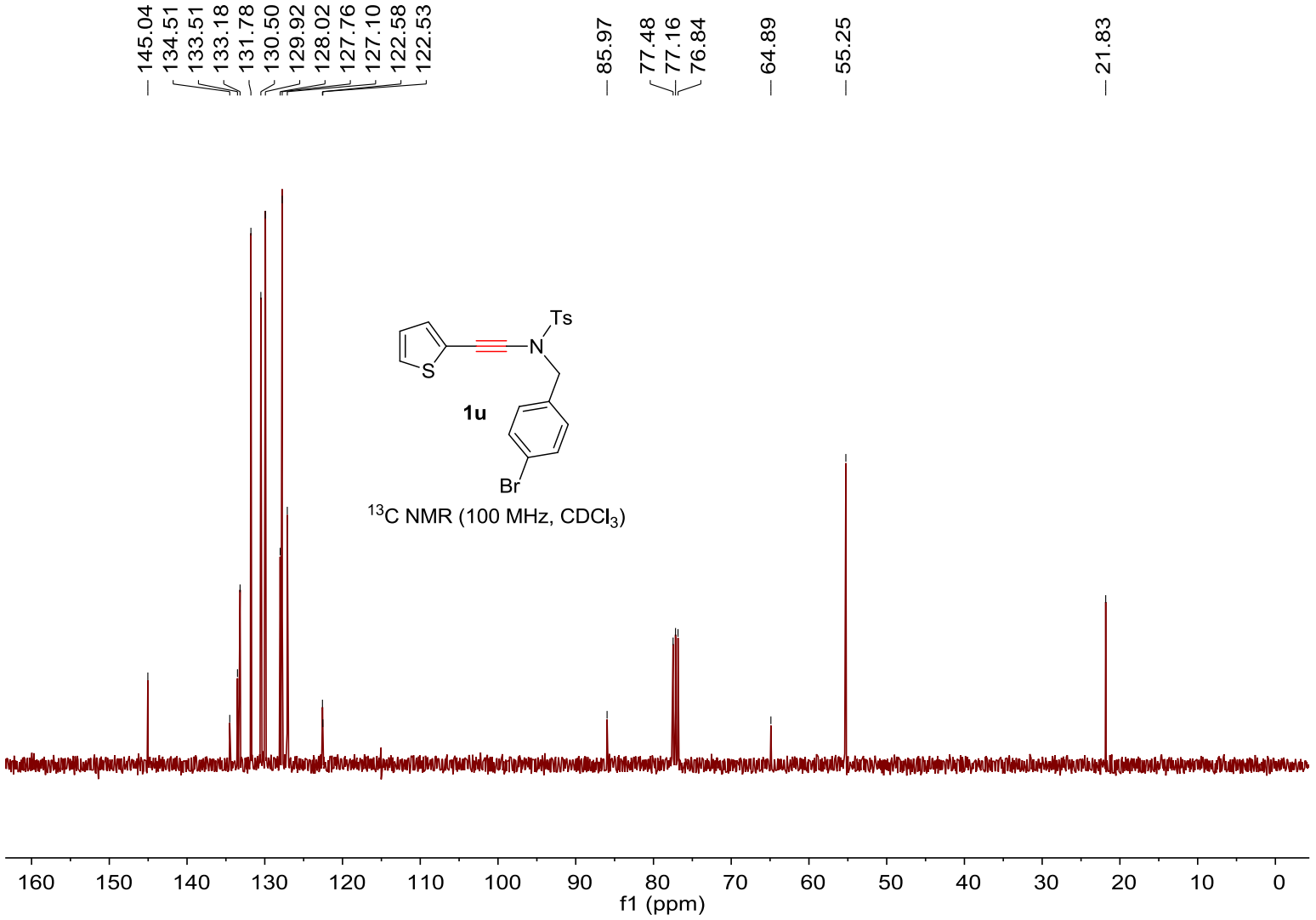
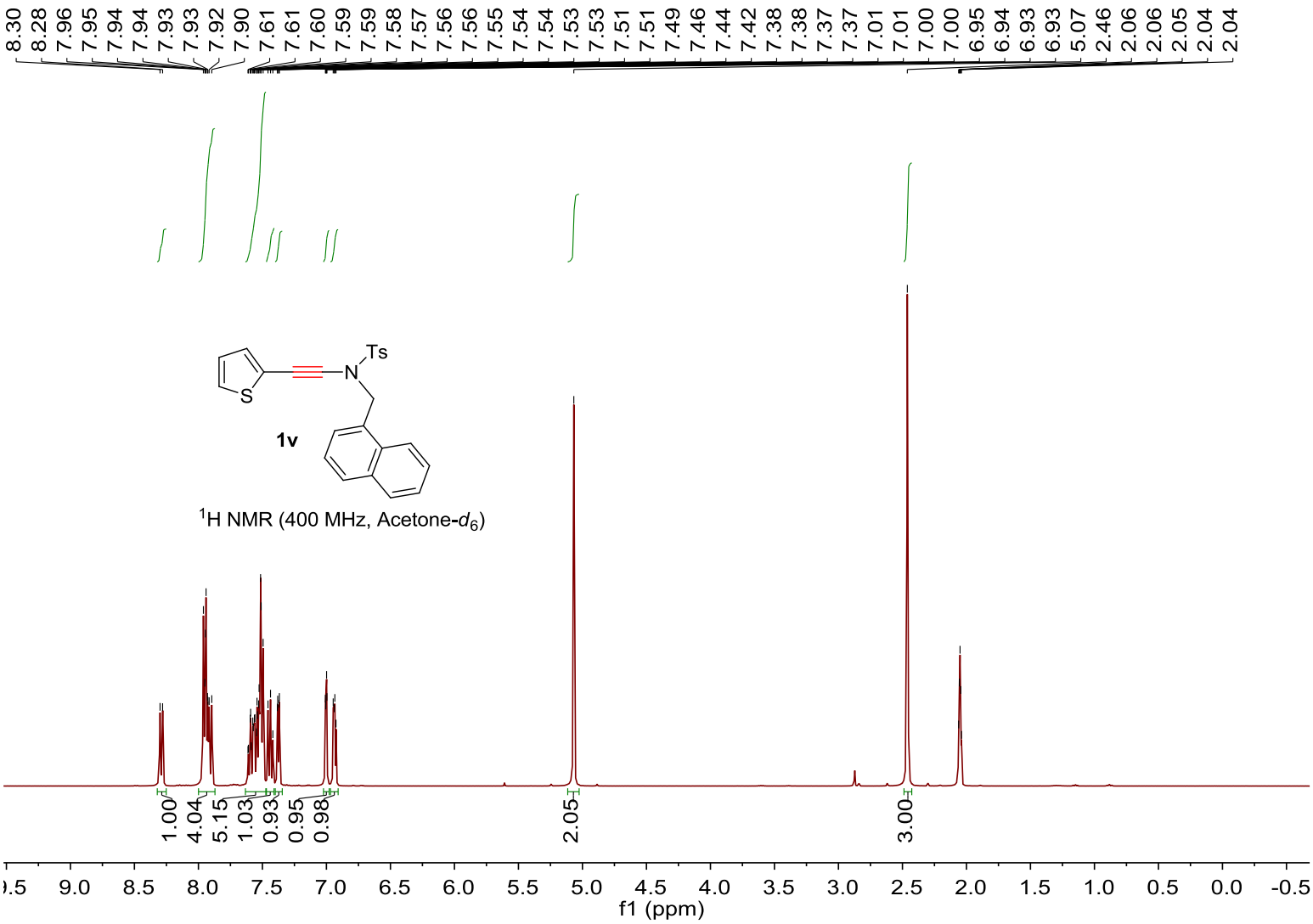
144.74
134.87
132.84
130.48
129.84
127.85
127.68
127.04
126.54
122.99
114.02
86.35
77.48
77.16
76.84
64.89
55.53
55.40
21.80
Ts
N
S
1s
MeO
13C NMR (100 MHz, CDCl3)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

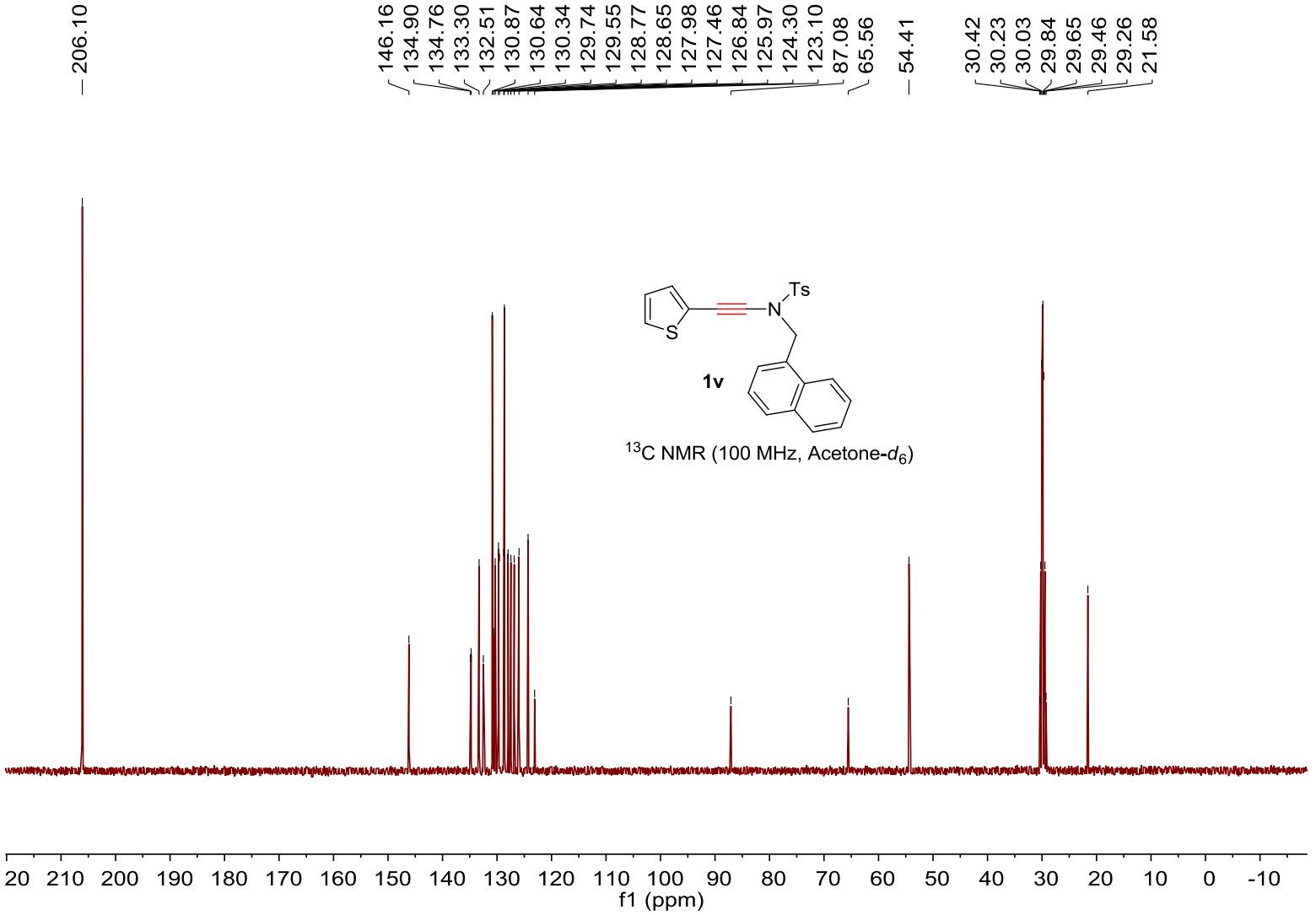

7.87
7.85
7.50
7.48
7.47
7.45
7.38
7.15
7.14
7.02
7.01
7.00
7.00
4.66
2.47
2.06
2.06
2.05
2.04
2.04
Ts
N
S
Cl
1t
1H NMR (400 MHz, Acetone-d6)
1.99
3.05
3.99
0.98
0.97
2.06
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


206.09
146.16
135.55
134.76
134.57
133.77
131.30
130.87
129.43
129.14
128.50
128.12
123.09
86.98
65.17
55.63
30.42
30.23
30.09
30.03
29.89
29.84
29.65
29.46
29.26
21.57
Ts
N
S
Cl
1t
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

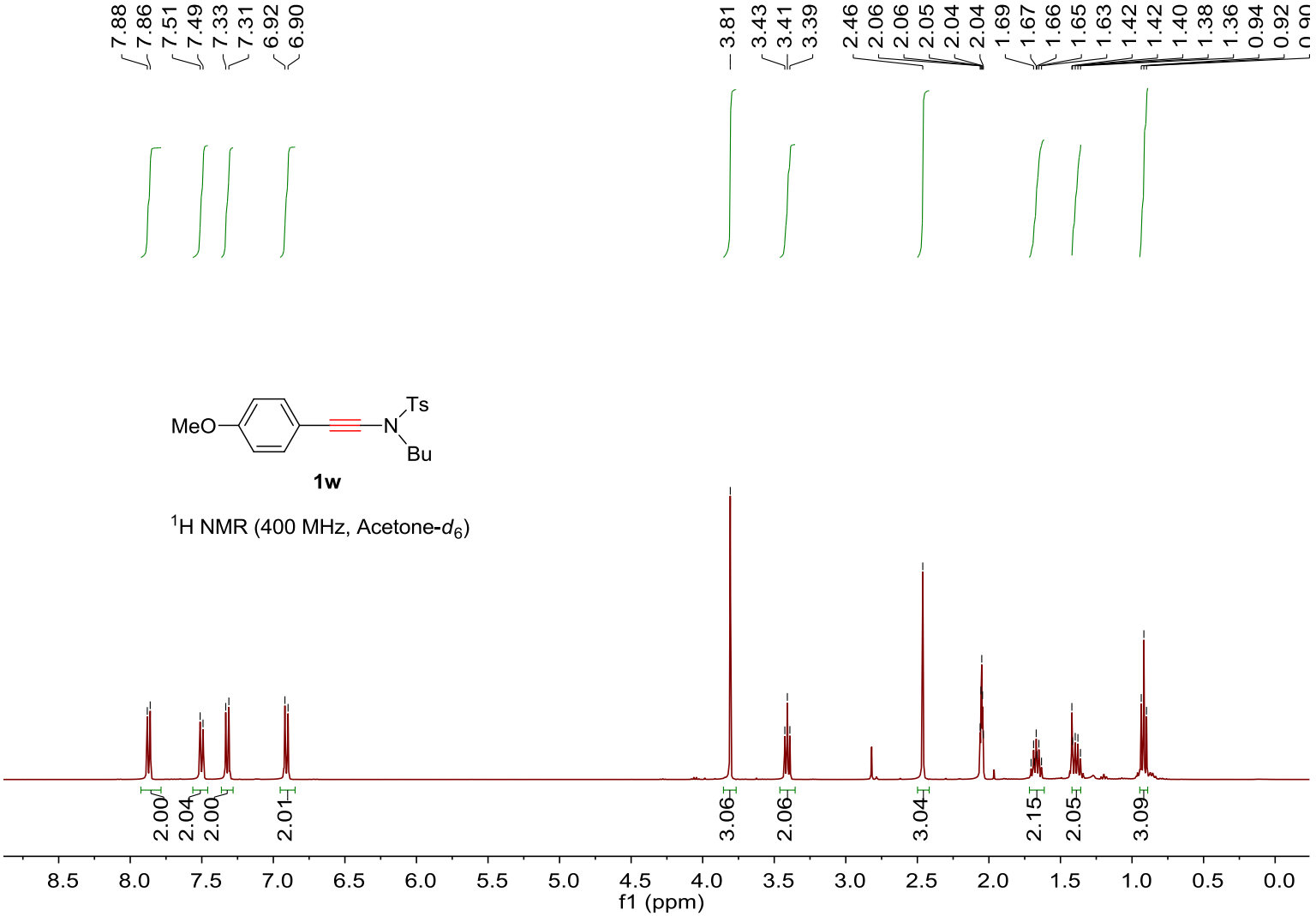

7.76
7.74
7.42
7.40
7.33
7.31
7.24
7.22
7.18
7.16
7.10
7.09
7.08
6.94
6.93
6.93
6.92
6.92
6.91
4.51
2.45
1.60
Ts
N
S
1u
Br
1H NMR (400 MHz, CDCl3)
2.01
2.00
2.01
1.22
2.01
0.98
1.01
2.02
3.00
f1 (ppm)

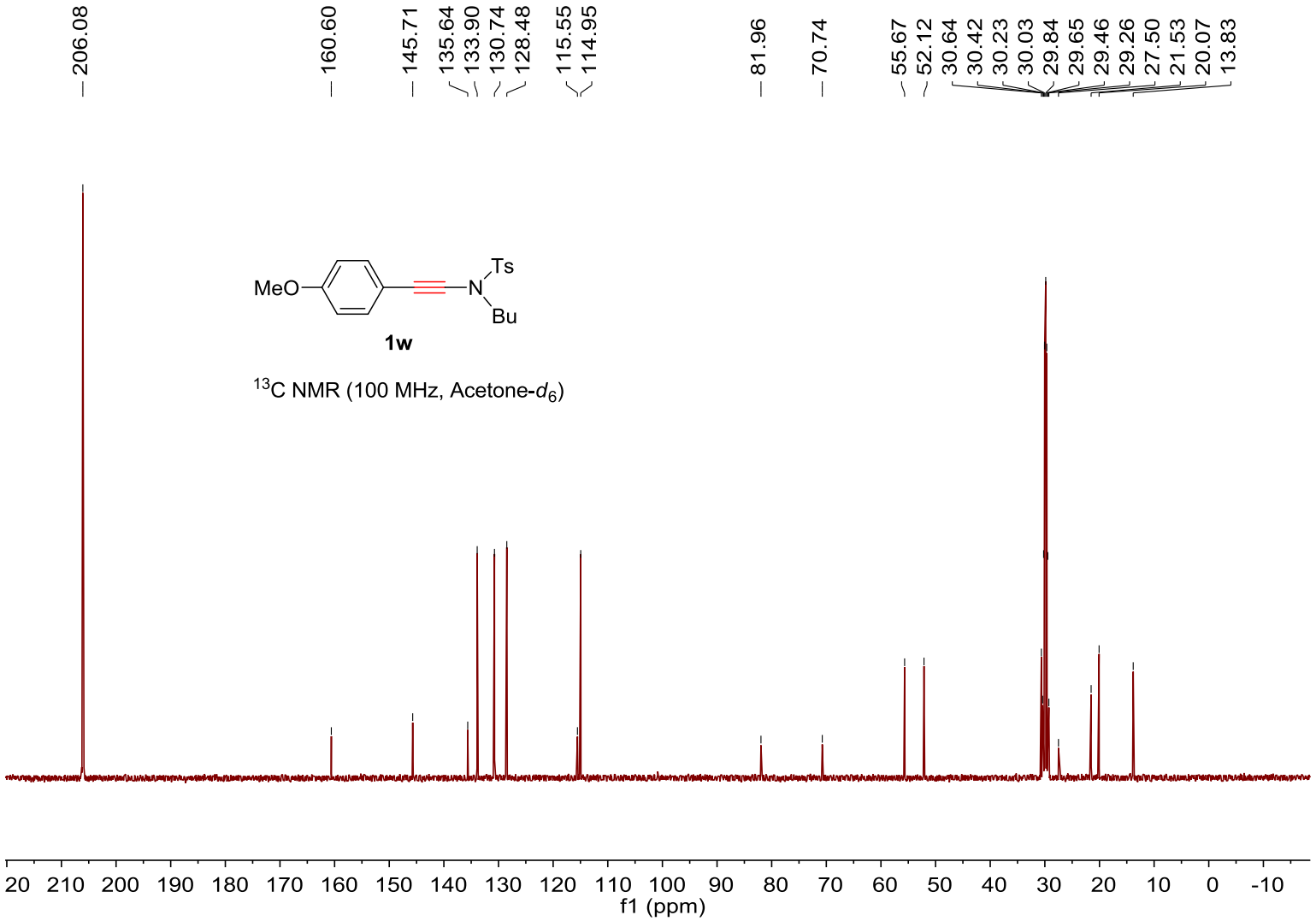

145.04
134.51
133.51
133.18
131.78
130.50
129.92
128.02
127.76
127.10
122.58
122.53
85.97
77.48
77.16
76.84
64.89
55.25
21.83
Ts
N
S
1u
Br
13C NMR (100 MHz, CDCl3)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.30 8.28 7.96 7.95 7.94 7.94 7.93 7.93 7.92 7.90 7.61 7.61 7.60 7.59 7.59 7.58 7.57 7.56 7.56 7.55 7.54 7.54 7.53 7.53 7.51 7.51 7.49 7.46 7.44 7.42 7.38 7.38 7.37 7.37 7.01 7.01 7.00 7.00 6.95 6.94 6.93 6.93 5.07 2.46 2.06 2.06 2.05 2.04 2.04
Ts
N
S
1v
1H NMR (400 MHz, Acetone-d6)
1.00 4.04 5.15 1.03 0.93 0.95 0.98 2.05 3.00
9.5 9.0 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 -0.5
f1 (ppm)

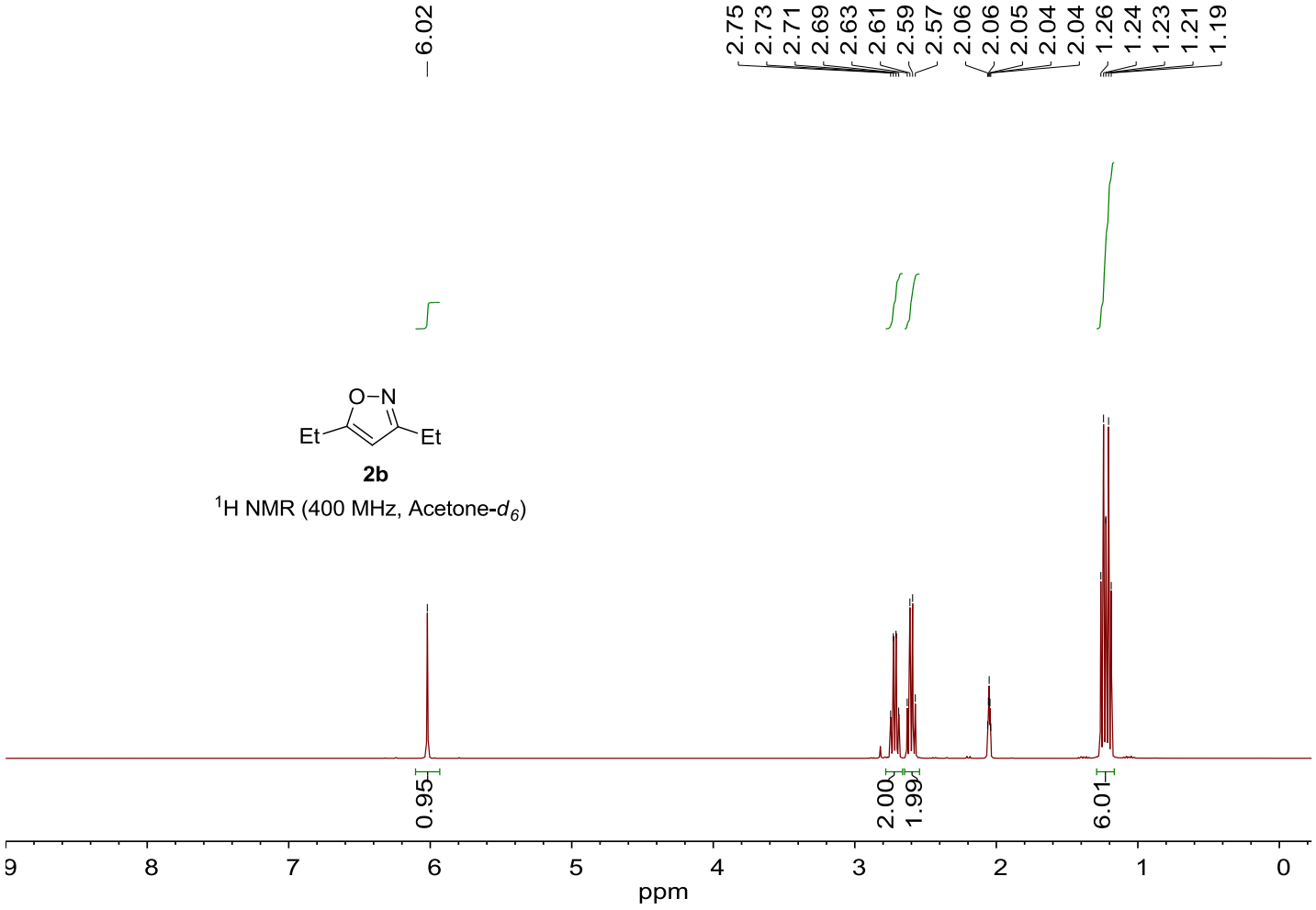


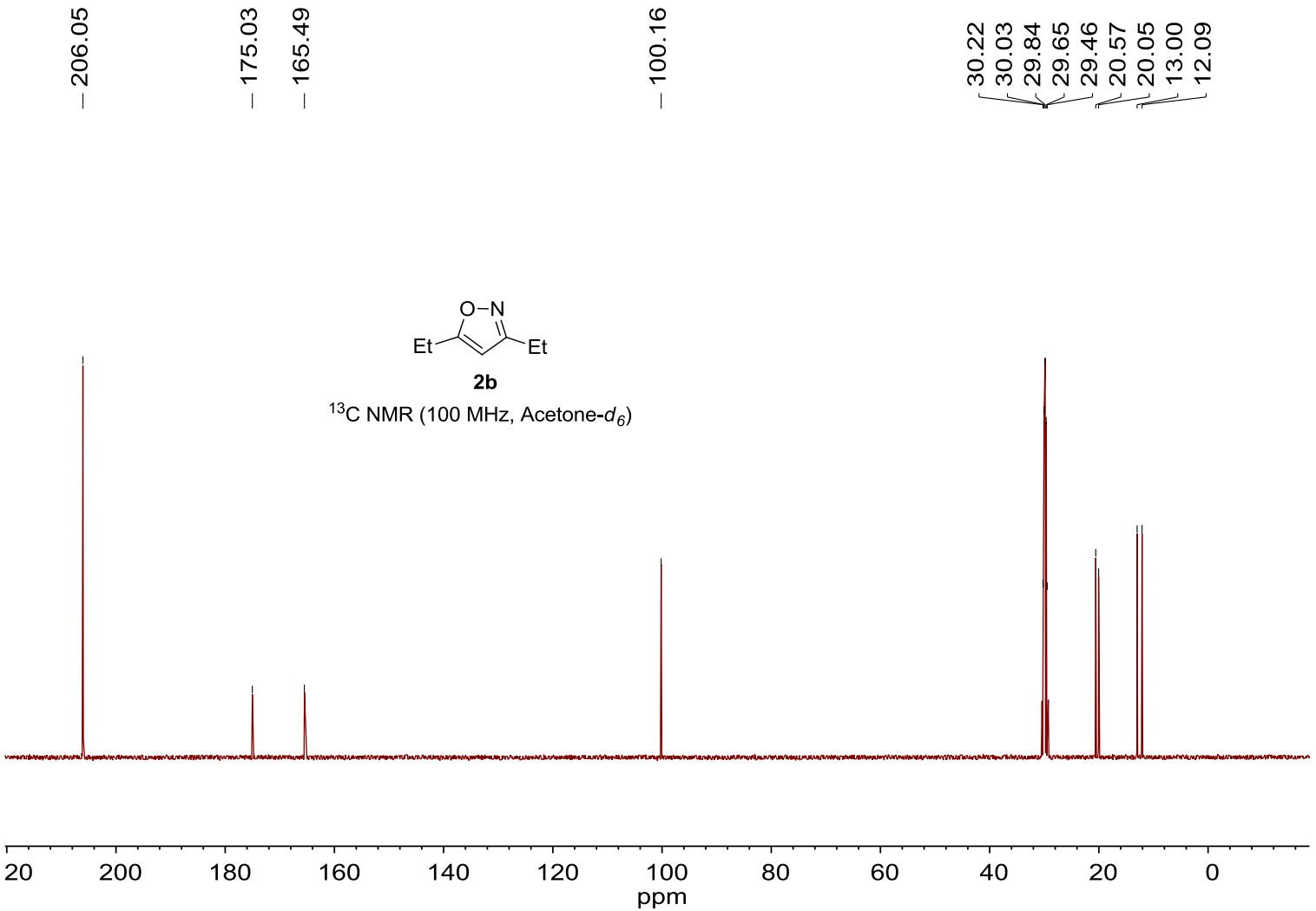
^{13}C NMR (100 MHz, Acetone-d_6)


7.88
7.86
7.51
7.49
7.33
7.31
6.92
6.90
3.81
3.43
3.41
3.39
2.46
2.06
2.06
2.05
2.04
2.04
1.69
1.67
1.66
1.65
1.63
1.42
1.42
1.40
1.38
1.36
0.94
0.92
MeO
N
Ts
Bu
1w
^{1}H NMR (400 MHz, Acetone-d_6)
2.00
2.04
2.00
2.01
3.06
2.06
3.04
2.15
2.05
3.09
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
f1 (ppm)

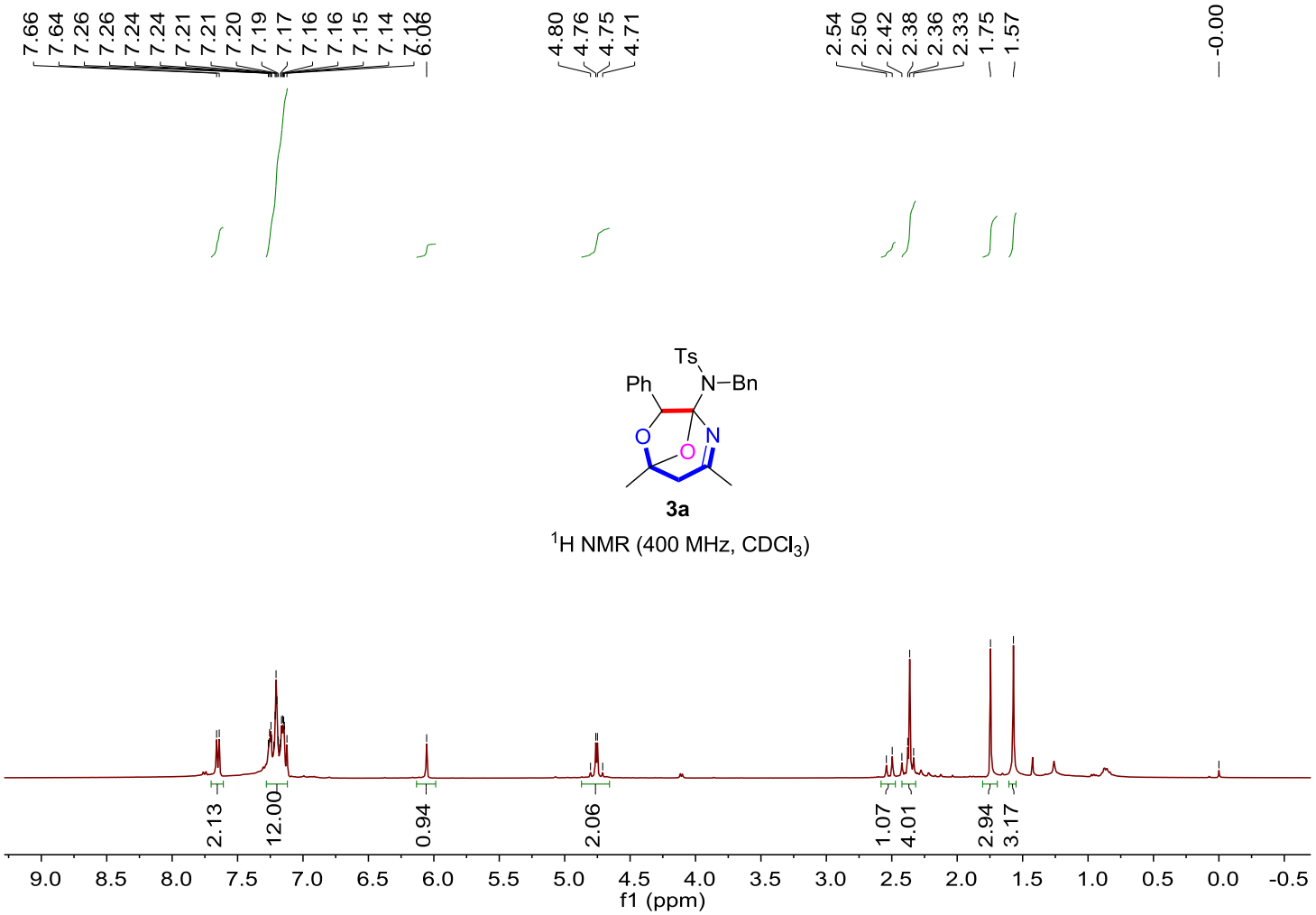

206.08
160.60
145.71
135.64
133.90
130.74
128.48
115.55
114.95
81.96
70.74
55.67
52.12
30.64
30.42
30.23
30.03
29.84
29.65
29.46
29.26
27.50
21.53
20.07
13.83
MeO
N
Ts
Bu
1w
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

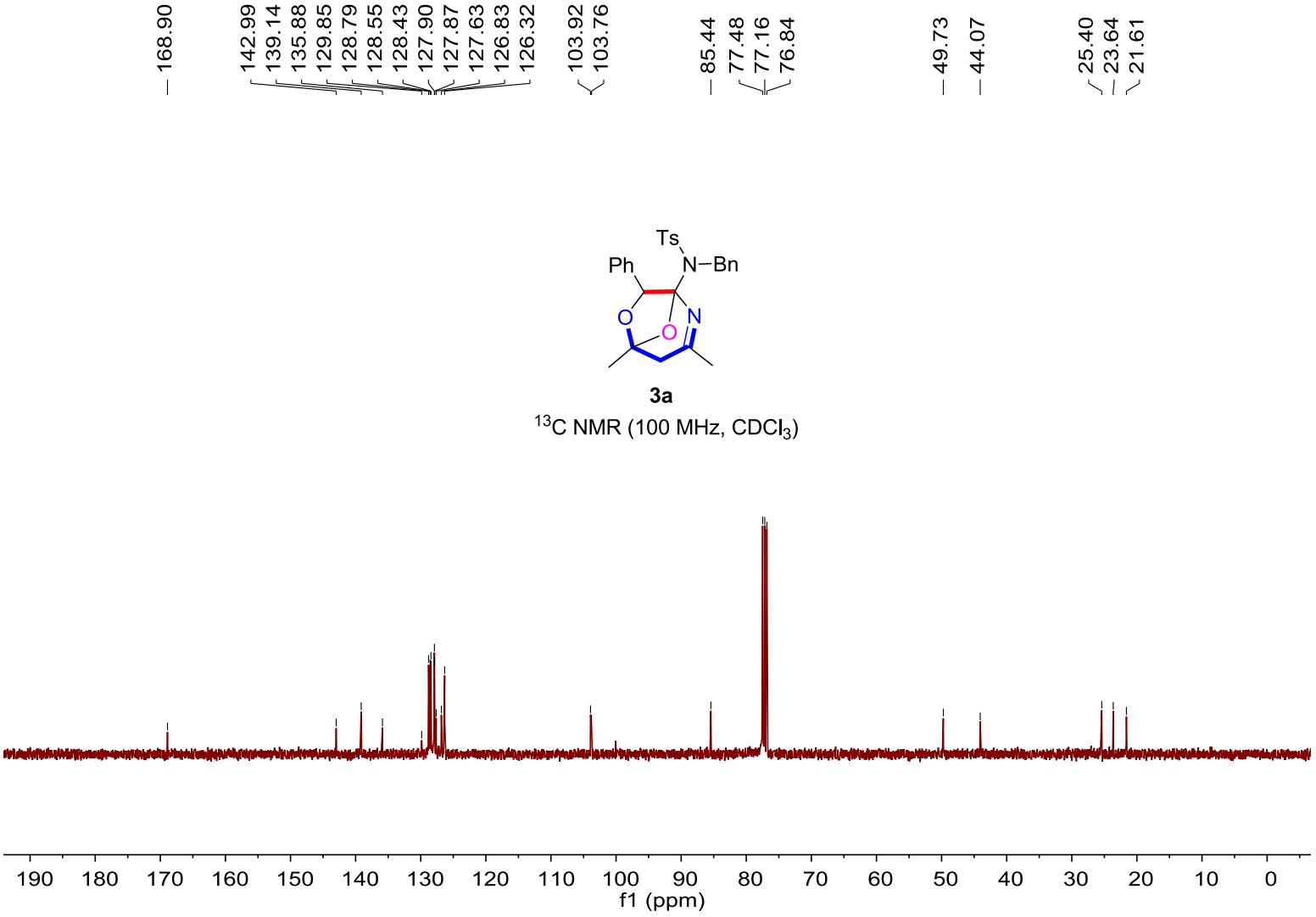
13. NMR spectroscopy of isoxazole 2b




206.05
175.03
165.49
100.16
30.22
30.03
29.84
29.65
29.46
20.57
20.05
13.00
12.09
O–N
Et
Et
2b
13C NMR (100 MHz, Acetone-d6)
20
200
180
160
140
120
100
80
60
40
20
0
ppm

