Supplementary Material (ESI) for Chemical Communications

α-Substituted Acylsilanes via a Highly Selective [1,4]-Wittig Rearrangement of α-Benzyloxyallylsilane

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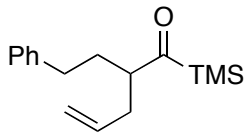
Supporting Information

Contents:

Materials and Methods: All air or moisture sensitive reactions were carried out in oven- or flame-dried glassware under nitrogen atmosphere, unless otherwise noted. All solvents were reagent grade. Anhydrous diethyl ether and tetrahydrofuran (THF) were freshly distilled under nitrogen from sodium benzophenoneketyl. Dichloromethane and triethylamine were freshly distilled from calcium hydride under nitrogen. Methyllithium, *n*-butyllithium, *sec*-butyllithium, and *tert*-butyllithium were purchased from Aldrich as diethyl ether, hexane, cyclohexane, and pentane solutions respectively. Except as otherwise indicated, all reactions were magnetically stirred and monitored by thin layer chromatography with 0.25-mm precoated silica gel plates. Flash chromatography was performed with silica gel 60 Å (particle size 230-400 Mesh ASTM). Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Proton and carbon NMR spectra were recorded on a 300 or 500 MHz spectrometer. Chemical shifts for ^{1}H NMR and ^{13}C NMR are reported in parts per million (ppm) relative to $CDCl_3$ (δ = 7.24 ppm for ^{1}H NMR or δ = 77.0 ppm for ^{13}C NMR).

Wittig rearrangements of α-benzyloxyallylsilane (1) and subsequent trapping experiments. Experimental details and spectroscopic data:

Preparation of (2-phenethyl-1-(trimethylsilyl)pent-4-en-1-one) (5) (Table 2, Entry 1):

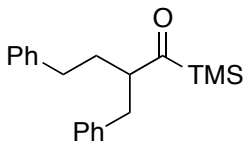


5

A solution of α-benzyloxyallylsilane (**1**) (106 mg, 0.48 mmol) in THF (0.065 M) was cooled to –78 °C under nitrogen. *s*-BuLi (1.3 M in cyclohexane, 1.5 equiv, 0.72 mmol, 554 μL) was added dropwise via syringe. The reaction mixture was stirred for 30 min. at –78 °C. The resultant enolate solution was transferred via canula to a THF solution of allyl bromide (323 mg, 1.92 mmol, 213 μL) and TEA (195 mg, 1.92 mmol, 270 μL) at –78 °C under nitrogen. The reaction was then stirred for 7 h, before being quenched with saturated aqueous NH_4Cl and diluted with diethyl ether. The phases were separated and the organic phase was washed with water and brine. The combined organics were dried over $MgSO_4$ and concentrated. The resulting residue was subjected to silica gel chromatography (0 to 2% EtOAc in hexane gradient) to afford 69 mg (55%) of (2-phenethyl-1-(trimethylsilyl)pent-4-en-1-one) (**5**) as a clear oil. IR (neat) 2953, 1715, 1640, 1454, 1250 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.10 (m, 5H), 5.70–5.61 (m, 1H), 5.02–4.96 (m, 2H), 3.02–2.97 (m, 1H), 2.5–2.45 (m, 2H), 2.40–2.32 (m, 1H), 2.11–2.04 (m, 1H), 1.97–1.89 (m, 1H), 1.63–1.54 (m, 1H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 250.5, 141.8,

135.8, 128.4, 128.3, 125.9, 116.6, 77.2, 54.6, 33.5, 30.6, –2.8; HRMS (EI) *m/z* 259.1528 [(M – H)$^+$; calcd for $C_{16}H_{23}OSi$, 259.1518].

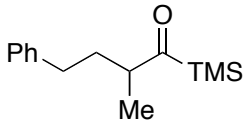
Preparation of 2-benzyl-4-phenyl-1-(trimethylsilyl)butan-1-one (6) (Table 2, Entry 2):



6

A solution of α-benzyloxyallylsilane (**1**) (99 mg, 0.45 mmol) in THF (0.065 M) was cooled to –78 °C under nitrogen. *s*-BuLi (1.3 M in cyclohexane, 1.5 equiv, 0.67 mmol, 513 μL) was added dropwise via syringe. The reaction mixture was stirred for 30 min. at –78 °C. The resultant enolate solution was transferred via canula to a THF solution of methyl iodide (307 mg, 1.80 mmol, 213 μL) and TEA (182 mg, 1.80 mmol, 250 μL) at –78 °C under nitrogen. The reaction was then stirred for 1.5 h, before being quenched with saturated aqueous NH_4Cl and diluted with diethyl ether. The phases were separated and the organic phase was washed with water and brine. The combined organics were dried over $MgSO_4$ and concentrated. The resulting residue was subjected to silica gel chromatography (0 to 2% EtOAc in hexane gradient) to afford 92 mg (66%) of 2-benzyl-4-phenyl-1-(trimethylsilyl)butan-1-one (**6**) as a light yellow oil. IR (neat) 3026, 2951, 1713, 1639, 1603, 1496, 1454, 1250 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32–7.13 (m, 10H), 3.43–3.33 (m, 1H), 3.12–2.94 (dd, *J* = 13.7, 7.8 Hz, 1H), 2.63–2.47 (m, 3H), 2.02–1.90 (m, 1H), 1.69–1.57 (m, 1H), 0.08 (s, 9H); ^{13}C (125 MHz, $CDCl_3$) δ 251.8, 141.7, 139.9, 129.0, 128.4, 128.3, 126.1, 125.9, 56.3, 35.9, 33.4, 31.3, –3.2; HRMS (EI) *m/z* 309.1669 [(M – H)$^+$; calcd for $C_{20}H_{25}OSi$, 309.1675].

Preparation of 2-methyl-4-phehyl-1-(trimethylsilyl)butan-1-one (7) (Table 2, Entry 3):

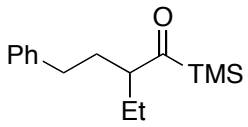


7

A solution of α-benzyloxyallylsilane (**1**) (98 mg, 0.0.445 mmol) in THF (0.065 M) was cooled to –78 °C under nitrogen. *s*-BuLi (1.3 M in cyclohexane, 1.5 equiv, 0.67 mmol, 513 μL) was added dropwise via syringe. The reaction mixture was stirred for 30 min. at –78 °C. The resultant enolate solution was transferred via canula to a THF solution of methyl iodide (252 mg, 1.78

mmol, 110 μL) and TEA (180 mg, 1.78 mmol, 248 μL) at –78 °C under nitrogen. The reaction was then stirred for 50 min, before being quenched with saturated aqueous NH_4Cl and diluted with diethyl ether. The phases were separated and the organic phase was washed with water and brine. The combined organics were dried over $MgSO_4$ and concentrated. The resulting residue was subjected to silica gel chromatography (0 to 2% EtOAc in hexane gradient) to afford 92 mg (73%) of 2-methyl-4-phehyl-1-(trimethylsilyl)butan-1-one (**7**) as a light yellow oil. IR (neat) 2963, 1713, 1639, 1604, 1454, 1250 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27–7.13 (m, 5H), 2.94–2.87 (m, 1H), 2.60–2.47 (m, 2H), 2.03–1.96 (m, 1H), 1.51–1.1.44 (m, 1H), 1.00 (d, J = 6.8 Hz, 3H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 250.4, 141.9, 128.3, 125.8, 49.6, 33.4, 32.6, 14.3, –2.7; HRMS (EI) *m/z* 233.1356 [$(M - H)^+$; calcd for $C_{14}H_{21}OSi$, 233.1362].

Preparation of 2-ethyl-4-phenyl-1-(trimethylsilyl)butan-1-one (8) and (*E*)-(1-ethoxy)-4-phenylbut-1-enyl)trimethylsilane (9) (Table 2, Entry 4):



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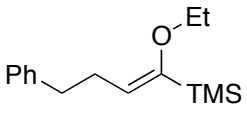
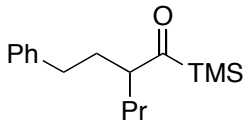


9

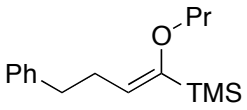
A solution of α-benzyloxyallylsilane (**1**) (121 mg, 0.55 mmol) in THF (0.065 M) was cooled to –78 °C under nitrogen. *s*-BuLi (1.3 M in cyclohexane, 1.5 equiv, 0.82 mmol, 634 μL) was added dropwise via syringe. The reaction mixture was stirred for 30 min. at –78 °C. The resultant enolate solution was transferred via canula to a THF solution of ethyl iodide (343 mg, 2.20 mmol, 176 μL) and HMPA (394 mg, 2.20 mmol, 250 μL) of HMPA at –78 °C under nitrogen. The reaction was then stirred for 17 h, before being quenched with saturated aqueous NH_4Cl and diluted with diethyl ether. The phases were separated and the organic phase was washed with water and brine. The combined organics were dried over $MgSO_4$ and concentrated. The resulting residue was subjected to silica gel chromatography (0 to 2% EtOAc in hexane gradient) to afford 112 mg (82%) of a 3:1 mixture of 2-ethyl-4-phenyl-1-(trimethylsilyl)butan-1-one (**8**) and (*E*)-(1-ethoxy)-4-phenylbut-1-enyl)trimethylsilane (**9**) as (ratio by ^{1}HNMR) as a light yellow oil. For **8**: IR (neat) 2961, 1713, 1639, 1454, 1250 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30–7.16 (m, 5H), 2.85–2.78 (m, 1H), 2.52–2.42 (m, 2H), 1.97–1.89 (m, 1H), 1.71–1.62 (m, 1H), 1.59–1.51 (m, 1H), 1.43–1.34 (m, 1H), 0.85 (*apparent* t, J = 7.8, 6.8 Hz, 3H), 0.21 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 251.2, 142.0, 128.4, 128.3, 125.8, 57.1, 33.7, 30.6, 22.3, 11.7, –2.7; HRMS (NH_3 CI) *m/z* 249.1676 [$(M+H)^+$; calcd for $C_{15}H_{25}OSi$, 249.1675]. For **9**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.33–7.16 (m, 5H), 5.10 (*apparent* t, J = 7.3, 6.8 Hz, 1H), 3.67–3.62 (q, J = 7.3, 6.8 Hz, 2H),

2.39–2.25 (m, 2H), 1.86–1.78 (m, 2H), 1.20–1.17 (*apparent* t, *J* = 7.3, 6.8 Hz, 3H), 0.12 (s, 9H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 161.2, 142.2, 128.4, 128.2, 128.1, 125.6, 66.2, 35.9, 27.2, 15.8, –0.66.

