Supplementary Information

Mesityllithium and p-(dimethylamino)phenyllithium for the selective alternate trilithiation of the hexaphenylbenzene framework

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Contents

General Information

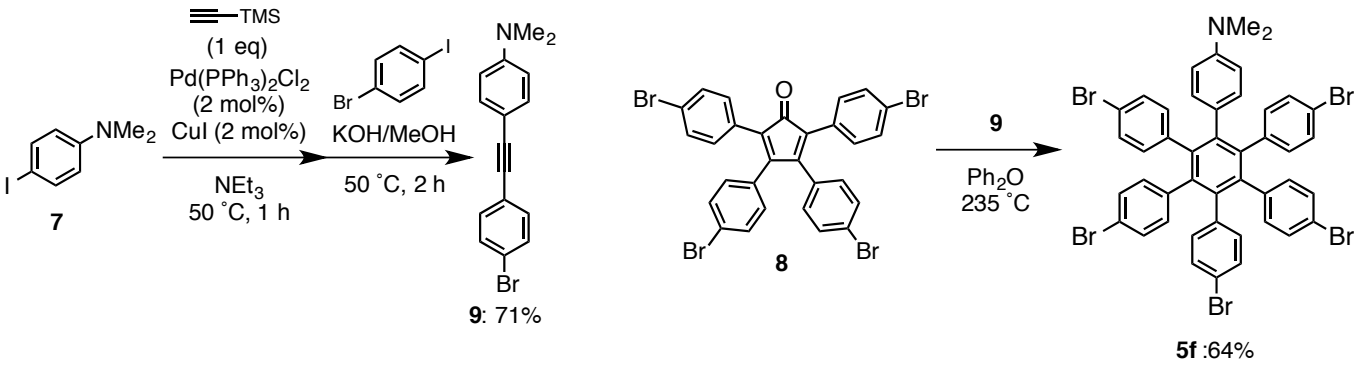
^{1}H NMR and ^{13}C NMR spectra were recorded with tetramethylsilane as the internal standard using a Bruker AV-500 (500 MHz) spectrometer. High-resolution mass spectra (HRMS) were obtained using a Waters Xevo G2 Tof mass spectrometer. Melting points were determined using a SCINICS SMP-300 instrument.

Materials

Unless otherwise noted, all solvents and reagents were obtained from commercial suppliers (TCI Co., Ltd., WAKO Pure Chemical Industries Ltd., KANTO Chemical Co., Ltd., and Sigma-Aldrich Co.) and were used as received. Compounds **1**,[1] **5a**-**e**,[2] 4-iodo-*N*,*N*-dimethylaniline (**7**)[3] and tetracyclone **8**[4] were prepared according to the literature.

Preparation of compound 5f

Scheme S1. Preparation of compound **5f**.



To the solution of compound **7** (3.00 g, 12.1 mmol), $Pd(PPh_3)_2Cl_2$ (169 mg, 2 mol%), CuI (46 mg, 2 mol%) in degassed NEt_3 (25 mL) was added trimethylsilylacetylene (1.73 mL, 12.1 mmol) at rt. The solution was stirred for 1 h at 50 ˚C. To the mixture were then added *p*-bromoiodobenzene (3.77 g, 13.3 mmol) and the methanol solution of KOH (0.35 g/mL, 8 mL). The mixture was vigorously stirred for 2 h at 50 ˚C. Then the solvent was removed in vacuo. After the addition of aq. NH_4Cl (20 mL) and CH_2Cl_2 (100 mL), the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL × 3) and the combined extracts were dried over anhydrous $MgSO_4$ and filtered. The concentration of the solution in vacuo resulted in the precipitation, which was collected by filtration to afford compound **9** (2.59 g, 71%) as a brown solid.

9: m.p. 145-146 ˚C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) δ 7.44 (d, *J* = 9.0 Hz, 2H), 7.39 (d, *J* = 9.0 Hz, 2H), 7.35 (d, *J* = 9.0 Hz, 2H), 6.66 (d, *J* = 9.0 Hz, 2H), 3.00 (s, 6H); ^{13}C {^{1}H} NMR (126 MHz, $CDCl_3$, 298 K) δ 150.36, 132.87, 132.82, 131.59, 123.32, 121.58, 111.94, 109.70, 92.03, 86.52, 40.33 (11 signals); HRMS (ASAP) Calcd for $[M+H]^+$ $C_{16}H_{15}{}^{79}BrN$ 300.0388, found 300.0392.

The mixture of compound **9** (0.708 g, 2.36 mmol) and tetracyclone **8** (1.50 g, 2.14 mmol) in degassed Ph_2O (2 mL) was stirred at 235 ˚C for 2.5 h. To the mixture was then added compound **9** (0.211 g, 0.703 mmol). The mixture was again stirred at 235 ˚C for 2.5 h. After cooling to rt and the addition of Et_2O (2 mL), the resulting

precipitation was filtered and thoroughly washed with Et_2O to afford compound **5f** (1.33 g, 64%) as a flesh-colored solid.

5f: m.p. >300 ˚C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) δ 7.05-7.02 (m, 10H), 6.64-6.60 (m, 10H), 6.52 (d, *J* = 9.0 Hz, 2H), 6.25 (d, *J* = 9.0 Hz, 2H), 2.80 (s, 6H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$, 298 K) δ 148.46, 141.33, 140.15, 139.40, 139.36, 139.08, 138.96, 138.67, 132.96, 132.86, 132.85, 131.90, 130.46, 130.45, 130.27, 127.19, 120.22, 120.19, 119.86, 111.35, 40.47 (21 signals); HRMS (ASAP) Calcd for $[M+H]^+$ $C_{44}H_{31}{}^{79}Br_3{}^{81}Br_2N$ 971.8337, found 971.8332.

Selective alternate trilithiation of compound 1 with *in situ* prepared MesLi or MapLi

To the suspension of compound **1** (0.200 g, 0.198 mmol) and MesBr (84 μL, 0.55 mmol) in THF (2 mL) was added the freshly titrated pentane solution of *t*-BuLi (1.68 M, 0.708 mL, 1.19 mmol) at –98 ˚C. After removal of the cooling bath, the reaction mixture was stirred for 30 min, and then quenched by the addition of TMSCl (0.151 mL, 1.19 mmol) at –98 ˚C. After the addition of water (10 mL) and $CHCl_3$ (10 mL), the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (10 mL × 3) and the combined extracts were dried over anhydrous $MgSO_4$, and filtered. Then the solvent was removed in vacuo and recrystallization from $CHCl_3$/EtOH afforded compound **4** (0.129 g, 66%) as a colorless solid.

To the suspension of compound **1** (0.200 g, 0.198 mmol) and MapBr (0.111 g, 0.555 mmol) in THF (2 mL) was added the freshly titrated pentane solution of *t*-BuLi (1.68 M, 0.708 mL, 1.19 mmol) at –98 ˚C. After removal of the cooling bath, the reaction mixture was stirred for 30 min, and then quenched by the addition of TMSCl (0.151 mL, 1.19 mmol) at –98 ˚C. After the addition of water (10 mL) and $CHCl_3$ (10 mL), the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (10 mL × 3) and the combined extracts were washed twice with aq.HCl (1 M). The resulting organic solution was dried over anhydrous $MgSO_4$, and filtered. Then the solvent was removed in vacuo and recrystallization from $CHCl_3$/EtOH afforded compound **4** (0.124 g, 63%) as a colorless solid.