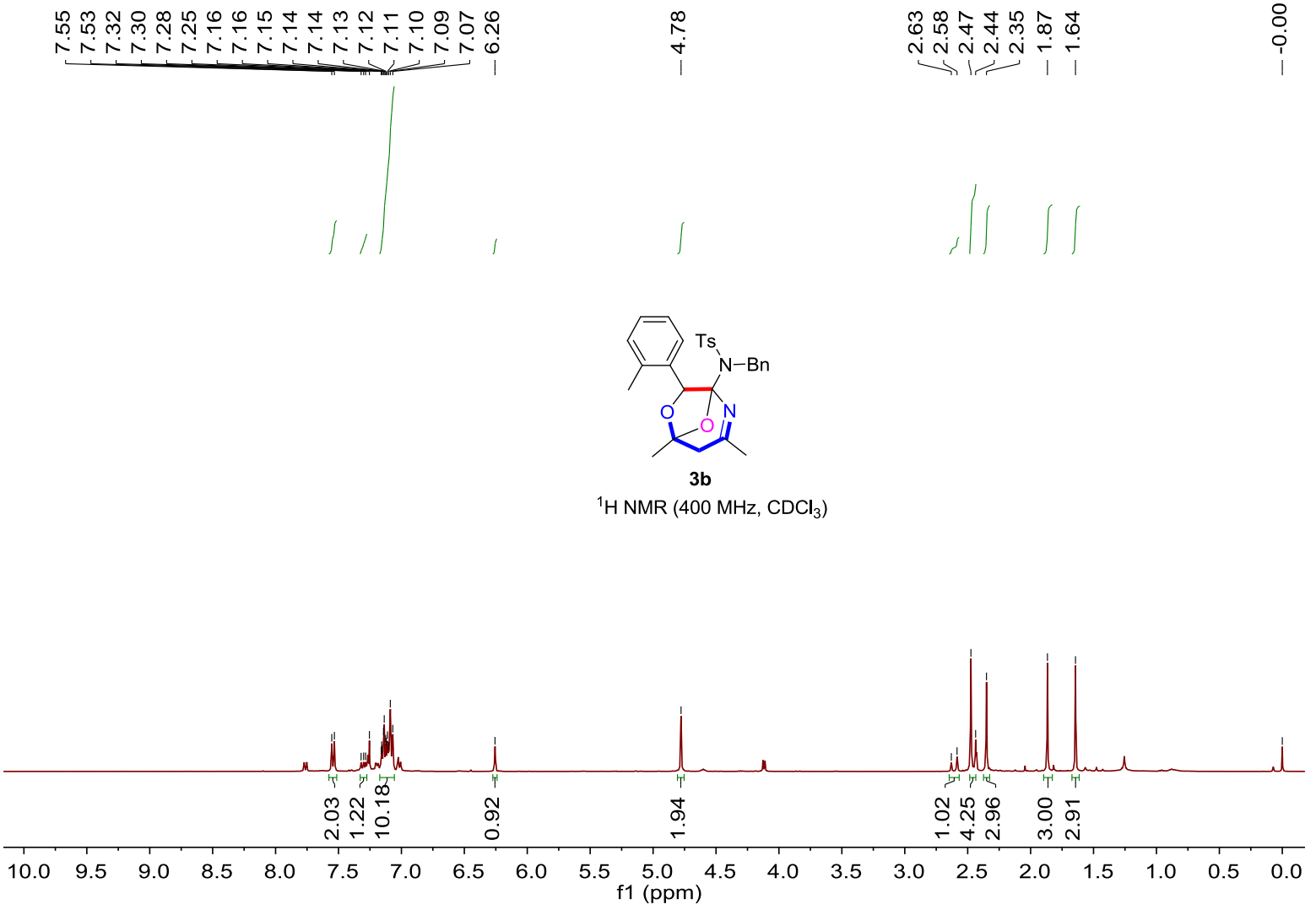
14. NMR spectroscopy of *O*-bridged tetrahydro-1,4-oxazepines





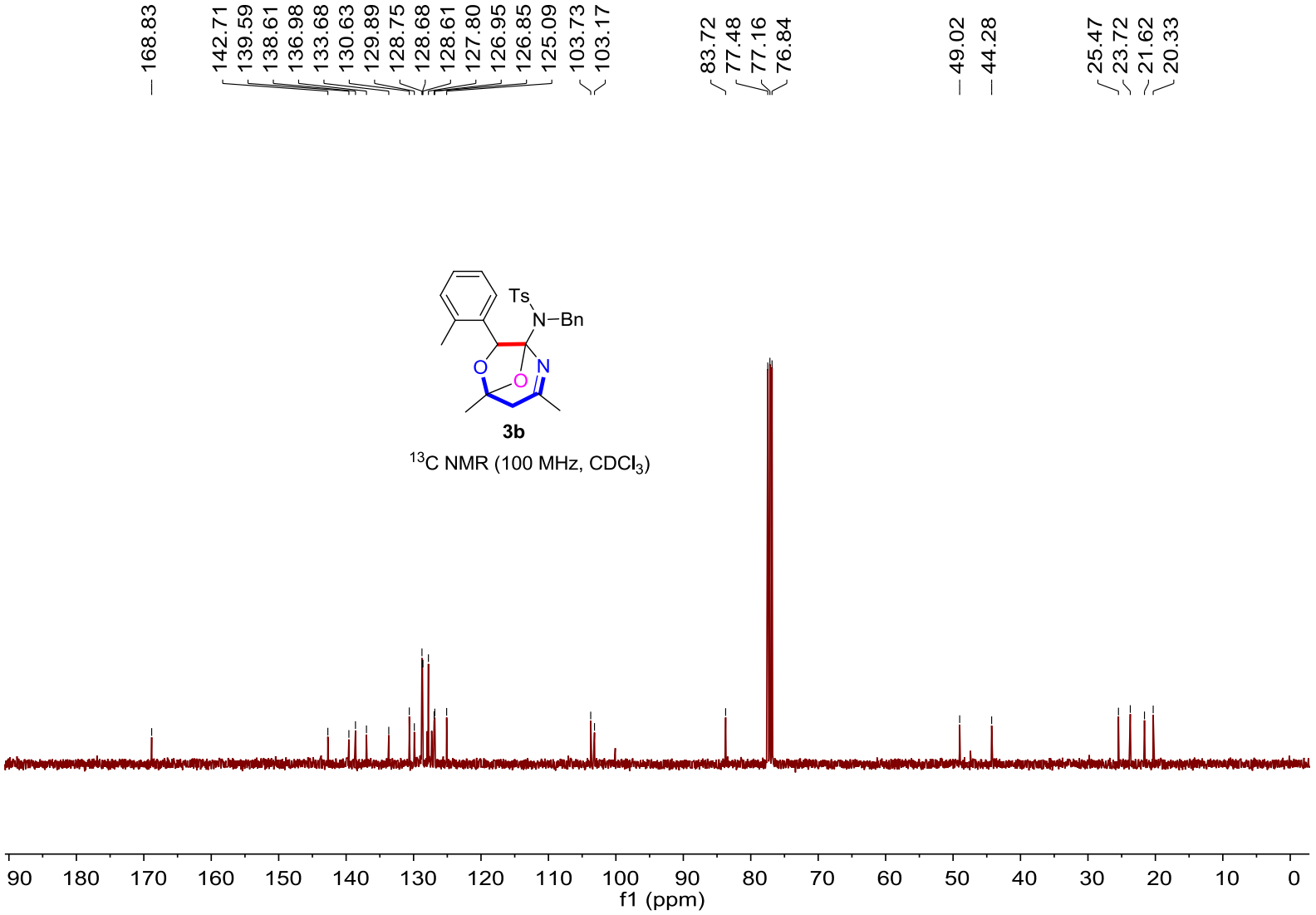
3a

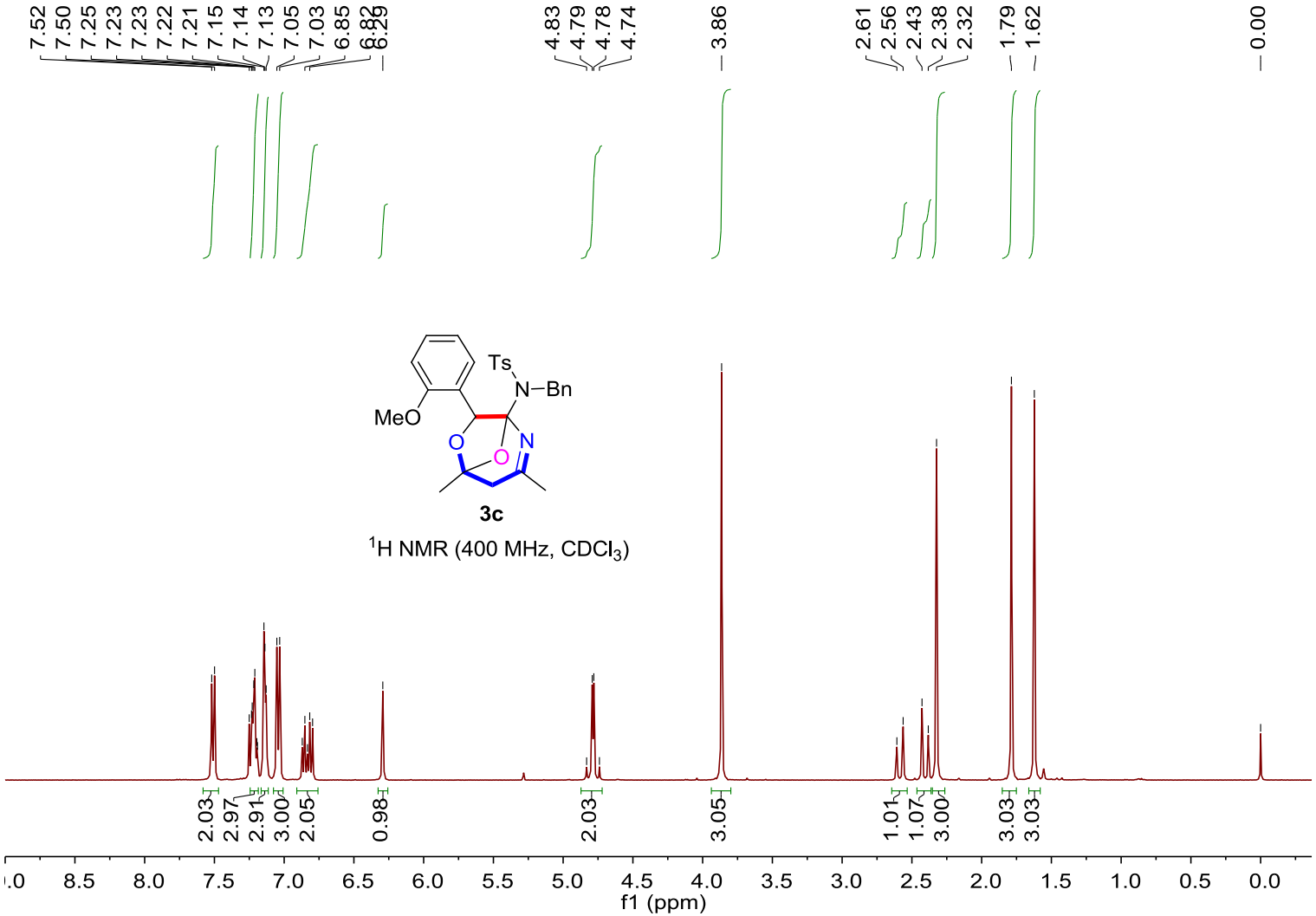
^{13}C NMR (100 MHz, $CDCl_3$)

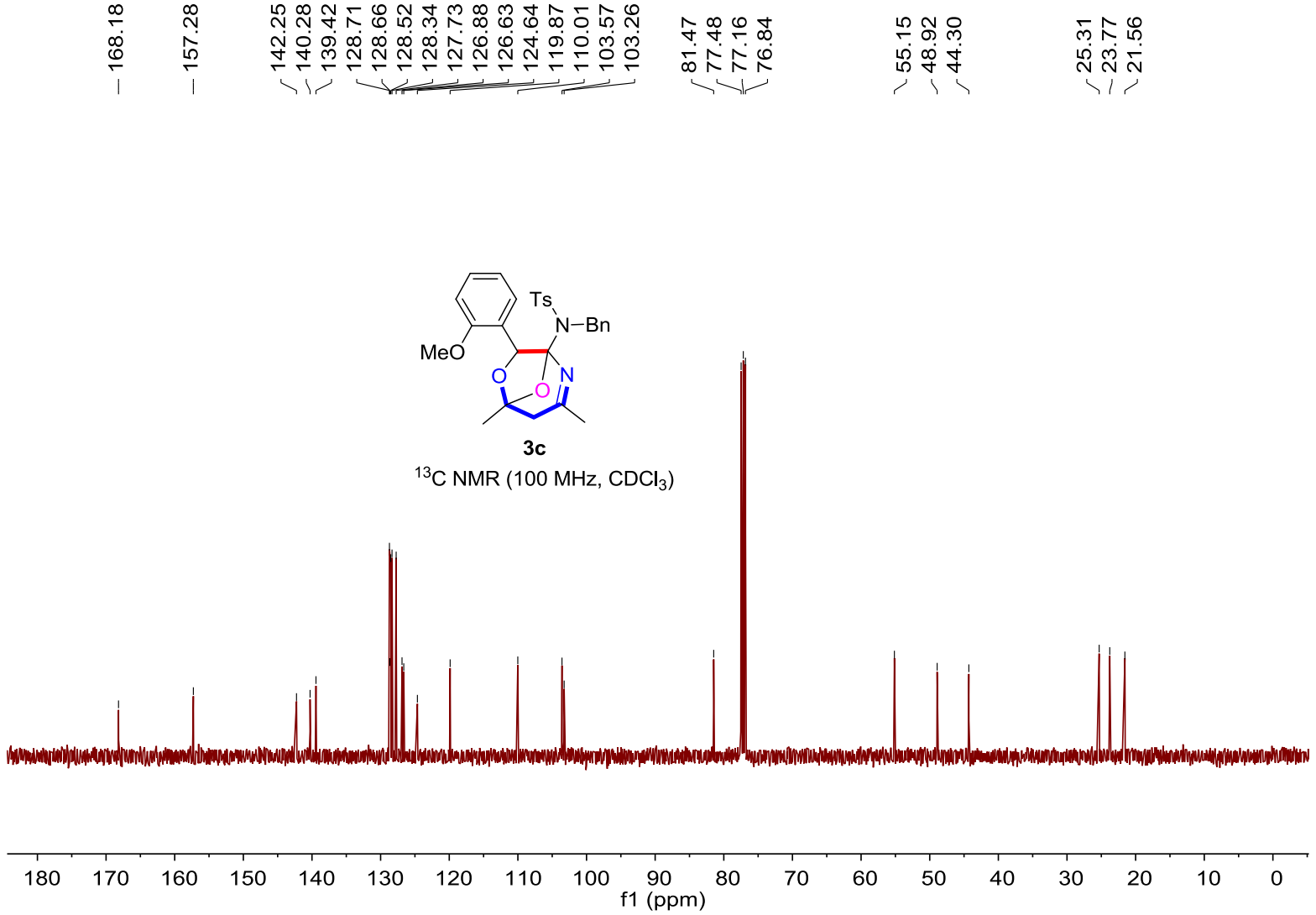


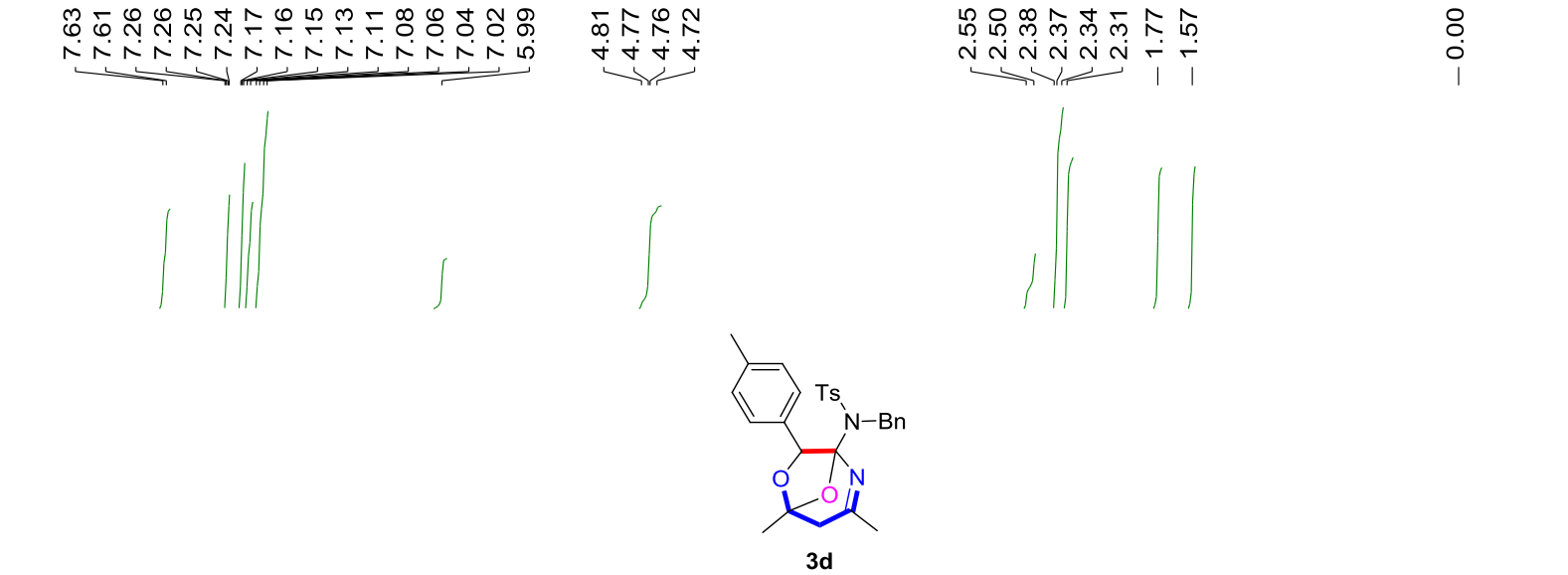
3b

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


168.83
142.71
139.59
138.61
136.98
133.68
130.63
129.89
128.75
128.68
128.61
127.80
126.95
126.85
125.09
103.73
103.17
83.72
77.48
77.16
76.84
49.02
44.28
25.47
23.72
21.62
20.33
Ts
N–Bn
O
O
N
3b
13C NMR (100 MHz, CDCl3)
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

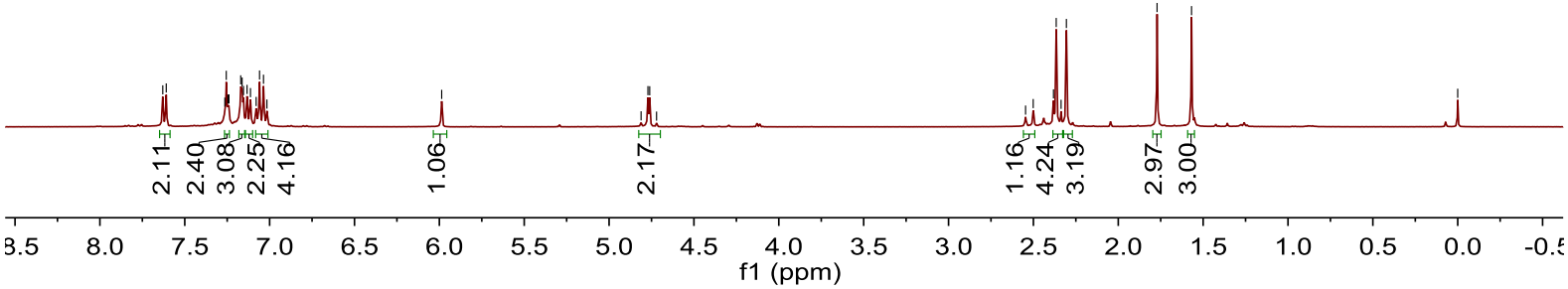

7.52
7.50
7.25
7.23
7.23
7.22
7.21
7.15
7.14
7.13
7.05
7.03
6.85
6.82
6.29
4.83
4.79
4.78
4.74
3.86
2.61
2.56
2.43
2.38
2.32
1.79
1.62
0.00
Ts
N–Bn
MeO
O
O
N
3c
1H NMR (400 MHz, CDCl3)
2.03
2.97
2.91
3.00
2.05
0.98
2.03
3.05
1.01
1.07
3.00
3.03
3.03
f1 (ppm)

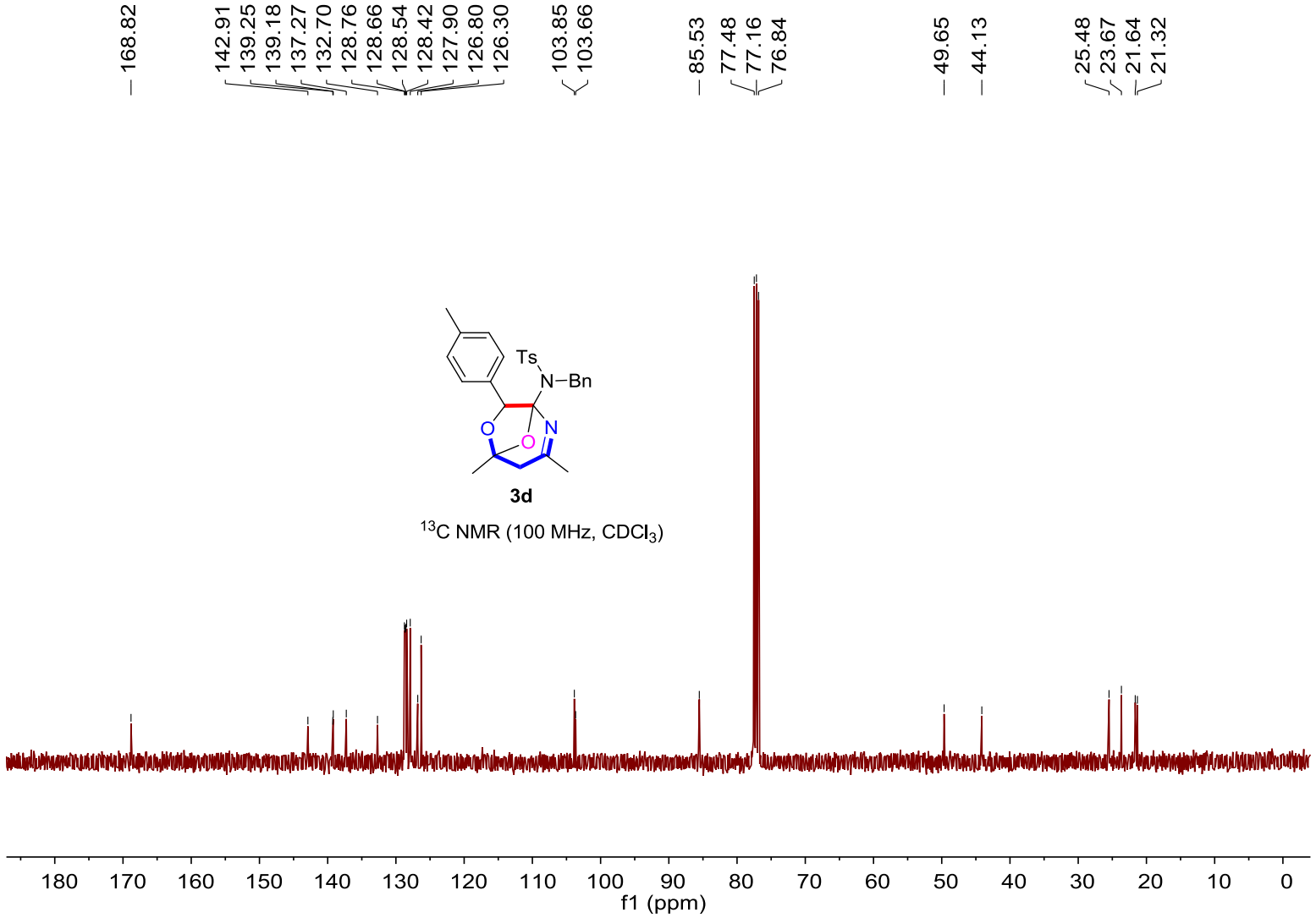

168.18
157.28
142.25
140.28
139.42
128.71
128.66
128.52
128.34
127.73
126.88
126.63
124.64
119.87
110.01
103.57
103.26
81.47
77.48
77.16
76.84
55.15
48.92
44.30
25.31
23.77
21.56
Ts
N–Bn
MeO
O
O
N
3c
13C NMR (100 MHz, CDCl3)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

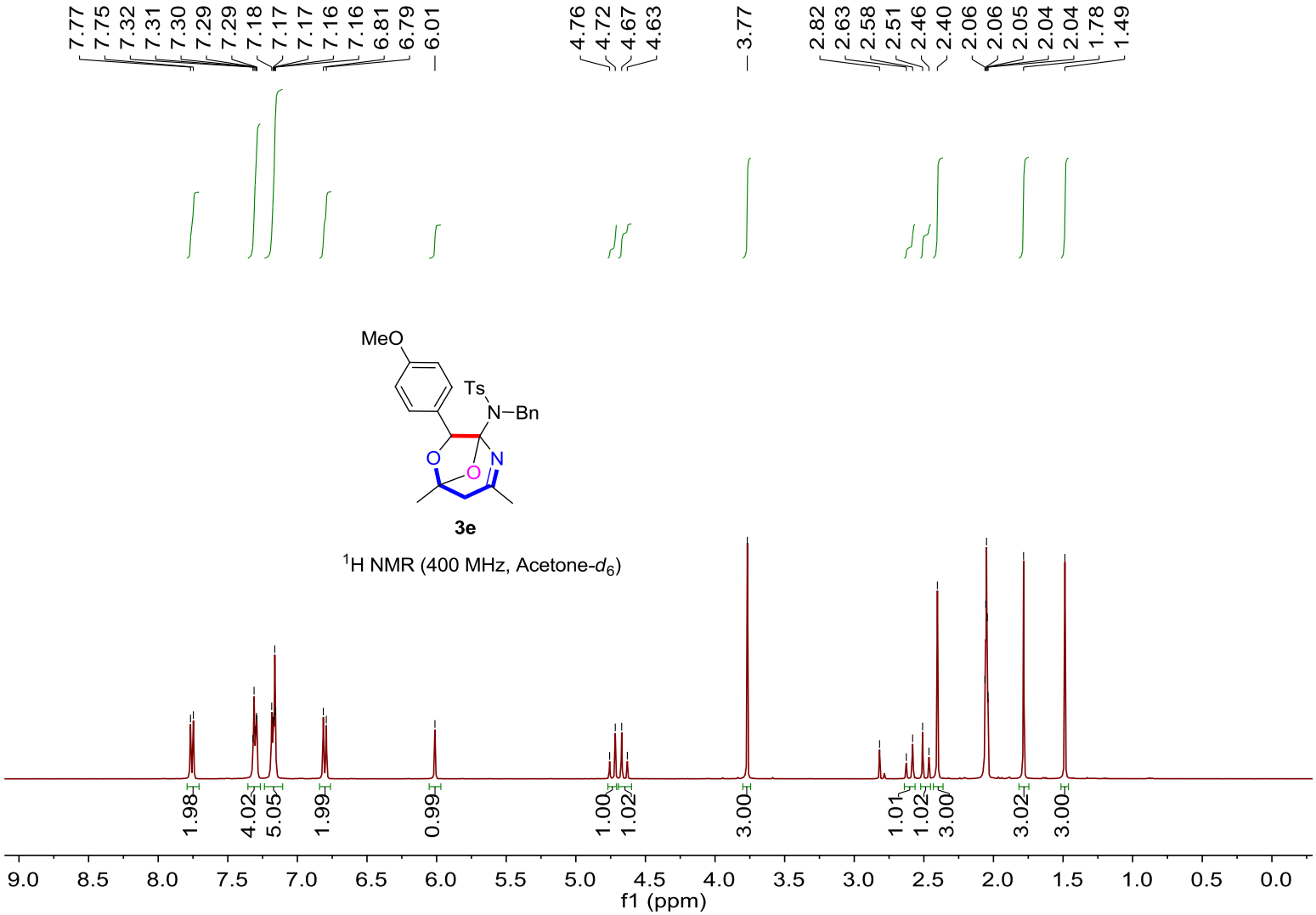


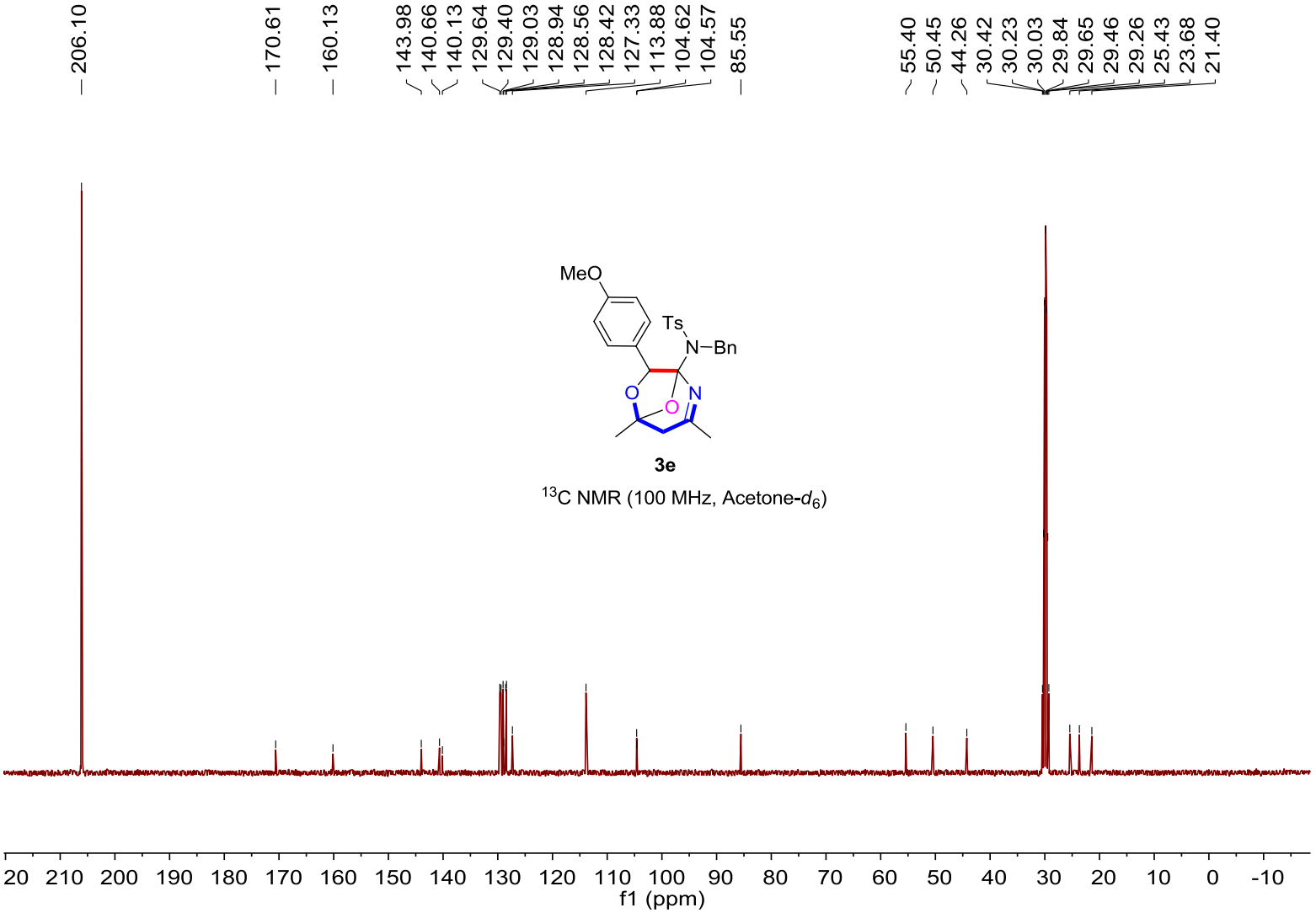
3d

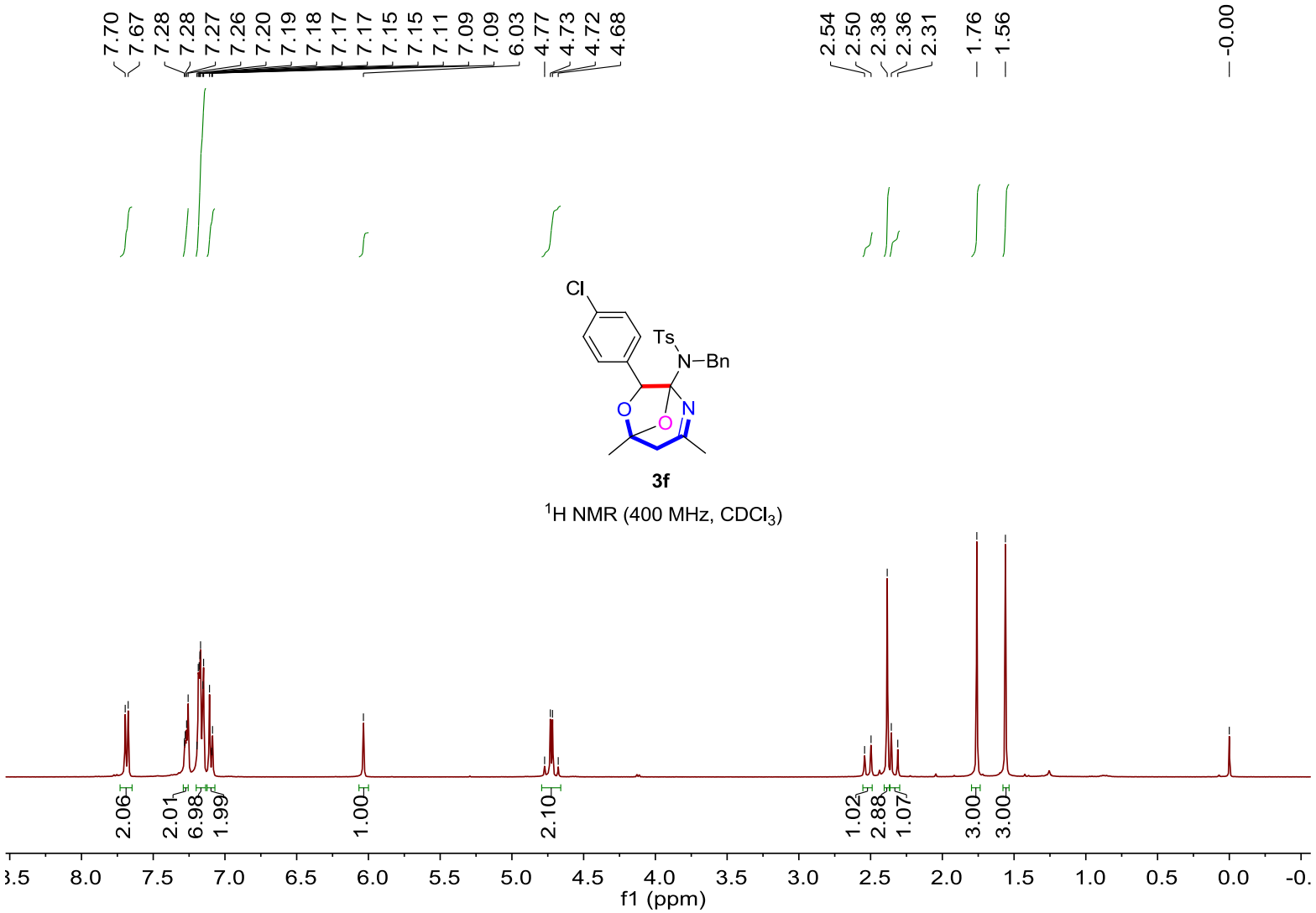
^{1}H NMR (400 MHz, $CDCl_3$)




168.82
142.91
139.25
139.18
137.27
132.70
128.76
128.66
128.54
128.42
127.90
126.80
126.30
103.85
103.66
85.53
77.48
77.16
76.84
49.65
44.13
25.48
23.67
21.64
21.32
Ts
N–Bn
O
O
N
3d
13C NMR (100 MHz, CDCl3)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

