Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

A convenient, economical and scalable multi-gram synthesis of 1-vinylcyclopropyl 4-methylbenzenesulfonate

O. Stephen Ojo,[a] Phillip A. Inglesby,[a] Daniela E. Negru[b] and P. Andrew Evans[*b]

[a] *Department of Chemistry, University of Liverpool, Crown Street, L69 7ZD, United Kingdom*

[b] *Department of Chemistry, Queen's University, 90 Bader Lane, Kingston, ON K7L 3N6, Canada*

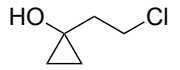
Contents of Supporting Information:

1. General Information

All reactions were carried out in flame-dried glassware under an atmosphere of argon using anhydrous solvent. Commercially available reagents were used as received from the following suppliers: ethyl 3-chloropropanoate (98%) and anhydrous potassium *tert*-butoxide (97%) were purchased from Alfa Aesar; titanium isopropoxide (98%), ammonium chloride (99.5%), sodium chloride (extra pure) were purchased from Acros Organics; ethylmagnesium bromide (3M in diethylether) and 4-(dimethylamino)pyridine (99%) were purchased from Sigma Aldrich; *p*-toluenesulfonyl chloride (98%) was purchased from Merck; magnesium sulphate (laboratory grade), triethylamine (laboratory grade), sodium hydrogen carbonate (analytical grade), 37% hydrochloric acid (analytical grade), petroleum ether (30-40 ^{o}C, laboratory grade), diethyl ether (laboratory grade, 99%, stabilized with BHT) and dichloromethane (HPLC grade) were purchased from Fisher Scientific. Anhydrous solvents were dried were obtained from a Grubbs solvent systems by passing the aforementioned solvents through activated alumina. Flash chromatography was performed using silica gel 60 (40-63 μm, *FluoroChem*) and gave spectroscopic data consistent with being ≥95% the assigned structure. IR spectra were recorded on an *Agilent Cary 630 FTIR* spectrometer; wavenumbers (ν) are given in cm^{-1}; and the abbreviations w (weak, <25%), m (medium, 25-50%), s (strong, 51-75%), vs (very strong, >75%) and br (broad) are used to describe the relative intensities of the IR absorbance bands. Mass spectra were obtained through the *Chemistry Department Mass Spectrometry Service* at the Queen's University. ^{1}H spectra were

recorded on a *Bruker Avance DRX-500* spectrometer using d[1]-chloroform at ambient temperature; chemical shifts (δ) are given in ppm. NMR data were calibrated using the signal of residual undeuterated solvent as an internal reference ($CHCl_3$, δ_H = 7.26 ppm, δ_C = 77.16 ppm). ^{1}H NMR data are reported as follows: chemical shift (multiplicity, 1st order spin system if available, coupling constant and integration). Coupling constants (*J*) are reported in Hz and apparent splitting patterns are designated using the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), quintet, sextet, m (multiplet), br (broad), app. (apparent) and combinations thereof. ^{13}C NMR spectra with complete proton decoupling were described with the aid of an APT sequence, separating methylene and quaternary carbons (e, even), from methyl and methine carbons (o, odd).

2. Spectral Data for 11, 12 and 1



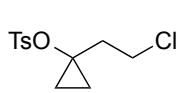
1-(2-Chloroethyl)cyclopropanol 11.[1]

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74 (t, *J* = 7.1 Hz, 2H), 2.71 (br. s, 1H), 1.99 (t, *J* = 7.1 Hz, 2H), 0.77 (app. t, *J* = 6.0 Hz, 2H), 0.52 (d, A of AB, J_{AB} = 5.3 Hz, 1H), 0.51 (d, B of AB, J_{AB} = 5.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 54.08 (e), 42.11 (e), 41.10 (e), 13.41 (e).

IR (Neat) 3324 (br, m), 3089 (w), 3008 (w), 2965 (w), 1452 (m), 1419 (m), 1247 (vs), 1138 (m), 1013 (vs), 956 (s), 743 (s), 696 (vs) cm^{-1}.

HRMS (EI) calculated for $C_5H_9{}^{35}ClO$ 120.0342, found 120.0338.