Preparation of 2-phenethyl-1-(trimethylsilyl)pentan-1-one (10) and (*E*)-trimethyl(4-phenyl-1-propoxybut-1-enyl)silane (11) (Table 2, Entry 5):



10



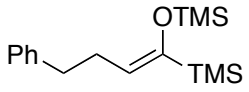
11

A solution of α-benzyloxyallylsilane (**1**) (129 mg, 0.59 mmol) in THF (0.065 M) was cooled to –78 °C under nitrogen. *s*-BuLi (1.3 M in cyclohexane, 1.5 equiv, 0.88 mmol, 680 μL) was added dropwise via syringe. The reaction mixture was stirred for 30 min. at –78 °C. The resultant enolate solution was transferred via canula to a THF solution of propyl iodide (398 mg, 2.34 mmol, 228 μL) and HMPA (420 mg, 2.34 mmol, 410 μL) of HMPA at –78 °C under nitrogen. The reaction was then stirred for 17 h, before being quenched with saturated aqueous NH_4Cl and diluted with diethyl ether. The phases were separated and the organic phase was washed with water and brine. The combined organics were dried over $MgSO_4$ and concentrated. The resulting residue was subjected to silica gel chromatography (0 to 2% EtOAc in hexane gradient) to afford 102 mg (66%) of 2-phenethyl-1-(trimethylsilyl)pentan-1-one (**10**) and (*E*)-trimethyl(4-phenyl-1-propoxybut-1-enyl)silane **(11**) as 3:1 mixture (ratio by ^{1}HNMR) as a light yellow oil. Resubjecting this material to a second silica gel column allowed for the isolation of pure **10** and a sample of **11** that was slightly contaminated by **10** and grease.

For **10**: IR (neat) 2957, 1717, 1638, 1454, 1250 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.12 (m, 5H), 2.92–2.86 (m, 1H), 2.52–2.44 (m, 2H), 1.95–1.88 (m, 1H), 1.65–1.51 (m, 2H), 1.32–1.17 (m, 3H), 0.86 (t, *J* = 6.8 Hz, 3H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 251.2, 142.0, 128.34, 128.32, 125.8, 55.3, 33.7, 31.5, 31.0, 20.6, 14.3, –2.7; HRMS (NH_3 CI) *m/z* 263.1821 [$(M + H)^+$; calcd for $C_{16}H_{27}OSi$, 263.1831].

For **11**: IR (neat) 2959,1605, 1454, 1248 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32–7.12 (m, 5H), 5.11–5.06 (*apparent* t, *J* = 6.8, 7.1 Hz, 1H), 3.57–3.53 (t, *J* = 6.6 Hz, 2H), 2.66–2.61 (dd, *J* = 8.5, 9.5 Hz, 2H), 2.502.42 (m, 2H), 1.65–1.53 (m, 2H), 0.96–0.91 (*apparent* t, *J* = 7.3, 7.6 Hz, 3H), 0.13 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 142.3, 128.4, 128.1, 125.6,125.5, 72.4, 35.9, 27.2, 23.6, 10.6, –0.5.

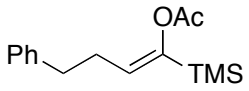
Preparation of (*E*)-1-(4-(trimethylsilyl)-4-(trimethylsilyloxy)but-3-enyl)benzene (12) (Table 2, Entry 7):



12

A solution of α-benzyloxyallylsilane (**1**) (126 mg, 0.572 mmol) in THF (0.065 M) was cooled to –78 °C under nitrogen. *s*-BuLi (1.3 M in cyclohexane, 1.5 equiv, 0.86 mmol, 660 μL) was added dropwise via syringe. The reaction mixture was stirred for 30 min. at –78 °C. The resultant enolate solution was transferred via canula to a THF solution of TMSCl (248 mg, 2.29 mmol, 290 μL) and TEA (231 mg, 2.29 mmol, 320 μL) at –78 °C under nitrogen. The reaction was then stirred for 1.5 h, before being quenched with saturated aqueous NH_4Cl and diluted with diethyl ether. The phases were separated and the organic phase was washed with water and brine. The combined organics were dried over $MgSO_4$ and concentrated. The resulting residue was subjected to silica gel chromatography (hexanes) to afford 142 mg (85%) of (*E*)-1-(4-(trimethylsilyl)-4-(trimethylsilyloxy)but-3-enyl)benzene (**12**) as clear oil. IR (neat) 3028, 2959, 1614, 1496, 1454, 1250, 1121 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.16 (m, 5H), 5.07–5.02 (t, *J* = 6.7 Hz, 1H), 2.66–2.60 (*apparent* t, *J* = 8.5, 7.4 Hz, 2H), 2.40–2.35 (m, 2H), 0.16 (s, 9H), 0.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 142.2. 128.4, 128.3, 125.7, 124.4, 35.7, 27.6, 0.9, –1.7; HRMS (NH_3 CI) *m/z* 293.1747 [$(M + H)^+$; calcd for $C_{16}H_{29}OSi_2$, 293.1757].

Preparation of (*E*)-4-phenyl-1-(trimethylsilyl)but-1-enyl acetate (13) (Table 2, Entry 8):

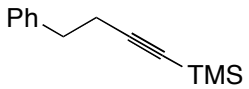


13

A solution of α-benzyloxyallylsilane (**1**) (89 mg, 0.40 mmol) in THF (0.065 M) was cooled to –78 °C under nitrogen. *s*-BuLi (1.3 M in cyclohexane, 1.5 equiv, 0.60 mmol, 460 μL) was added dropwise via syringe. The reaction mixture was stirred for 30 min. at –78 °C. The resultant enolate solution was transferred via canula to a THF solution of acetyl chloride (127 mg, 1.62 mmol, 115 μL) at –78 °C under nitrogen. The reaction was then stirred for 1.5 h, before being quenched with saturated aqueous NH_4Cl and diluted with diethyl ether. The phases were separated and the organic phase was washed with water and brine. The combined organics were dried over $MgSO_4$ and concentrated. The resulting residue was subjected to silica gel

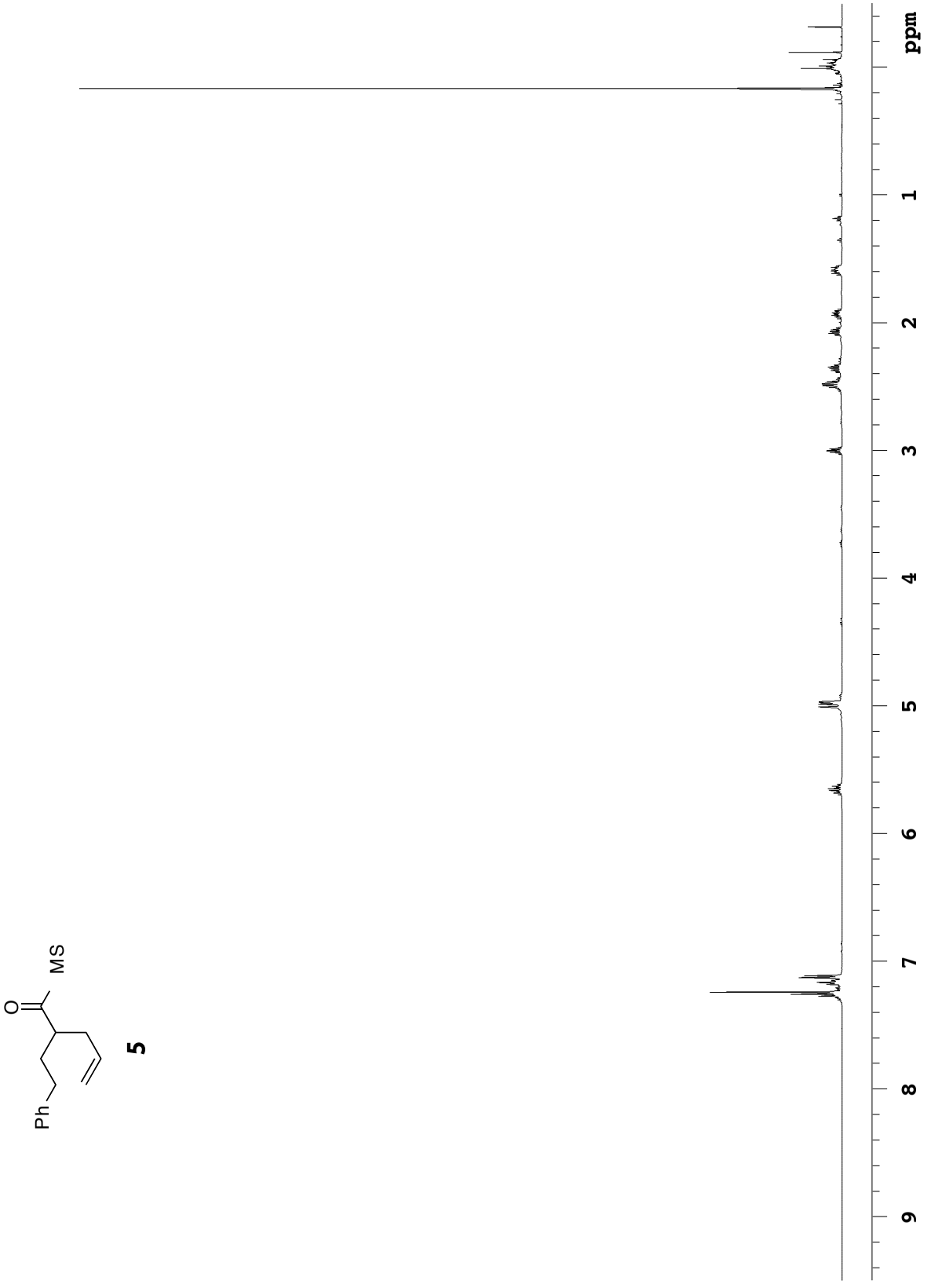
chromatography (0 to 2% EtOAc in hexane gradient) to afford 73 mg (69%) of (*E*)-4-phenyl-1-(trimethylsilyl)but-1-enyl acetate (**13**) as a clear oil. IR (neat) 3086, 3026, 2955, 2922, 2849, 1745, 1603, 1496, 1454, 1369, 1230, 1089, 1039 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30–7.15 (m, 5H), 5.51–5.48 (t, *J* = 7.0 Hz, 1H), 2.68–2.64 (*apparent* t, *J* = 8.4, 7.5 Hz, 2H), 2.36–2.31 (*apparent* quintet, *J* = 8.4, 7.5, 7.1 Hz, 2H), 2.11 (s, 3H), 0.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 155.3, 141.6, 130.5, 128.4, 128.3, 125.9, 35.0, 27.6, 20.5, –1.5; HRMS (EI) *m/z* 262.1387 [(M^+); calcd for $C_{15}H_{22}O_2Si$, 262.1389]. For a prior preparation of **13** see Motoki, Y.; Kazuyoshi, U.; Koichi, N. *Bull. Chem. Soc. Jpn*. **2005**, *78*, 477–486.

Preparation of trimethyl(4-phenylbut-1-ynyl)silane (14) (Table 2, Entry 9):



14

A solution of α-benzyloxyallylsilane (**1**) (85 mg, 0.39 mmol) in THF (0.065 M) was cooled to –78 °C under nitrogen. *s*-BuLi (1.3 M in cyclohexane, 1.5 equiv, 0.58 mmol, 450 μL) was added dropwise via syringe. The reaction mixture was stirred for 30 min. at –78 °C. The resultant enolate solution was transferred via canula to a THF solution of perfluoro-1-butanesulfonyl fluoride (128 mg, 0.43 mmol, 76 μL) at –78 °C under nitrogen. The reaction was then stirred for 5 h, before being quenched with saturated aqueous NH_4Cl and diluted with diethyl ether. The phases were separated and the organic phase was washed with water and brine. The combined organics were dried over $MgSO_4$ and concentrated. The resulting residue was subjected to silica gel chromatography (0 to 2% EtOAc in hexane gradient) to afford 45 mg (58%) of trimethyl(4-phenylbut-1-ynyl)silane (**14**) as a clear oil. IR (neat) 2959, 2175, 1603, 1496, 1454, 1250 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.20 (m, 5H), 2.85–2.80 (t, *J* = 7.7 Hz, 2H), 2.51–2.46 (t, *J* = 7.7 Hz, 2H), 0.13 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6, 128.5, 128.3, 126.2, 106.6, 85.2, 35.1, 22.1, 0.1; HRMS (EI) *m/z* 202.1174 [(M^+); calcd for $C_{13}H_{18}Si$, 202.1178]. For a prior preparation of **14** see: (a) Jiang, H.; Zhu, S. *Tetrahedron Lett*. **2005**, *46*, 517–519. (b) Shimizu, K.; Takimoto, M.; Sato, Y.; Mori, M. *Org. Lett*. **2005**, *7*, 195–197. (c) Murakami, M.; Hayashi, M.; Ito, Y. J. Org. Chem. 1994, 59, 7910–7914. (d) Miyachi, N.; Shibasaki, M. *J. Org. Chem*. **1990**, *55*, 1975–1976. (e) Negishi, E.; Matsushita, H.; Kobayashi, M.; Rand, C. *Tetrahedron Lett*. **1983**, *24*, 3823–3824.