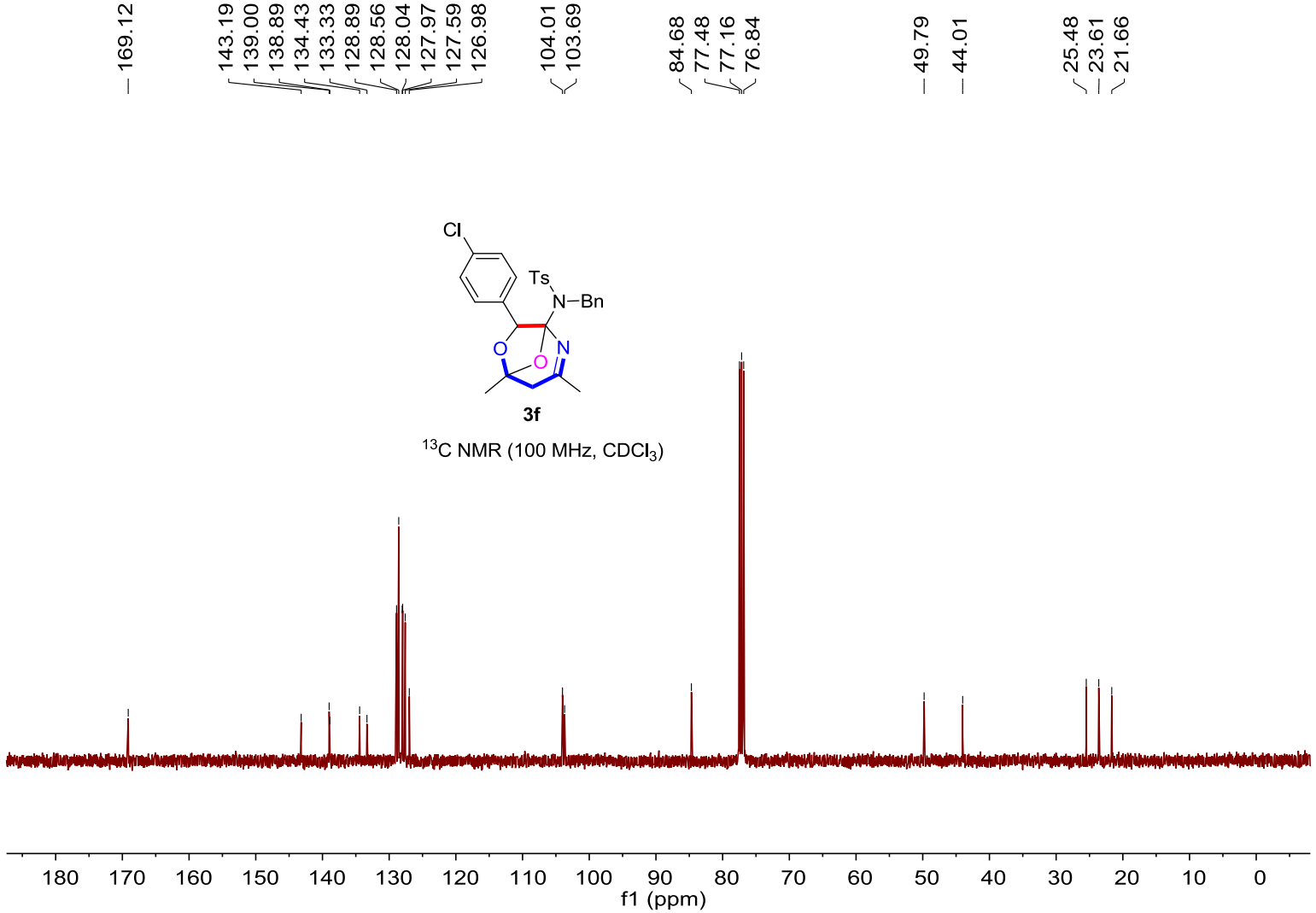

7.77
7.75
7.32
7.31
7.30
7.29
7.29
7.18
7.17
7.17
7.16
7.16
6.81
6.79
6.01
4.76
4.72
4.67
4.63
3.77
2.82
2.63
2.58
2.51
2.46
2.40
2.06
2.06
2.05
2.04
2.04
1.78
1.49
MeO
Ts
N–Bn
O
O
N
3e
1H NMR (400 MHz, Acetone-d6)
1.98
4.02
5.05
1.99
0.99
1.00
1.02
3.00
1.01
1.02
3.00
3.02
3.00
9.0
8.5
8.0
7.5
7.0
6.5
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
f1 (ppm)

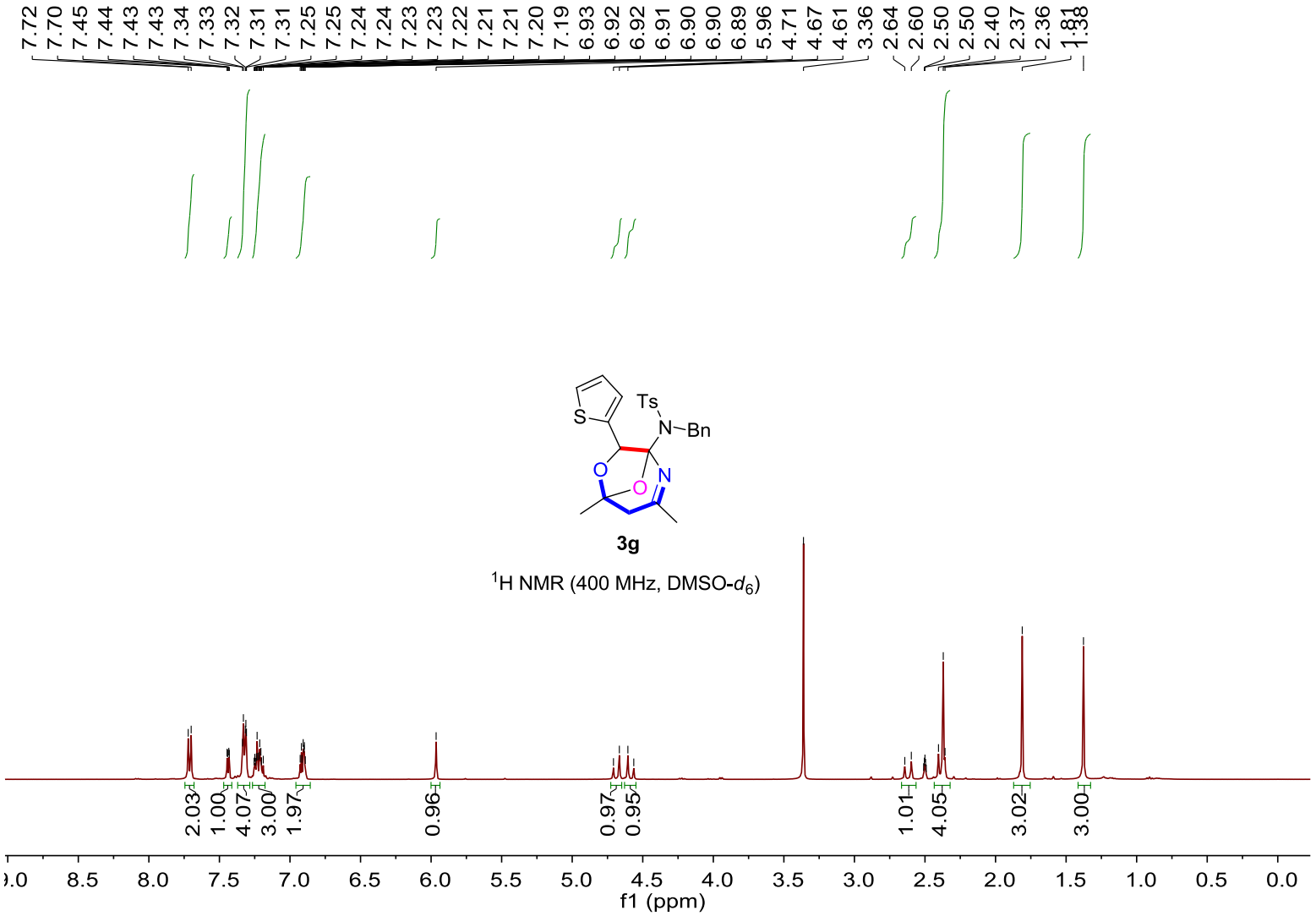

206.10
170.61
160.13
143.98
140.66
140.13
129.64
129.40
129.03
128.94
128.56
128.42
127.33
113.88
104.62
104.57
85.55
55.40
50.45
44.26
30.42
30.23
30.03
29.84
29.65
29.46
29.26
25.43
23.68
21.40
MeO
Ts
N–Bn
O
O
N
3e
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

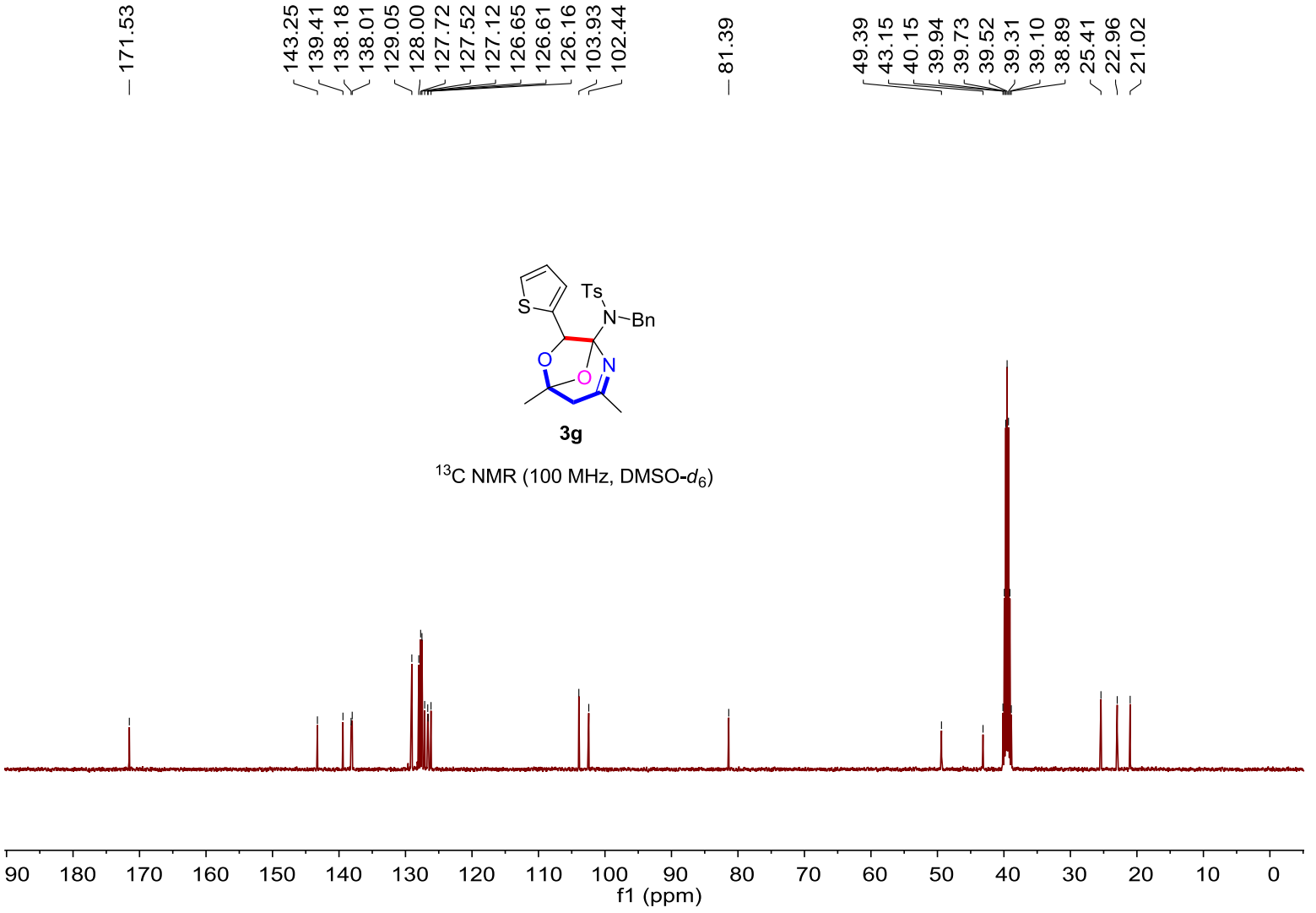


3f

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

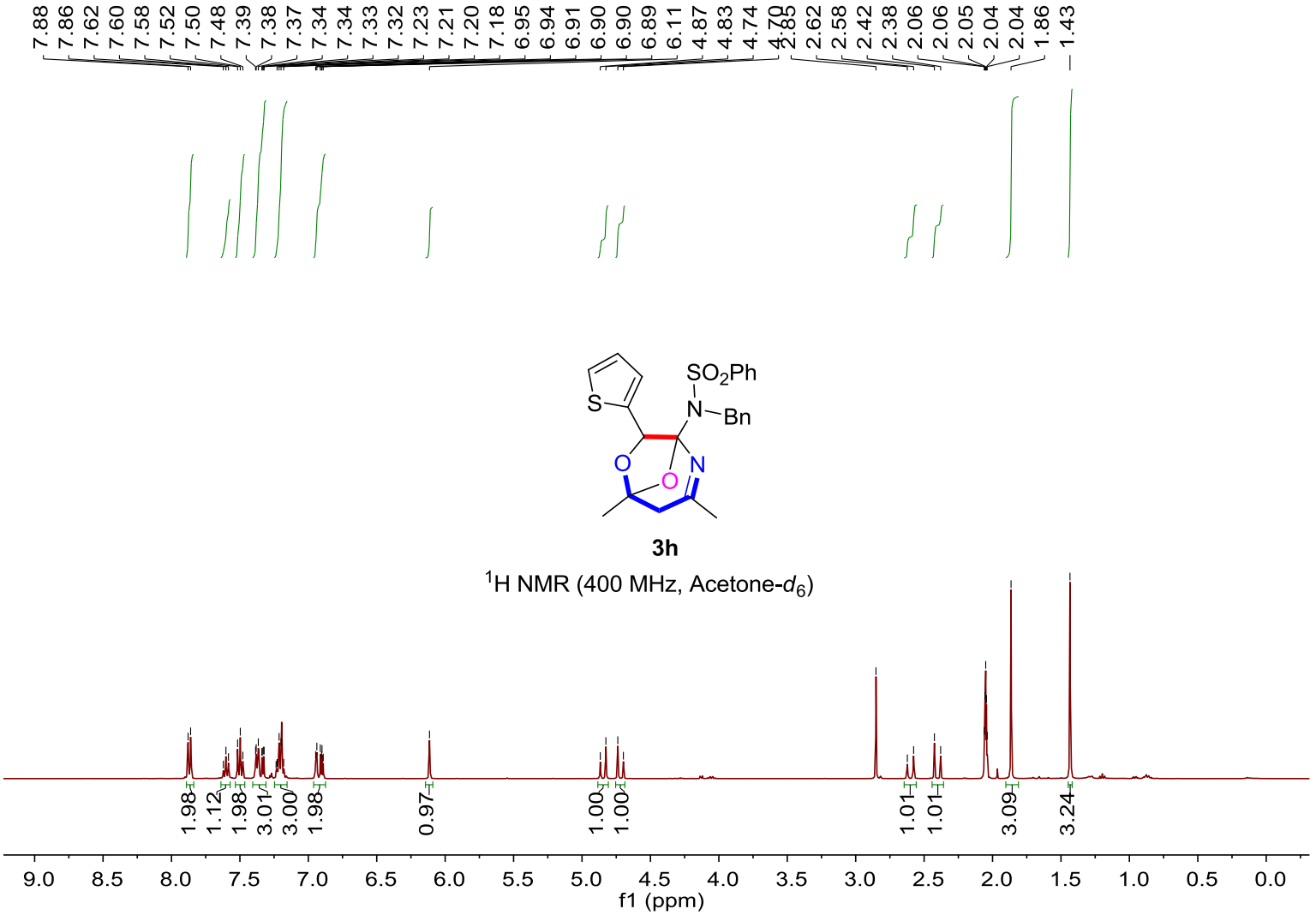

169.12
143.19
139.00
138.89
134.43
133.33
128.89
128.56
128.04
127.97
127.59
126.98
104.01
103.69
84.68
77.48
77.16
76.84
49.79
44.01
25.48
23.61
21.66
Cl
Ts
N–Bn
O
O
N
3f
13C NMR (100 MHz, CDCl3)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

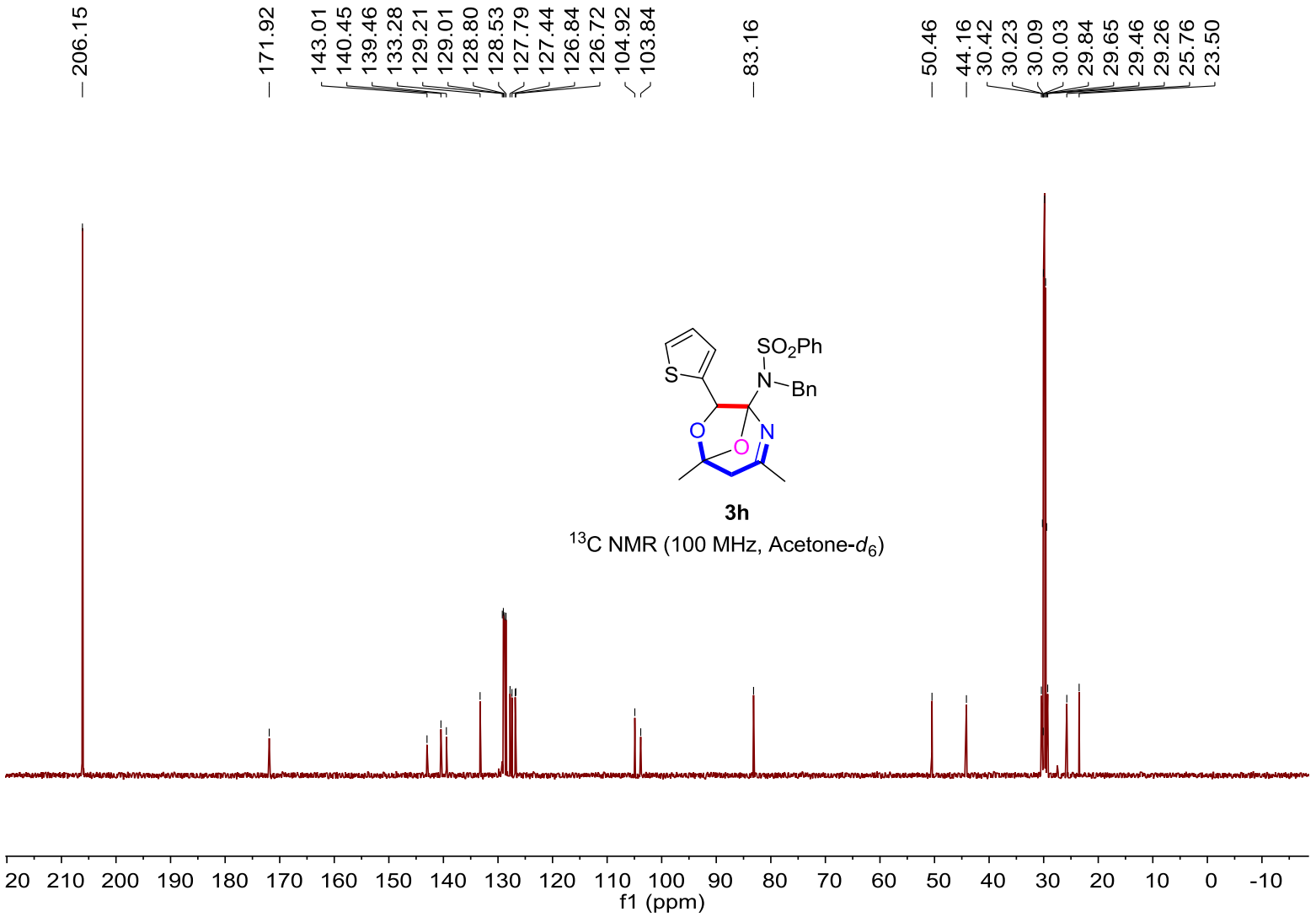

7.72
7.70
7.45
7.44
7.43
7.43
7.34
7.33
7.32
7.31
7.31
7.25
7.25
7.24
7.24
7.23
7.23
7.22
7.21
7.21
7.20
7.19
6.93
6.92
6.92
6.91
6.90
6.90
6.89
5.96
4.71
4.67
4.61
3.36
2.64
2.60
2.50
2.50
2.40
2.37
2.36
1.81
1.38
S
Ts
N
Bn
O
O
N
3g
1H NMR (400 MHz, DMSO-d6)
2.03
1.00
4.07
3.00
1.97
0.96
0.97
0.95
1.01
4.05
3.02
3.00
9.0
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
f1 (ppm)

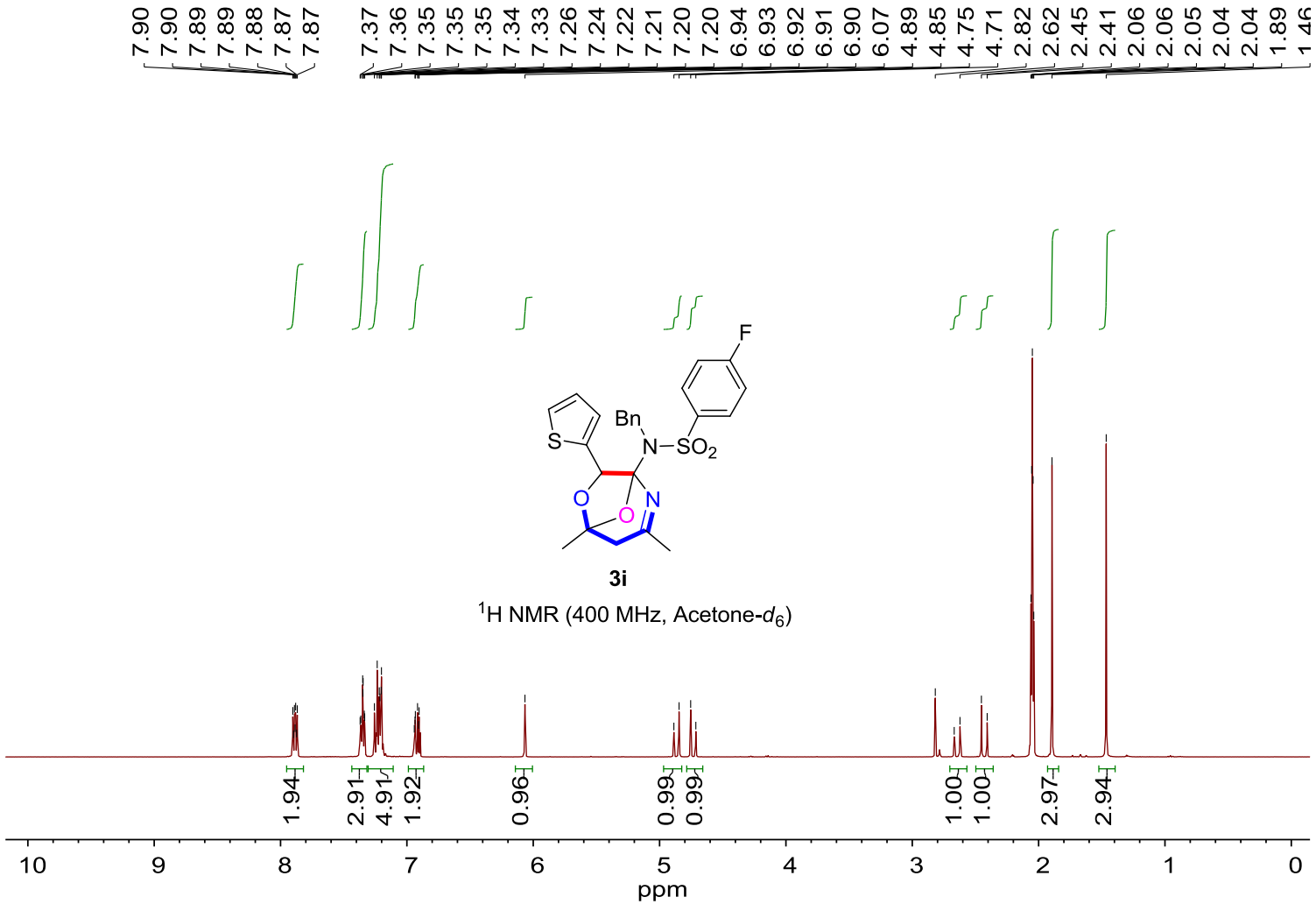


3g

^{13}C NMR (100 MHz, DMSO-d_6)

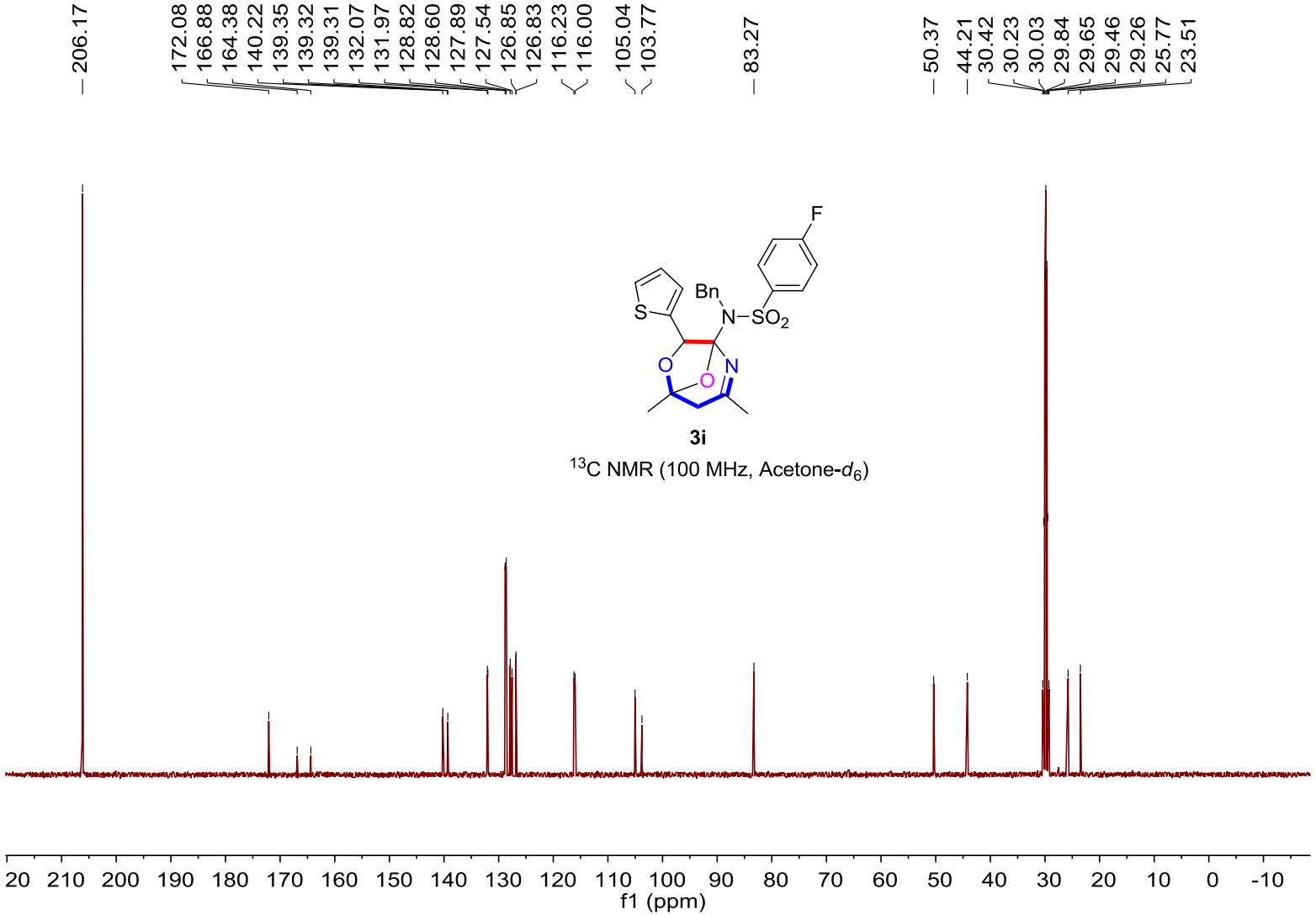

7.88
7.86
7.62
7.60
7.58
7.52
7.50
7.48
7.39
7.38
7.37
7.34
7.34
7.33
7.32
7.23
7.21
7.20
7.18
6.95
6.94
6.91
6.90
6.90
6.89
6.11
4.87
4.83
4.74
4.70
2.85
2.62
2.58
2.42
2.38
2.06
2.06
2.05
2.04
2.04
1.86
1.43
SO2Ph
N
Bn
S
O
O
N
3h
1H NMR (400 MHz, Acetone-d6)
1.98
1.12
1.98
3.01
3.00
1.98
0.97
1.00
1.00
1.01
1.01
3.09
3.24
9.0
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
f1 (ppm)


206.15
171.92
143.01
140.45
139.46
133.28
129.21
129.01
128.80
128.53
127.79
127.44
126.84
126.72
104.92
103.84
83.16
50.46
44.16
30.42
30.23
30.09
30.03
29.84
29.65
29.46
29.26
25.76
23.50
SO2Ph
N
Bn
S
O
O
N
3h
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



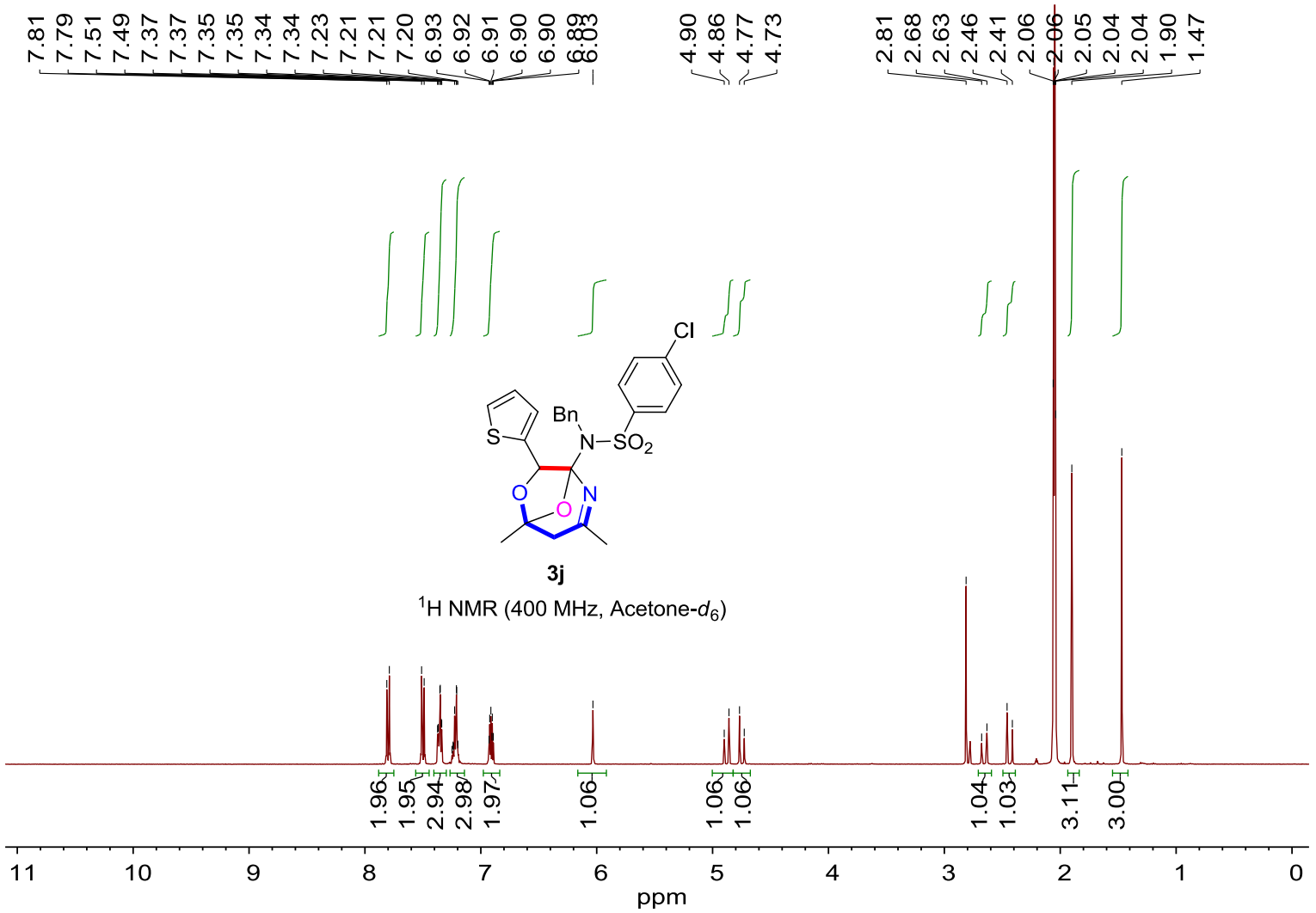
3i

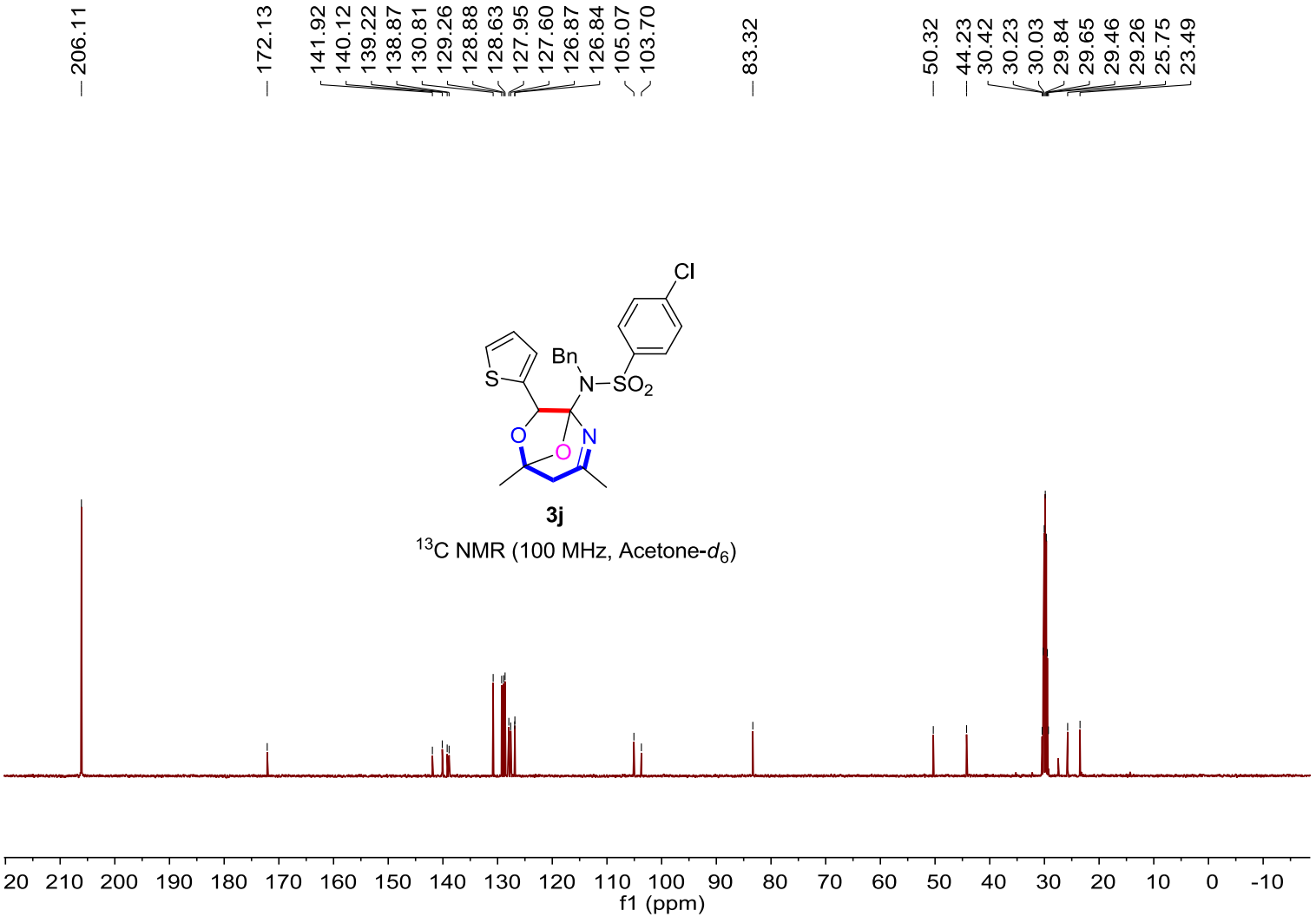
^{1}H NMR (400 MHz, Acetone-d_6)