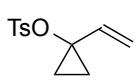
1-(2-Chloroethyl)cyclopropyl 4-methylbenzenesulfonate 12.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 3.70 (t, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 2.23 (t, *J* = 7.1 Hz, 2H), 1.12 (app. t, *J* = 7.1 Hz, 2H), 0.72 (app. t, *J* = 7.2 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 145.10 (e), 134.98 (e), 130.04 (o), 127.67 (o), 64.54 (e), 40.78 (e), 39.22 (e), 21.80 (o), 11.59 (e).

IR (Neat) 2970 (w), 1598 (w), 1452 (w), 1359 (s), 1347 (s), 1172 (vs), 1094 (s), 896 (vs), 813 (vs), 690 (s) cm^{-1}.

HRMS (ESI, $[M+H]^+$) calculated for $C_{12}H_{16}{}^{35}ClO_3S$ 275.0503, found 275.0498.



1-Vinylcyclopropyl 4-methylbenzenesulfonate 1.[2]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.2 Hz, 2H), 5.89

[1] O. G. Kulinkovich, Y. Y. Kozyrkov, A. V. Bekish, E. A. Matiushenkov and I. L. Lysenko, *Synthesis*, 2005, **10**, 1713.
[2] A. Stolle, J. Ollivier, P. P. Piras, J. Salaün and A. de Meijere, *J. Am. Chem. Soc.*, 1992, **114**, 4051

(dd, J = 17.2, 10.8 Hz, 1H), 5.10 (d, J = 17.2 Hz, 1H), 5.01 (d, J = 11.1 Hz, 1H), 2.45 (s, 3H), 1.36 (d, A of AB, J_{AB} = 6.3 Hz, 1H), 1.35 (d, B of AB, J_{AB} = 6.1 Hz, 1H), 0.92 (dd, A of ABM, J_{AB} = 5.6 Hz, J_{AM} = 1.0 Hz, 1H), 0.91 (dd, B of ABM, J_{AB} = 6.0 Hz, J_{BM} = 0.8 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 144.84 (e), 136.62 (o), 135.01 (e), 129.83 (o), 127.94 (o), 113.52 (e), 65.47 (e), 21.73 (o), 14.04 (e).

IR (Neat) 3003 (w), 1644 (w), 1596 (m), 1349 (vs), 1294 (m), 1165 (vs), 1089 (s), 1032 (s), 949 (vs), 906 (vs), 819 (vs) cm^{-1}.

HRMS (ESI, $[M+H]^+$) calculated for $C_{12}H_{15}O_3S$ 239.0736, found 239.0729.

3. Procedure for the Synthesis ACP 2a.[3] Sodium hydride (0.46 g, 11.6 mmol; 60% in mineral oil) was suspended in anhydrous *N*,*N*-dimethylformamide (25 mL) and stirred at room temperature under an atmosphere of argon. *N*-allyl-4-methyl-benzenesulfonamide (2.45 g, 11.6 mmol) was added and the reaction mixture was stirred for *ca*. 1 hour. Tris(dibenzylideneacetone)dipalladium (0.082 g, 0.09 mmol), 1,2-bis(diphenylphosphino)ethane (0.071 g, 0.18 mmol) and 1-vinylcyclopropyl 4-methylbenzenesulfonate **1** (2.0 g, 8.9 mmol) were dissolved in anhydrous tetrahydrofuran (25 mL) and stirred at room temperature for *ca*. 30 minutes before being added *via* Teflon® cannula to the solution of the anion. The resulting mixture was stirred for *ca*. 12 hours (t.l.c. control), diluted with deionized water (30 mL) and partitioned with diethyl ethyl (3 x 40 mL). The combined organic phases were washed with water (3 x 30 mL), saturated aqueous NaCl solution (30 mL), dried (anhyd. $MgSO_4$), filtered and concentrated *in vacuo* to afford the crude product. Purification by flash chromatography (SiO_2, eluting with 10-20% diethyl ether/petroleum ether) afforded the alkylidenecyclopropane **2a** (2.19 g, 7.2 mmol, 89%).