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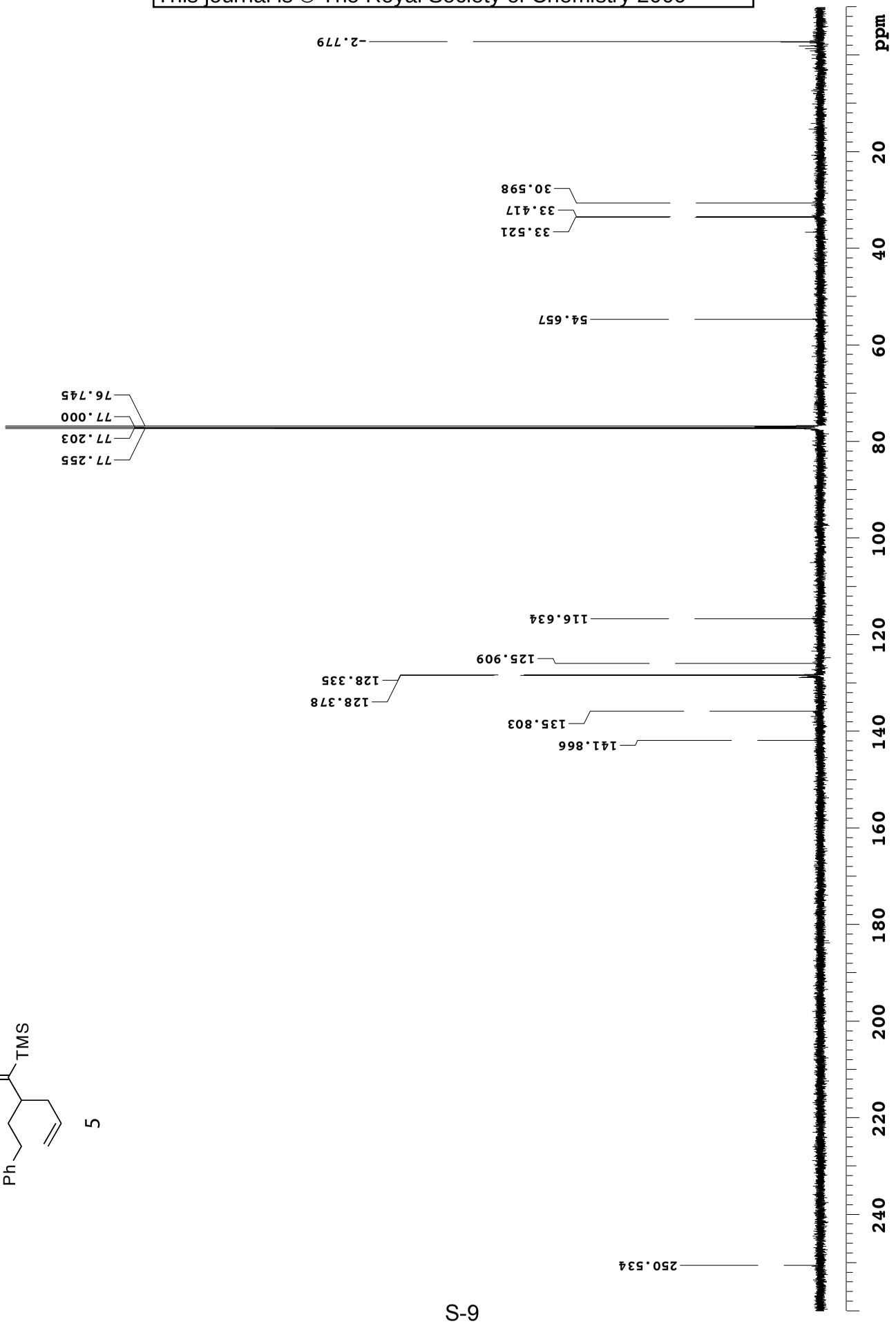
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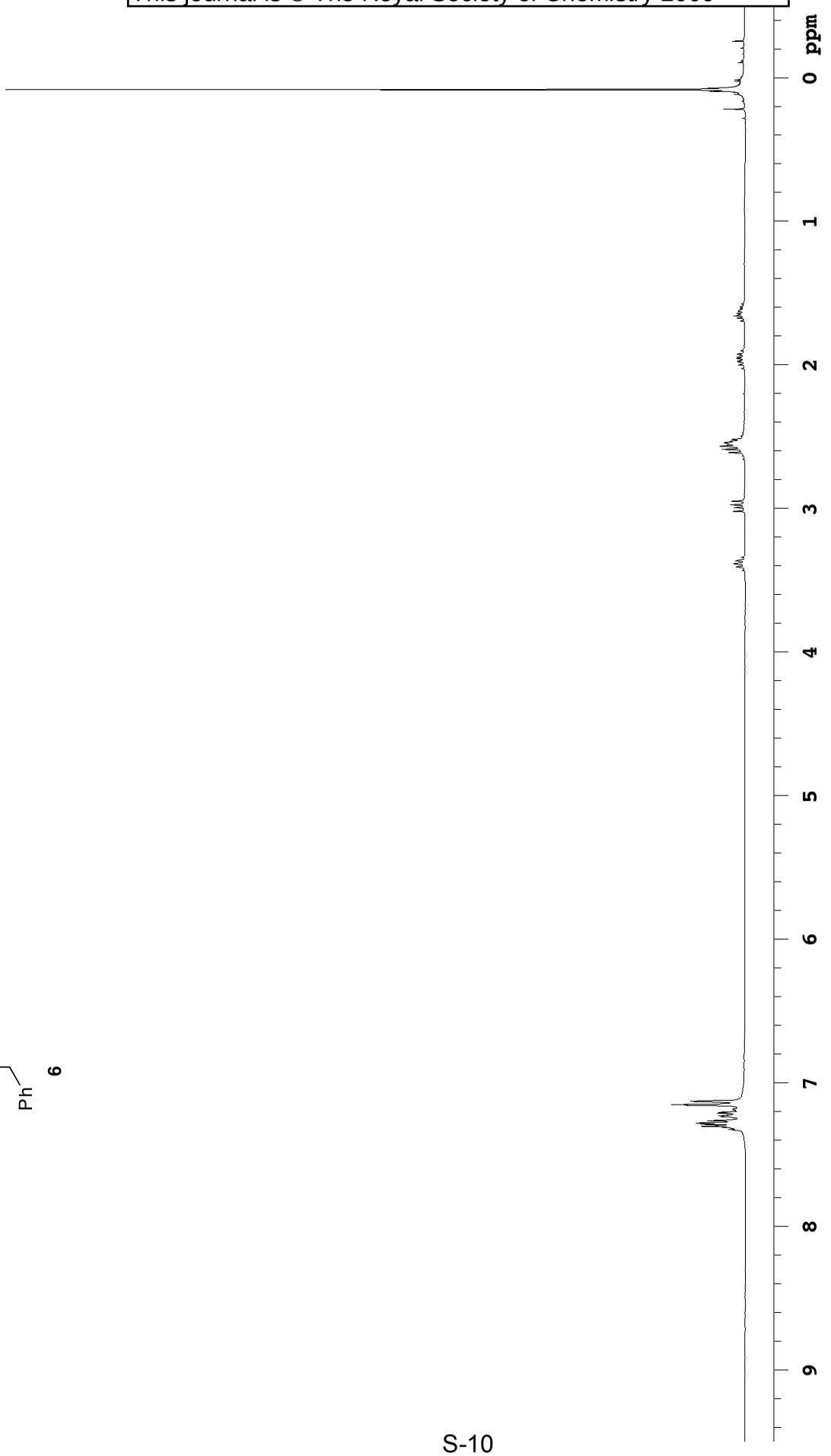