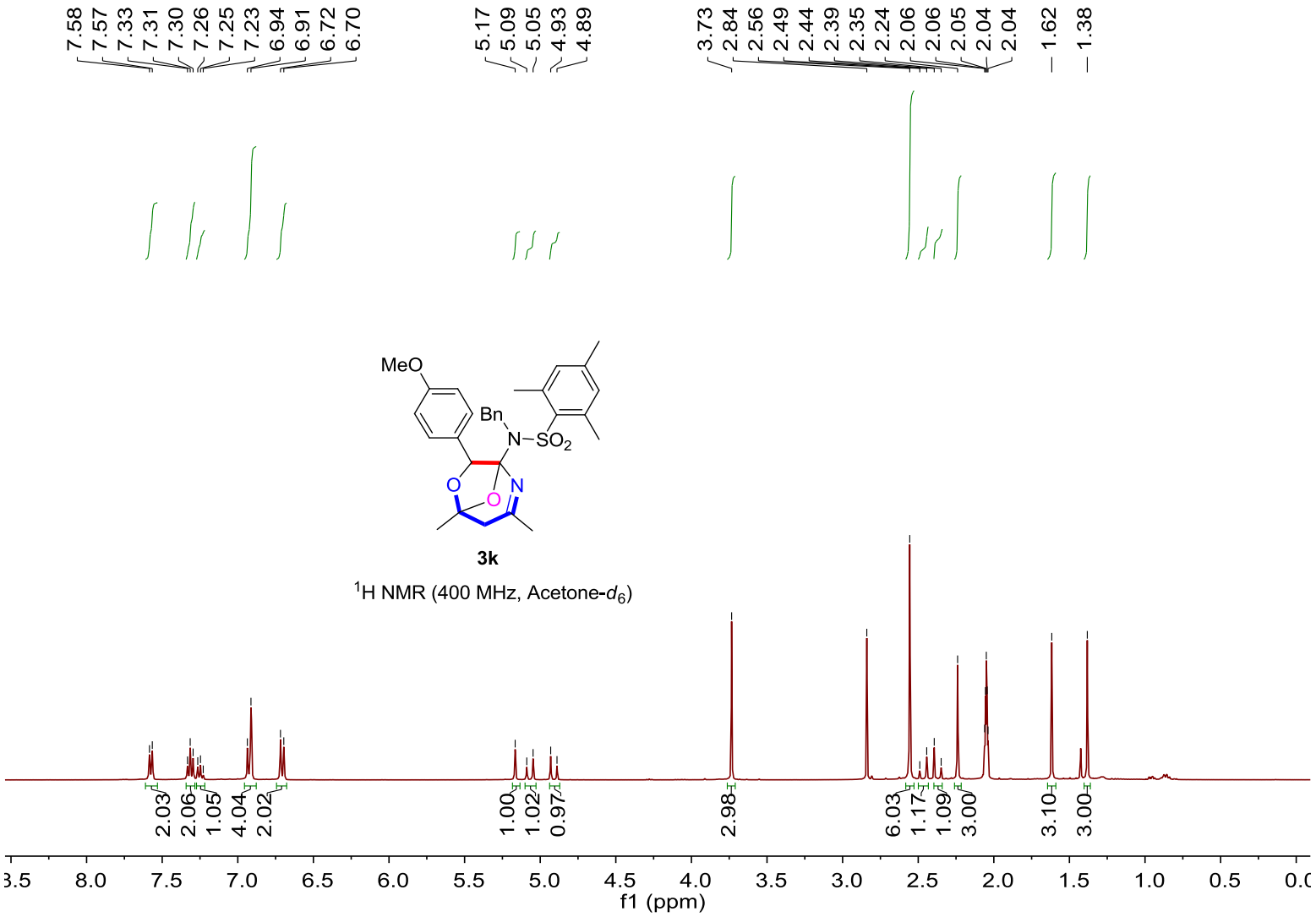


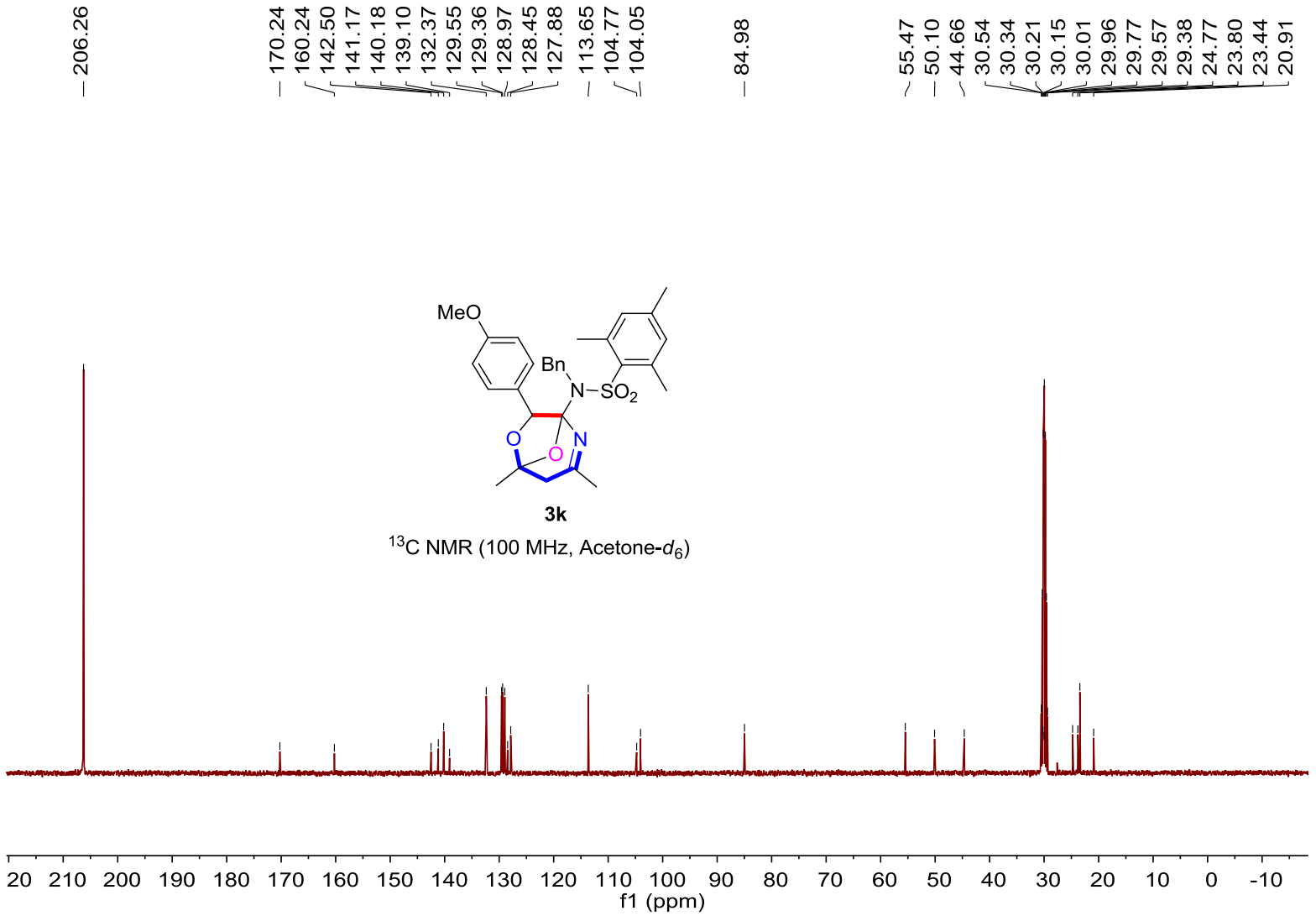
3i

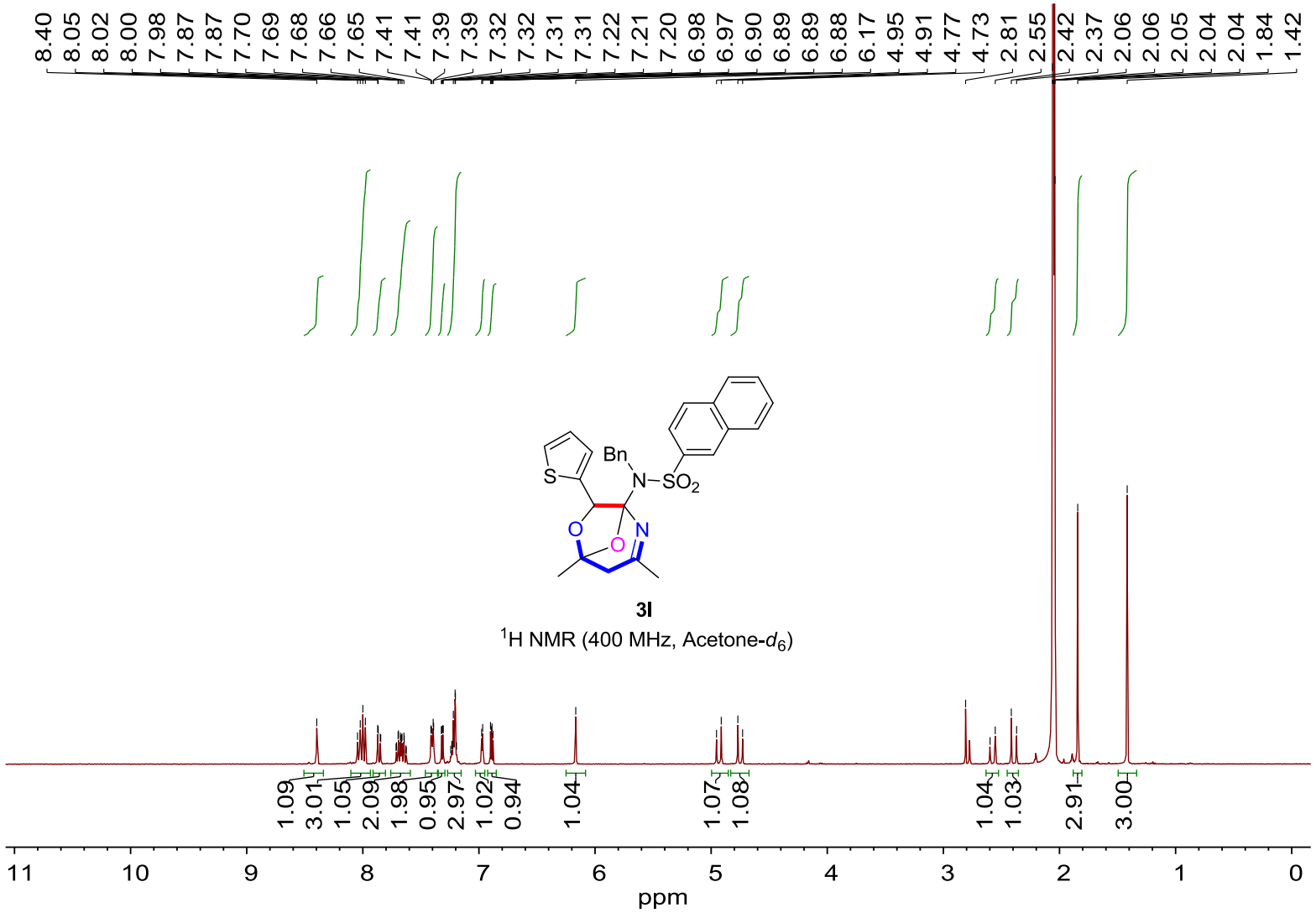
^{13}C NMR (100 MHz, Acetone-d_6)


7.81
7.79
7.51
7.49
7.37
7.37
7.35
7.35
7.34
7.34
7.23
7.21
7.21
7.20
6.93
6.92
6.91
6.90
6.90
6.89
6.83
4.90
4.86
4.77
4.73
2.81
2.68
2.63
2.46
2.41
2.06
2.06
2.05
2.04
2.04
1.90
1.47
Cl
Bn
N–SO2
S
O
O
N
3j
1H NMR (400 MHz, Acetone-d6)
1.96
1.95
2.94
2.98
1.97
1.06
1.06
1.06
1.04
1.03
3.11
3.00
11
10
9
8
7
6
5
4
3
2
1
0
ppm


206.11
172.13
141.92
140.12
139.22
138.87
130.81
129.26
128.88
128.63
127.95
127.60
126.87
126.84
105.07
103.70
83.32
50.32
44.23
30.42
30.23
30.03
29.84
29.65
29.46
29.26
25.75
23.49
Cl
Bn
S
N–SO2
O
O
N
3j
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

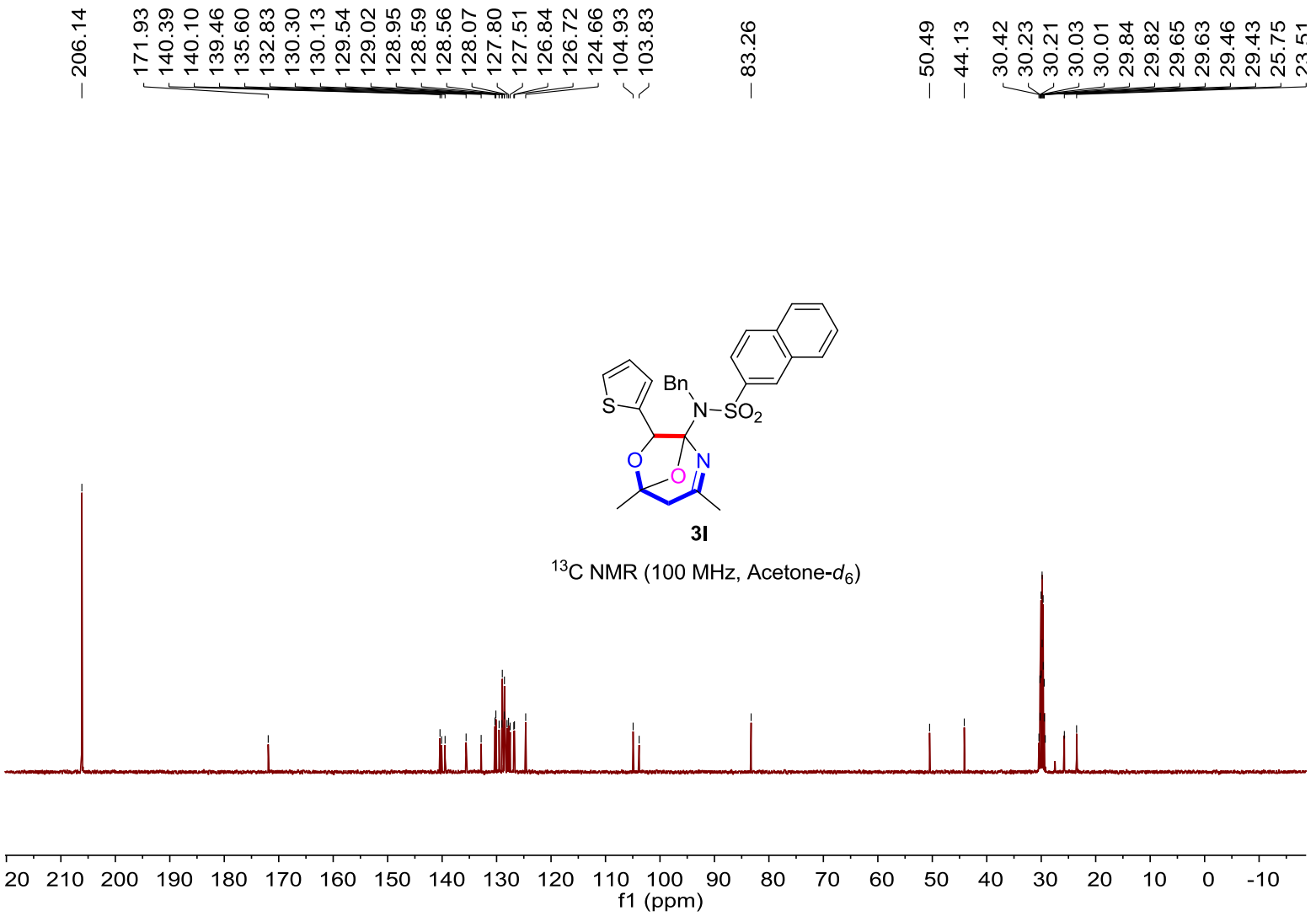

7.58
7.57
7.33
7.31
7.30
7.26
7.25
7.23
6.94
6.91
6.72
6.70
5.17
5.09
5.05
4.93
4.89
3.73
2.84
2.56
2.49
2.44
2.39
2.35
2.24
2.06
2.06
2.05
2.04
2.04
1.62
1.38
MeO
Bn
N–SO2
O
O
N
3k
1H NMR (400 MHz, Acetone-d6)
2.03
2.06
1.05
4.04
2.02
1.00
1.02
0.97
2.98
6.03
1.17
1.09
3.00
3.10
3.00
f1 (ppm)

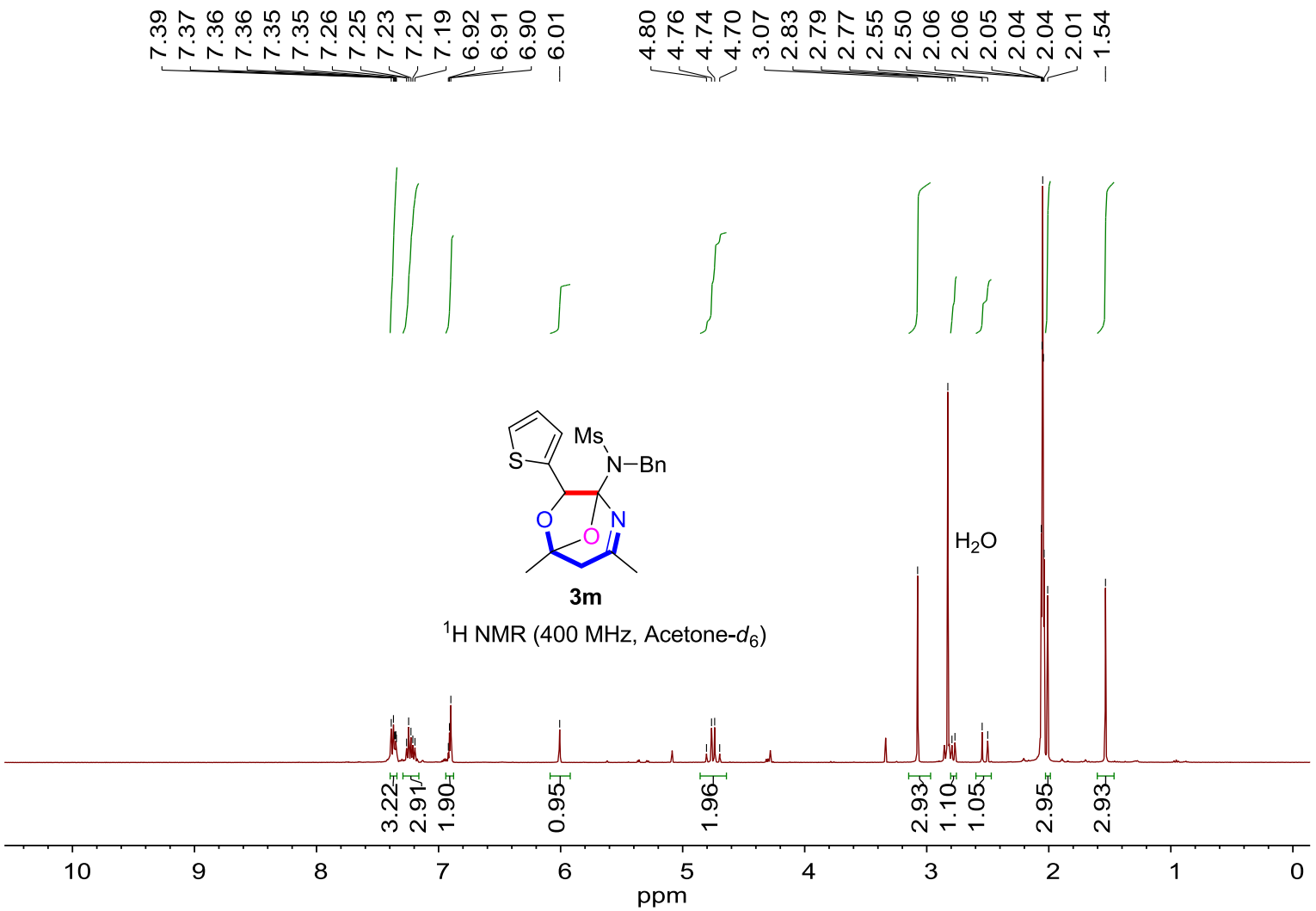

206.26
170.24
160.24
142.50
141.17
140.18
139.10
132.37
129.55
129.36
128.97
128.45
127.88
113.65
104.77
104.05
84.98
55.47
50.10
44.66
30.54
30.34
30.21
30.15
30.01
29.96
29.77
29.57
29.38
24.77
23.80
23.44
20.91
MeO
Bn
N–SO2
O
O
N
3k
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

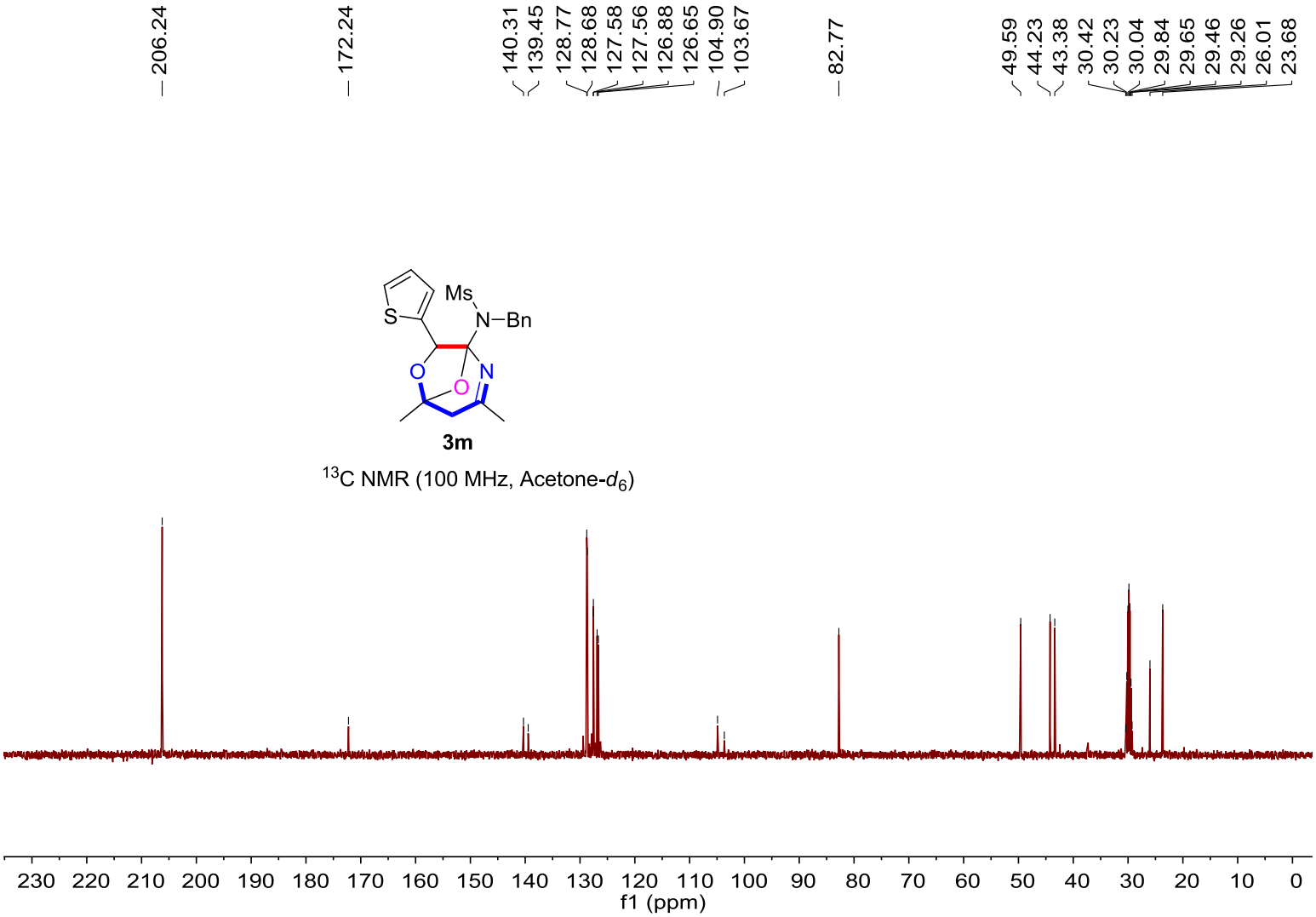


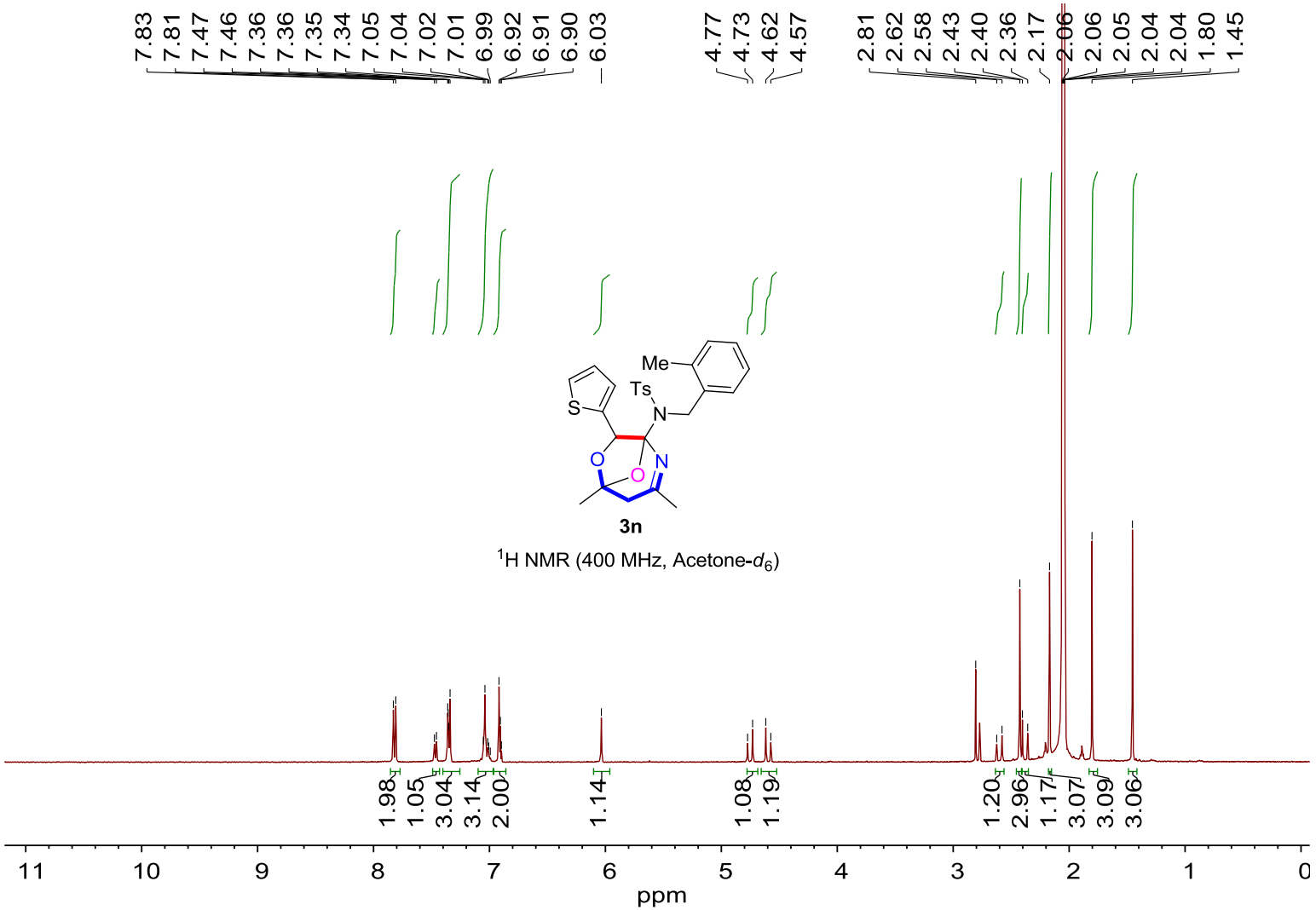
3l

^{1}H NMR (400 MHz, Acetone-d_6)


206.14
171.93
140.39
140.10
139.46
135.60
132.83
130.30
130.13
129.54
129.02
128.95
128.59
128.56
128.07
127.80
127.51
126.84
126.72
124.66
104.93
103.83
83.26
50.49
44.13
30.42
30.23
30.21
30.03
30.01
29.84
29.82
29.65
29.63
29.46
29.43
25.75
Bn
N–SO2
S
O
O
N
3l
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

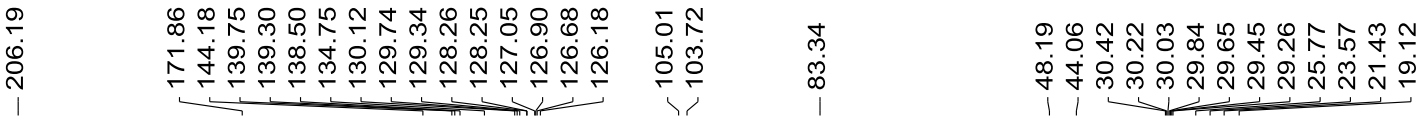

7.39
7.37
7.36
7.36
7.35
7.35
7.26
7.25
7.23
7.21
7.19
6.92
6.91
6.90
6.01
4.80
4.76
4.74
4.70
3.07
2.83
2.79
2.77
2.55
2.50
2.06
2.06
2.05
2.04
2.04
2.01
1.54
Ms
N–Bn
S
O
O
N
H2O
3m
1H NMR (400 MHz, Acetone-d6)
3.22
2.91
1.90
0.95
1.96
2.93
1.10
1.05
2.95
2.93
10
9
8
7
6
5
4
3
2
1
0
ppm

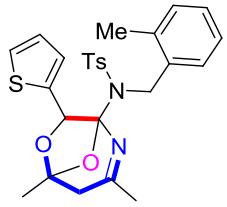

206.24
172.24
140.31
139.45
128.77
128.68
127.58
127.56
126.88
126.65
104.90
103.67
82.77
49.59
44.23
43.38
30.42
30.23
30.04
29.84
29.65
29.46
29.26
26.01
23.68
Ms
N–Bn
S
O
O
N
3m
13C NMR (100 MHz, Acetone-d6)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



3n

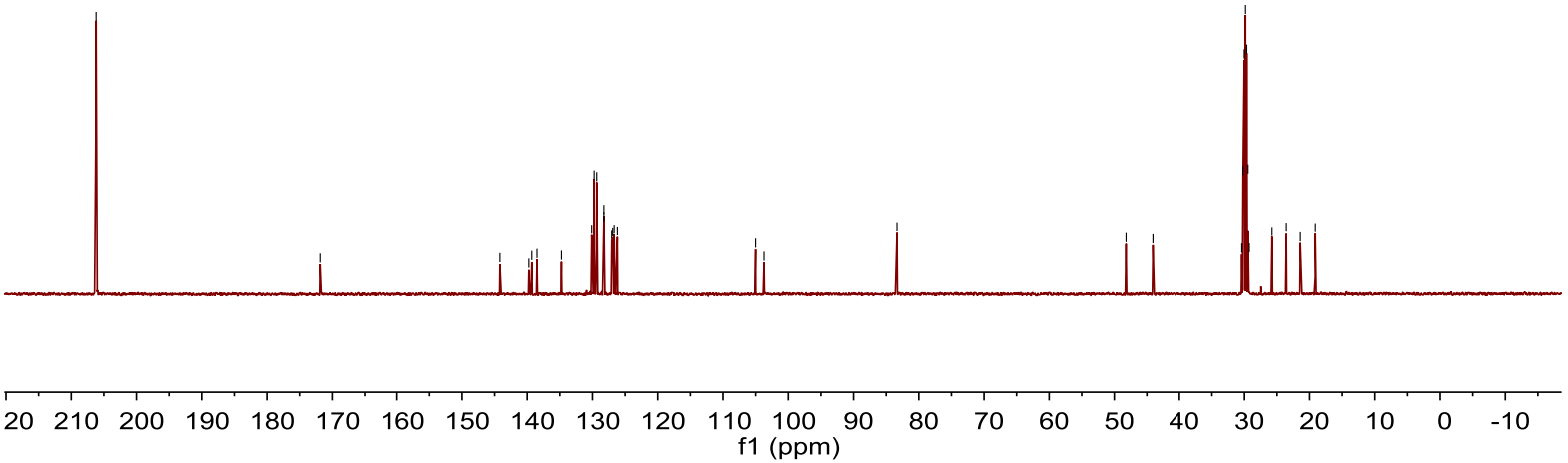
^{1}H NMR (400 MHz, Acetone-d_6)