4. Spectral Data for ACP 2a

***N*-Allyl-*N*-(2-cyclopropylidenethyl)-4-methylbenzenesulfonamide 2a.**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 5.64 (ddt, J = 16.8, 10.5, 6.3 Hz, 1H), 5.60-5.58 (m, 1H), 5.12-5.06 (m, 2H), 3.94 (d, J = 6.8 Hz, 2H), 3.78 (d, J = 6.3 Hz, 2H), 2.43 (s, 3H), 1.07-1.02 (m, 2H), 1.00-0.95 (m, 2H).

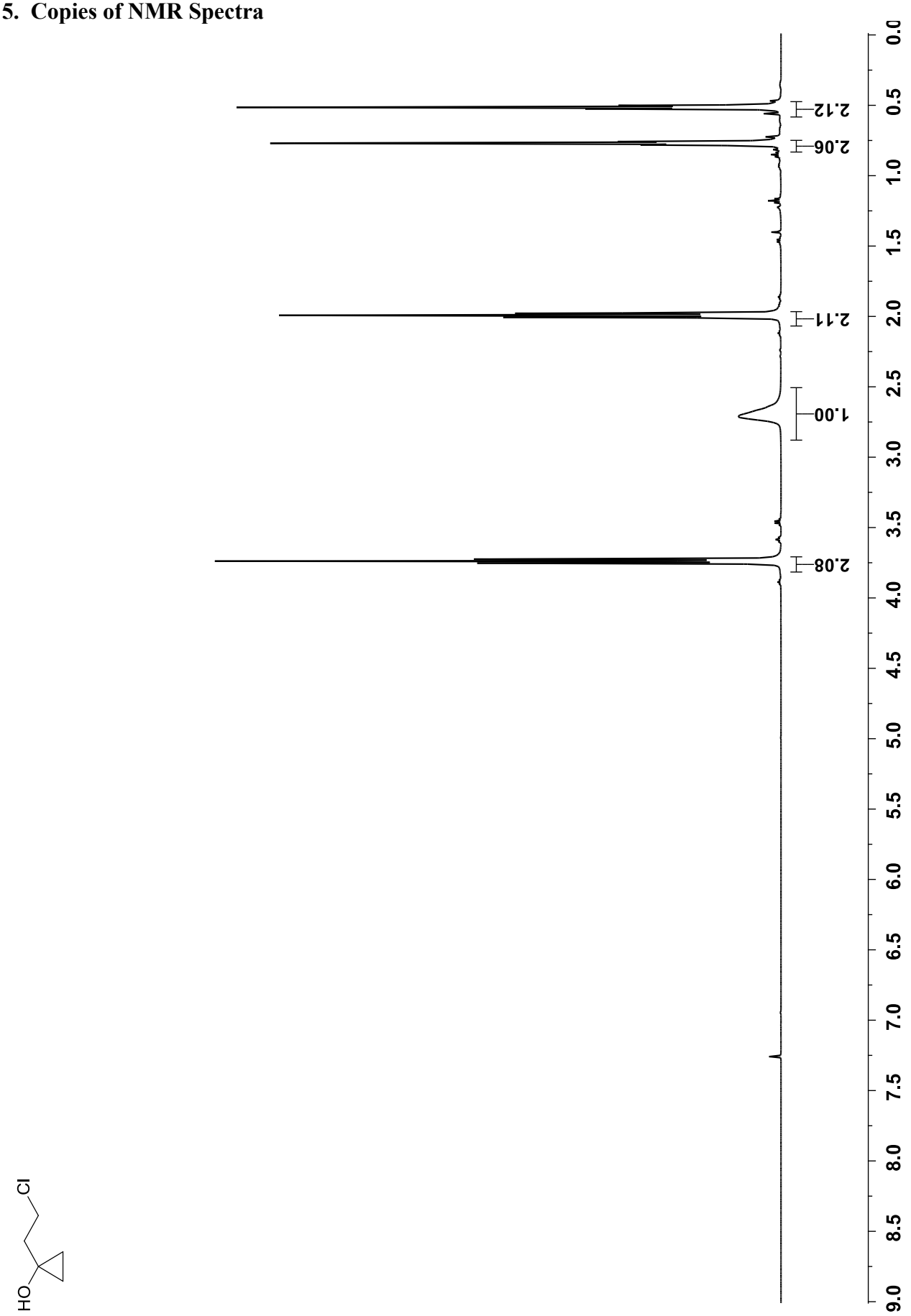
^{13}C NMR (125 MHz, $CDCl_3$) δ 143.21 (e), 137.67 (e), 133.16 (o), 129.75 (o), 127.39 (e), 127.27 (o), 118.50 (e), 112.76 (o), 49.51 (e), 48.30 (e), 21.67 (o), 2.59 (e), 2.04 (e).