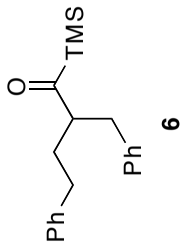

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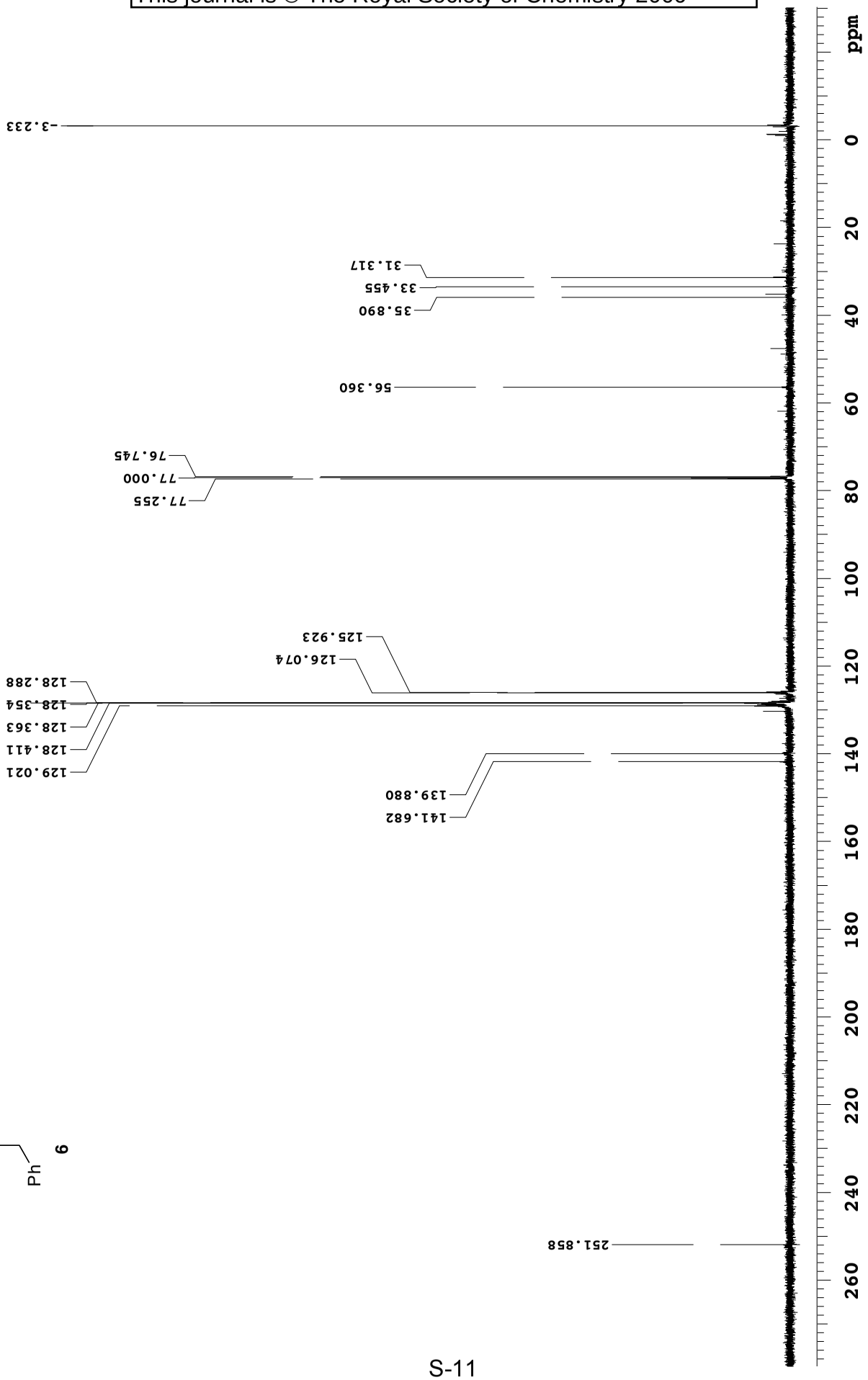
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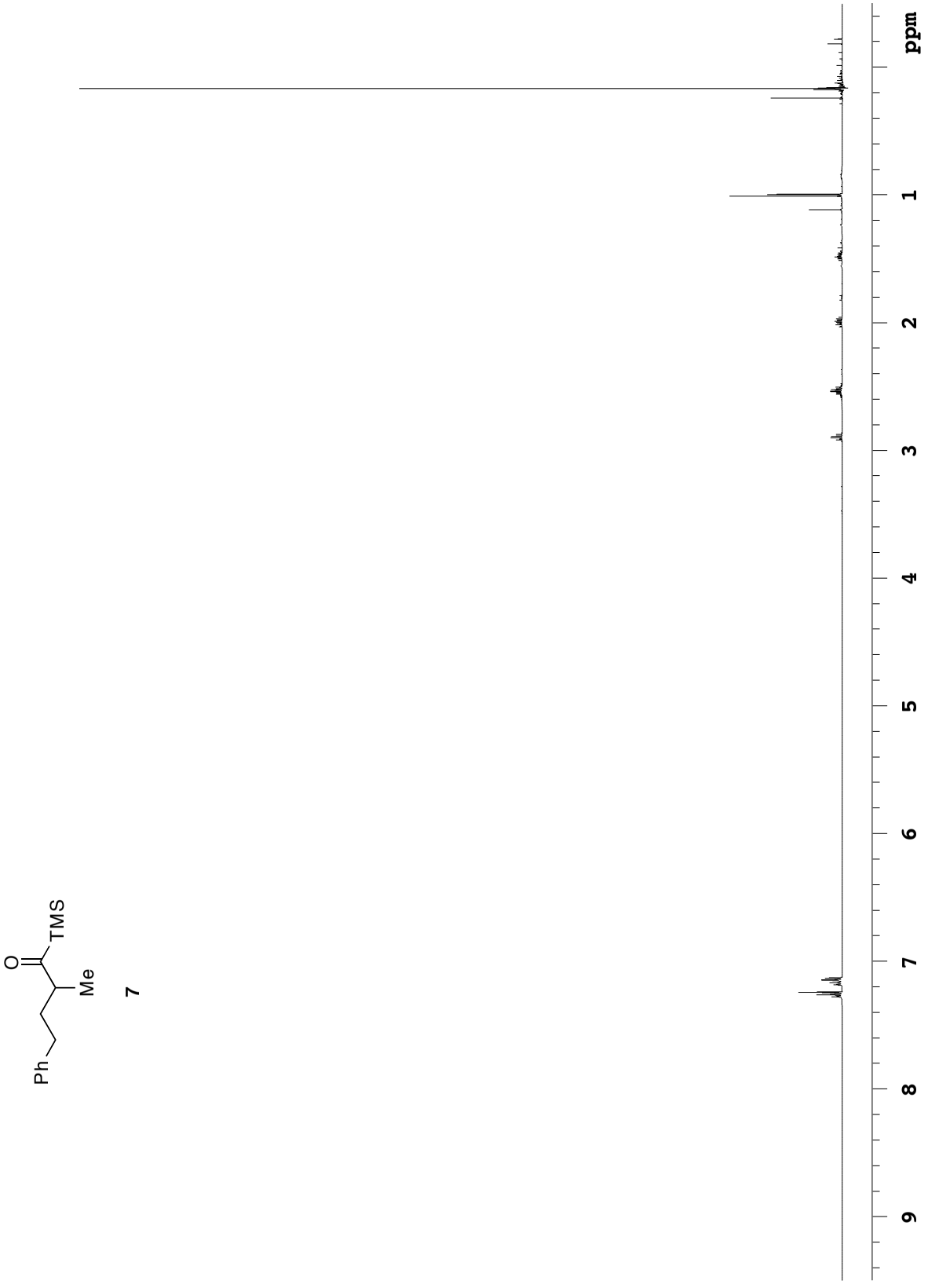
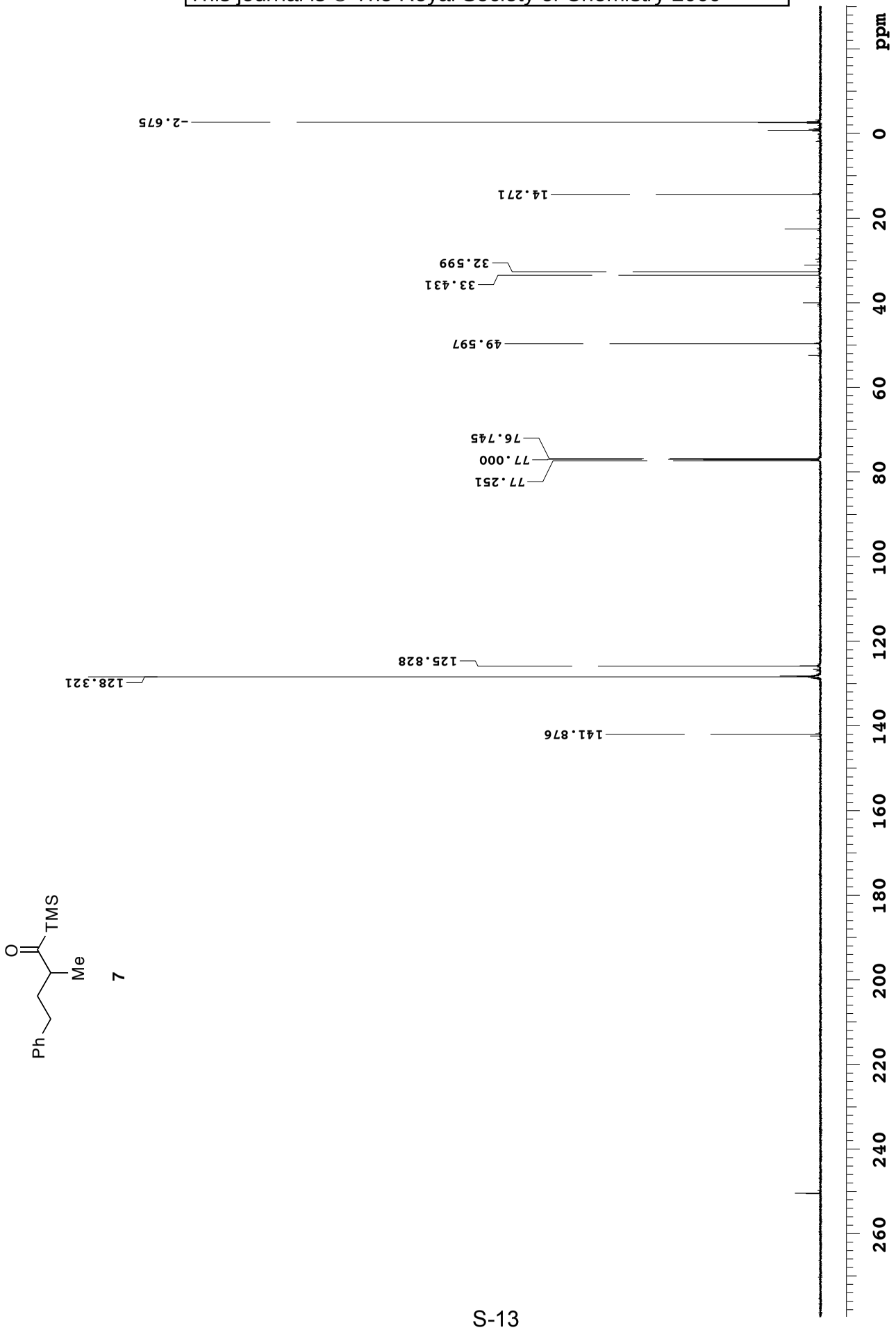
Ph