Selective alternate trilithiation of compounds 5a-f with *in situ* prepared MesLi

To the suspension of pentabrominated HPB derivatives **5a-f** (**5a**: 0.200 g, **5b**: 0.200 g, **5c**: 0.150 g, **5d**: 0.150 g, **5e**: 0.150 g, **5f**: 0.200 g,) and MesBr (2.8 equiv.) in THF (2 mL) was added the freshly titrated pentane solution of *t*-BuLi (6 equiv.) at –98 ˚C. After removal of the cooling bath, the reaction mixture was stirred for 30-40 min. Then the reaction was quenched by the addition of TMSCl (6 equiv.) at –98 ˚C. After the addition of aq. NH_4Cl (10 mL) and $CHCl_3$ (10 mL), the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (10 mL × 3) and the combined extracts were dried over anhydrous $MgSO_4$, and filtered. Then the solvent was removed in vacuo and recrystallization from $CHCl_3$/EtOH afforded compounds **6a-f** (**6a**: 128 mg (65%), **6b**: 149 mg (76%), **6c**: 80 mg (54%), **6d**: 98 mg, (67%), **6e**: 88 mg (60%), **6f**: 114 mg (58%)) as a colorless solid.

The spectroscopic data of **6a** and **6b** were in agreement with those reported in the literature.[2]

6c: m.p. 296-299 ˚C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) δ 7.03 (d, *J* = 8.2 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 4H), 6.95 (d, *J* = 8.6 Hz, 4H), 6.84-6.80 (m, 3H), 6.77-6.74 (m, 2H), 6.73 (d, *J* = 8.2 Hz, 4H), 6.73 (d, *J* = 8.2 Hz, 2H), 6.64 (d, *J* = 8.6 Hz, 4H), 0.14 (s, 9H), 0.11 (s, 18H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, 298 K) δ 140.75, 140.70, 140.64, 140.49, 140.29, 140.26, 139.65, 139.24, 137.52, 137.21, 133.13, 131.99, 131.81, 131.45, 130.73, 129.84, 126.69, 125.31, 119.50, –1.03, –1.06 (21 signals; One signal in an aromatic region was not observed because of overlapping.); HRMS (ASAP) Calcd for $[M]^+$ $C_{51}H_{52}{}^{79}Br_2Si_3$ 906.1744, found 906.1756.

6d: m.p. >300 ˚C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) δ 7.02 (d, *J* = 8.2 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 4H), 6.94 (d, *J* = 8.6 Hz, 4H), 6.73 (d, *J* = 8.2 Hz, 4H), 6.72 (d, *J* = 8.2 Hz, 2H), 6.63 (d, *J* = 8.6 Hz, 4H), 6.62 (s, 4H), 2.08 (s, 3H) 0.14 (s, 9H), 0.12 (s, 18H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, 298 K) δ 140.85, 140.80, 140.71, 140.54, 140.08, 139.72, 139.19, 137.46, 137.16, 137.07, 134.57, 133.13, 131.97, 131.78, 131.29, 130.74, 129.81, 127.38, 119.45, 21.08, –1.04 (21 signals; One signal in an aromatic region and one signal from TMS group were not observed because of overlapping.); HRMS (ASAP) Calcd for $[M]^+$ $C_{52}H_{54}{}^{79}Br_2Si_3$ 920.1900, found 920.1909.

6e: m.p. 286-289 ˚C; ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) δ 7.02 (d, *J* = 8.2 Hz, 2H), 7.02 (d, *J* = 8.2 Hz, 4H), 6.94 (d, *J* = 8.5 Hz, 4H), 6.73 (d, *J* = 8.2 Hz, 4H), 6.72 (d, *J* = 8.2 Hz, 2H), 6.65 (d, *J* = 8.9 Hz, 2H), 6.63 (d, *J* = 8.5 Hz, 4H), 6.37 (d, *J* = 8.9 Hz, 2H), 3.60 (s, 3H), 0.14 (s, 9H), 0.12 (s, 18H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, 298 K) δ 157.22, 140.98, 140.83, 140.53, 140.28, 140.12, 139.72, 139.24, 137.48, 137.11, 133.13, 132.72, 132.50, 131.98, 131.87, 130.78, 130.74, 129.82, 119.47, 112.31, 55.15, –1.03 (22 signals; One signal from TMS group was not observed because of overlapping.); HRMS (ASAP) Calcd for $[M]^+$ $C_{52}H_{54}{}^{79}Br_2Si_3O$ 936.1849, found 936.1843.

6f: m.p. 254 ˚C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) δ 7.02 (d, *J* = 8.2 Hz, 4H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.94 (d, *J* = 8.2 Hz, 4H), 6.74 (d, *J* = 8.2 Hz, 4H), 6.72 (d, *J* = 8.2 Hz, 2H), 6.63 (d, *J* = 8.2 Hz, 2H), 6.56 (d, *J* = 8.8 Hz, 4H), 6.22 (d, *J* = 8.8 Hz, 2H), 2.72 (s, 6H), 0.14 (s, 9H), 0.12 (s, 18H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, 298 K) δ 148.37, 141.13 141.04, 140.83, 140.67, 139.90, 139.74, 139.15, 137.35, 136.78, 133.18, 132.19, 131.93, 131.81, 130.87, 130.79, 129.77, 128.75, 119.37, 111.57, 40.80, –1.02 (22 signals; One signal from TMS group was not observed because of overlapping.); HRMS (ASAP) Calcd for $[M+H]^+$ $C_{53}H_{58}{}^{79}Br_2NSi_3$ 950.2244, found 950.2244.

Large-scale synthesis of compounds 4 and 6c from granular lithium and MapBr

To granular lithium (1.86 g, 0.268 mol) was added the solution of MapBr (26.8 g, 0.134 mol) in Et_2O (100 mL) dropwise in 10 min. During the addition, the solution spontaneously refluxed. After the addition, the mixture was refluxed for 1 h. Then THF (200 mL) and compound **1** (30.0 g, 29.8 mmol) was added at 0 ˚C. The mixture was stirred for 20 min at 0 ˚C and transferred to another reaction vessel containing TMSCl (34.0 mL, 0.268 mol) at 0 ˚C. Then the solvent was removed in vacuo. After the addition of water (100 mL) and $CHCl_3$ (100 mL), the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (100 mL × 3) and the combined extracts were washed twice with aq.HCl (1 M). The resulting organic solution was dried over anhydrous $MgSO_4$, and filtered. Then the solvent was removed in vacuo and recrystallization from $CHCl_3$/EtOH afforded compound **4** (19.5 g, 66%) as a colorless solid.

To granular lithium (0.556 g, 80.1 mmol) was added the solution of MapBr (8.02 g, 40.1 mmol) in Et_2O (25 mL) dropwise in 10 min. During the addition, the solution spontaneously refluxed. Then the mixture was refluxed for 1 h. Then THF (50 mL) and compound **5c** (8.27 g, 8.90 mmol) was added at 0 ˚C. The mixture was stirred for 20 min at 0 ˚C. To the resulted solution was then added TMSCl (10.2 mL, 80.1 mmol) at 0 ˚C, and the solvent was removed in vacuo. After the addition of water (50 mL) and $CHCl_3$ (50 mL), the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (50 mL × 3) and the combined extracts were washed twice with aq.HCl (1 M). The resulting organic solution was dried over anhydrous $MgSO_4$, and filtered. Then the solvent was removed in vacuo and recrystallization from $CHCl_3$/EtOH (twice) afforded compound **6c** (3.87 g, 48%) as a colorless solid.

Attempted alternate trilithiation of compound 1 with PhLi

To the suspension of compound **1** (0.200 g, 0.198 mmol) in THF (2 mL) was added the diethyl ether and cyclohexane solution of PhLi (1.07 M, 0.556 mL, 0.594 mmol) at 0 ˚C. The reaction mixture was stirred at rt for 20 min, and then quenched by the addition of TMSCl (0.15 mL, 1.2 mmol) at –98 ˚C. After the addition of water and $CHCl_3$, the organic layer was analyzed by ^{1}H NMR spectroscopy.