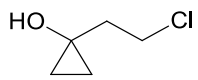
IR (Neat) 3053 (w), 2982 (w), 2924 (m), 2856 (w), 1598 (m), 1495 (w), 1444 (m), 1339 (s), 1156 (vs), 1091 (s), 929 (s), 900 (s), 718 (s) cm^{-1}.

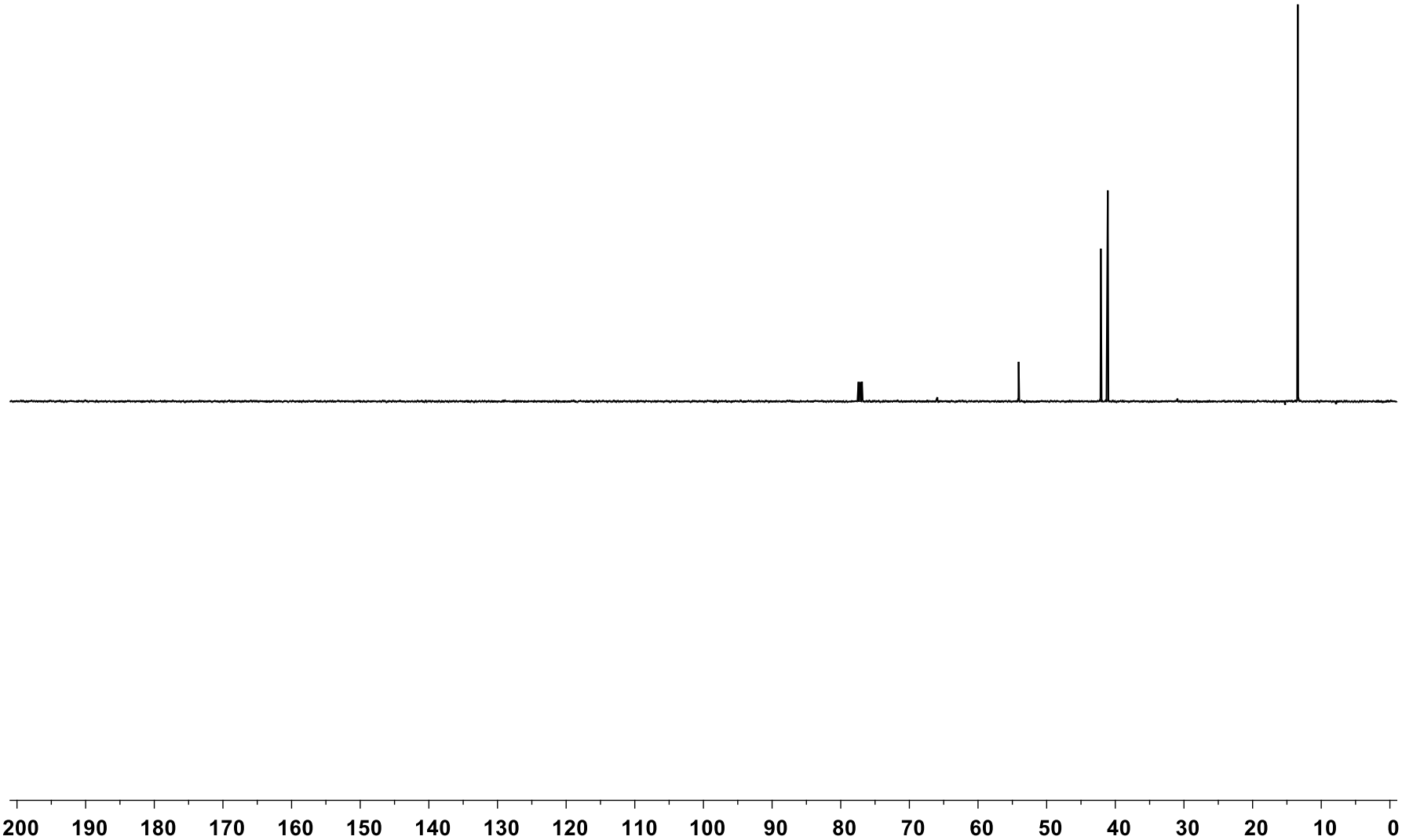
HRMS (CI, $[M+H]^+$) calculated for $C_{15}H_{20}NO_2S$ 278.1215, found 278.1221.