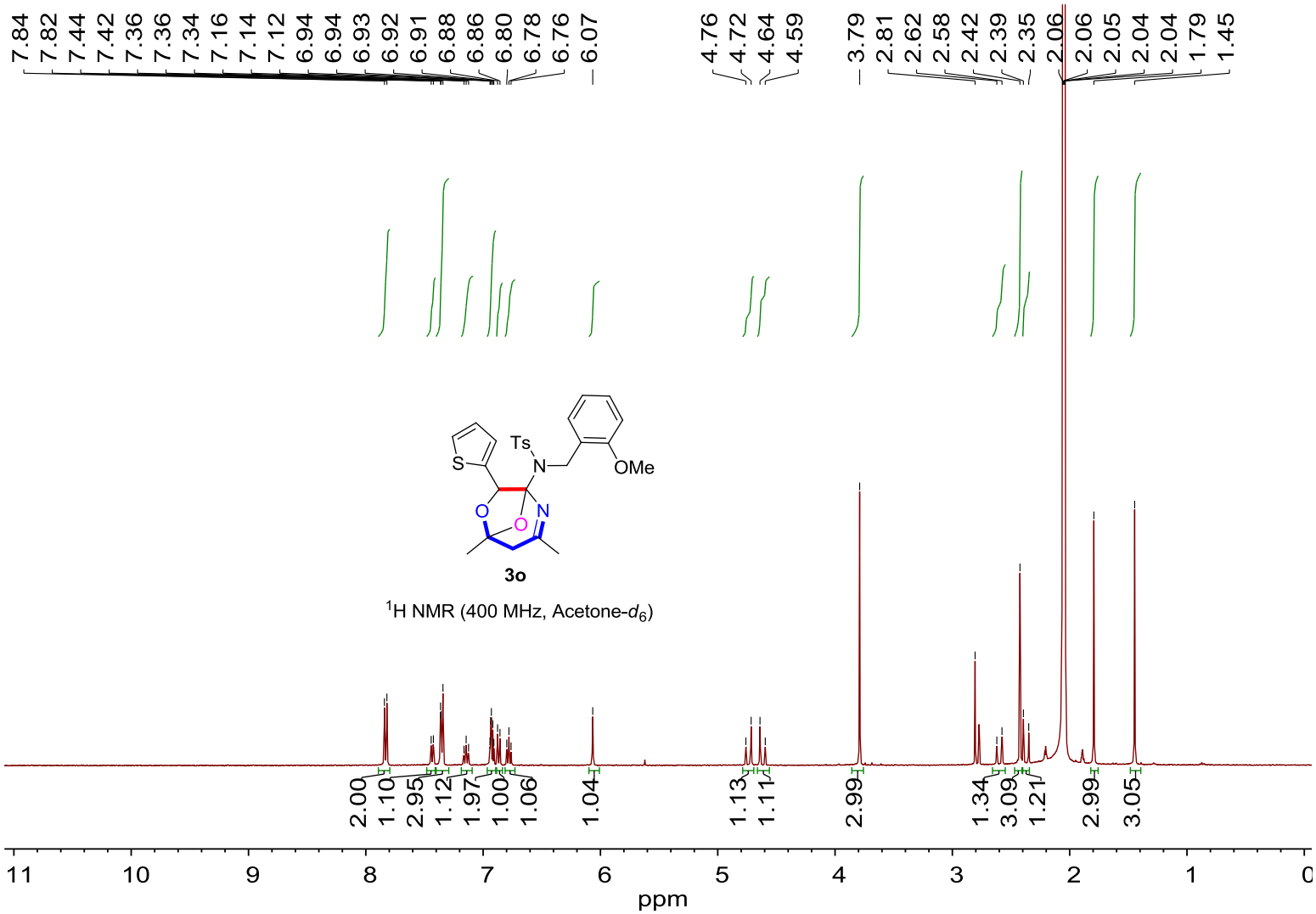


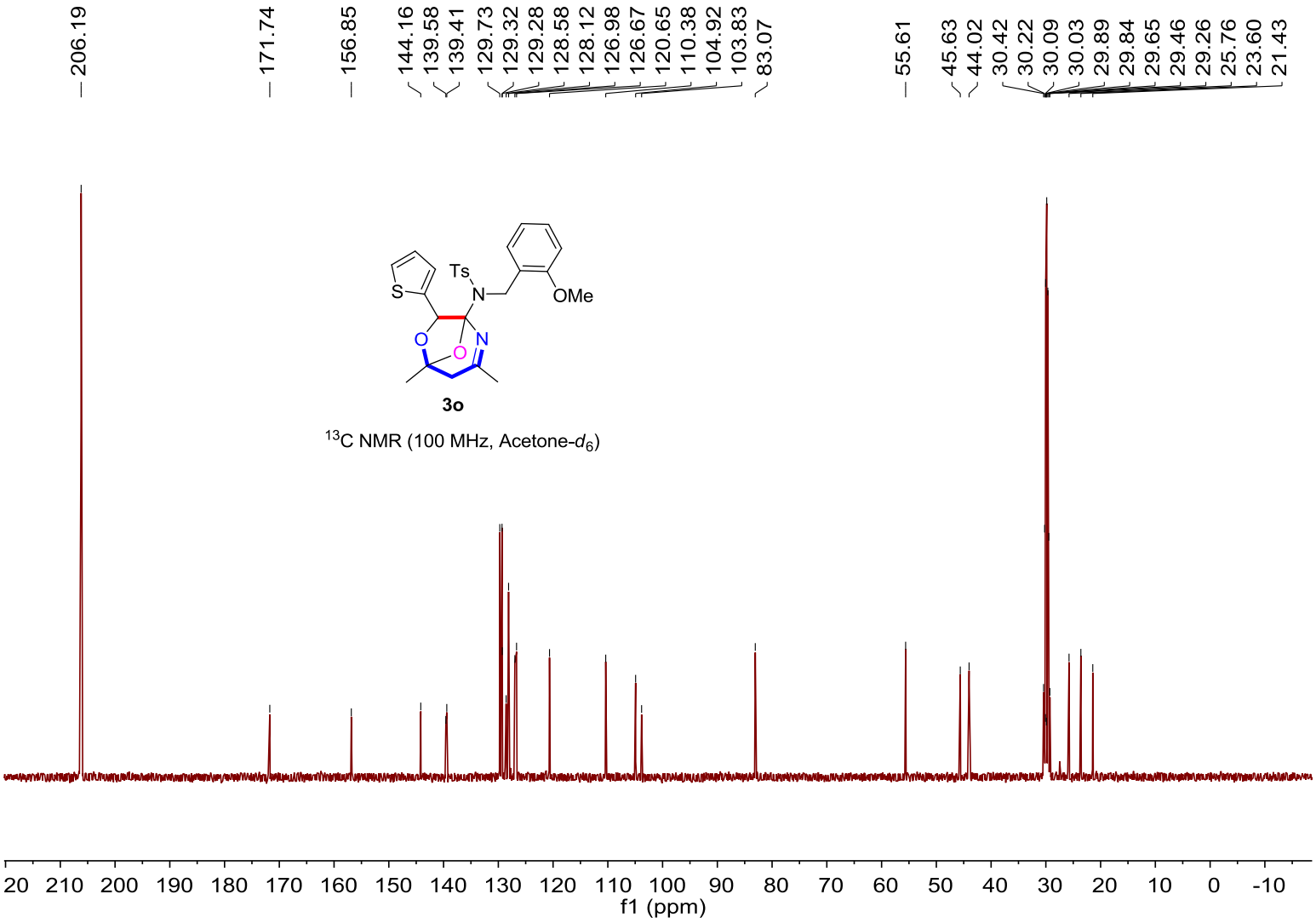


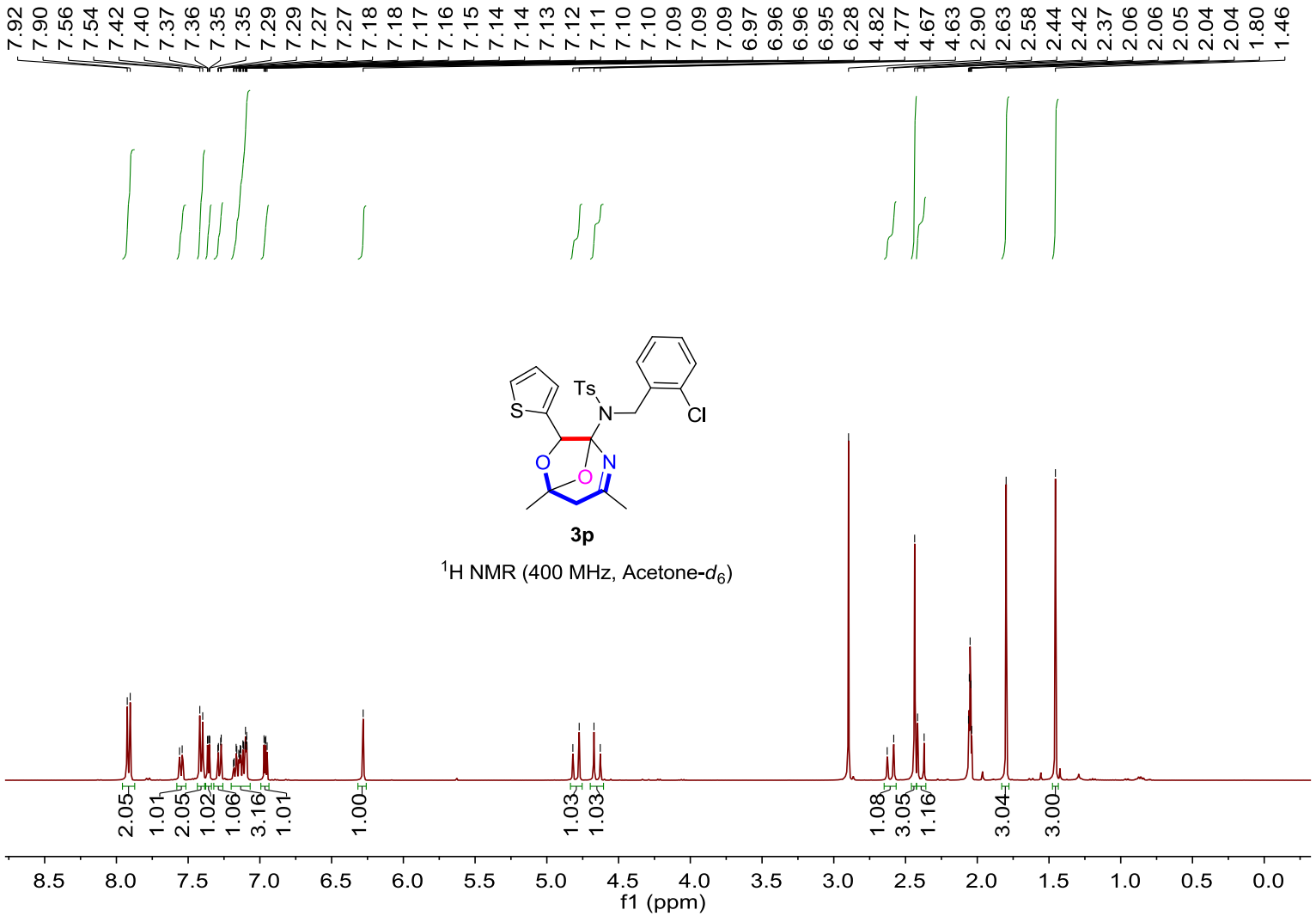
3n

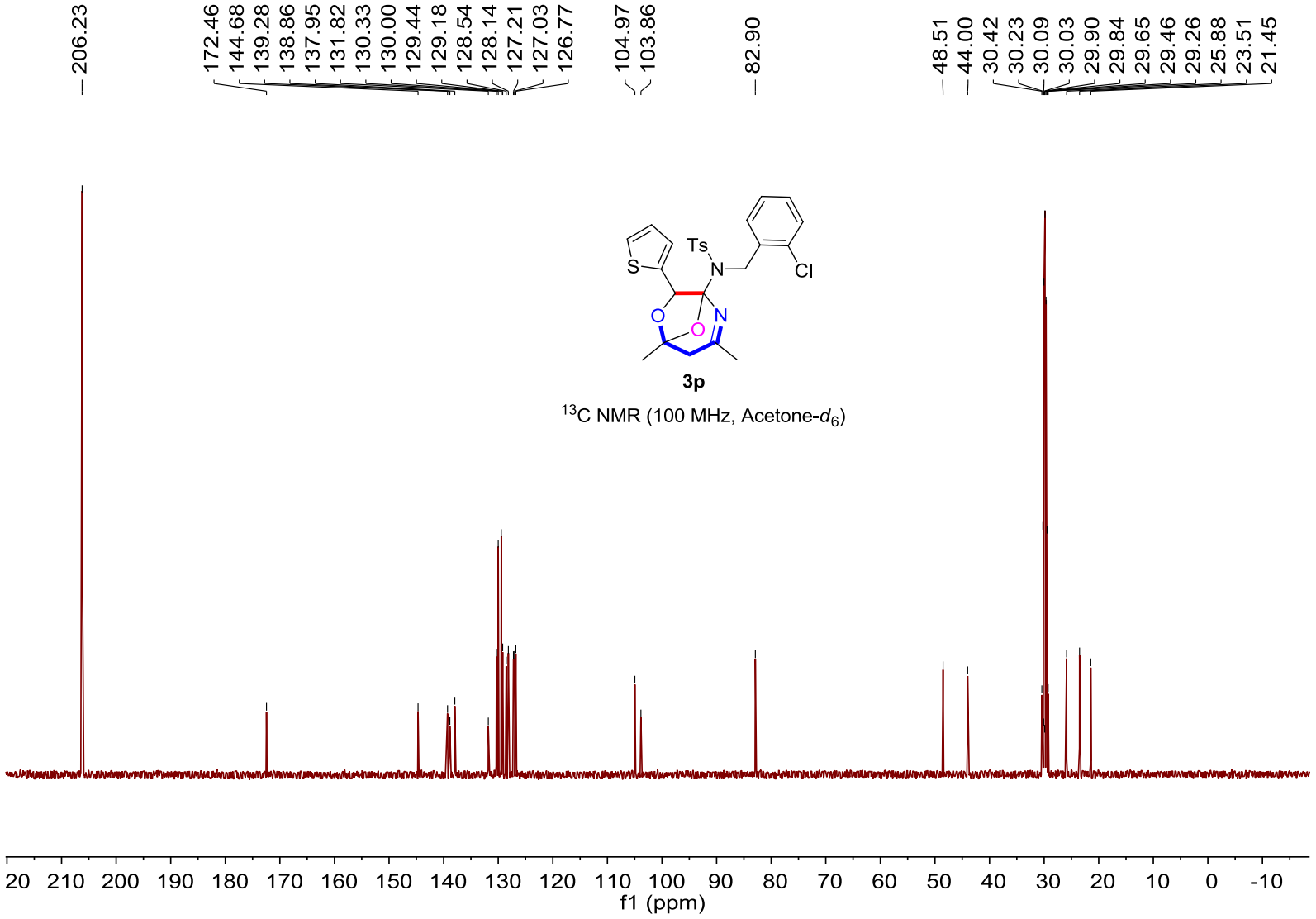
^{13}C NMR (100 MHz, Acetone-d_6)

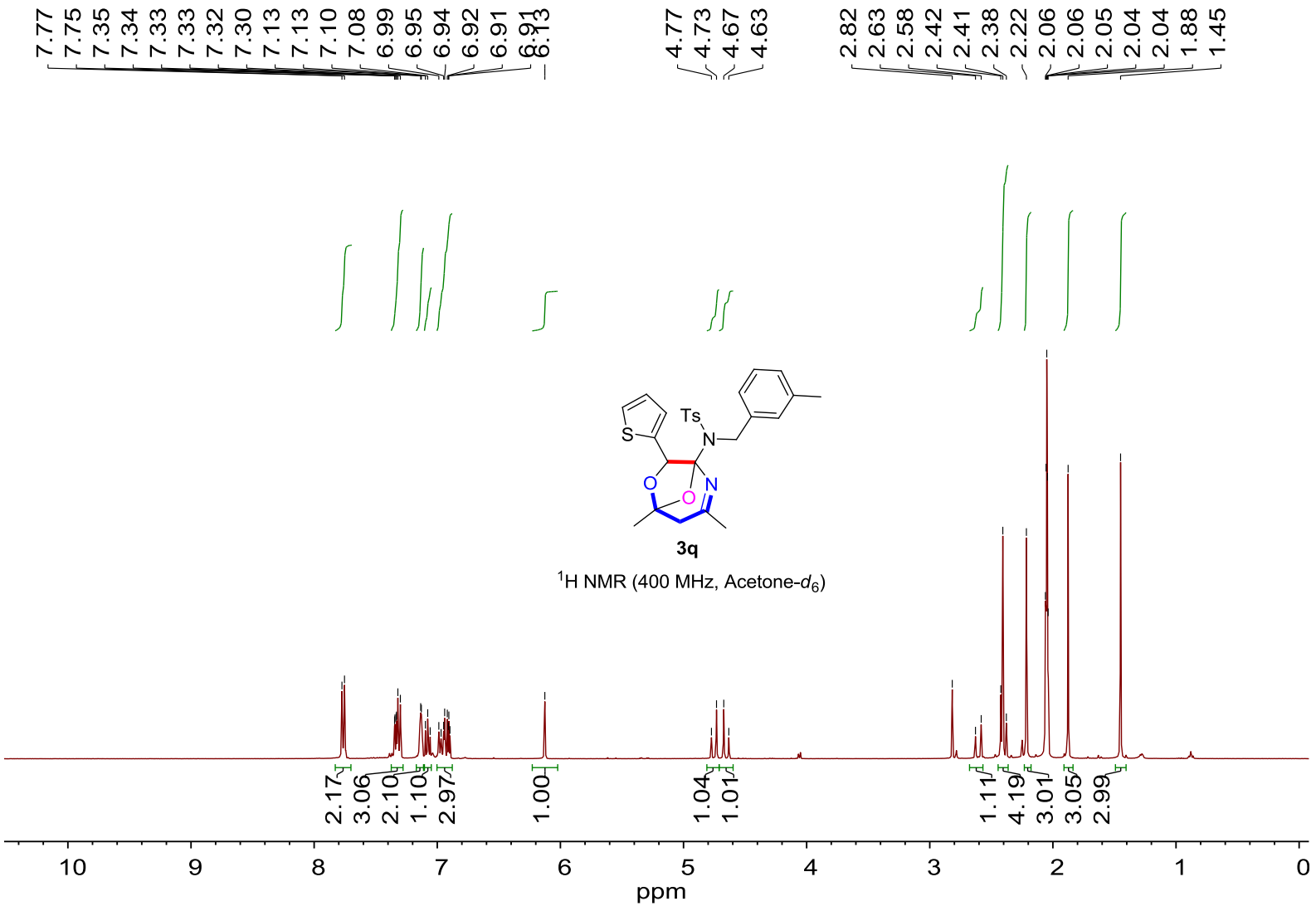


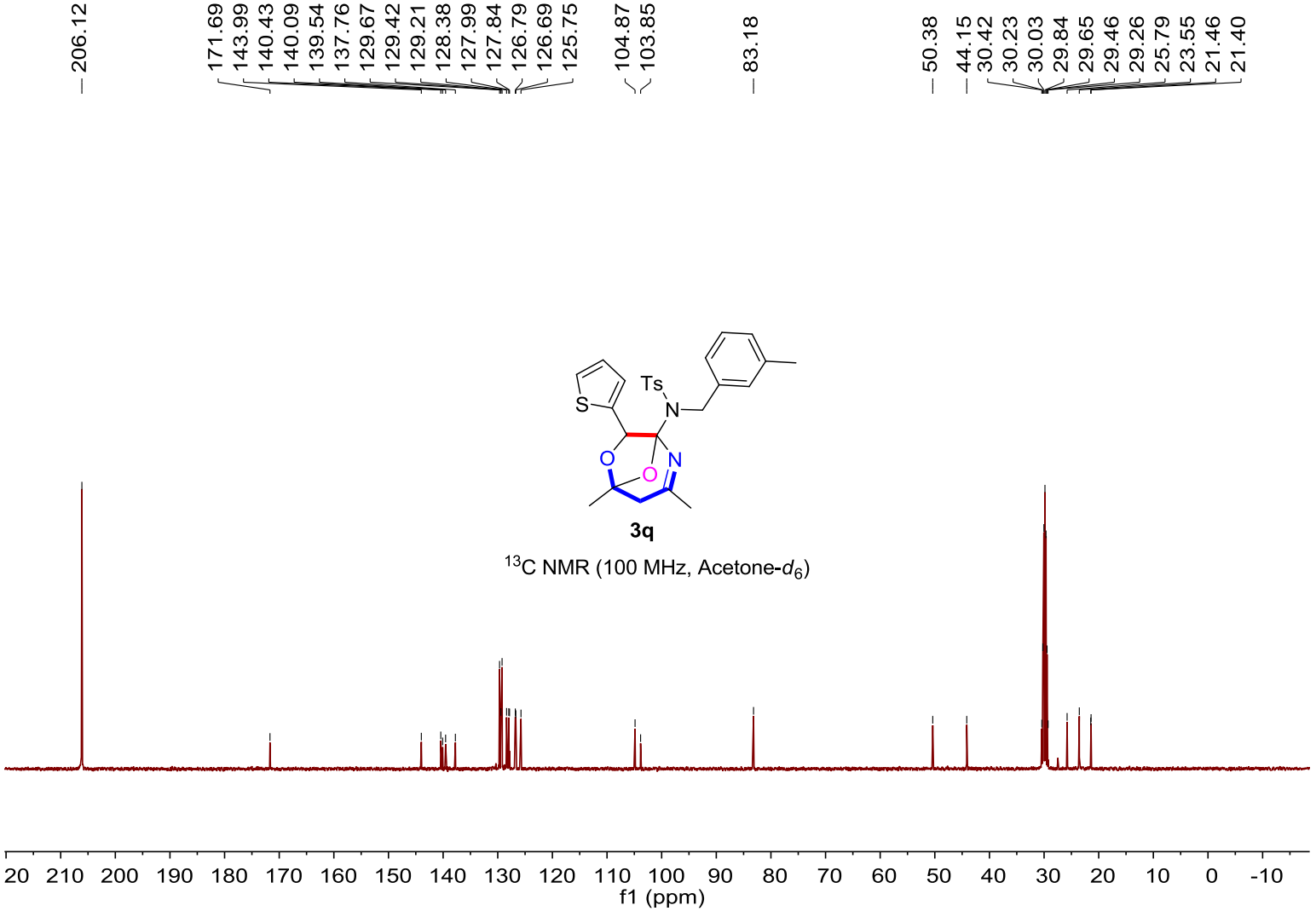

7.84
7.82
7.44
7.42
7.36
7.36
7.34
7.16
7.14
7.12
6.94
6.94
6.93
6.92
6.91
6.88
6.86
6.80
6.78
6.76
6.07
4.76
4.72
4.64
4.59
3.79
2.81
2.62
2.58
2.42
2.39
2.35
2.06
2.06
2.05
2.04
2.04
1.79
1.45
Ts
N
S
OMe
O
O
N
3o
1H NMR (400 MHz, Acetone-d6)
2.00
1.10
2.95
1.12
1.97
1.00
1.06
1.04
1.13
1.11
2.99
1.34
3.09
1.21
2.99
3.05
11
10
9
8
7
6
5
4
3
2
1
0
ppm

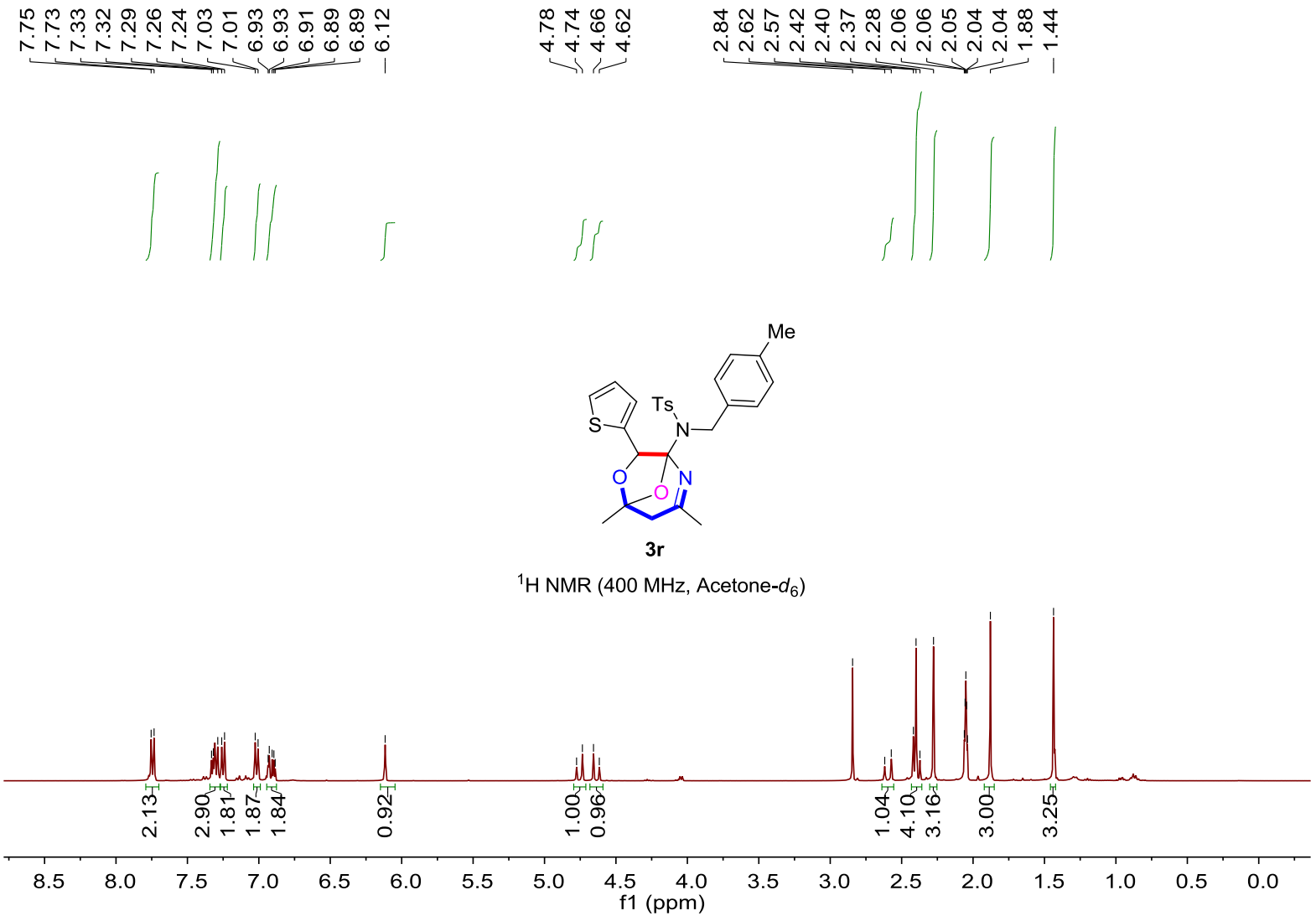

206.19
171.74
156.85
144.16
139.58
139.41
129.73
129.32
129.28
128.58
128.12
126.98
126.67
120.65
110.38
104.92
103.83
83.07
55.61
45.63
44.02
30.42
30.22
30.09
30.03
29.89
29.84
29.65
29.46
29.26
25.76
23.60
21.43
Ts
N
S
OMe
O
O
N
3o
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

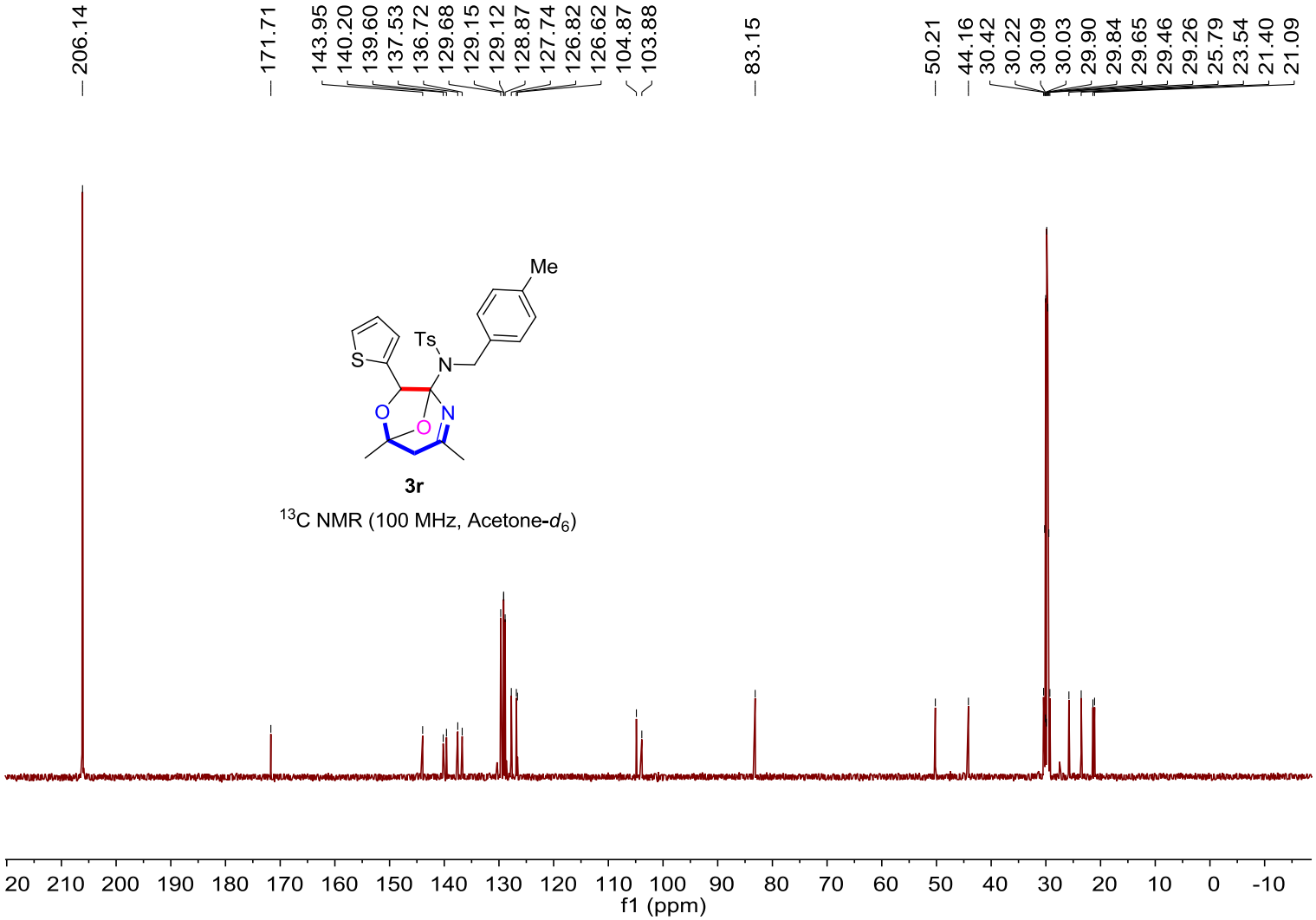

7.92 7.90 7.56 7.54 7.42 7.40 7.37 7.36 7.35 7.35 7.29 7.29 7.27 7.27 7.18 7.18 7.17 7.16 7.15 7.14 7.14 7.13 7.12 7.11 7.10 7.10 7.09 7.09 7.09 6.97 6.96 6.96 6.95 6.28 4.82 4.77 4.67 4.63 2.90 2.63 2.58 2.44 2.42 2.37 2.06 2.06 2.05 2.04 2.04 1.80 1.46
Ts
N
S
Cl
O
O
N
3p
1H NMR (400 MHz, Acetone-d6)
2.05 1.01 2.05 1.02 1.06 3.16 1.01 1.00 1.03 1.03 1.08 3.05 1.16 3.04 3.00
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
f1 (ppm)

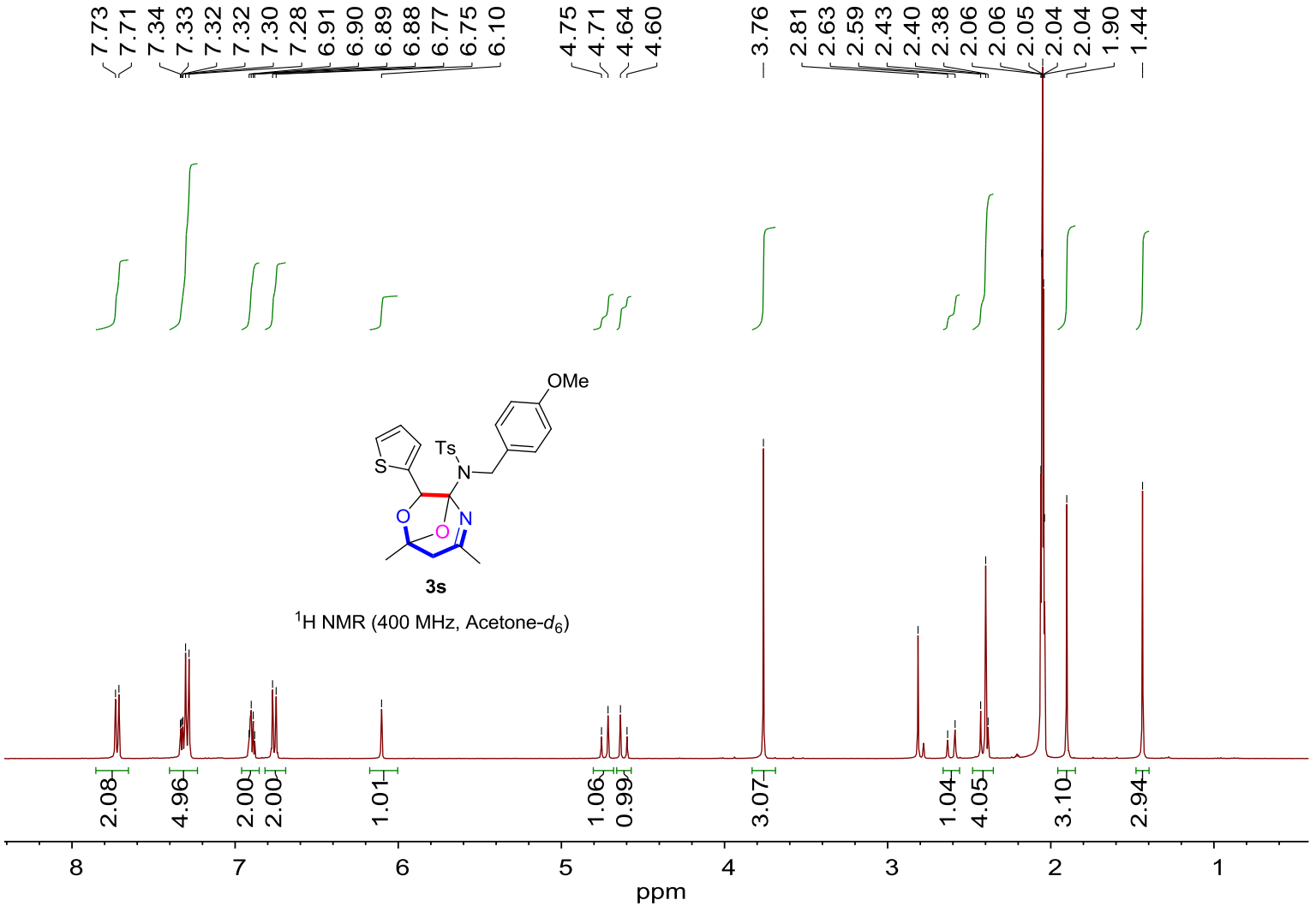

206.23
172.46
144.68
139.28
138.86
137.95
131.82
130.33
130.00
129.44
129.18
128.54
128.14
127.21
127.03
126.77
104.97
103.86
82.90
48.51
44.00
30.42
30.23
30.09
30.03
29.90
29.84
29.65
29.46
29.26
25.88
23.51
21.45
Ts
N
S
Cl
O
O
N
3p
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

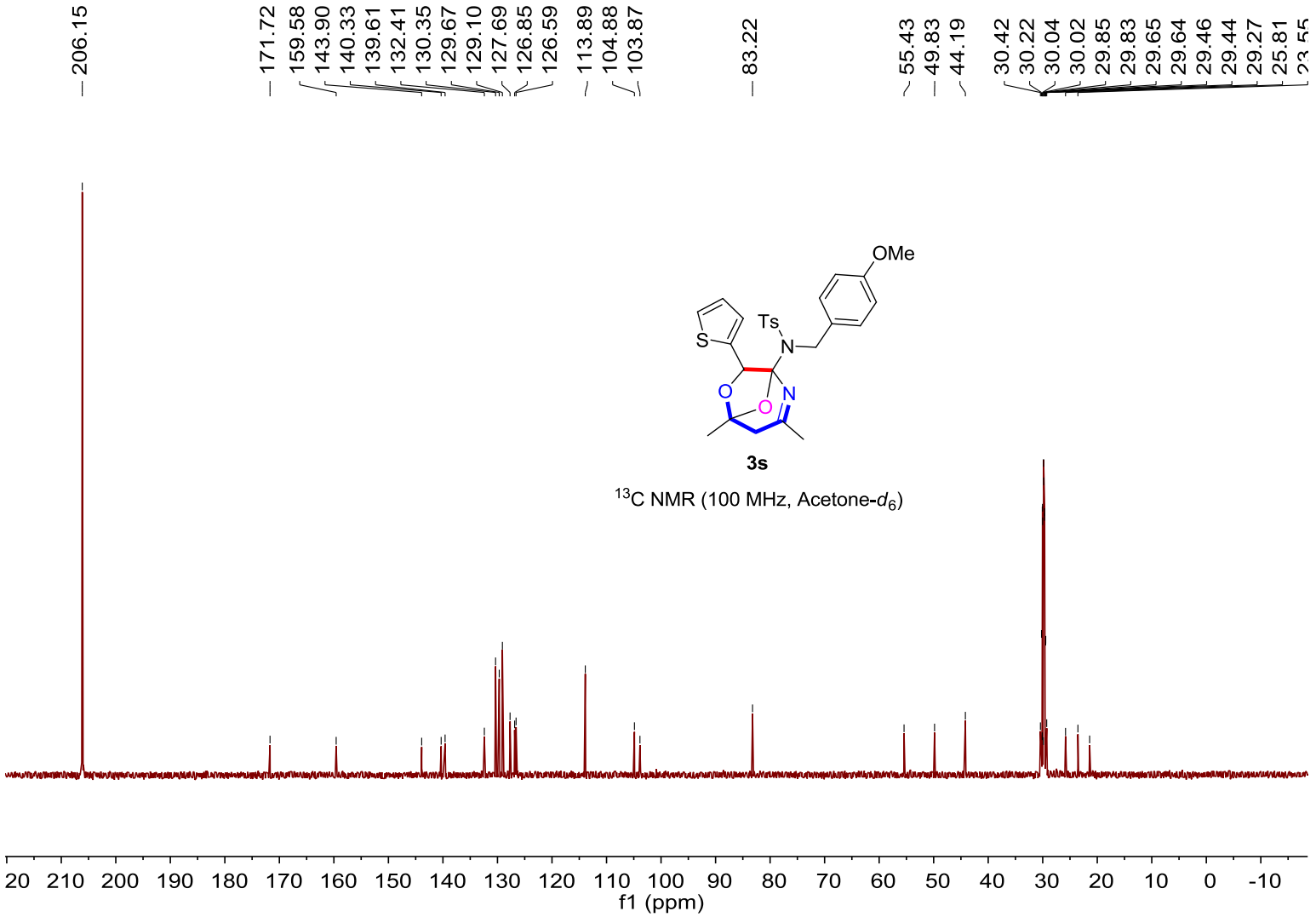

7.77
7.75
7.35
7.34
7.33
7.33
7.32
7.30
7.13
7.13
7.10
7.08
6.99
6.95
6.94
6.92
6.91
6.91
6.13
4.77
4.73
4.67
4.63
2.82
2.63
2.58
2.42
2.41
2.38
2.22
2.06
2.06
2.05
2.04
2.04
1.88
1.45
Ts
S
N
O
O
N
3q
1H NMR (400 MHz, Acetone-d6)
2.17
3.06
2.10
1.10
2.97
1.00
1.04
1.01
1.11
4.19
3.01
3.05
2.99
10
9
8
7
6
5
4
3
2
1
0
ppm