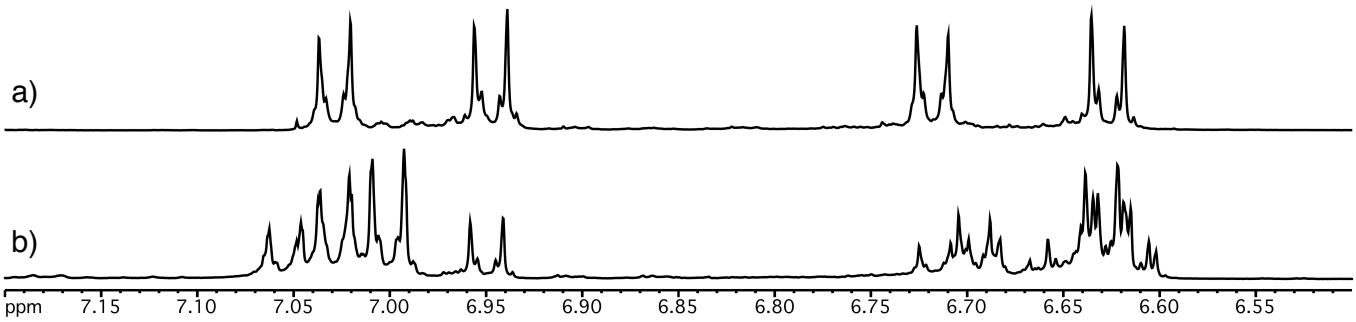
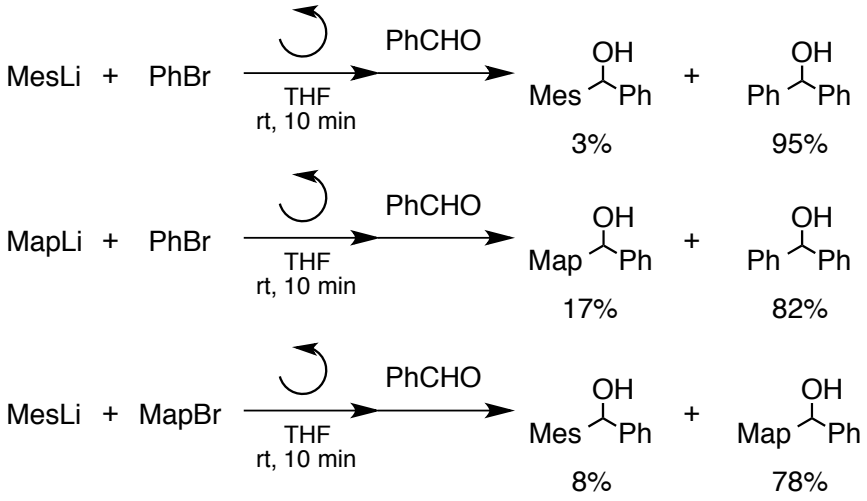


Figure S1. Partial ^{1}H NMR spectra (500 MHz, $CDCl_3$, 298 K) of the crude mixture obtained in the lithiation of compound **1** with a) *t*-BuLi (6 equiv.) or b) PhLi (3 equiv.).

Equilibration experiments with MesLi and MapLi

To the solution of Ar^1Br (1.3 mmol) in THF (4 mL) was added the pentane solution of *t*-BuLi (2.6 mmol) at –98 ˚C. After removal of the cooling bath, the solution was stirred for 20 min. Then Ar^2Br (1.3 mmol) was added to the solution, and the mixture was stirred at rt for 10 min. Then the reaction mixture was quenched with benzaldehyde (0.20 mL). After the addition of aq.NH_4Cl (10 mL), the product was extracted with CH_2Cl_2 (10 mL ×3). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. Then the solvent was removed in vacuo and ^{1}H NMR yields of the benzhydrol derivatives were determined with $CHCl_2CHCl_2$ as an internal standard.

Scheme S2. Comparison of the relative thermodynamic stability of PhLi, MesLi and MapLi as an aryllithium by equilibration experiments.



Confirmation of the *in situ* preparation of MesLi

The *in situ* preparation of MesLi was confirmed by the comparison of the crude product obtained by the rapid quenching of the lithiation reaction of compound **1** in the absence or the presence of MesBr. While three equivalents of lithiation of substrate **1** were completed in the absence of MesBr in 2.5 min after removal of the cooling bath, almost all of substrate **1** remained unreacted in the presence of MesBr in 2.5 min. This should be due to the selective lithiation of MesBr by *t*-BuLi.

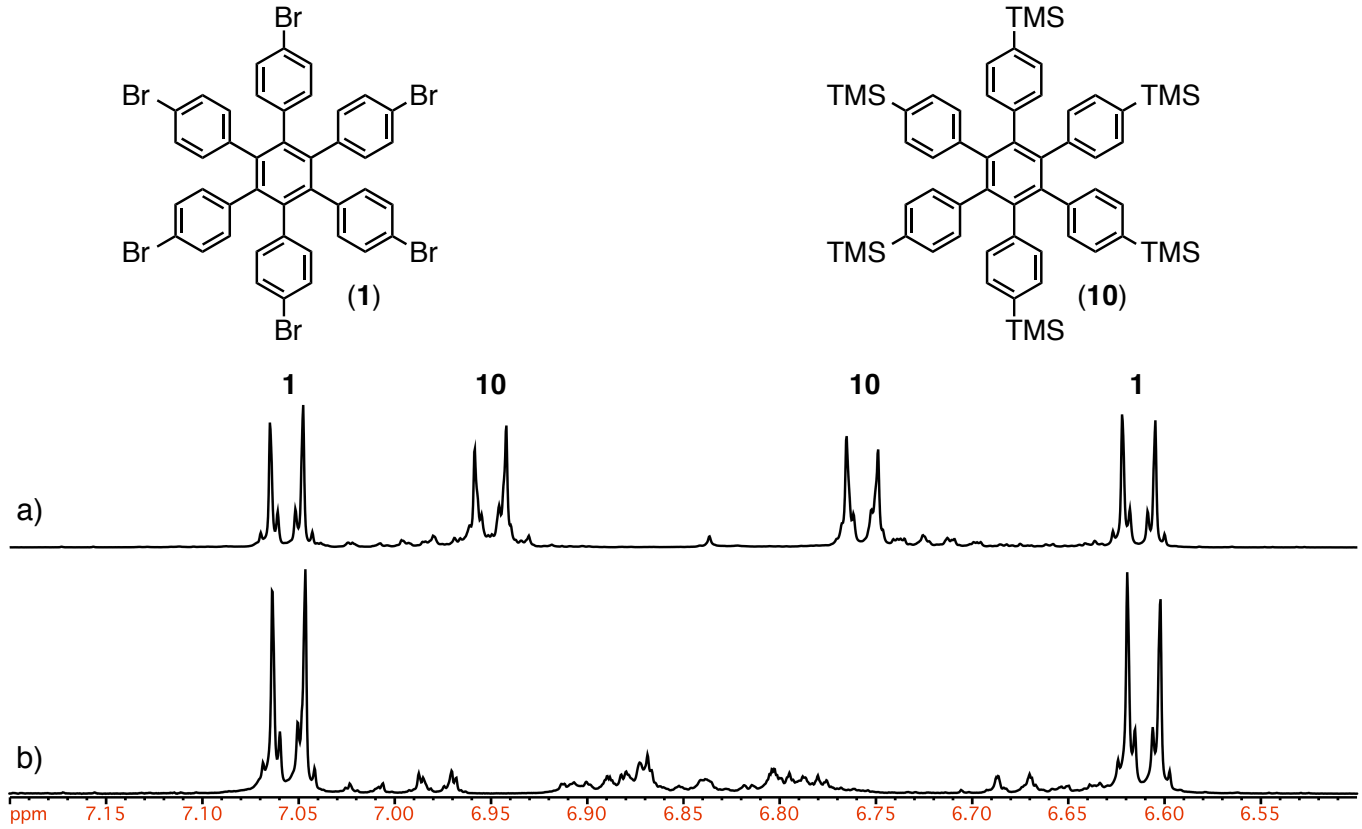


Figure S2. Partial ^{1}H NMR spectra (500 MHz, $CDCl_3$, 298 K) of the crude mixture obtained by quenching with TMSCl 2.5 min after removal of the cooling bath a) in the absence of MesBr, b) in the presence of MesBr.