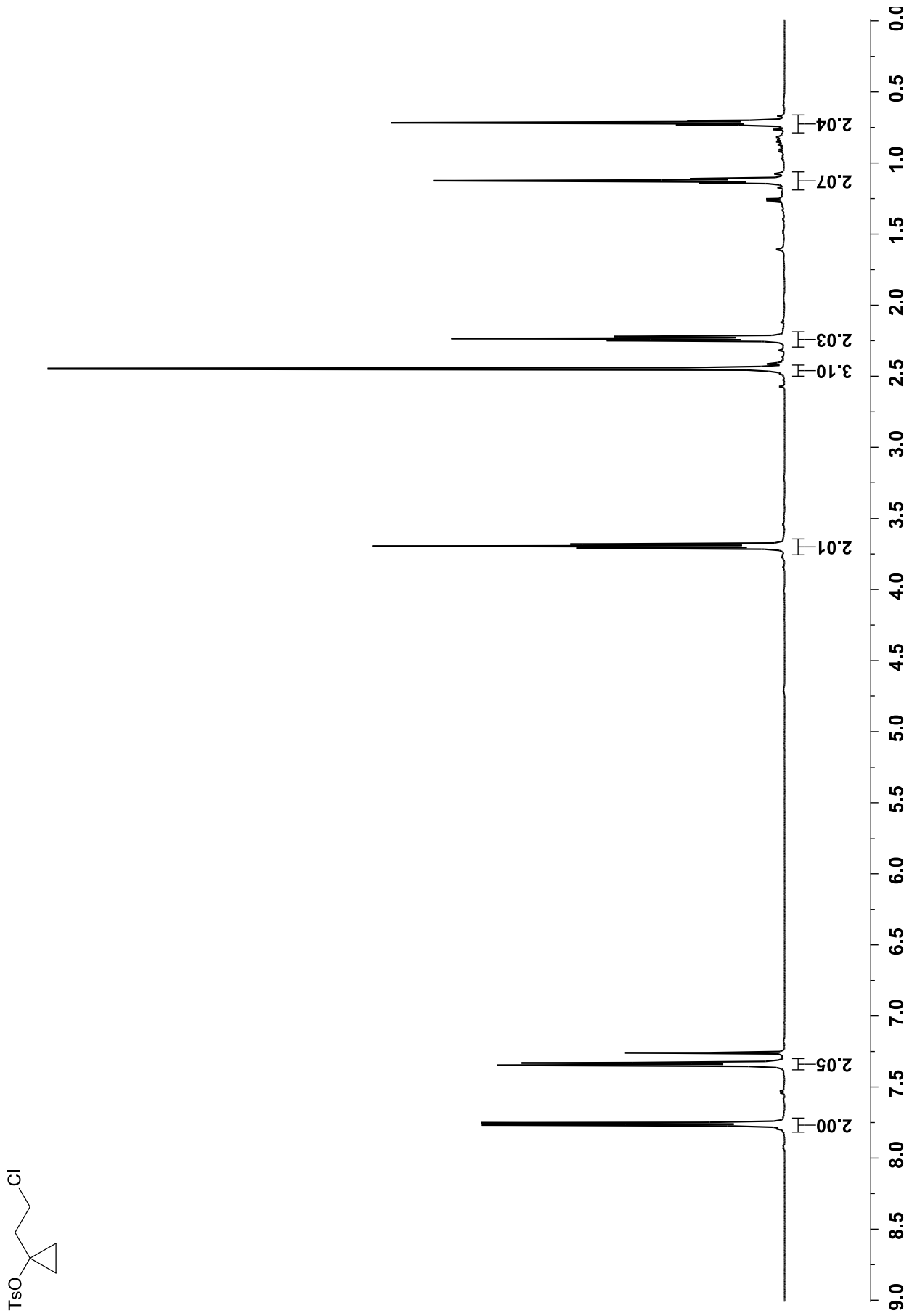
[3] P. A. Evans and P. A. Inglesby, *J. Am. Chem. Soc.*, 2008, **130**, 12838.