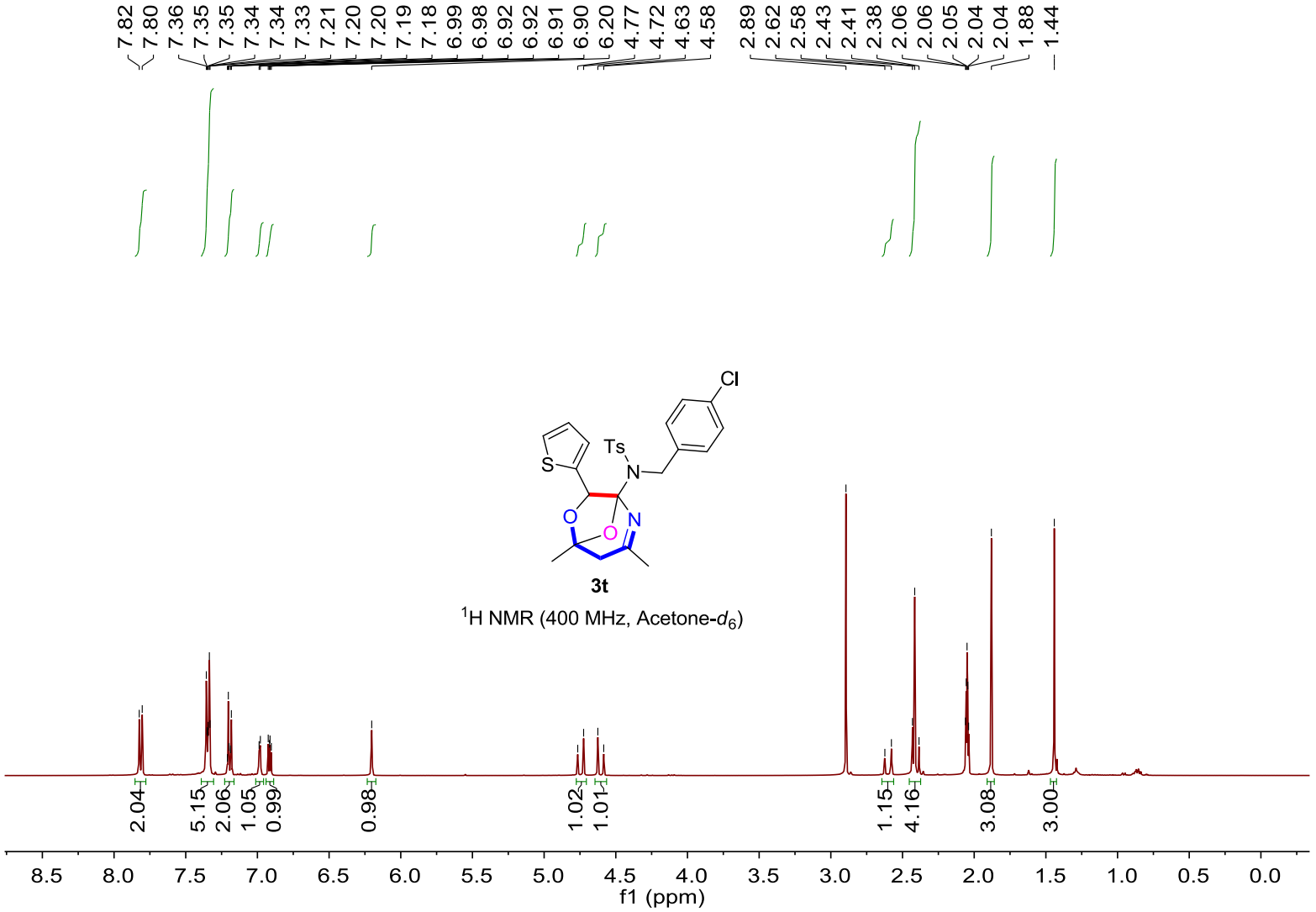

206.12
171.69
143.99
140.43
140.09
139.54
137.76
129.67
129.42
129.21
128.38
127.99
127.84
126.79
126.69
125.75
104.87
103.85
83.18
50.38
44.15
30.42
30.23
30.03
29.84
29.65
29.46
29.26
25.79
23.55
21.46
21.40
Ts
S
N
O
O
N
3q
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

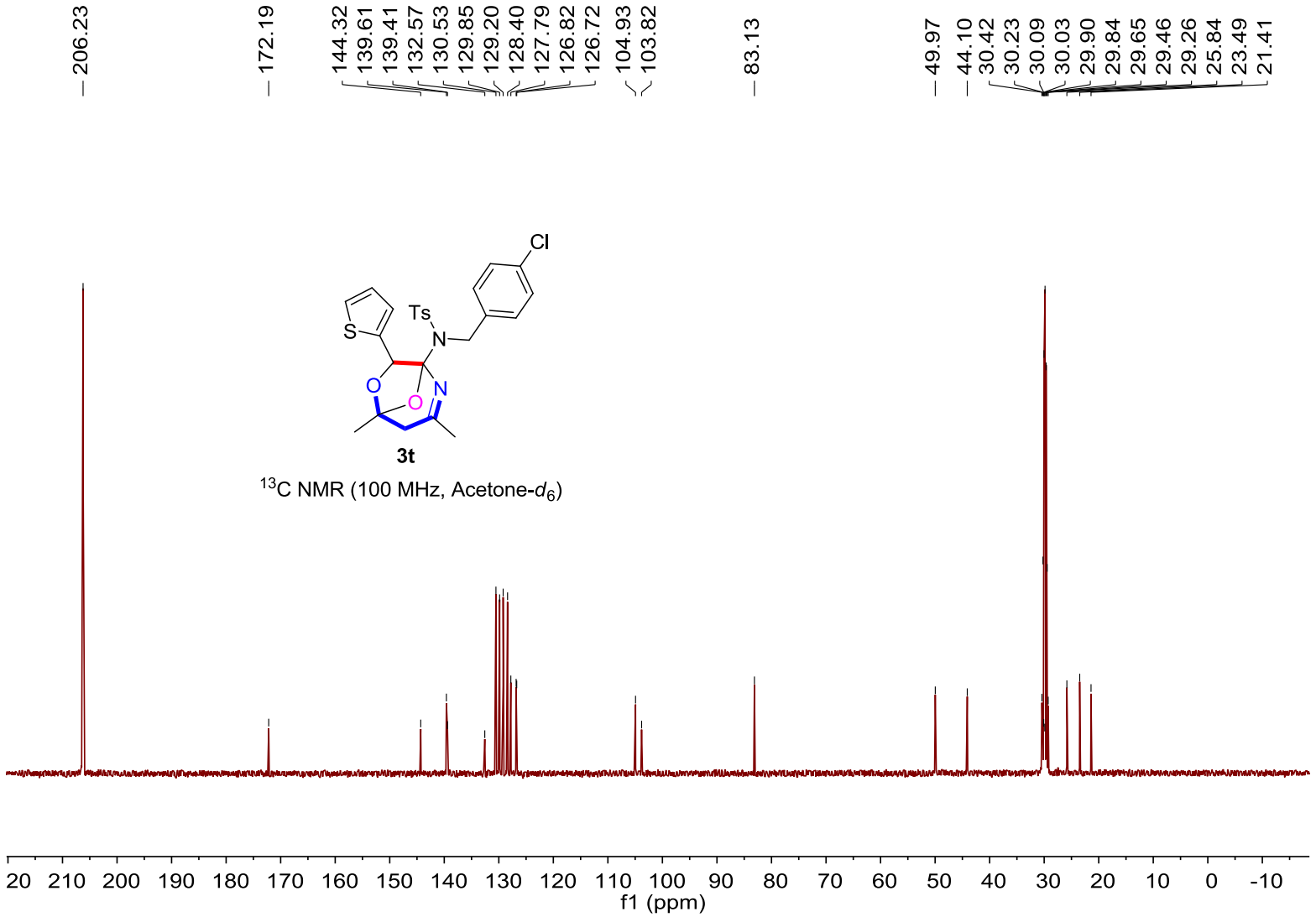

7.75
7.73
7.33
7.32
7.29
7.26
7.24
7.03
7.01
6.93
6.93
6.91
6.89
6.89
6.12
4.78
4.74
4.66
4.62
2.84
2.62
2.57
2.42
2.40
2.37
2.28
2.06
2.06
2.05
2.04
2.04
1.88
1.44
Me
Ts
S
N
O
O
N
3r
1H NMR (400 MHz, Acetone-d6)
2.13
2.90
1.81
1.87
1.84
0.92
1.00
0.96
1.04
4.10
3.16
3.00
3.25
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

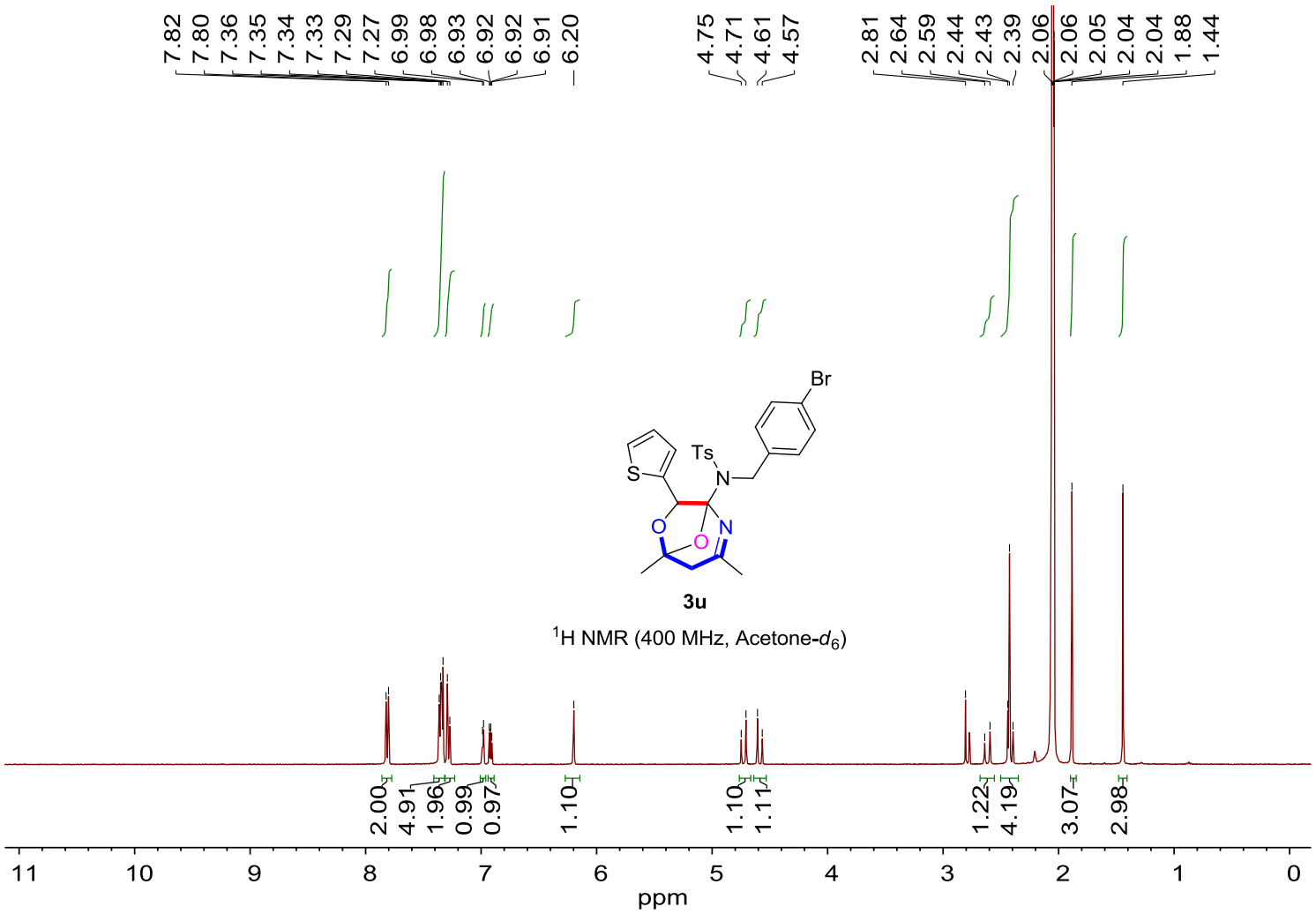

206.14
171.71
143.95
140.20
139.60
137.53
136.72
129.68
129.15
129.12
128.87
127.74
126.82
126.62
104.87
103.88
83.15
50.21
44.16
30.42
30.22
30.09
30.03
29.90
29.84
29.65
29.46
29.26
25.79
23.54
21.40
21.09
Me
Ts
S
N
O
O
N
3r
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

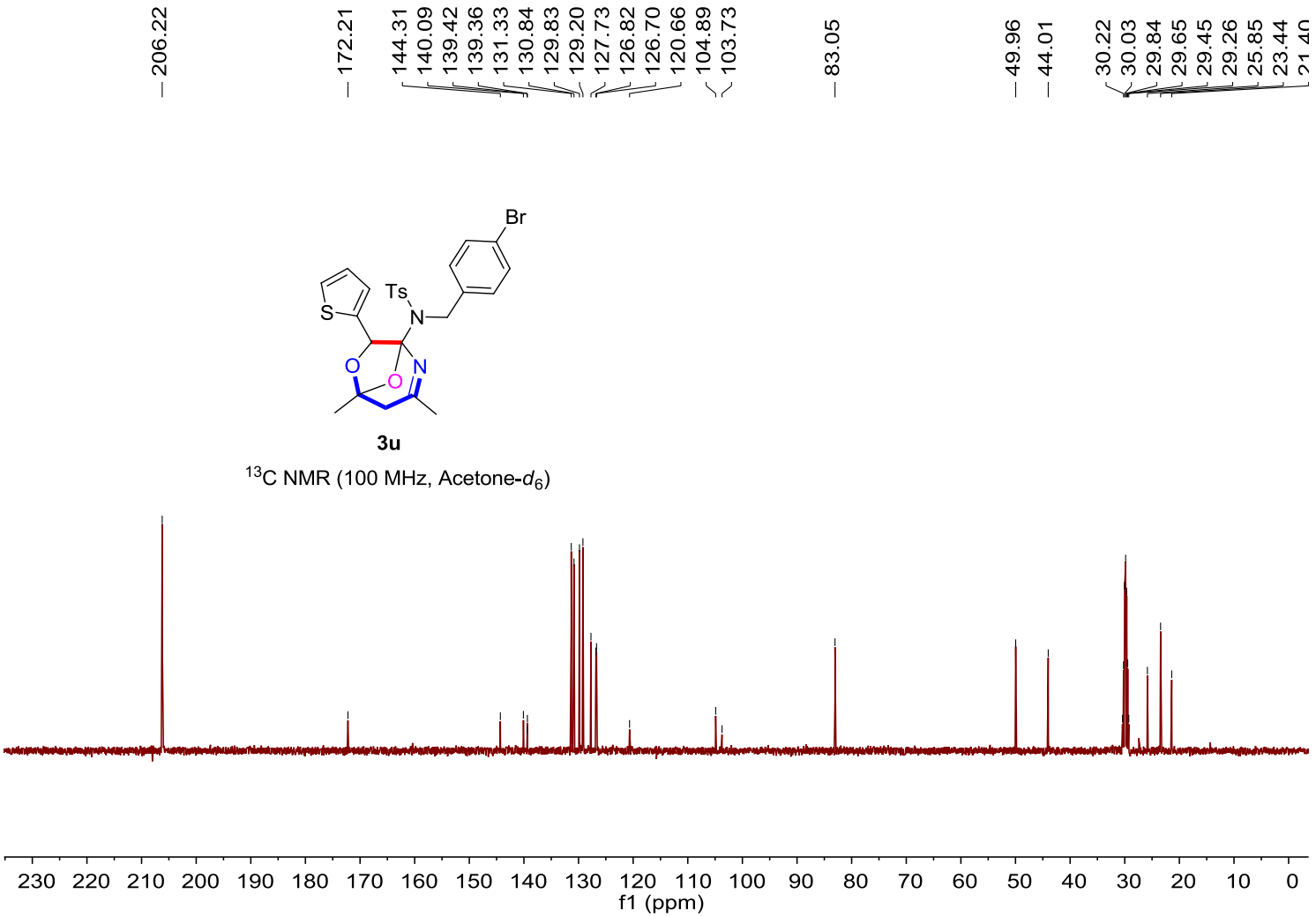

7.73
7.71
7.34
7.33
7.32
7.32
7.30
7.28
6.91
6.90
6.89
6.88
6.77
6.75
6.10
4.75
4.71
4.64
4.60
3.76
2.81
2.63
2.59
2.43
2.40
2.38
2.06
2.06
2.05
2.04
2.04
1.90
1.44
OMe
Ts
S
N
O
O
N
3s
1H NMR (400 MHz, Acetone-d6)
2.08
4.96
2.00
2.00
1.01
1.06
0.99
3.07
1.04
4.05
3.10
2.94
8
7
6
5
4
3
2
1
ppm

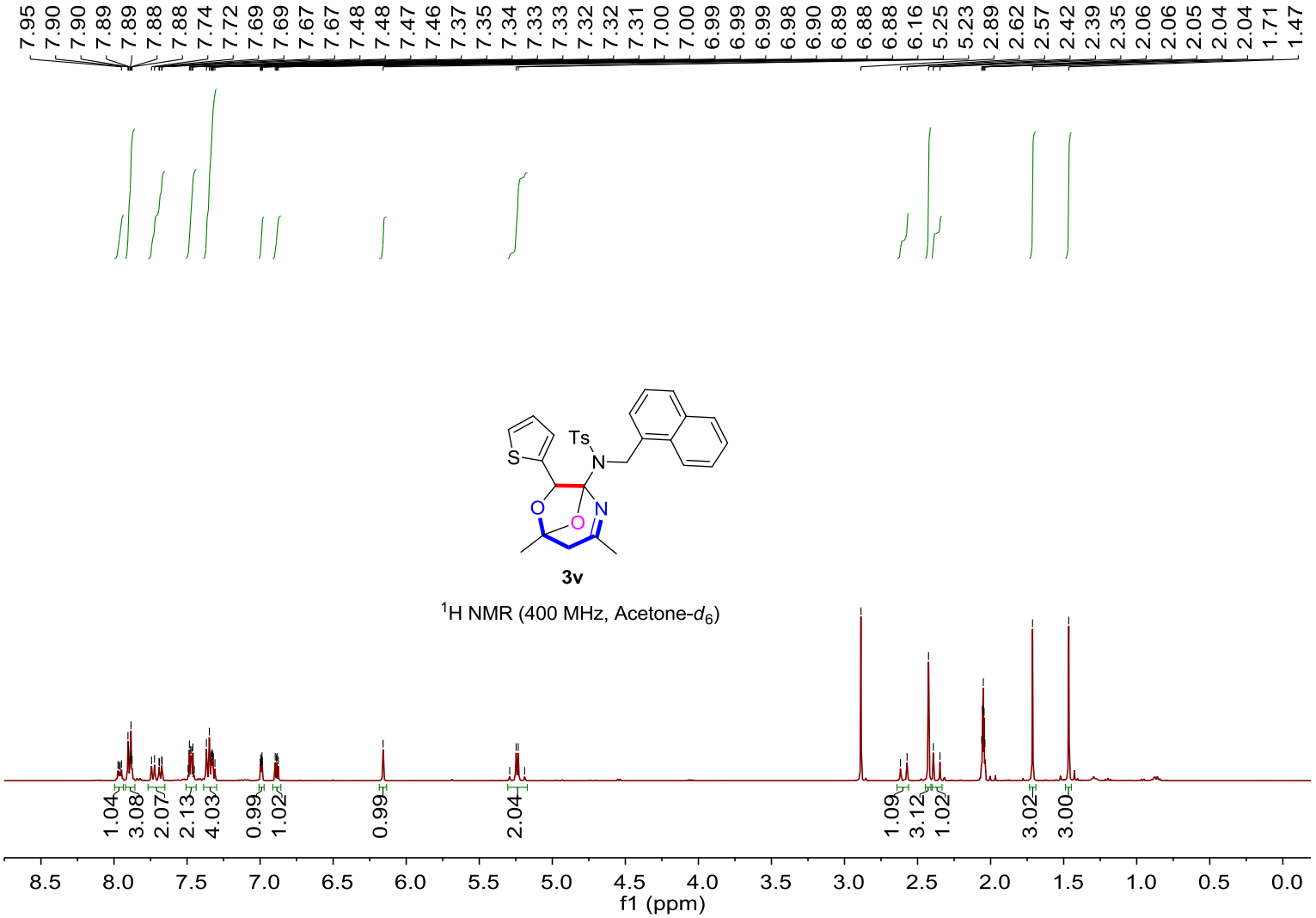

206.15
171.72
159.58
143.90
140.33
139.61
132.41
130.35
129.67
129.10
127.69
126.85
126.59
113.89
104.88
103.87
83.22
55.43
49.83
44.19
30.42
30.22
30.04
30.02
29.85
29.83
29.65
29.64
29.46
29.44
29.27
25.81
OMe
Ts
S
N
O
O
N
3s
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

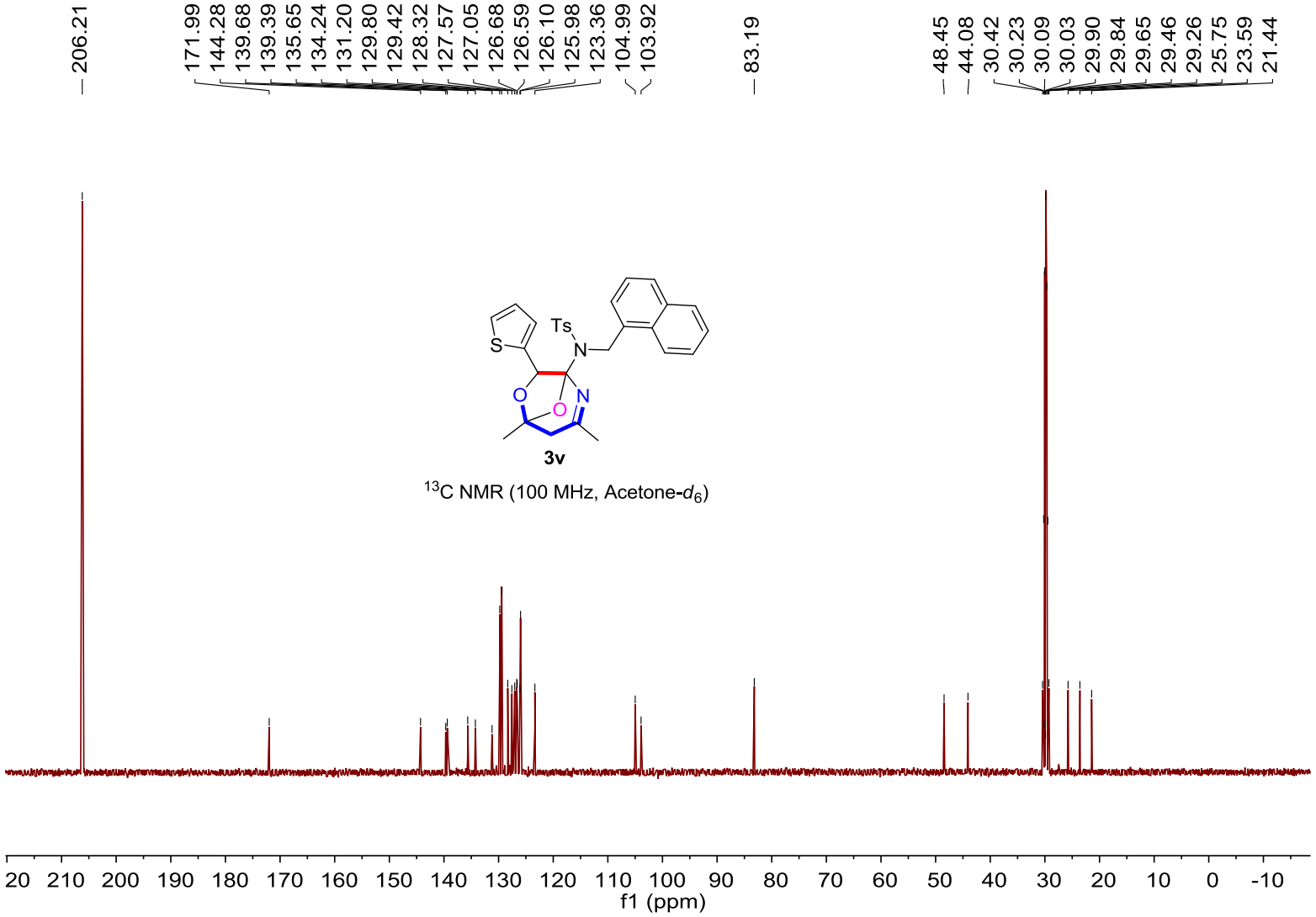

7.82
7.80
7.36
7.35
7.35
7.34
7.34
7.33
7.21
7.20
7.20
7.19
7.18
6.99
6.98
6.92
6.92
6.91
6.90
6.20
4.77
4.72
4.63
4.58
2.89
2.62
2.58
2.43
2.41
2.38
2.06
2.06
2.05
2.04
2.04
1.88
1.44
Cl
Ts
N
S
O
O
N
3t
1H NMR (400 MHz, Acetone-d6)
2.04
5.15
2.06
1.05
0.99
0.98
1.02
1.01
1.15
4.16
3.08
3.00
8.5
8.0
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
f1 (ppm)

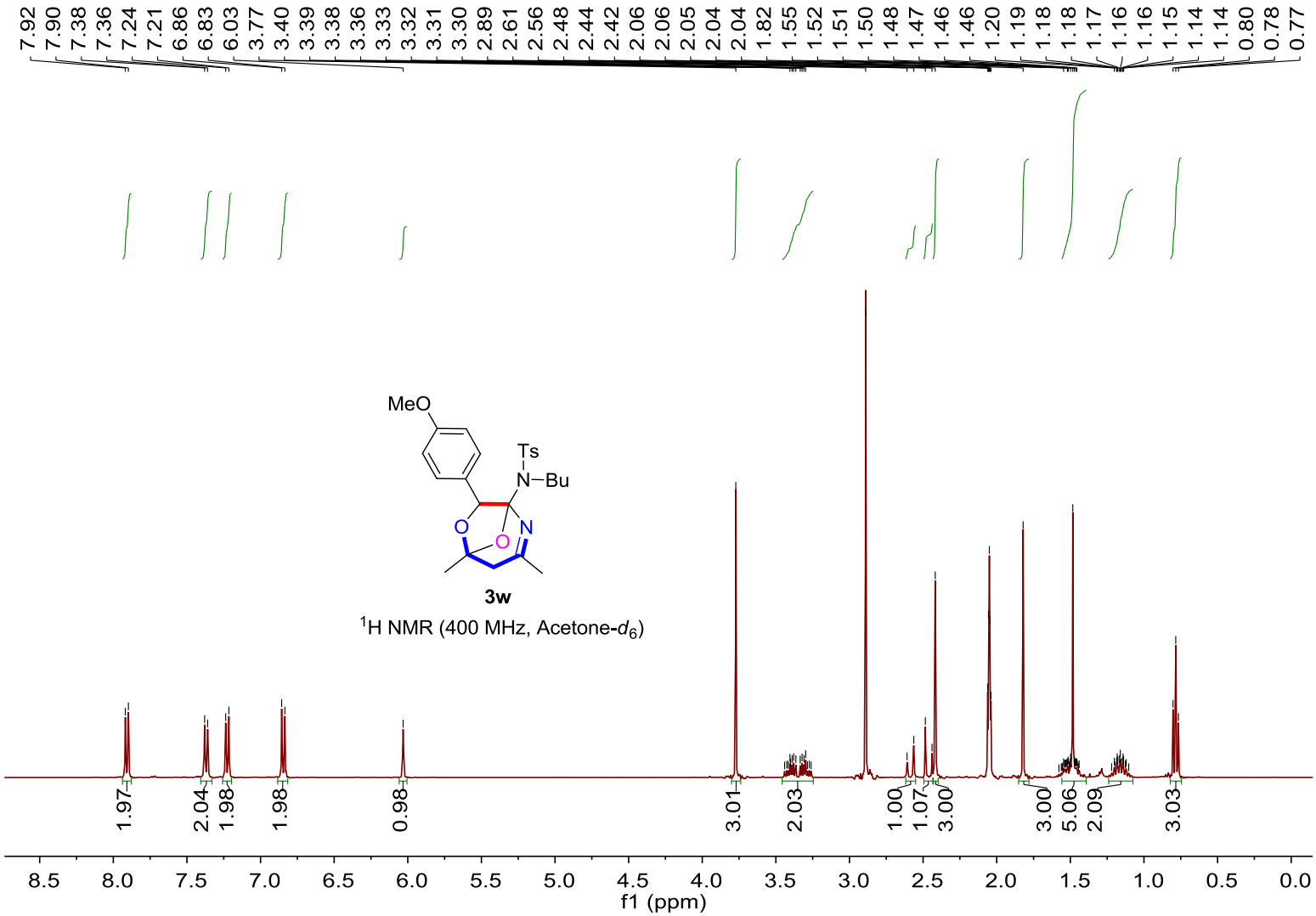

206.23
172.19
144.32
139.61
139.41
132.57
130.53
129.85
129.20
128.40
127.79
126.82
126.72
104.93
103.82
83.13
49.97
44.10
30.42
30.23
30.09
30.03
29.90
29.84
29.65
29.46
29.26
25.84
23.49
21.41
Cl
Ts
S
N
O
O
N
3t
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

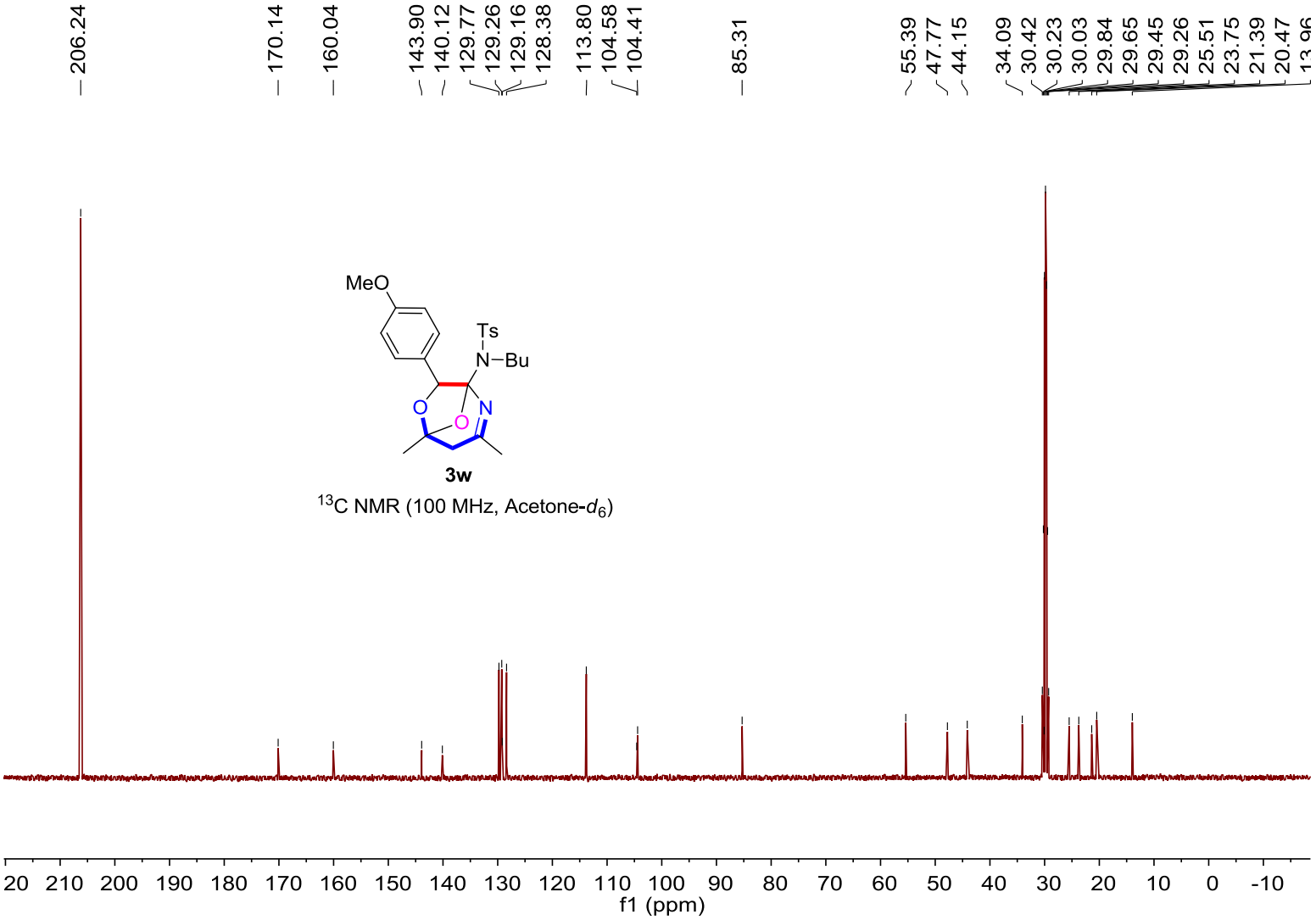

7.82
7.80
7.36
7.35
7.34
7.33
7.29
7.27
6.99
6.98
6.93
6.92
6.92
6.91
6.20
4.75
4.71
4.61
4.57
2.81
2.64
2.59
2.44
2.43
2.39
2.06
2.06
2.05
2.04
2.04
1.88
1.44
Br
Ts
S
N
O
O
N
3u
1H NMR (400 MHz, Acetone-d6)
2.00
4.91
1.96
0.99
0.97
1.10
1.10
1.11
1.22
4.19
3.07
2.98
11
10
9
8
7
6
5
4
3
2
1
0
ppm


206.22
172.21
144.31
140.09
139.42
139.36
131.33
130.84
129.83
129.20
127.73
126.82
126.70
120.66
104.89
103.73
83.05
49.96
44.01
30.22
30.03
29.84
29.65
29.45
29.26
25.85
23.44
Br
Ts
N
S
O
O
N
3u
13C NMR (100 MHz, Acetone-d6)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.95 7.90 7.90 7.89 7.89 7.88 7.88 7.74 7.72 7.69 7.69 7.67 7.67 7.48 7.48 7.47 7.46 7.37 7.35 7.34 7.33 7.33 7.32 7.32 7.31 7.00 7.00 6.99 6.99 6.99 6.98 6.90 6.89 6.88 6.88 6.16 5.25 5.23 2.89 2.62 2.57 2.42 2.39 2.35 2.06 2.06 2.05 2.04 2.04 1.71 1.47
S
Ts
N
O
O
N
3v
1H NMR (400 MHz, Acetone-d6)
1.04 3.08 2.07 2.13 4.03 0.99 1.02 0.99 2.04 1.09 3.12 1.02 3.02 3.00
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
f1 (ppm)

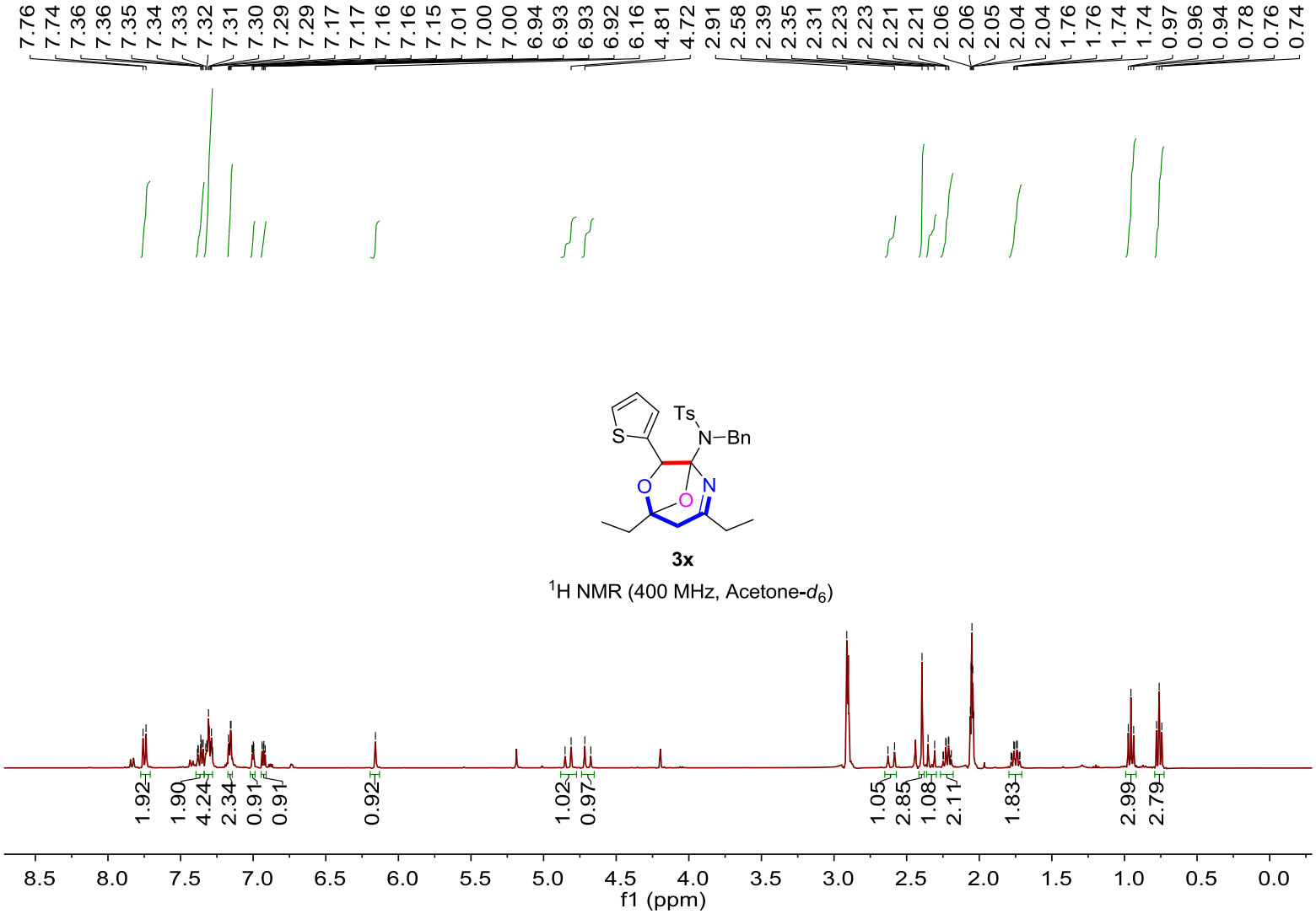

206.21
171.99
144.28
139.68
139.39
135.65
134.24
131.20
129.80
129.42
128.32
127.57
127.05
126.68
126.59
126.10
125.98
123.36
104.99
103.92
83.19
48.45
44.08
30.42
30.23
30.09
30.03
29.90
29.84
29.65
29.46
29.26
25.75
23.59
21.44
Ts
S
N
O
O
N
3v
13C NMR (100 MHz, Acetone-d6)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.92 7.90 7.38 7.36 7.24 7.21 6.86 6.83 6.03 3.77 3.40 3.39 3.38 3.36 3.33 3.32 3.31 3.30 2.89 2.61 2.56 2.48 2.44 2.42 2.06 2.06 2.05 2.04 2.04 1.82 1.55 1.52 1.51 1.50 1.48 1.47 1.46 1.46 1.20 1.19 1.18 1.18 1.17 1.16 1.16 1.15 1.14 1.14 0.80 0.78 0.77
MeO
Ts
N–Bu
O
O
N
3w
1H NMR (400 MHz, Acetone-d6)
1.97 2.04 1.98 1.98 0.98 3.01 2.03 1.00 1.07 3.00 3.00 5.06 2.09 3.03
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
f1 (ppm)