Attempted alternate trilithiation of compound 1 with *in situ* prepared PhLi and *p*-$CF_3C_6H_4Li$

To the suspension of compound **1** (0.200 g, 0.198 mmol) and ArBr (2.8 equiv.) in THF (2 mL) was added the freshly titrated pentane solution of *t*-BuLi (1.74 M, 0.684 mL, 1.19 mmol) at –98 ˚C. After removal of the cooling bath, the reaction mixture was stirred for 30 min, and then quenched by the addition of TMSCl (0.151 mL, 1.19 mmol) at –98 ˚C. After the addition of water (10 mL) and $CHCl_3$ (10 mL), the organic layer was analyzed by ^{1}H NMR spectroscopy.

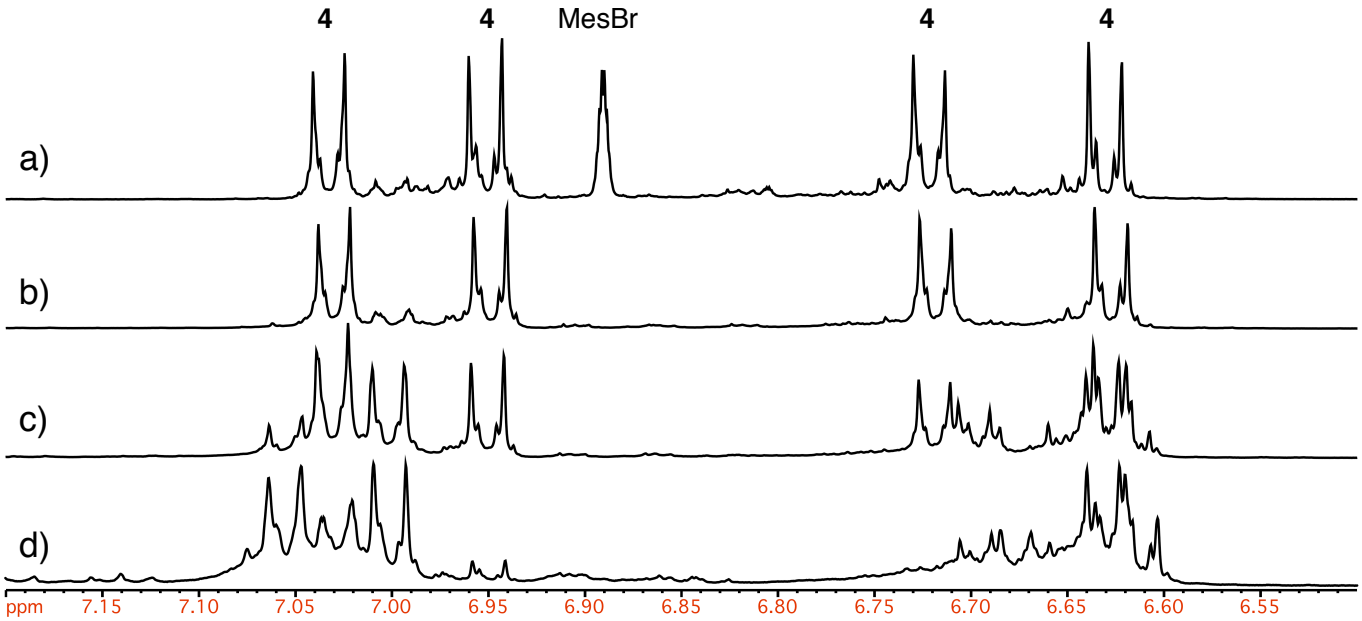


Figure S3. Partial ^{1}H NMR spectra (500 MHz, $CDCl_3$, 298 K) of the crude mixture obtained with various kinds of *in situ* prepared ArLi reagents: a) MesBr, b) MapBr, c) PhBr, d) *p*-$CF_3C_6H_4Br$.

Attempted lithiation of compound 1 with excess amount of MesLi or MapLi

To the suspension of compound **1** (0.200 g, 0.198 mmol) and ArBr (4.5 equiv.) in THF (2 mL) was added the freshly titrated pentane solution of *t*-BuLi (1.82 M, 0.981 mL, 1.79 mmol) at –98 ˚C. After removal of the cooling bath, the reaction mixture was stirred for 30 min, and then quenched by the addition of TMSCl (0.151 mL, 1.19 mmol) at –98 ˚C. After the addition of water (10 mL) and $CHCl_3$ (10 mL), the organic layer was analyzed by ^{1}H NMR spectroscopy. As for the reaction with MapBr, the organic layer was washed twice with aq.HCl (1 M), dried over anhydrous $MgSO_4$, and filtered. Then the solvent was removed in vacuo and recrystallization from $CHCl_3$/EtOH afforded compound **4** (0.128 g, 65%) as a colorless solid.

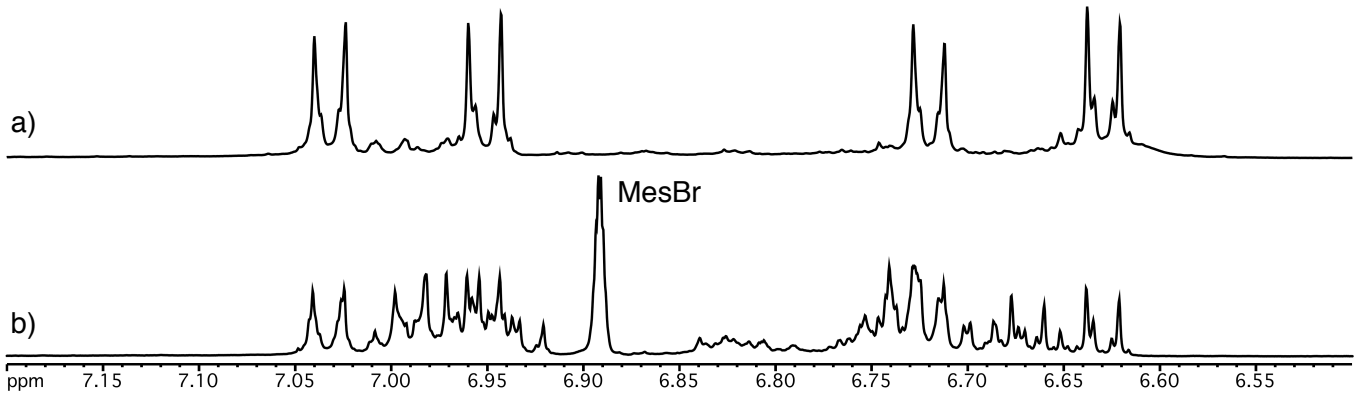


Figure S4. Partial ^{1}H NMR spectra (500 MHz, $CDCl_3$, 298 K) of the crude mixture obtained with 4.5 equiv. of a) MapLi or b) MesLi.