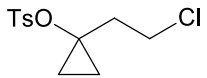
5. Copies of NMR Spectra

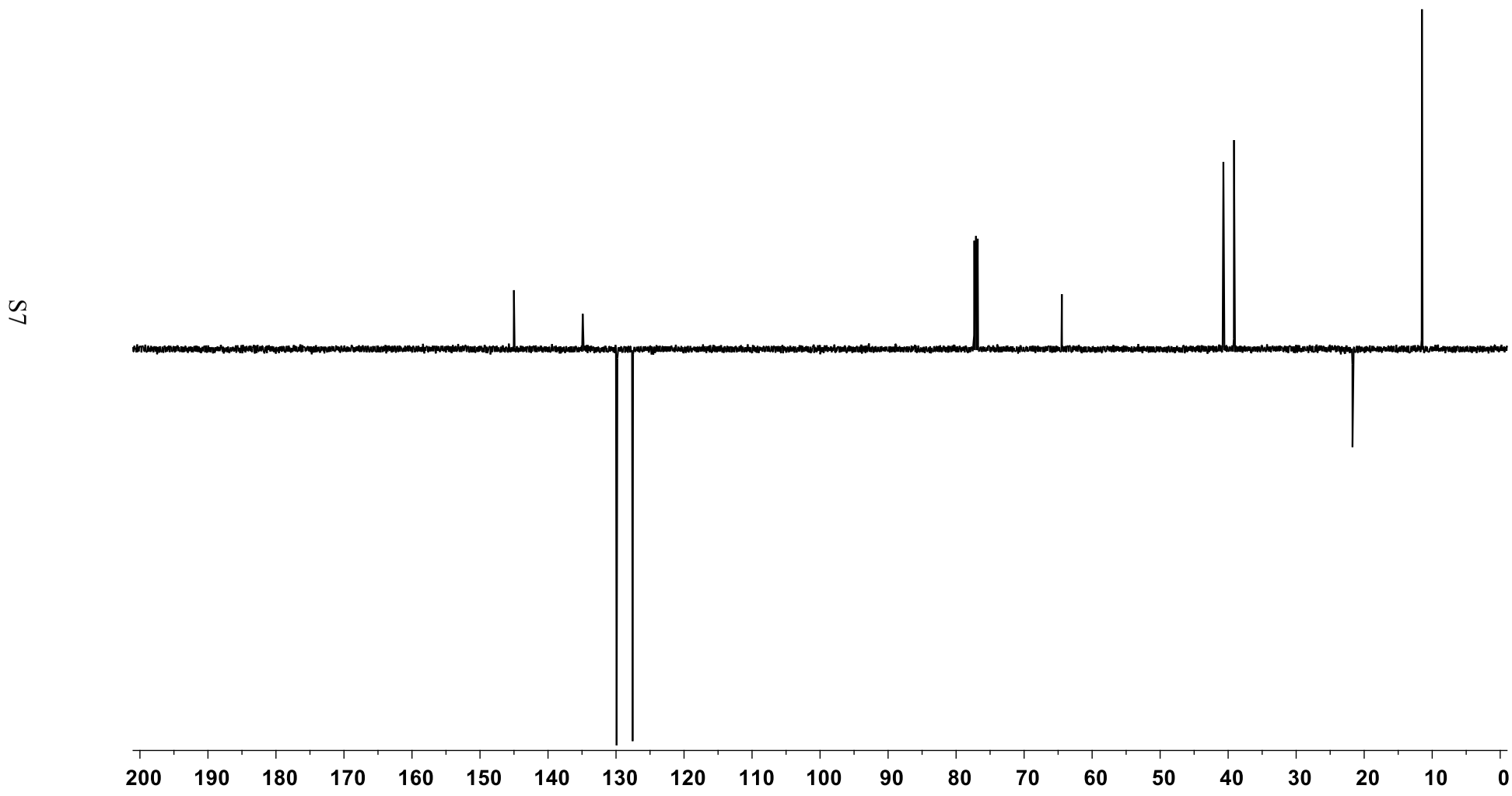


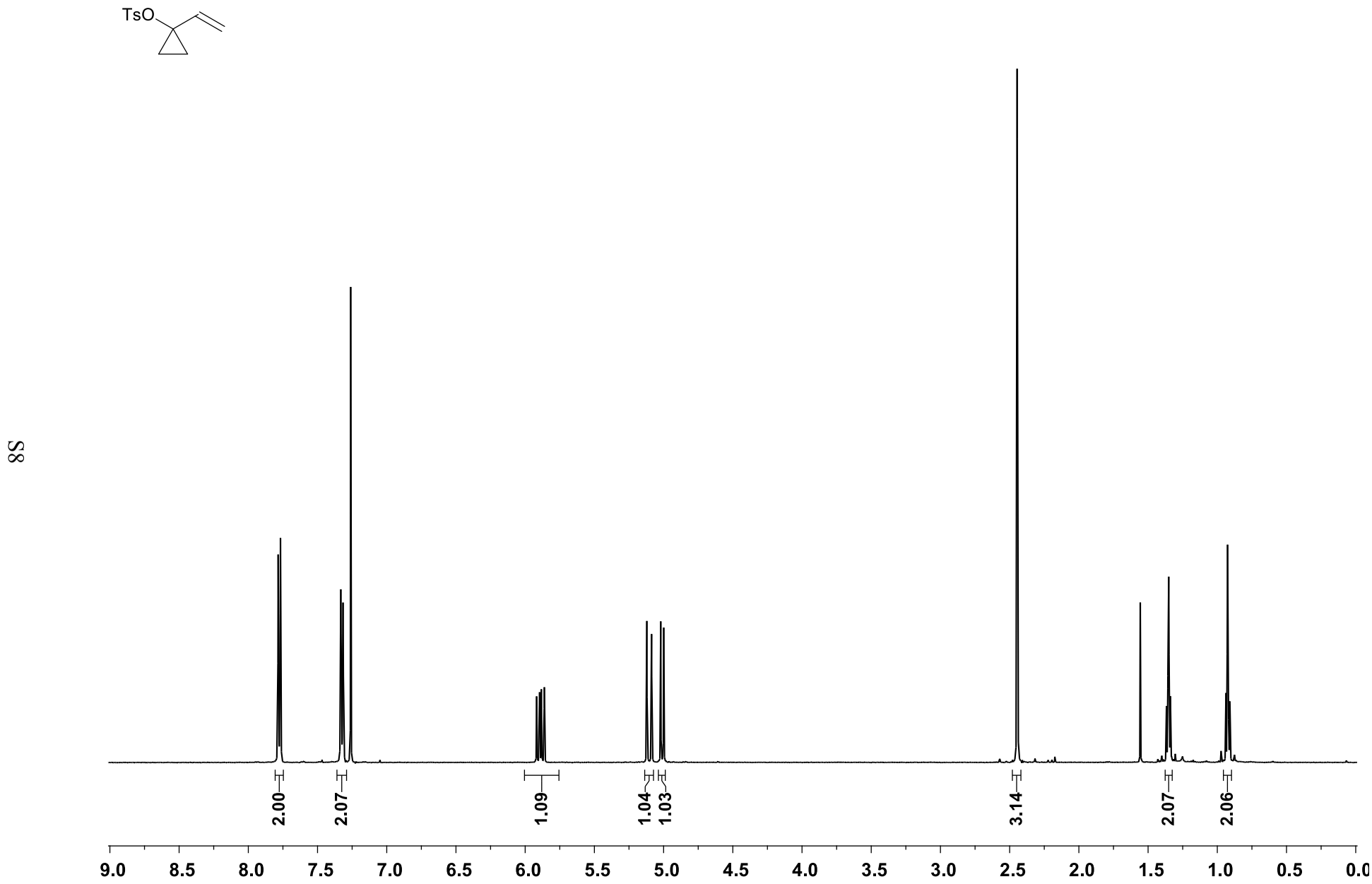

HO
Cl

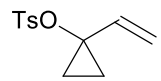