6


O
TMS
Me
Ph
7
ppm
1
2
3
4
5
6
7
8
9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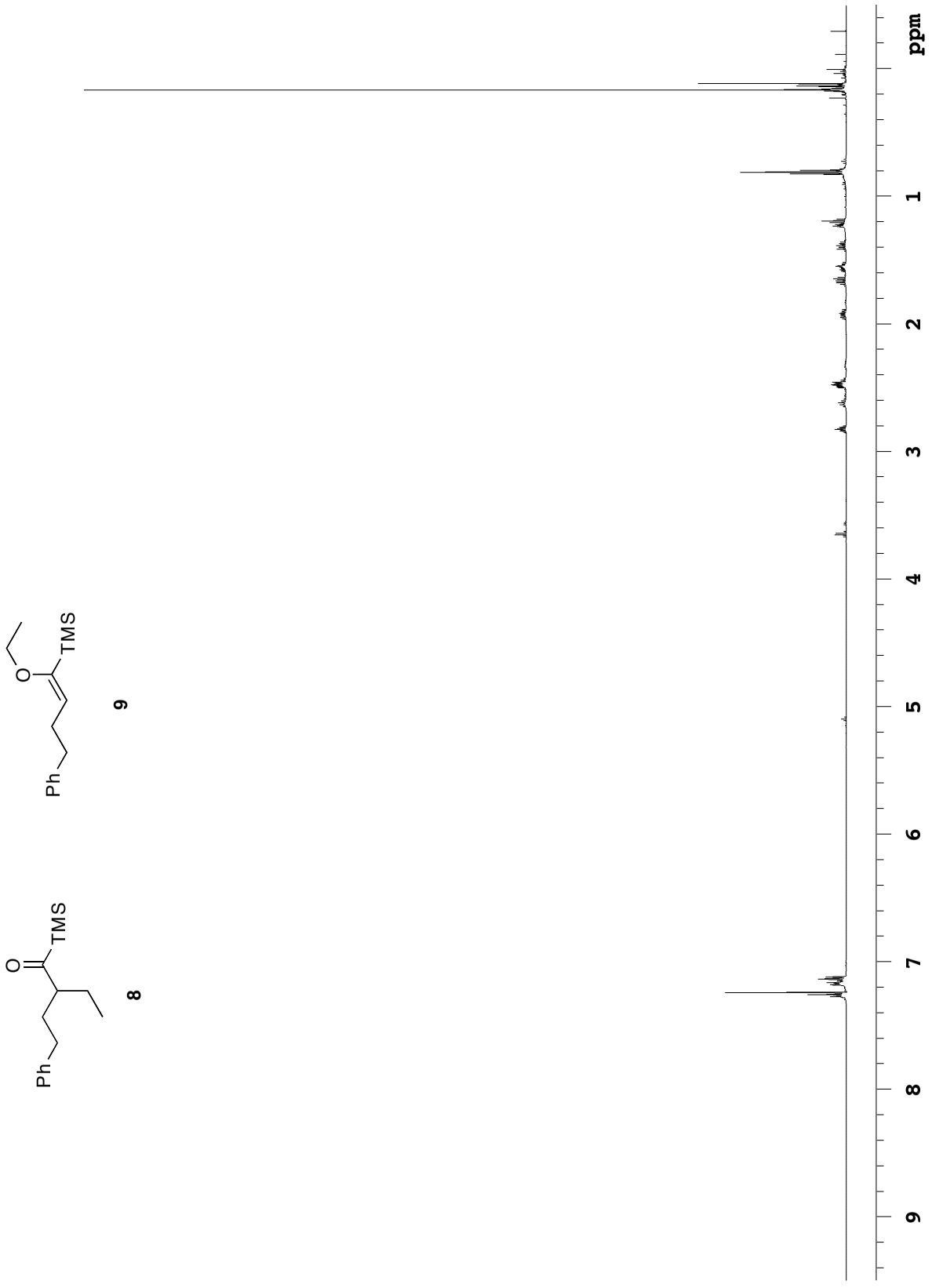
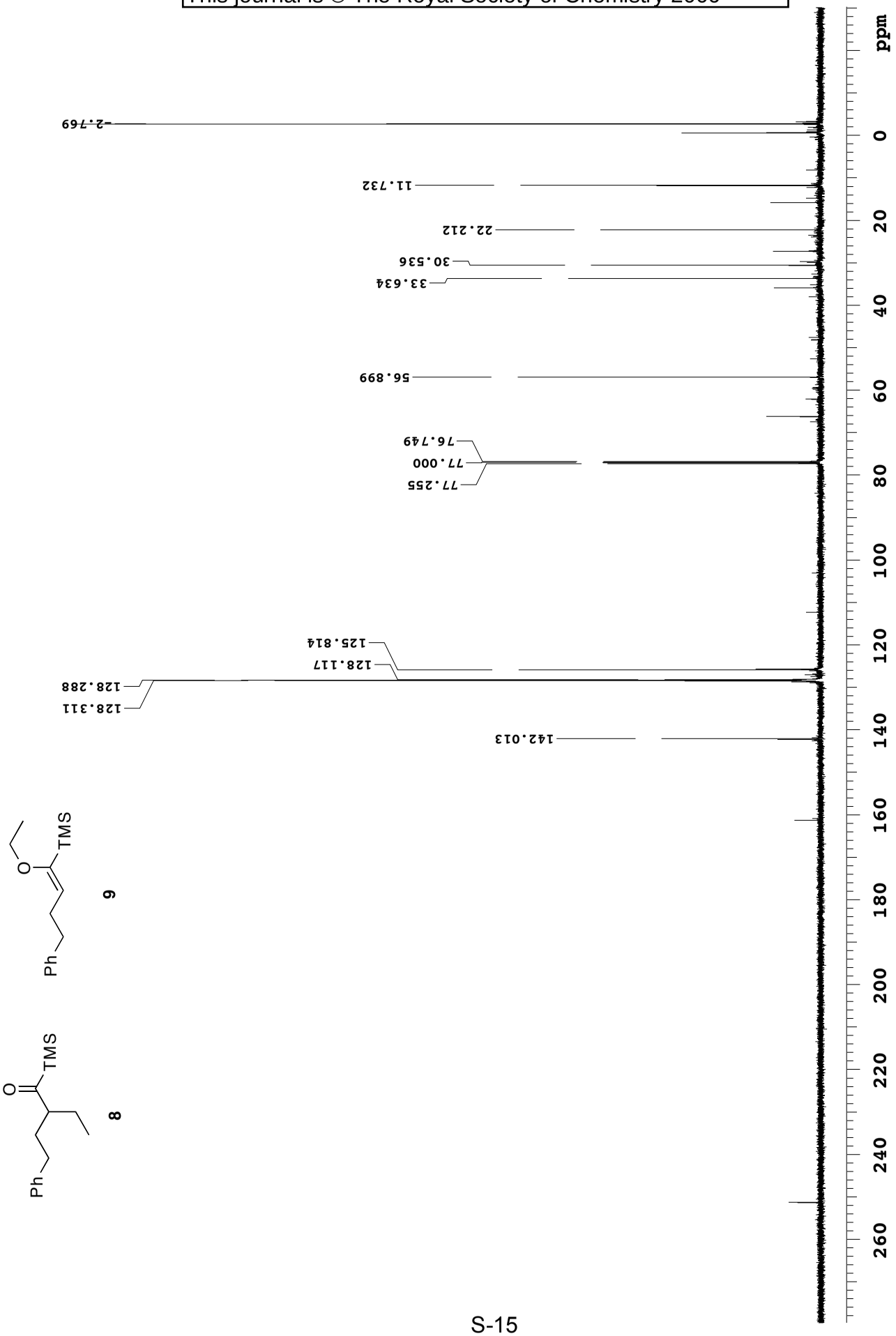
14.271
32.599
33.431
49.597
76.745
77.000
77.251
125.828
128.321
141.876
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240
260

TMS
O
Me
Ph

7


ppm
1
2
3
4
5
6
7
8
9
O
TMS
Ph
9
O
TMS
Ph
8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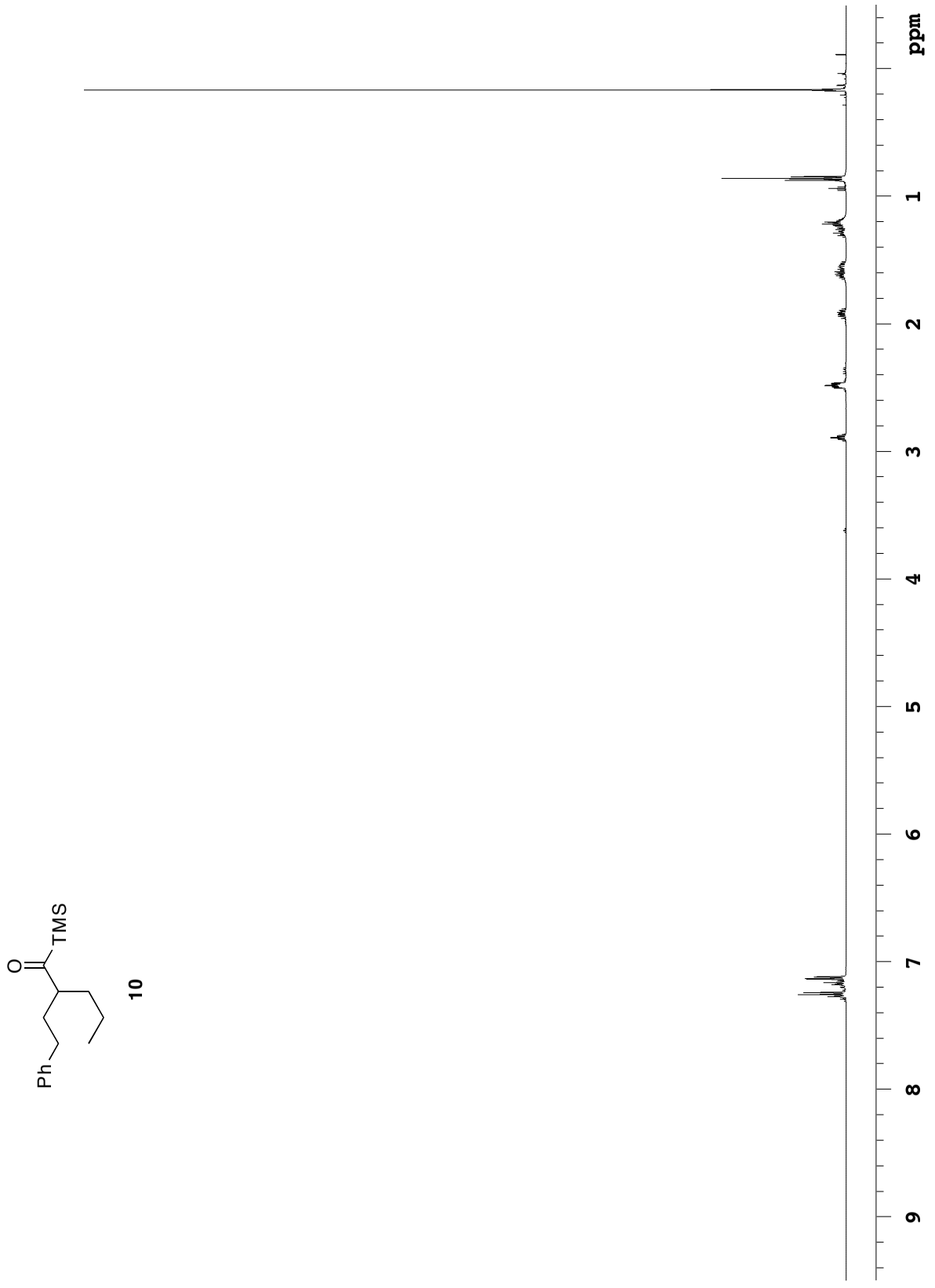
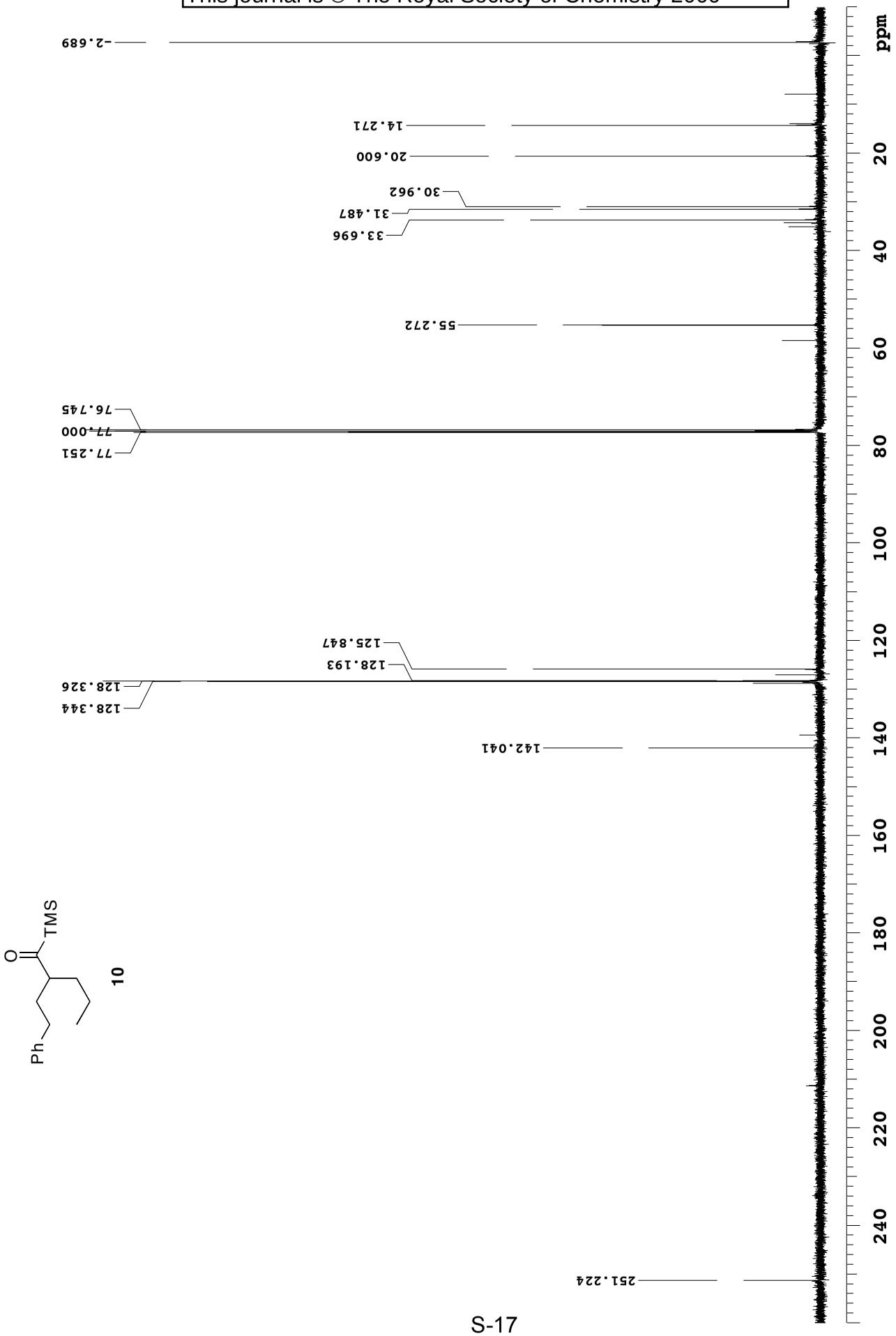
11.732
22.212
30.536
33.634
56.899
76.749
77.000
77.255
125.814
128.117
128.288
128.311
142.013
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240
260
TMS
O
Ph
9
TMS
O
Ph
8