References

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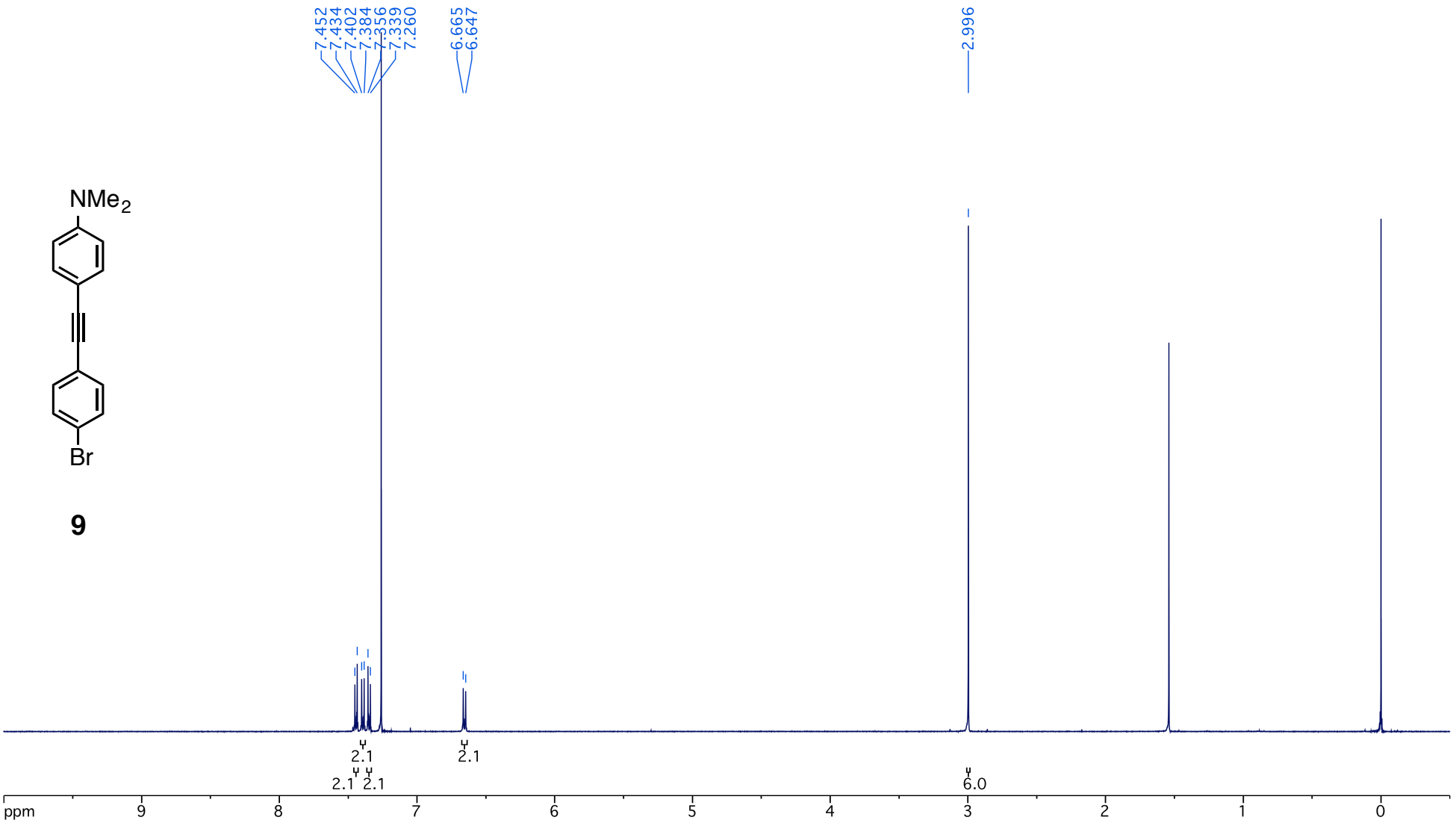
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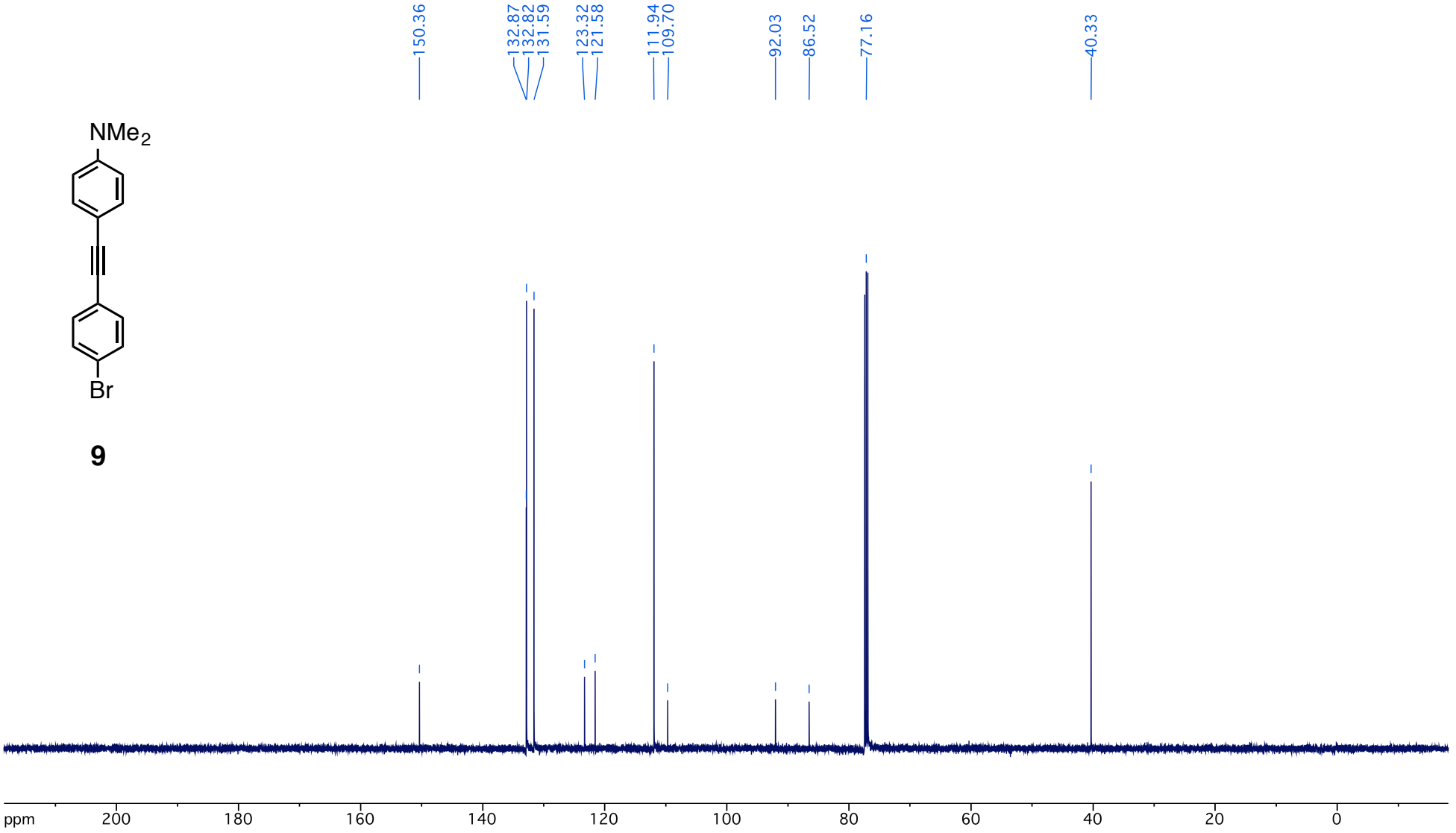
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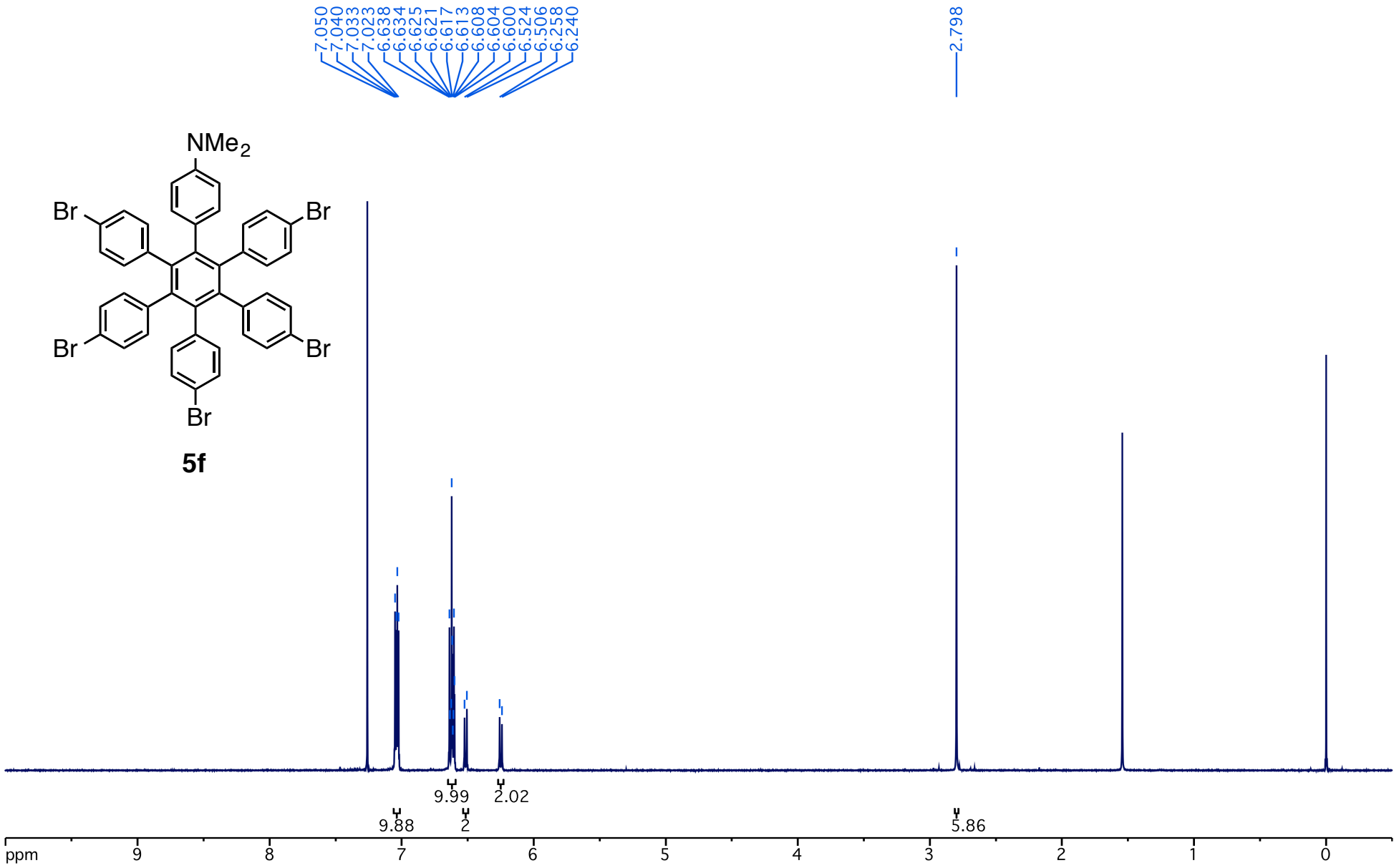