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

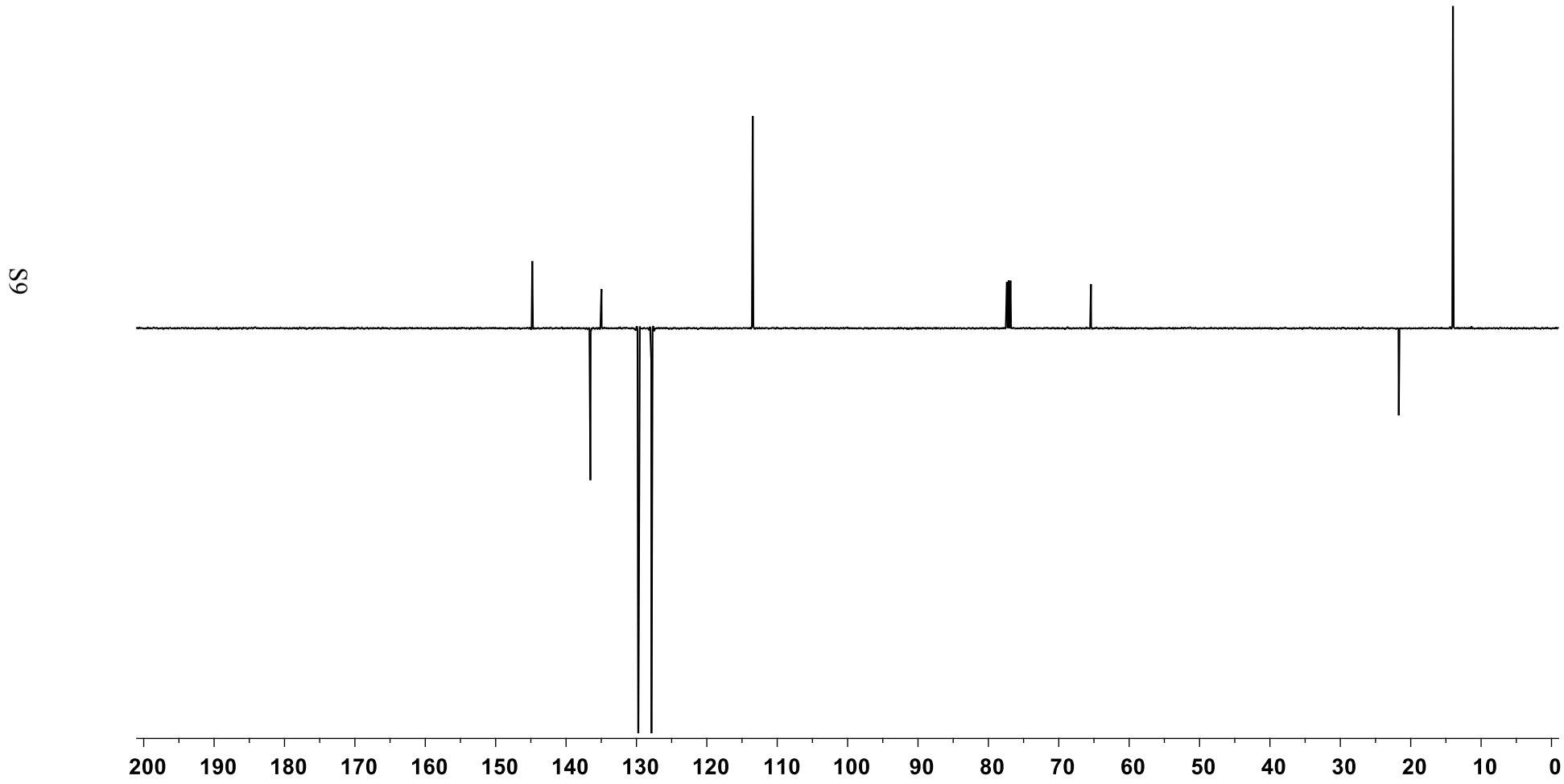

Cl
TsO
2.04
2.07
2.03
3.10
2.01
2.05
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


TsO
Cl


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


TsO
2.00
2.07
1.09
1.04
1.03
3.14
2.07
2.06
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


TsO


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0