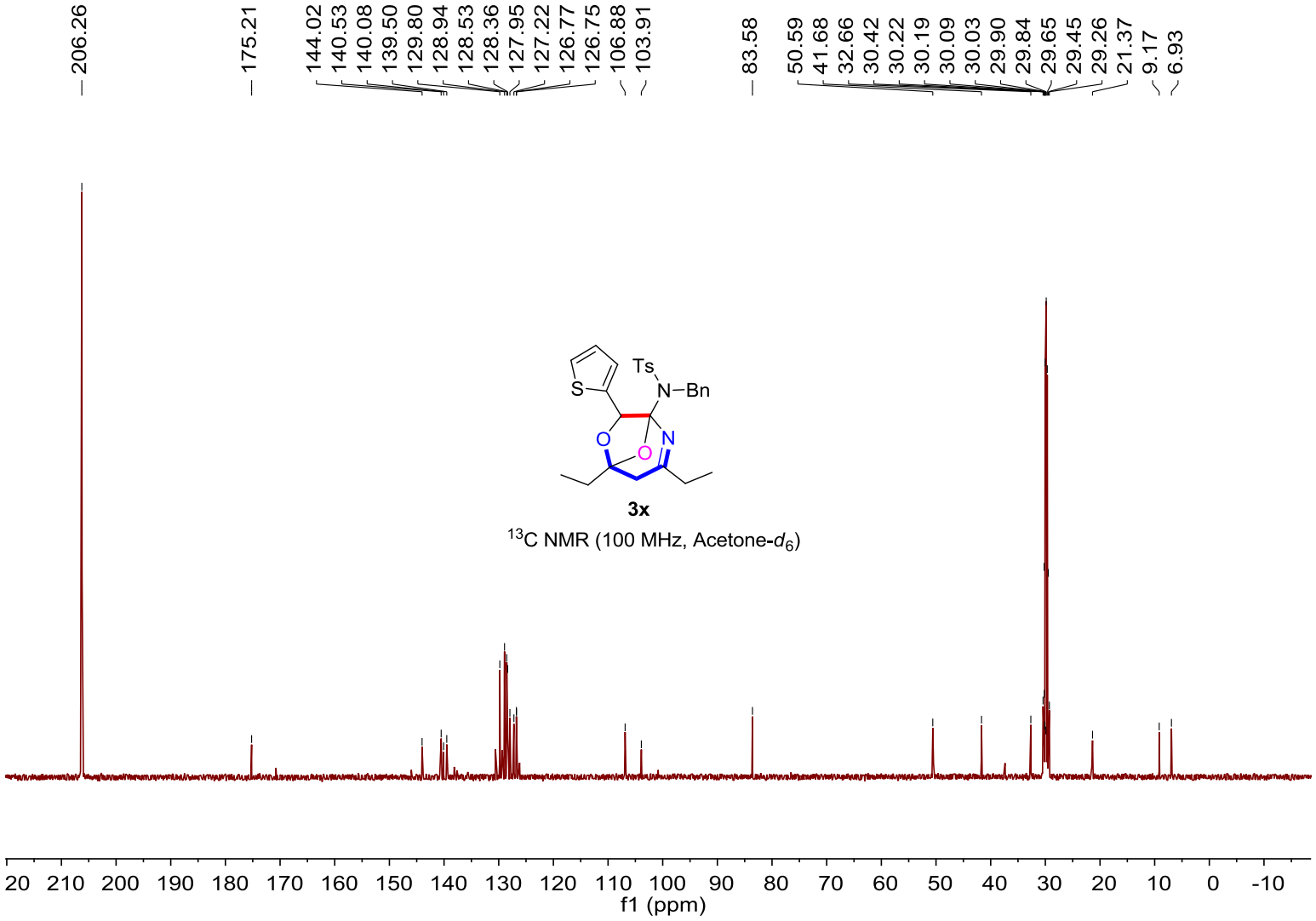
3w

^{13}C NMR (100 MHz, Acetone-d_6)



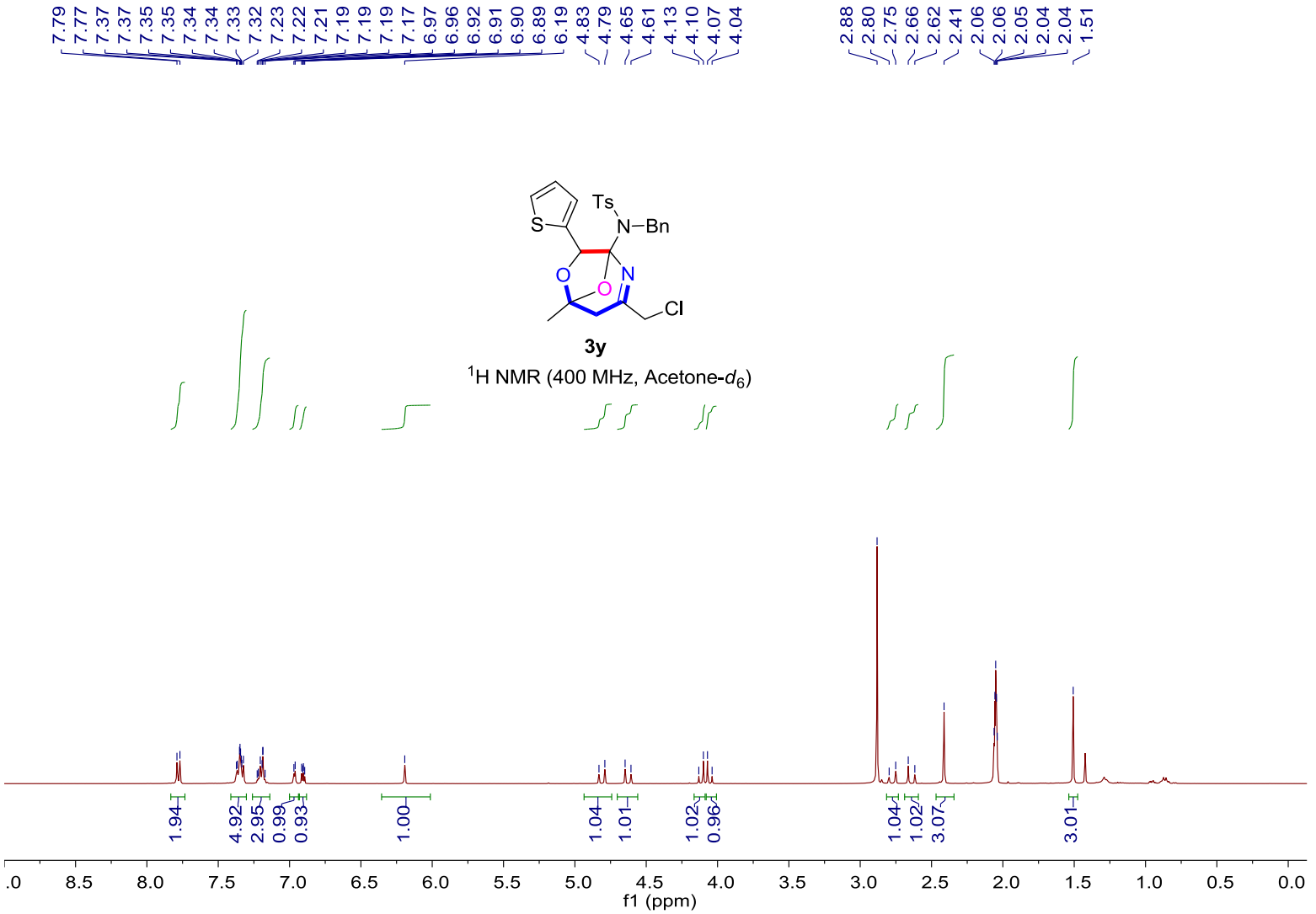
3x

^{1}H NMR (400 MHz, Acetone-d_6)



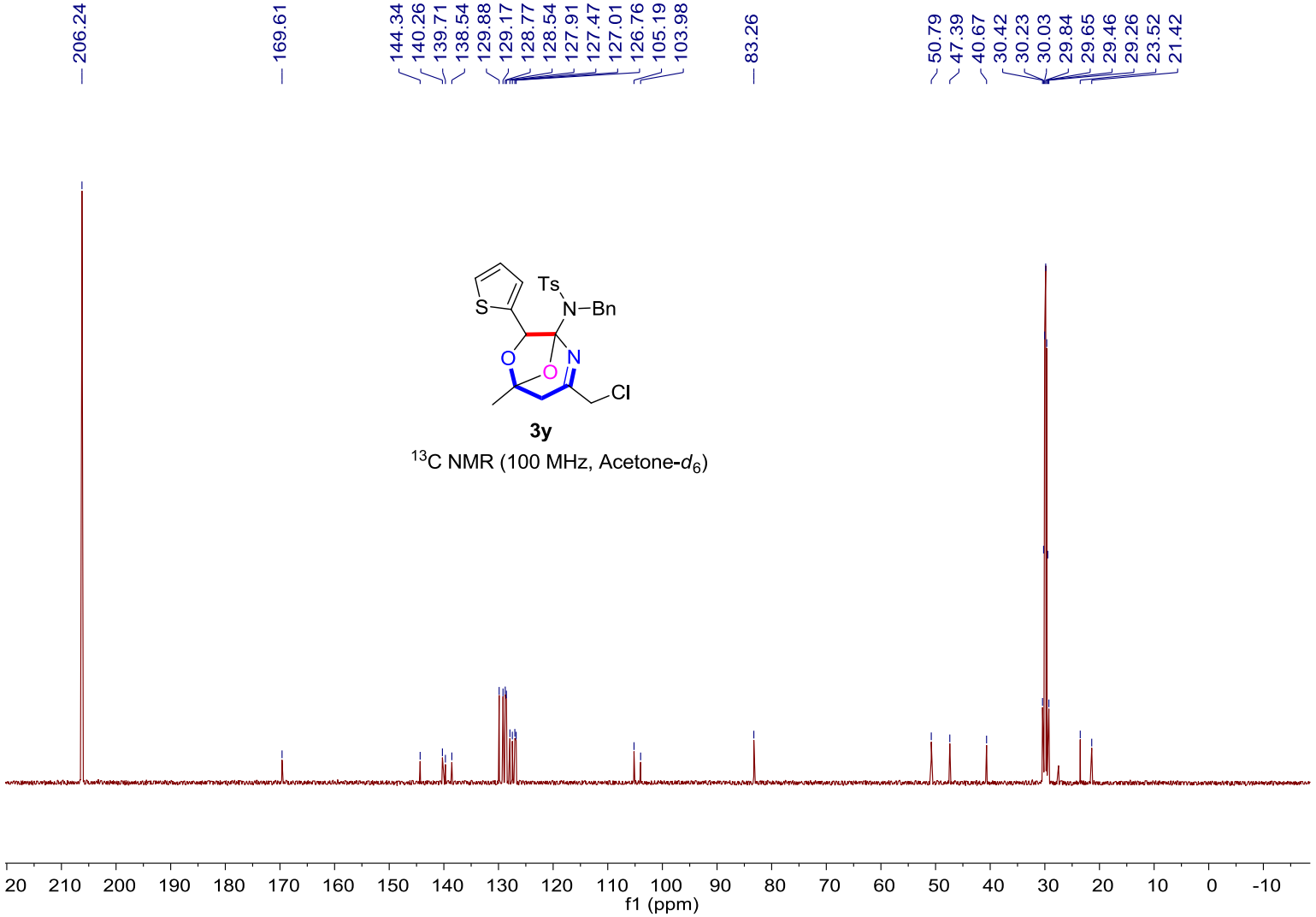
3x

^{13}C NMR (100 MHz, Acetone-d_6)



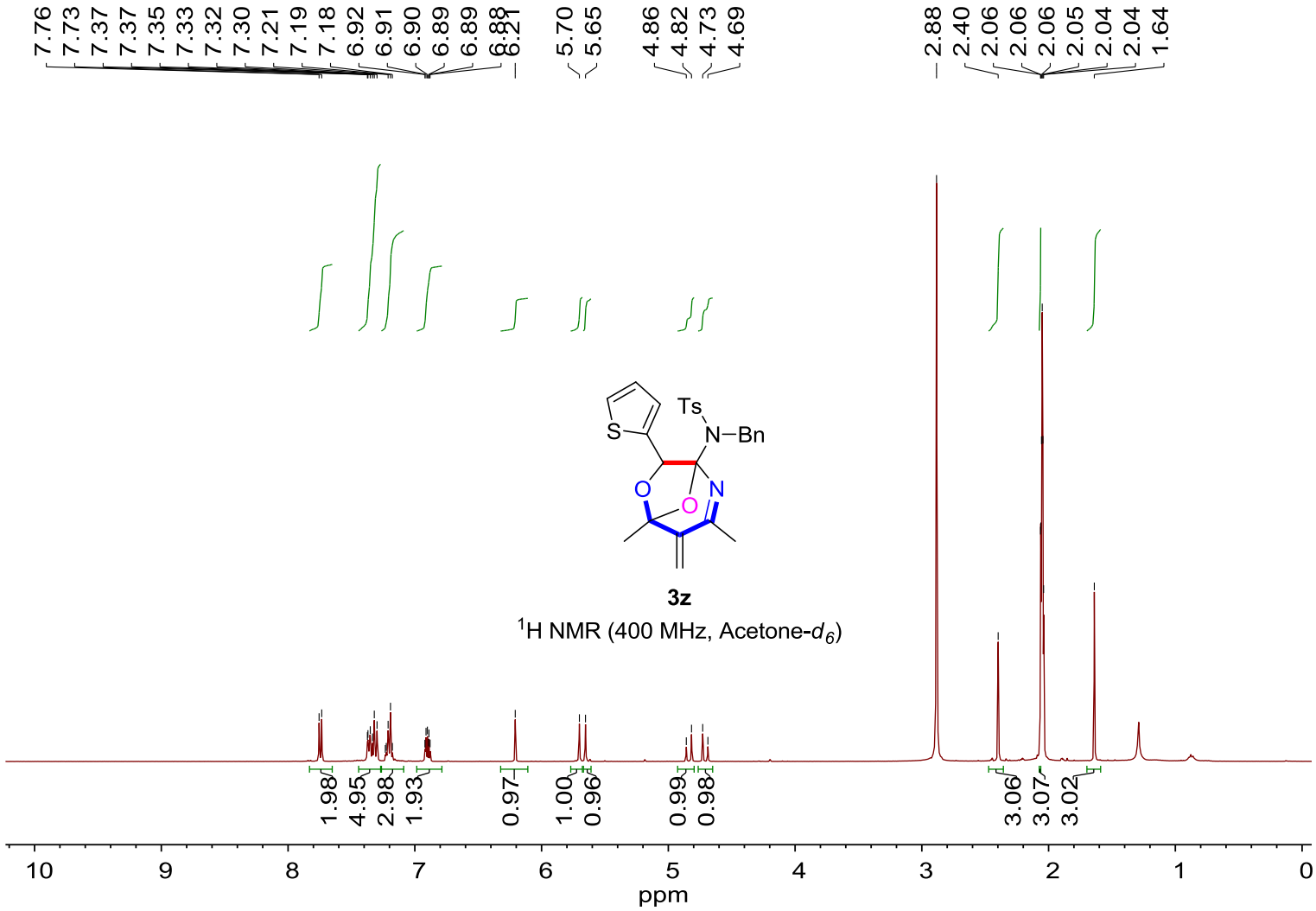
3y

^{1}H NMR (400 MHz, Acetone-d_6)



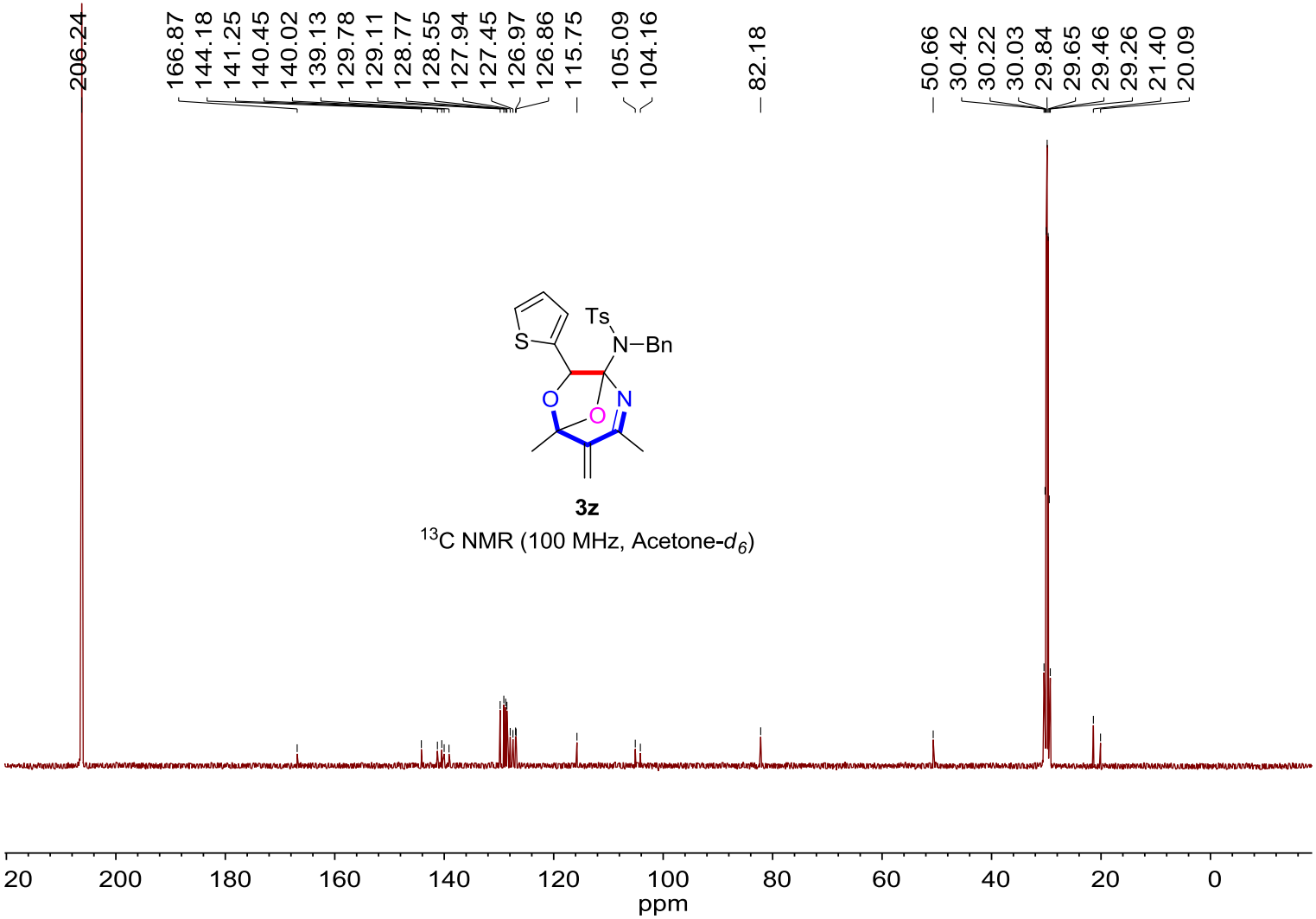
3y

^{13}C NMR (100 MHz, Acetone-d_6)



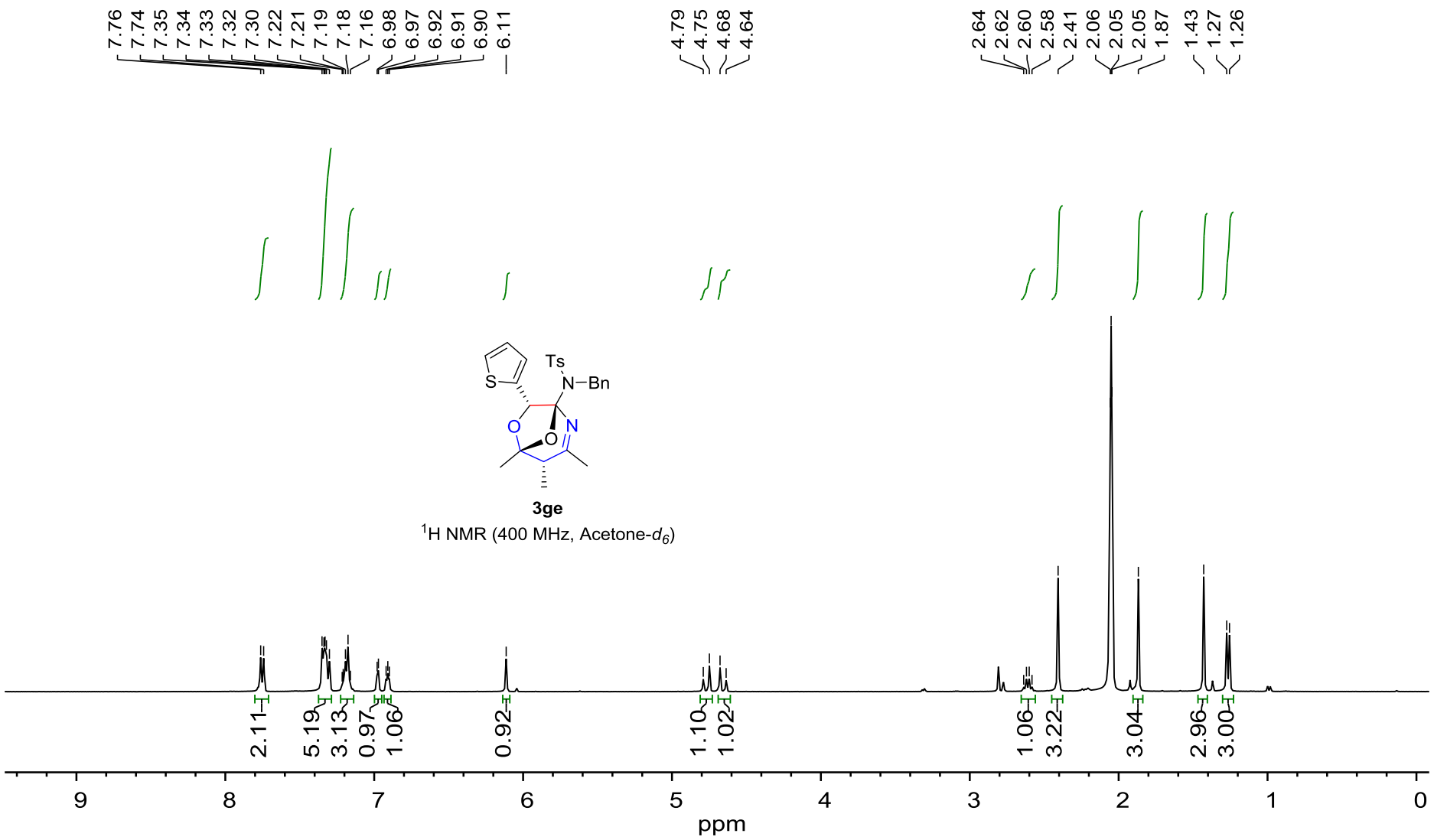
3z

^{1}H NMR (400 MHz, Acetone-d_6)



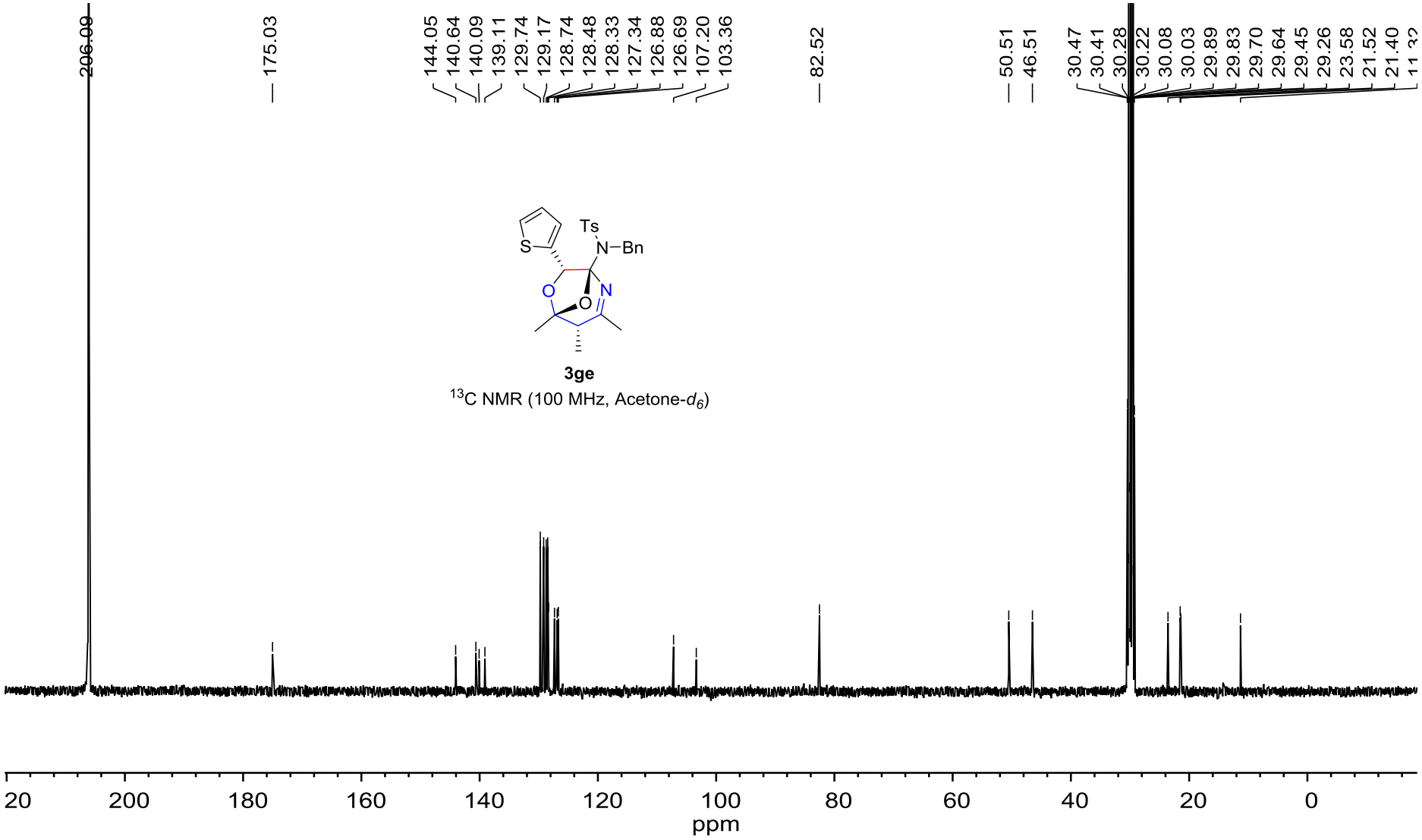
3z

^{13}C NMR (100 MHz, Acetone-d_6)



3ge

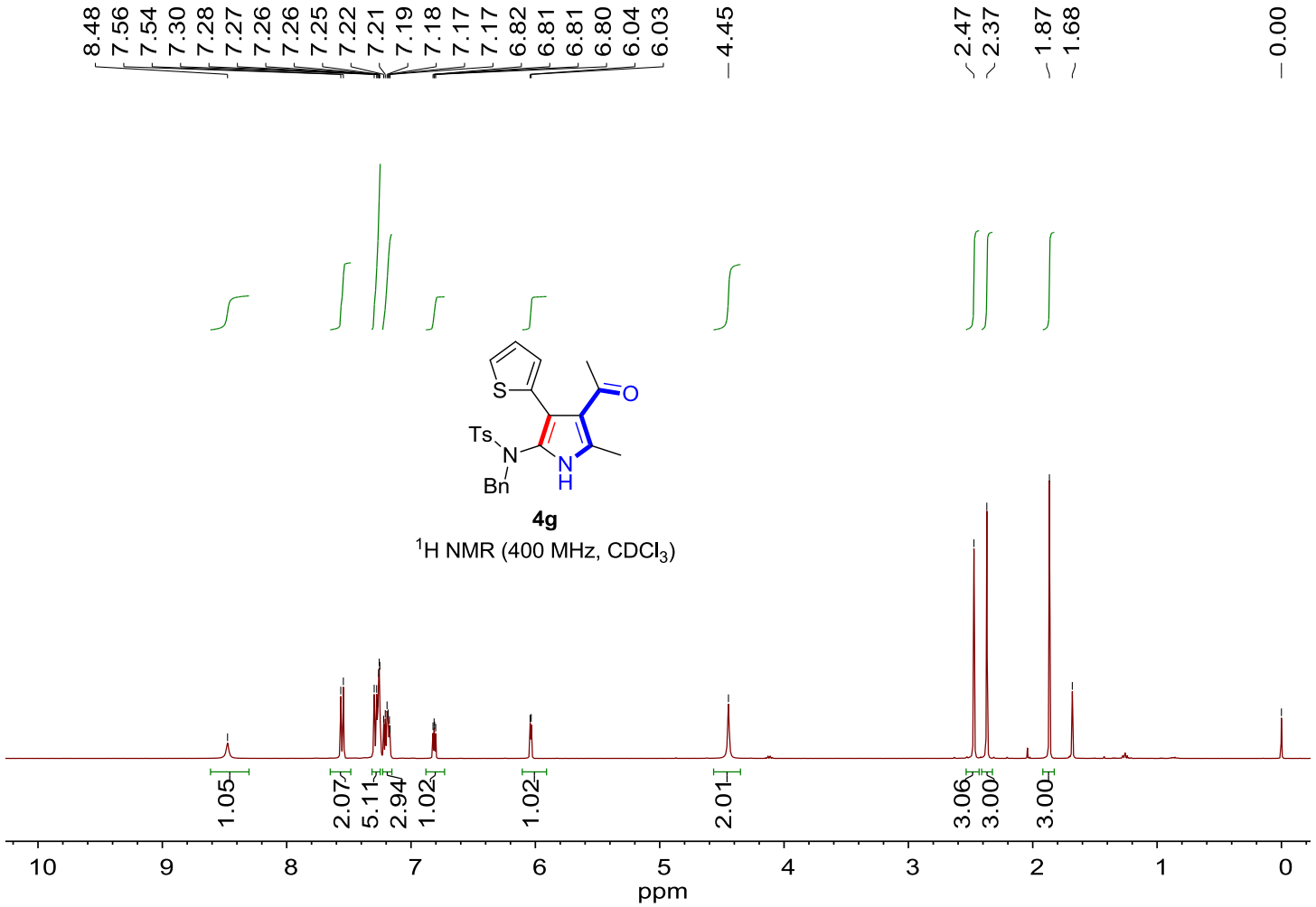
^{1}H NMR (400 MHz, Acetone-d_6)

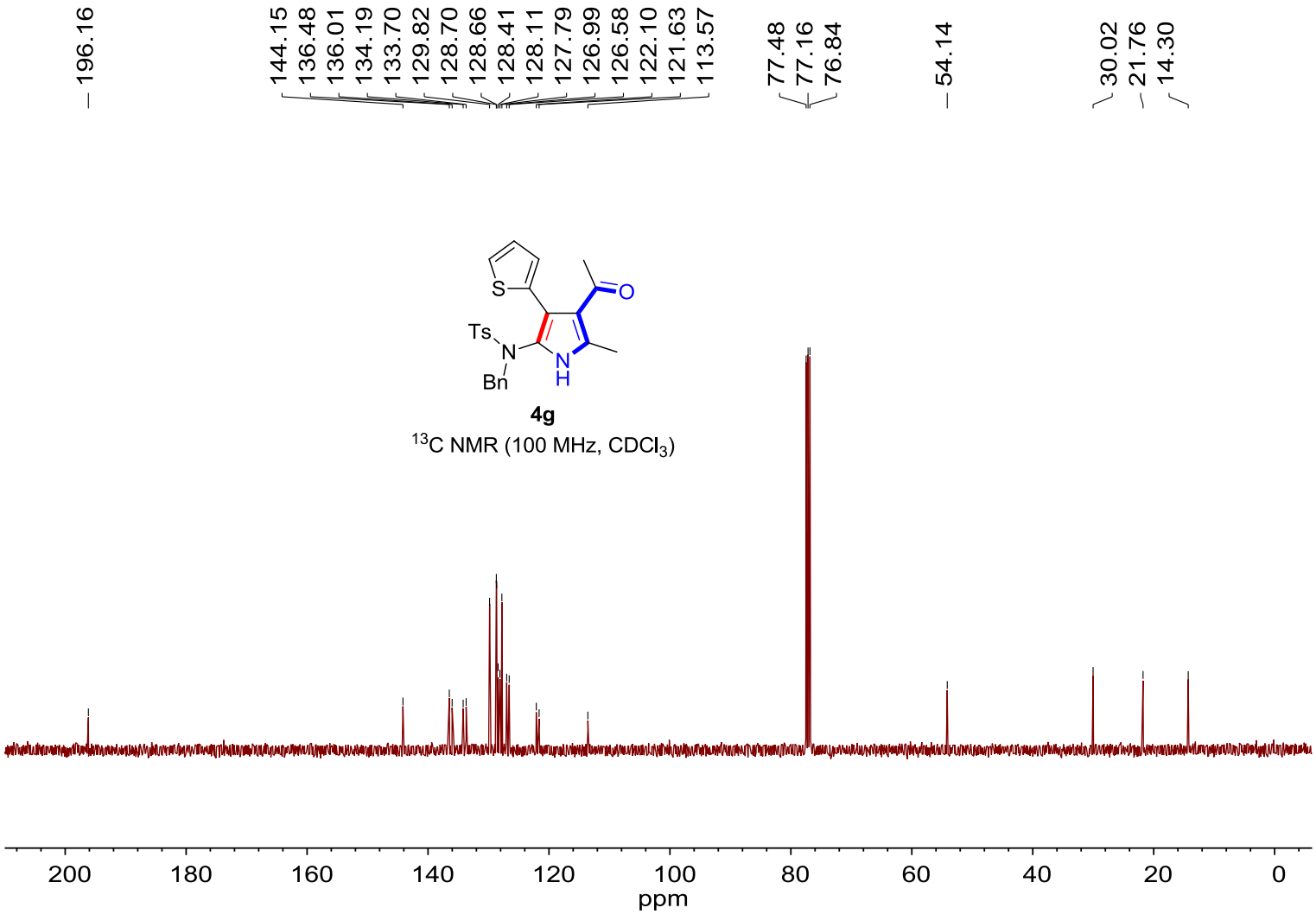


3ge

^{13}C NMR (100 MHz, Acetone-d_6)