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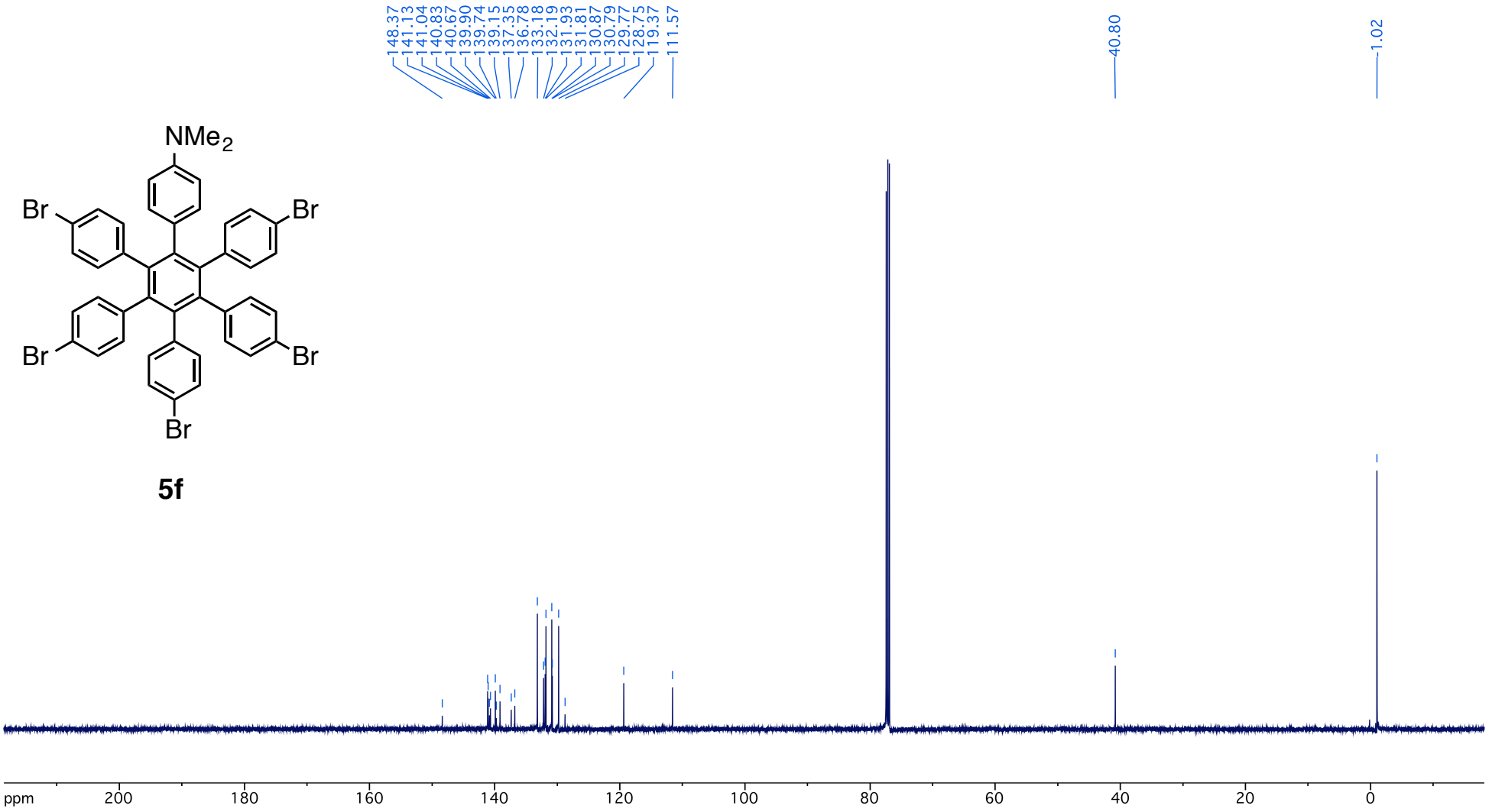
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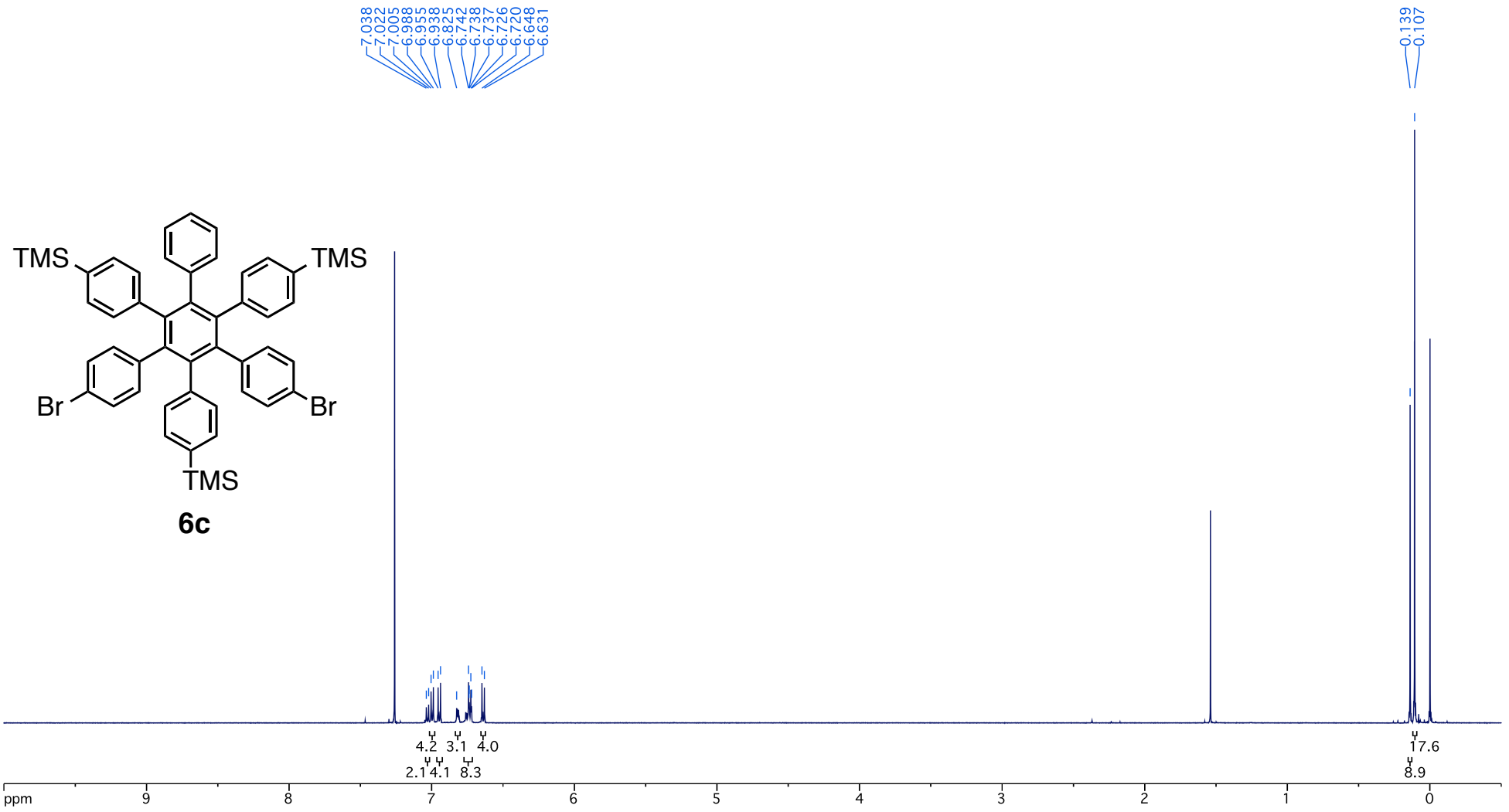
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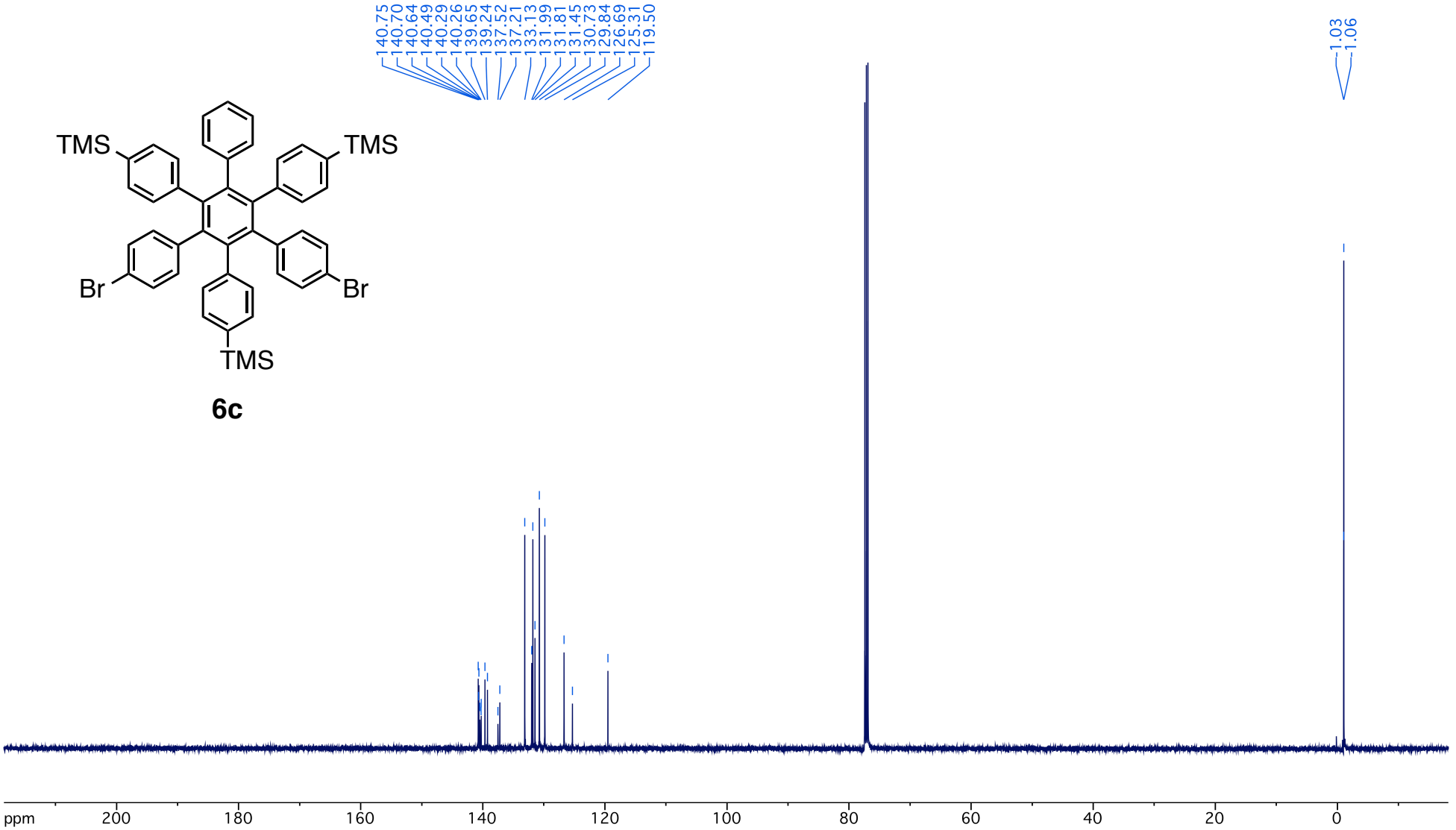