10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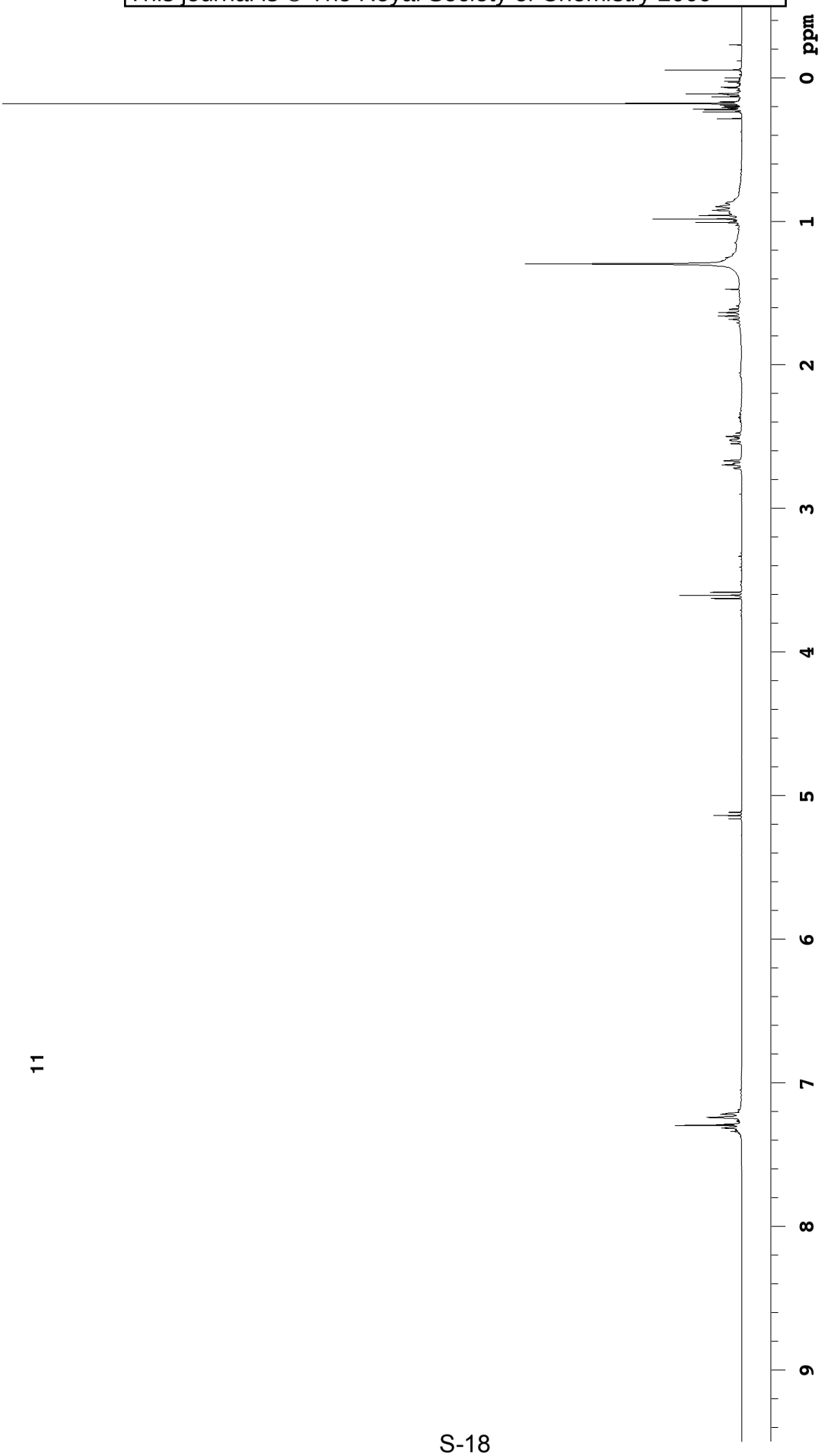
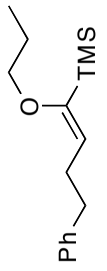
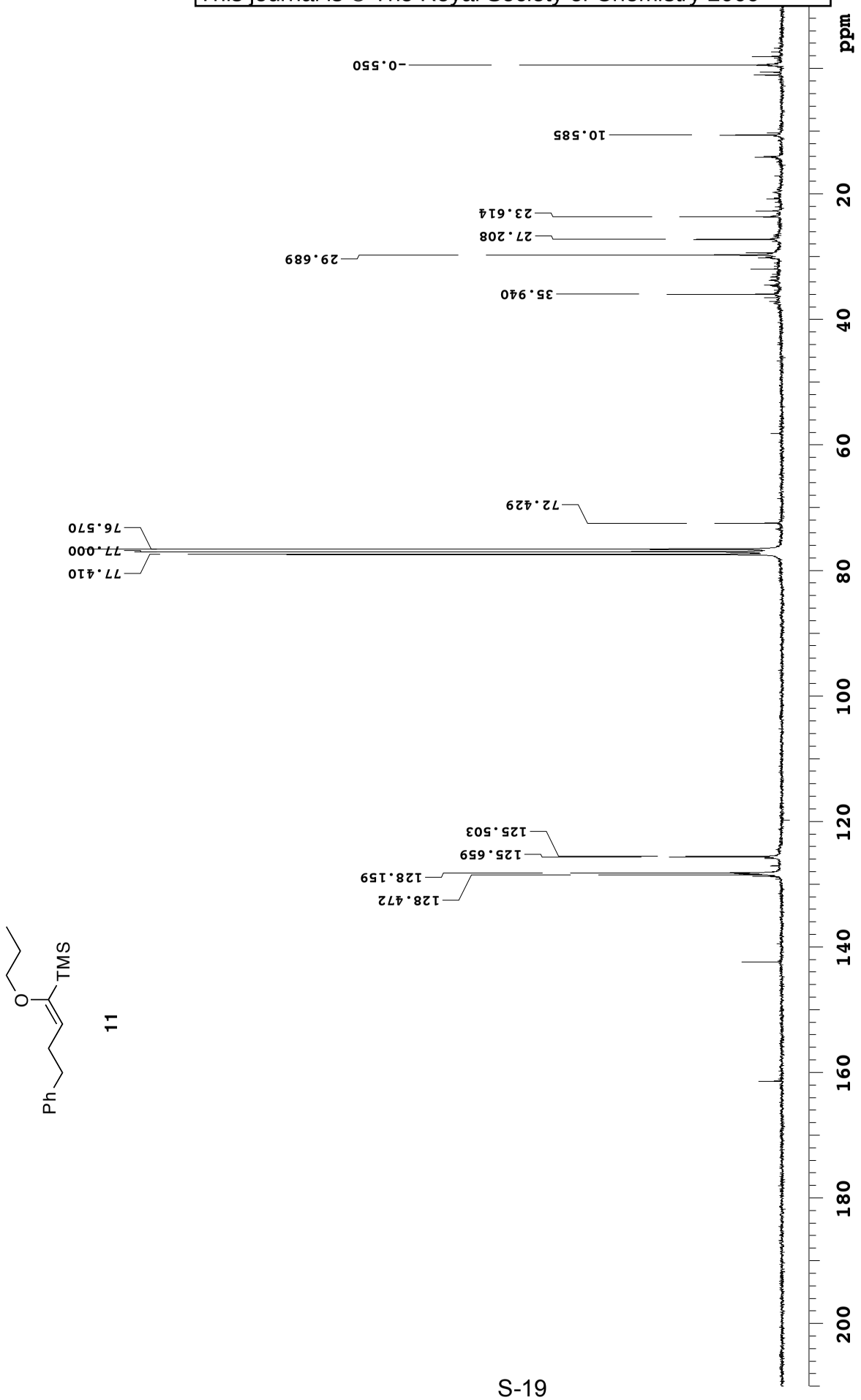
14.271
20.600
30.962
31.487
33.696
55.272
76.745
77.000
77.251
125.847
128.193
128.326
128.344
142.041
251.224
ppm
20
40
60
80
100
120
140
160
180
200
220
240
O
TMS
Ph
10