15. NMR spectroscopy of pyrrole 4g

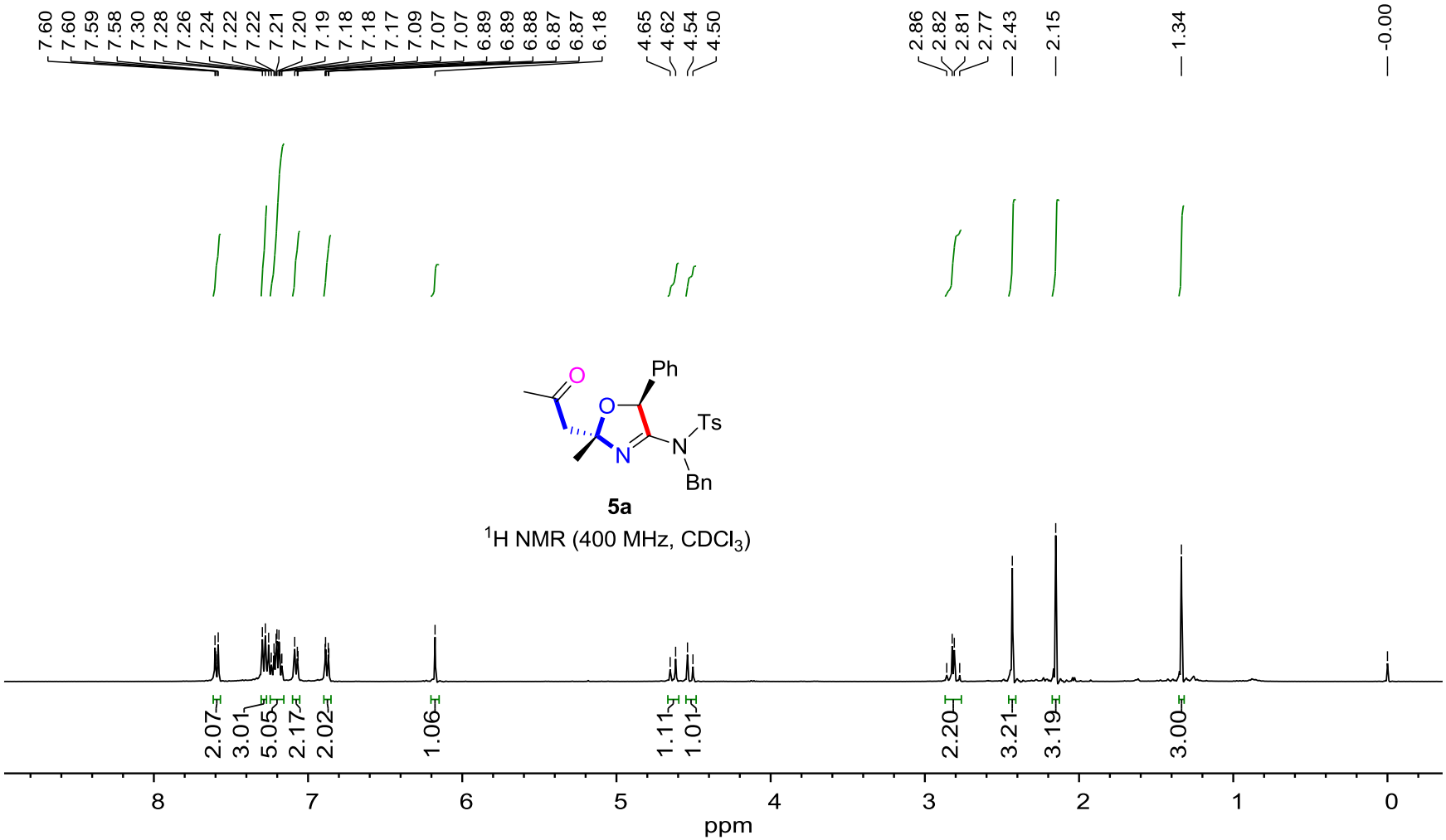


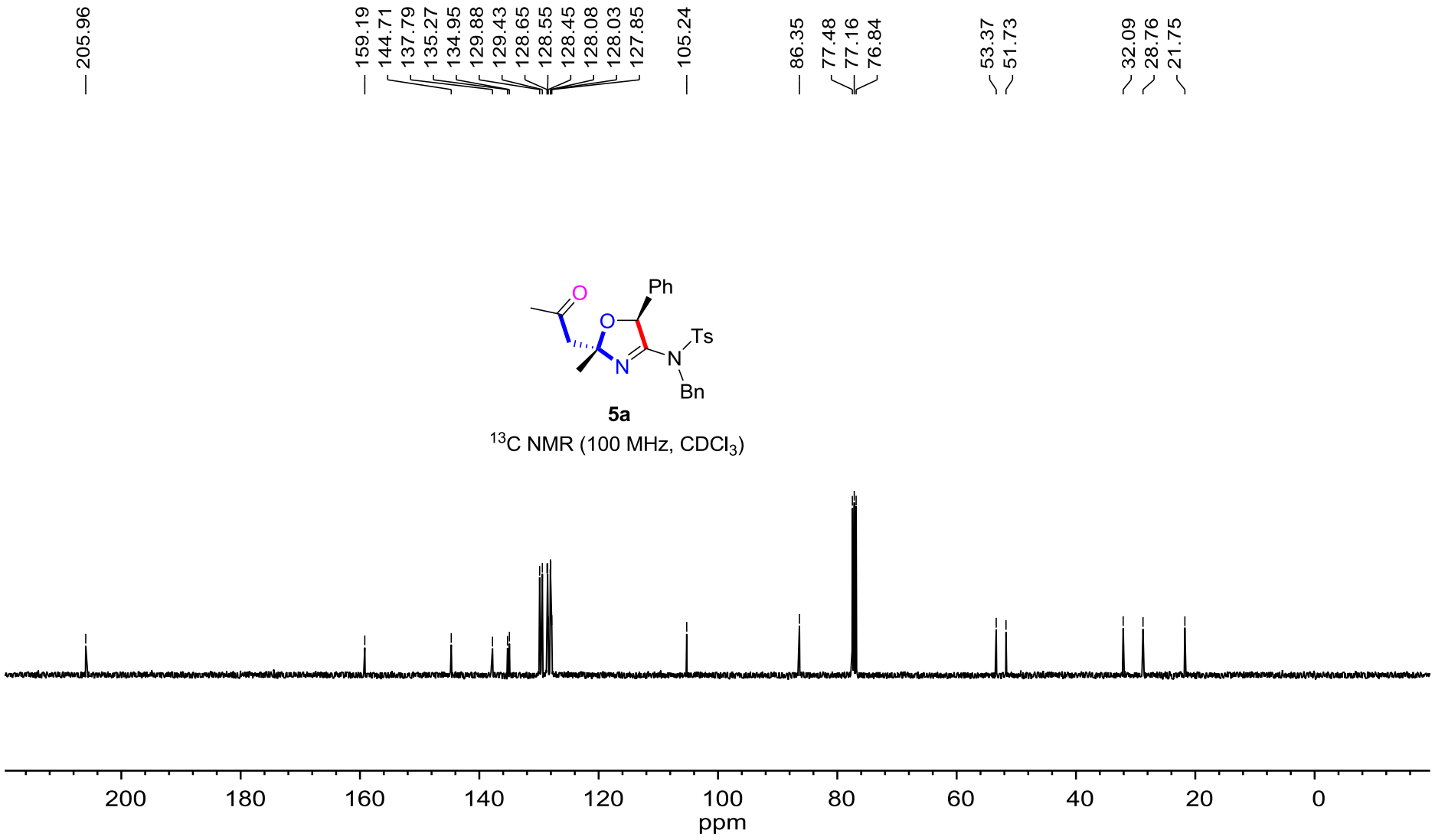


4g

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

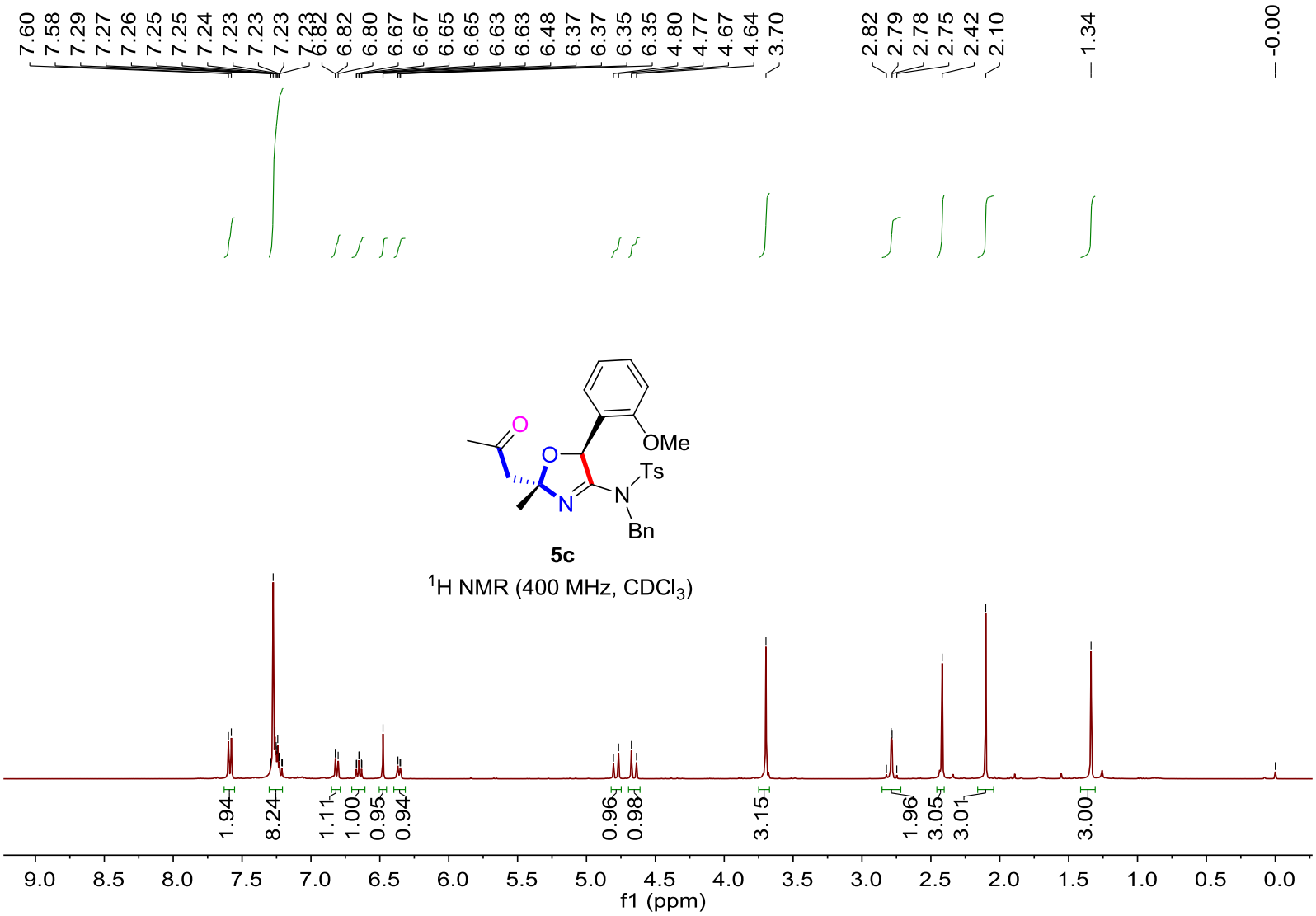
16. NMR spectroscopy of dihydrooxazoles 5

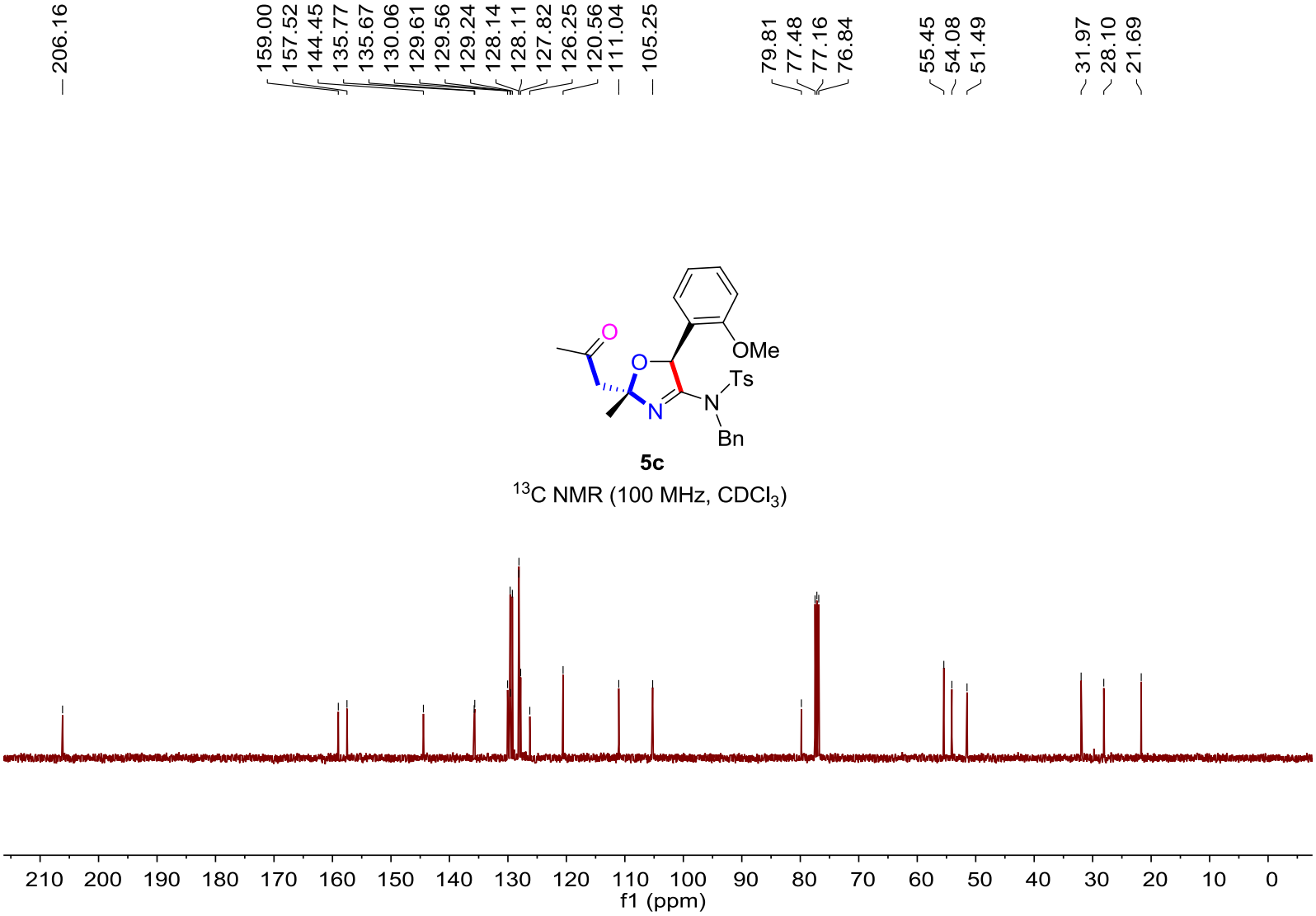




5a

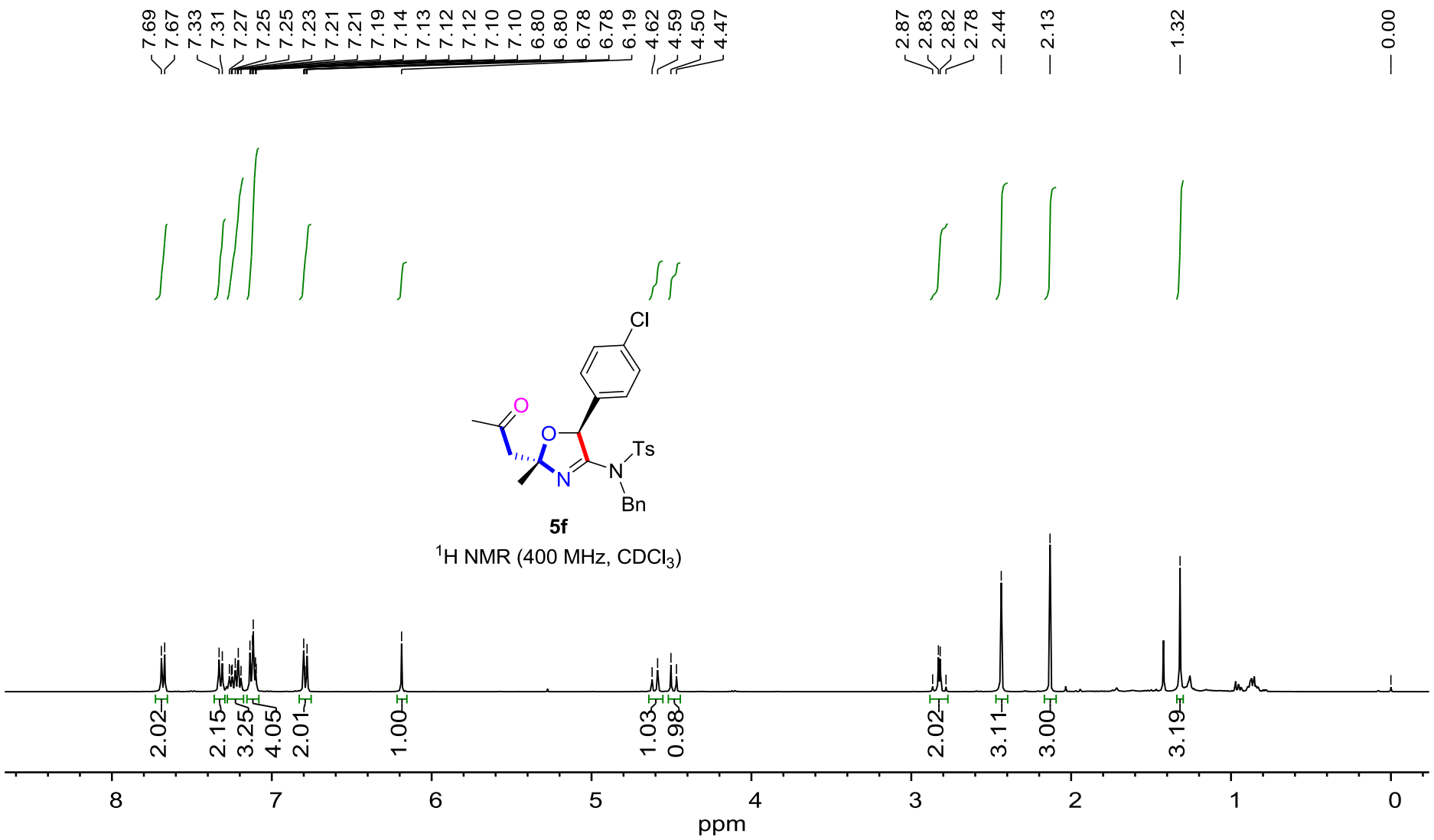
^{13}C NMR (100 MHz, $CDCl_3$)

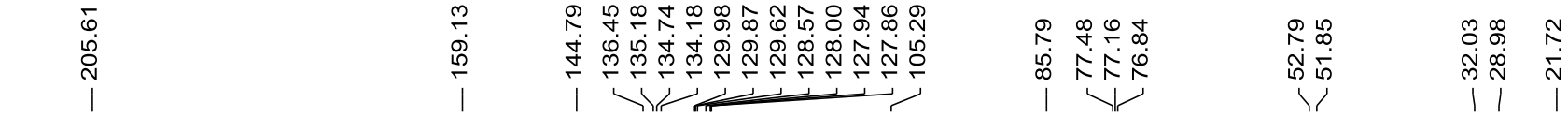

7.60
7.58
7.29
7.27
7.26
7.25
7.25
7.24
7.23
7.23
7.23
6.82
6.82
6.80
6.67
6.67
6.65
6.65
6.63
6.63
6.48
6.37
6.37
6.35
6.35
4.80
4.77
4.67
4.64
3.70
2.82
2.79
2.78
2.75
2.42
2.10
1.34
-0.00
O
O
N
OMe
Ts
N
Bn
5c
1H NMR (400 MHz, CDCl3)
1.94
8.24
1.11
1.00
0.95
0.94
0.96
0.98
3.15
1.96
3.05
3.01
3.00
9.0
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
f1 (ppm)

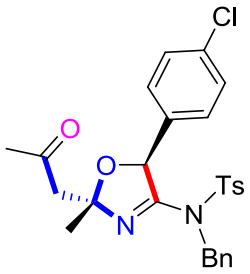


5c

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

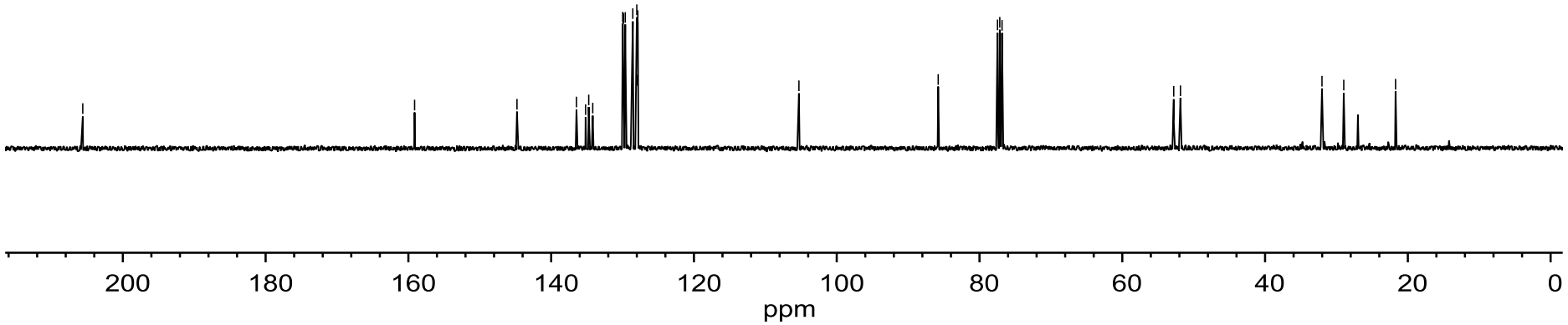

7.69
7.67
7.33
7.31
7.27
7.25
7.25
7.23
7.21
7.21
7.19
7.14
7.13
7.12
7.12
7.10
7.10
6.80
6.80
6.78
6.78
6.19
4.62
4.59
4.50
4.47
2.87
2.83
2.82
2.78
2.44
2.13
1.32
0.00
Cl
O
O
N
N
Ts
Bn
5f
1H NMR (400 MHz, CDCl3)
2.02
2.15
3.25
4.05
2.01
1.00
1.03
0.98
2.02
3.11
3.00
3.19
8
7
6
5
4
3
2
1
0
ppm

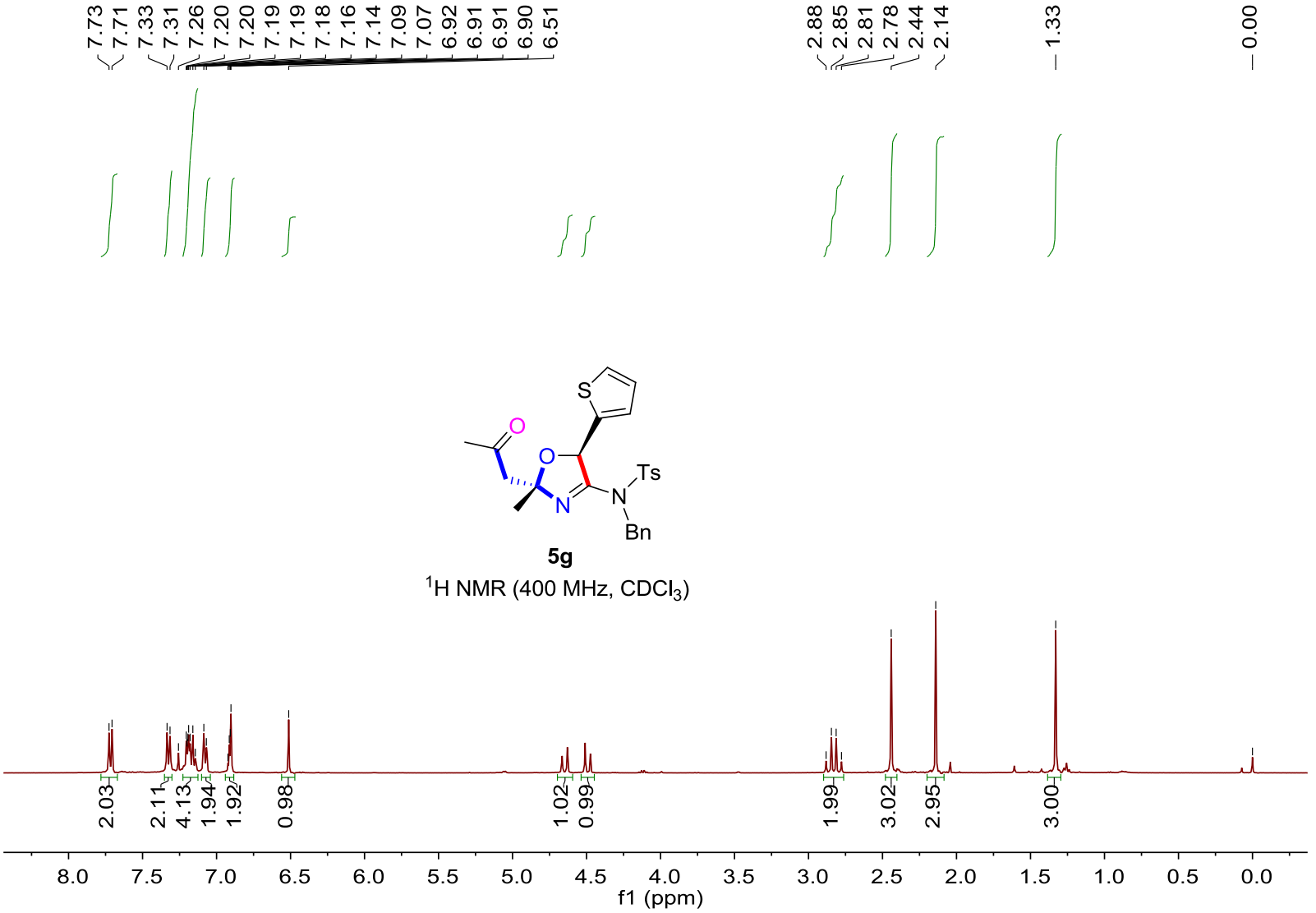


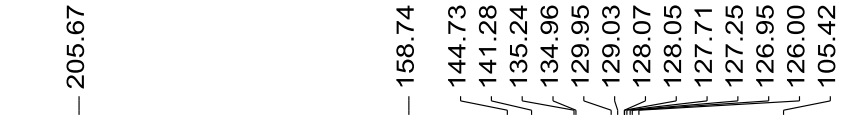


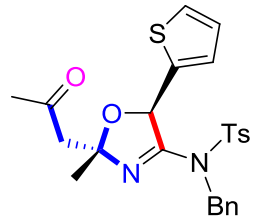
5f

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



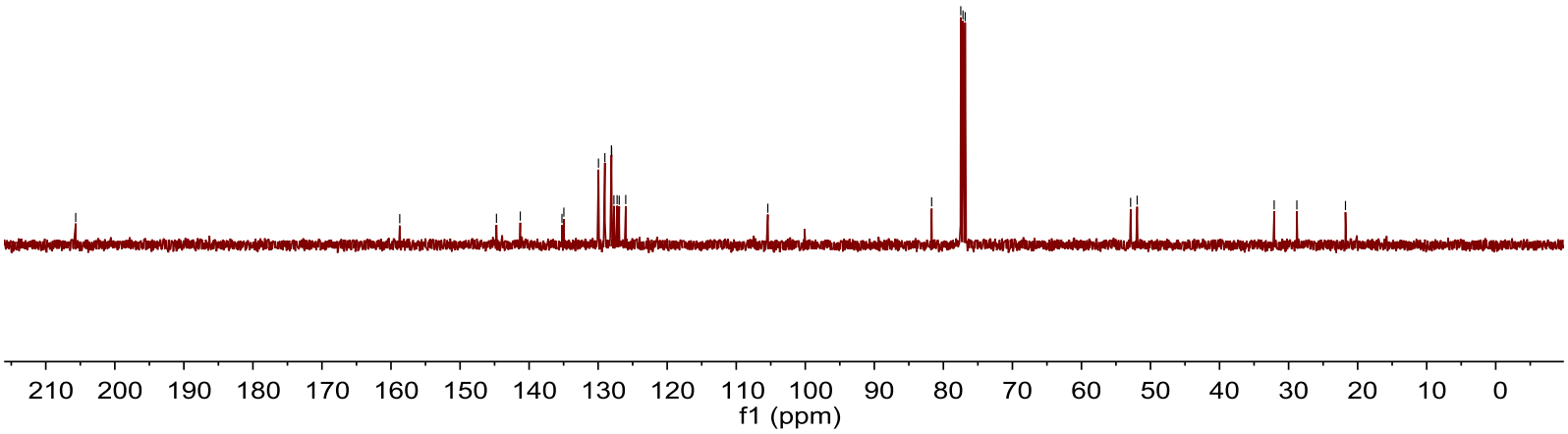

7.73
7.71
7.33
7.31
7.26
7.20
7.20
7.19
7.19
7.18
7.16
7.14
7.09
7.07
6.92
6.91
6.91
6.90
6.51
2.88
2.85
2.81
2.78
2.44
2.14
1.33
0.00
S
O
O
N
N
Ts
Bn
5g
1H NMR (400 MHz, CDCl3)
2.03
2.11
4.13
1.94
1.92
0.98
1.02
0.99
1.99
3.02
2.95
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



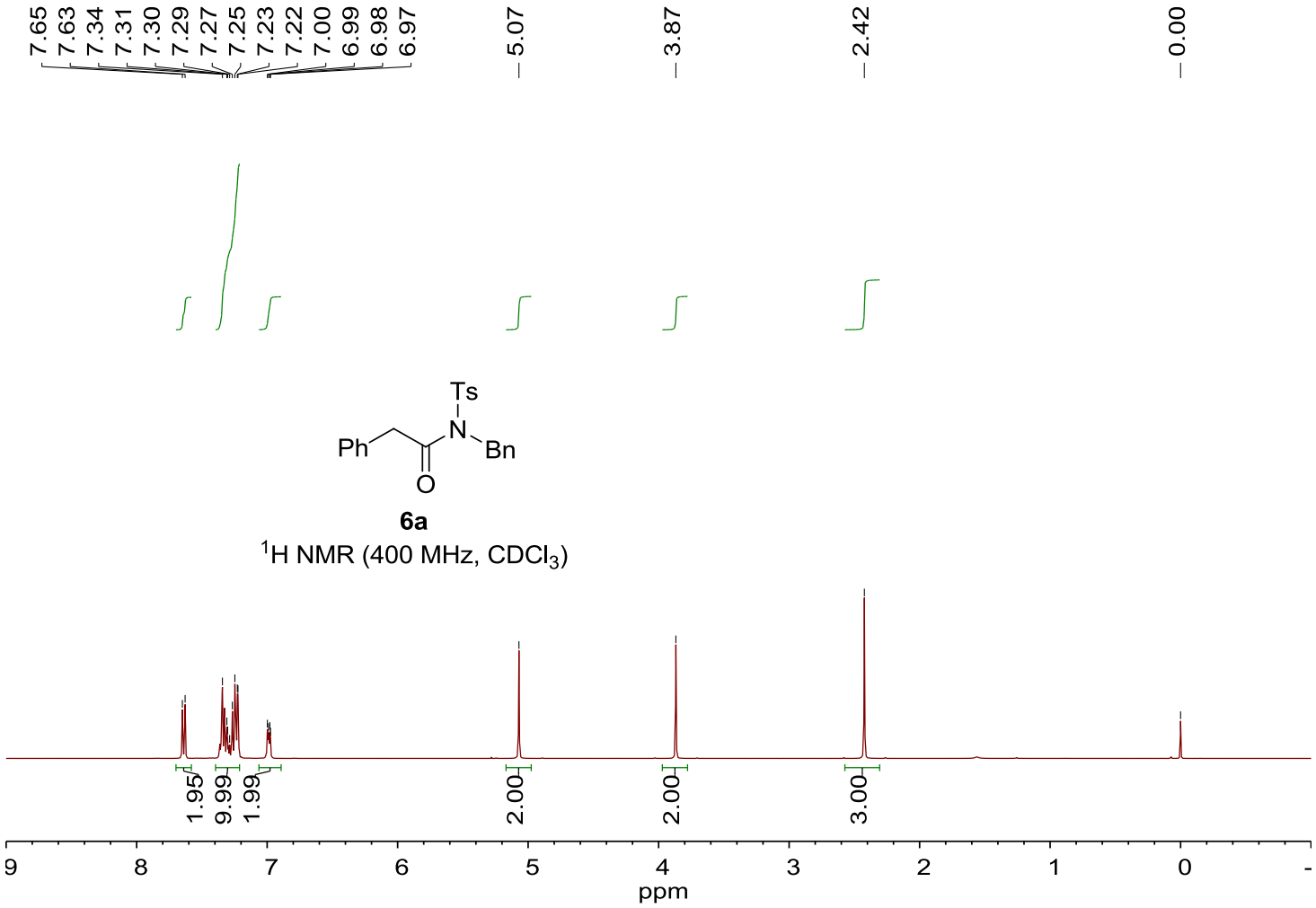


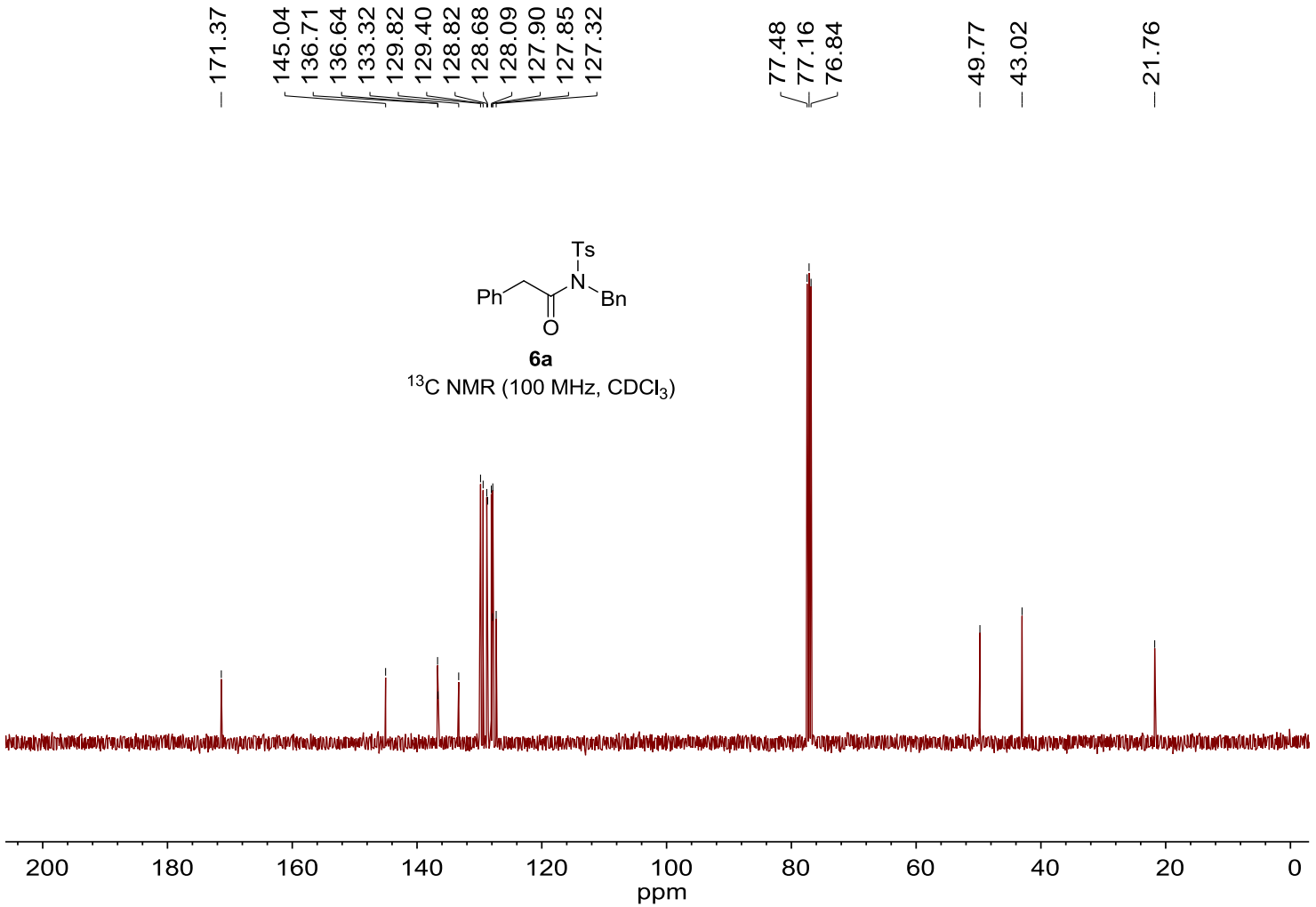
5g

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



17. NMR spectroscopy of amide 6a





6a

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