11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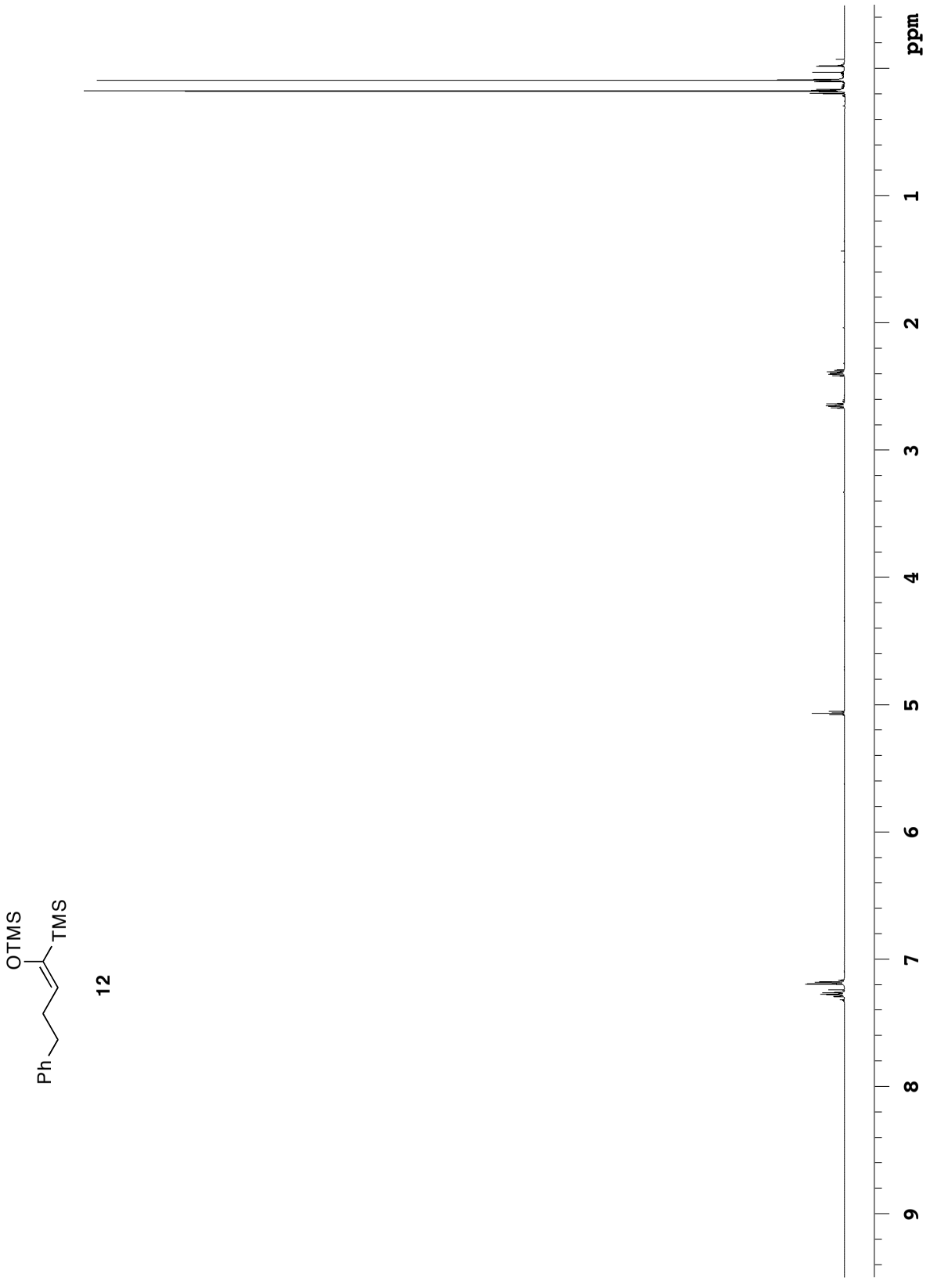
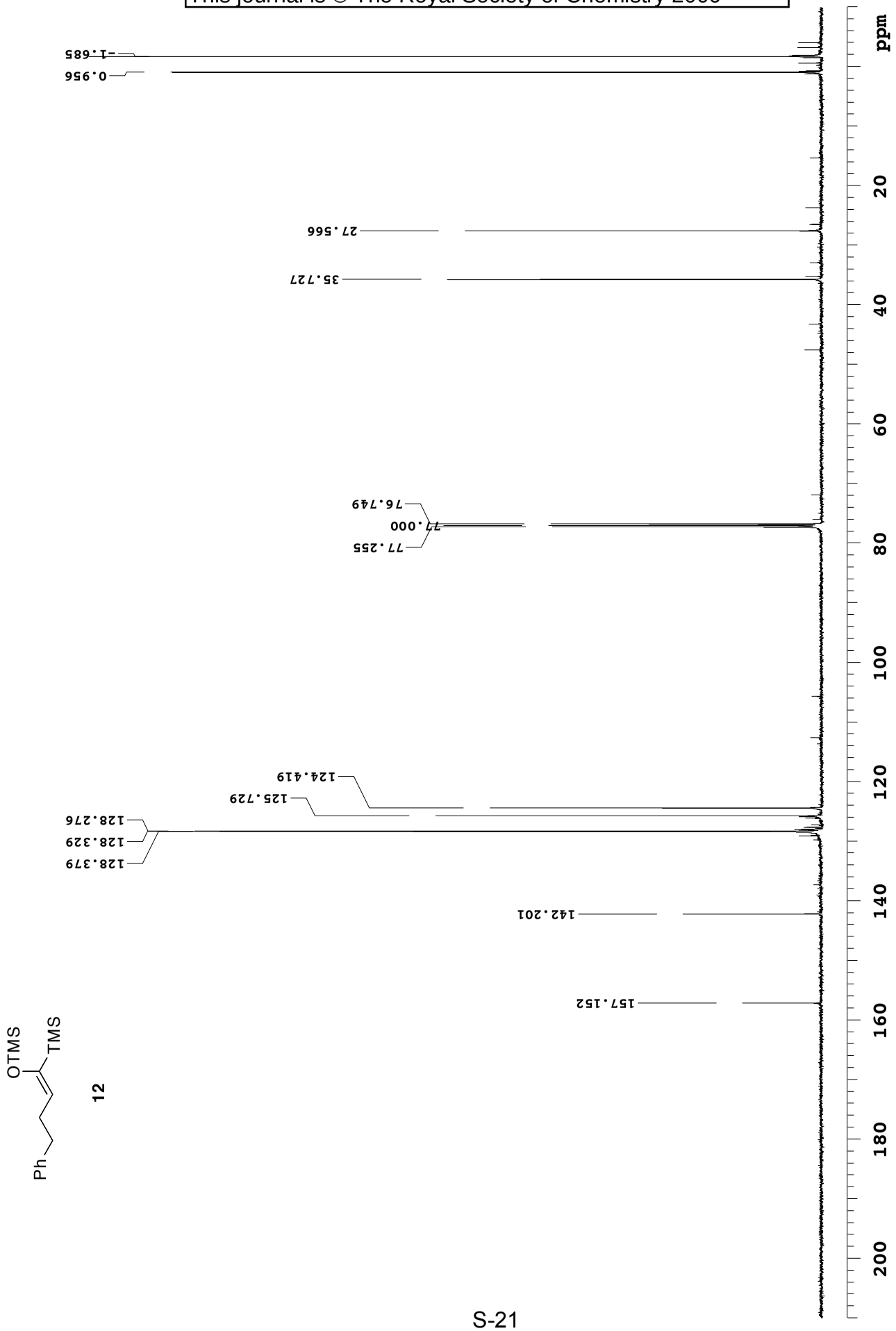
23.614
27.208
29.689
35.940
72.429
76.570
77.000
77.410
125.503
125.659
128.159
128.472
ppm
20
40
60
80
100
120
140
160
180
200
TMS
O
Ph

11


OTMS
TMS
Ph
12
ppm
1
2
3
4
5
6
7
8
9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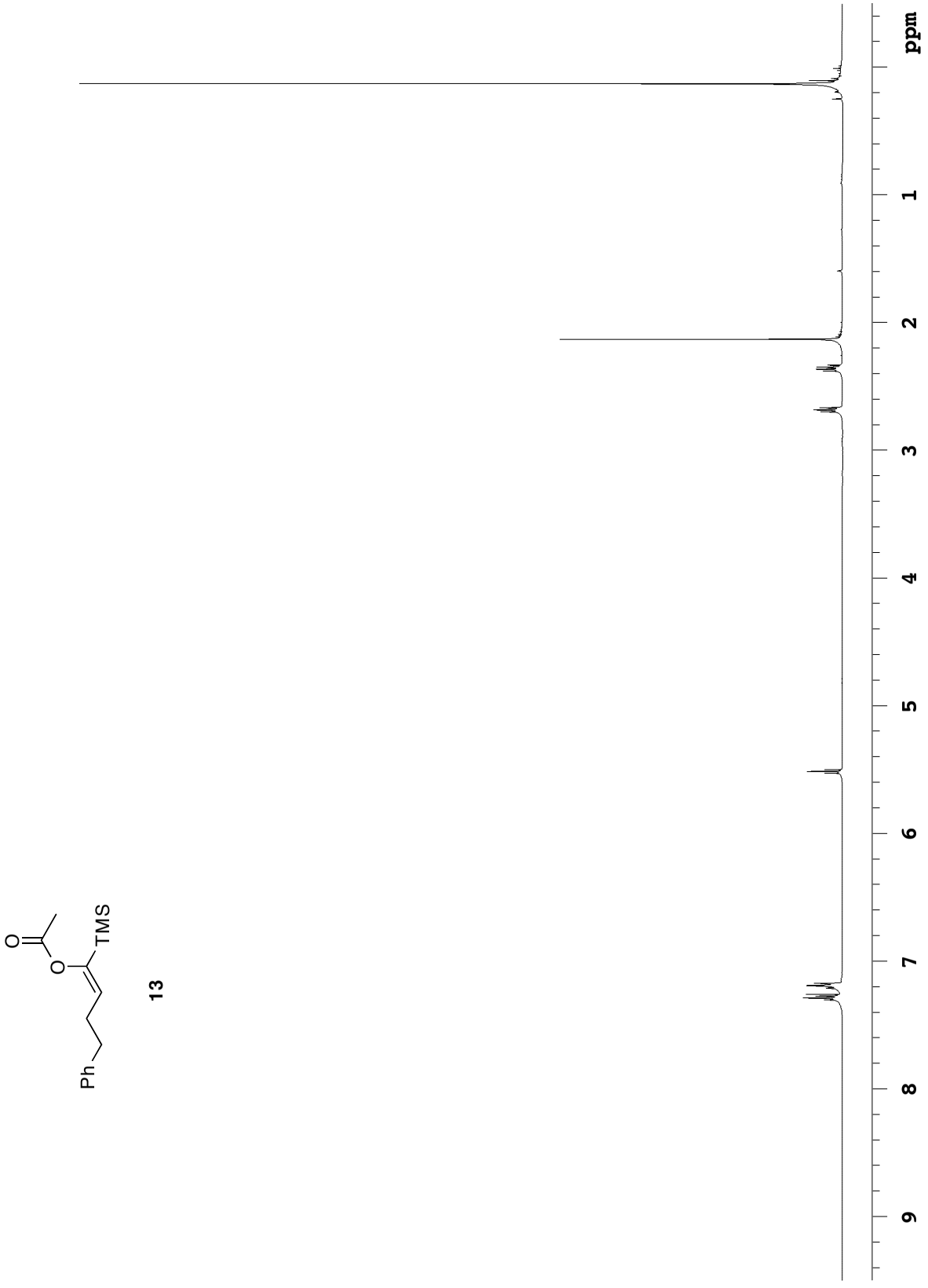
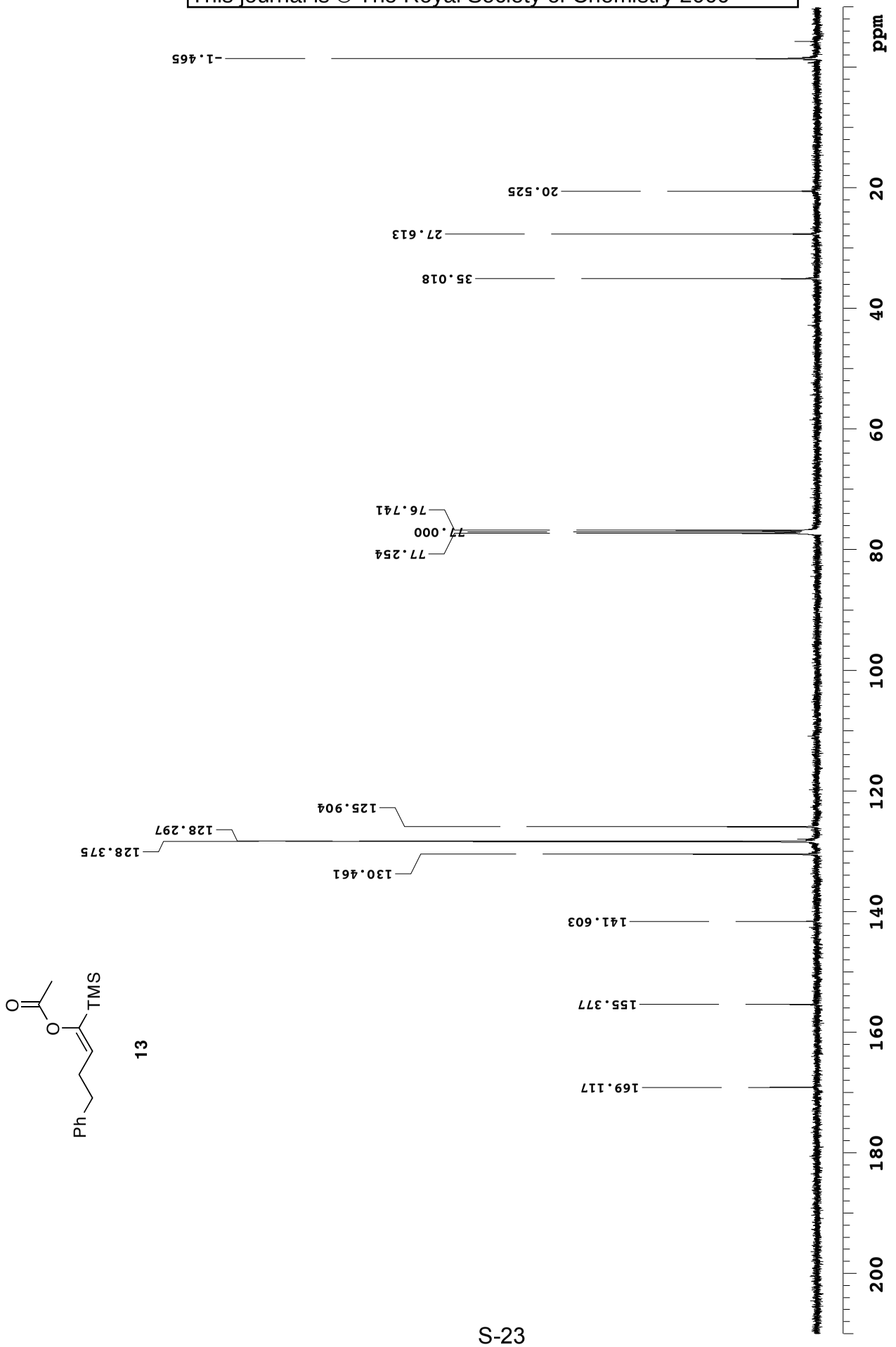
0.956
27.566
35.727
76.749
77.000
77.255
124.419
125.729
128.276
128.329
128.379
142.201
157.152
ppm
20
40
60
80
100
120
140
160
180
200
OTMS
TMS
Ph
12


O
O
TMS
Ph
13
ppm
1
2
3
4
5
6
7
8
9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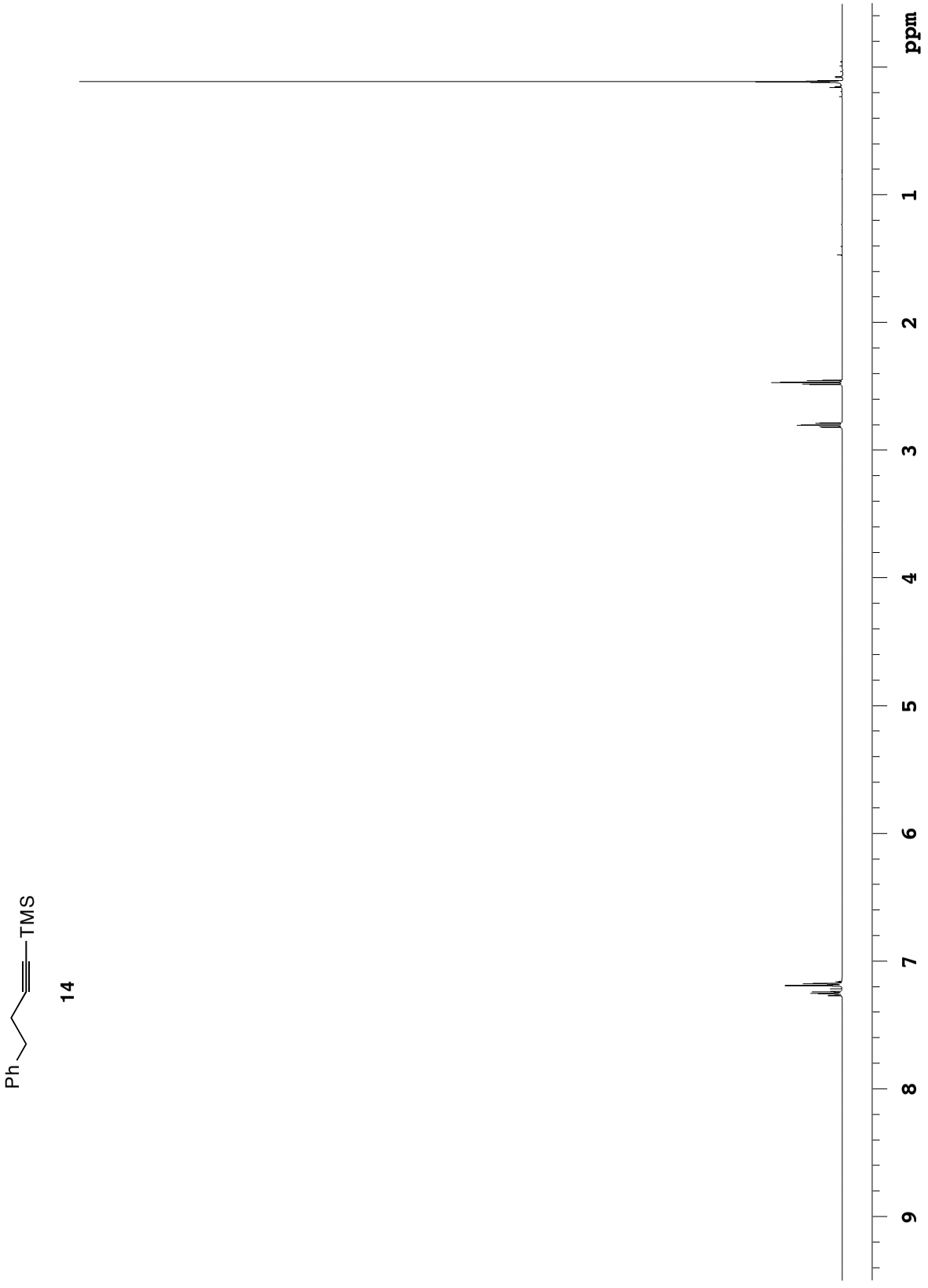
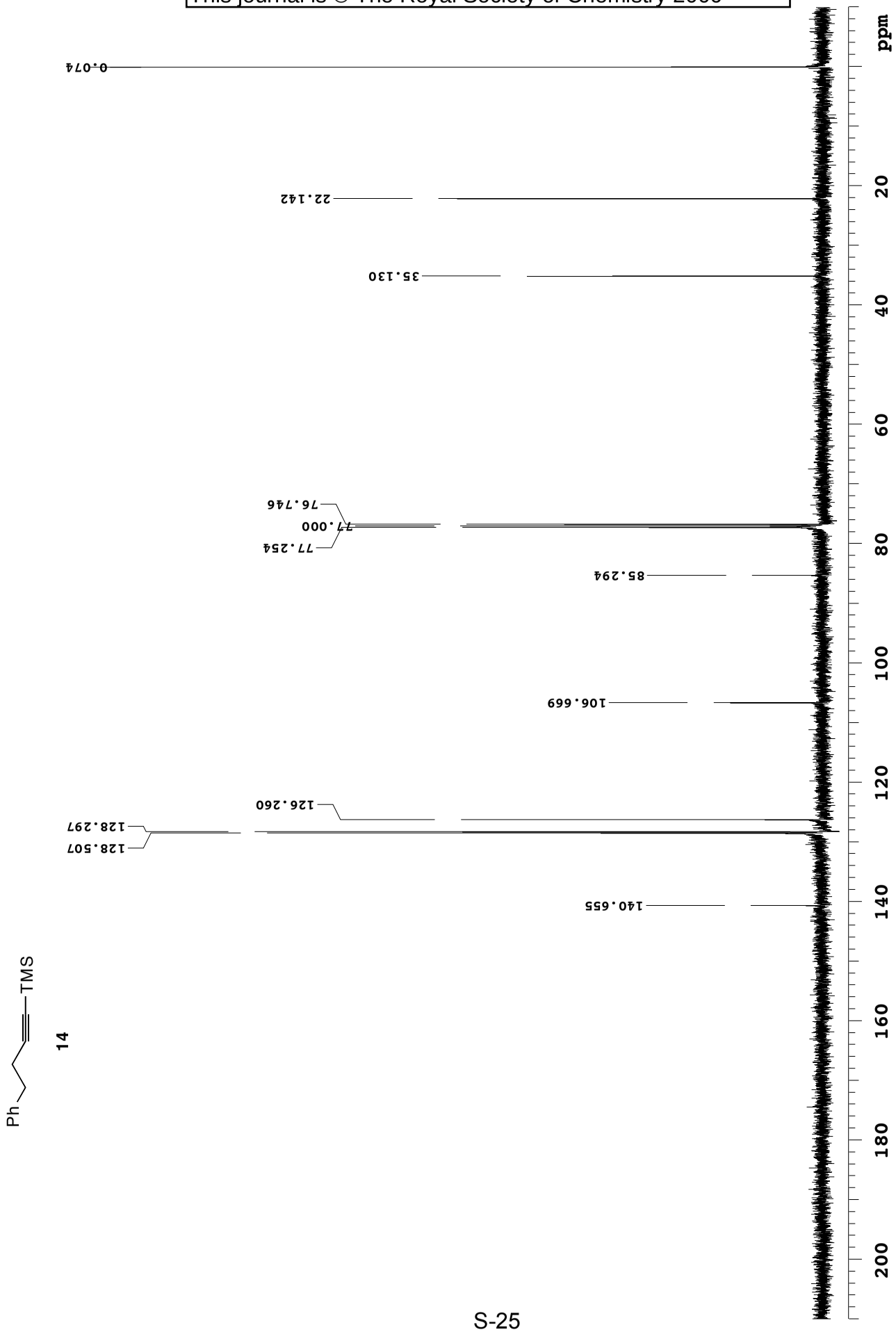
20.525
27.613
35.018
76.741
77.000
77.254
125.904
128.297
128.375
130.461
141.603
155.377
169.117
ppm
20
40
60
80
100
120
140
160
180
200
O
O
TMS
Ph
13


Ph
TMS
14
ppm
1
2
3
4
5
6
7
8
9


0.074
22.142
35.130
76.746
77.000
77.254
85.294
106.669
126.260
128.297
128.507
140.655
ppm
20
40
60
80
100
120
140
160
180
200
TMS
Ph
14