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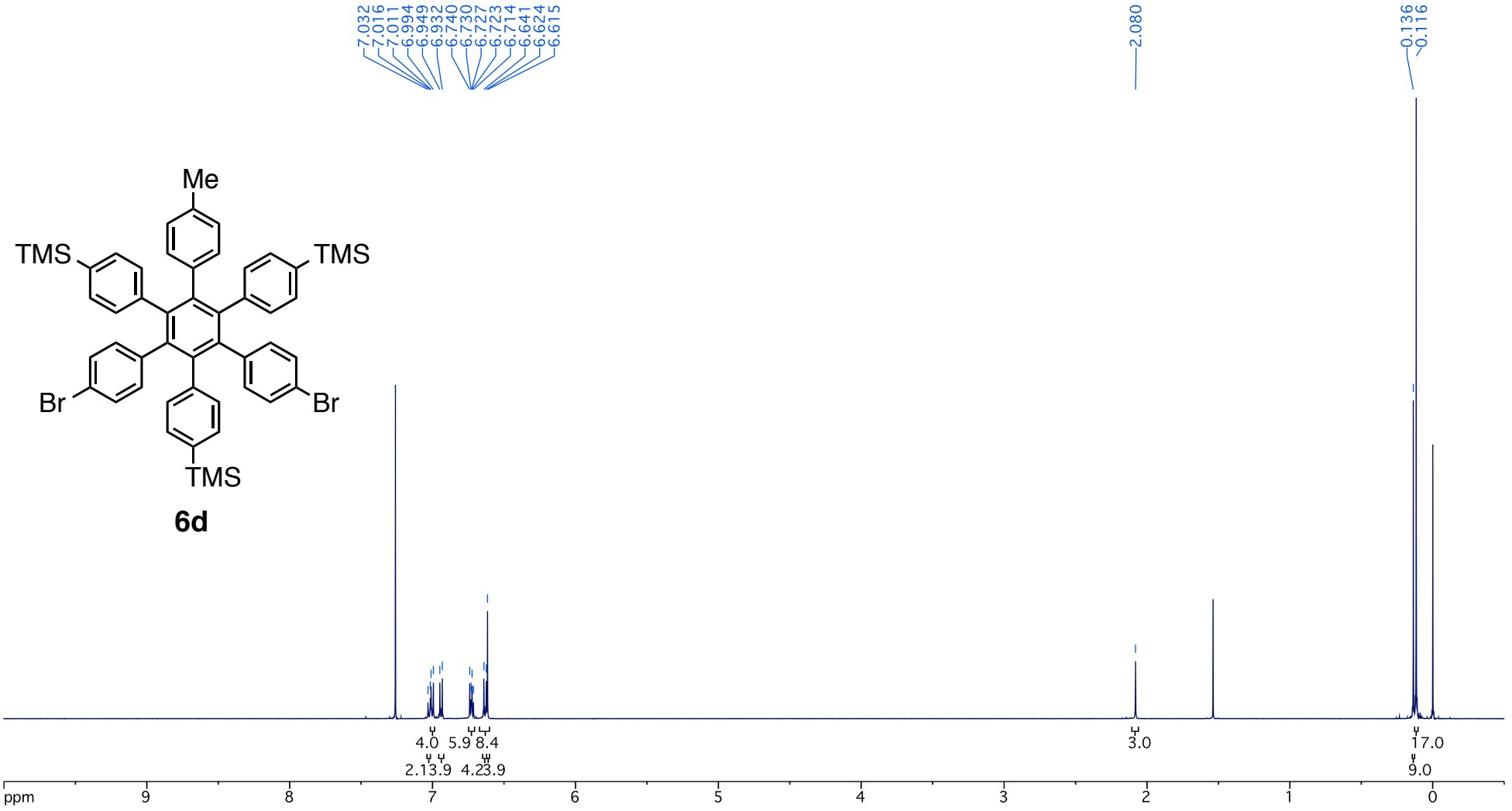
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6.740
6.730
6.727
6.723
6.714
6.641
6.624
6.615
2.080
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0.116
Me
TMS
TMS
Br
Br
TMS
6d
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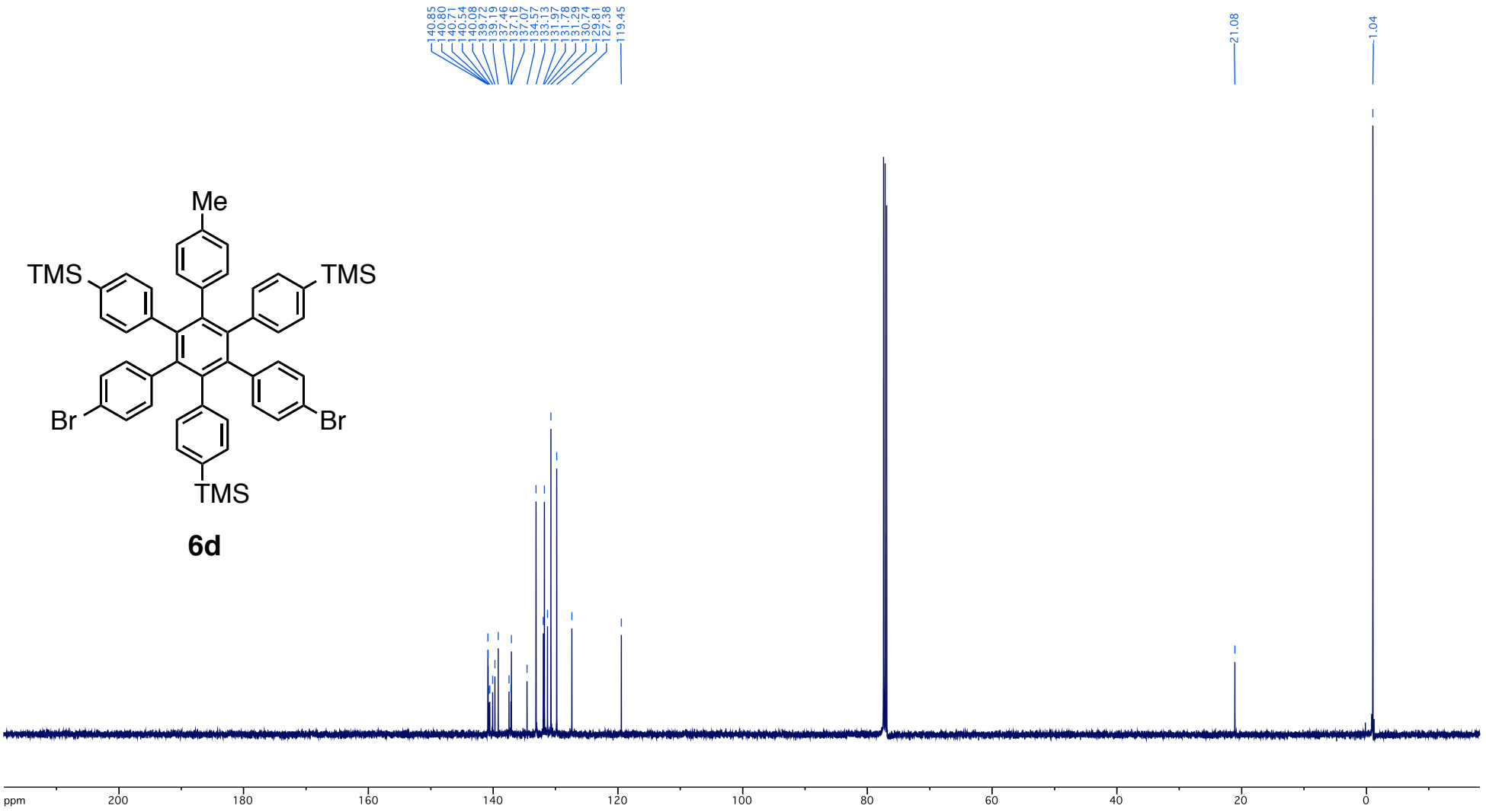
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133.13
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131.78
131.29
130.74
129.81
127.38
119.45
21.08
1.04
Me
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Br
TMS
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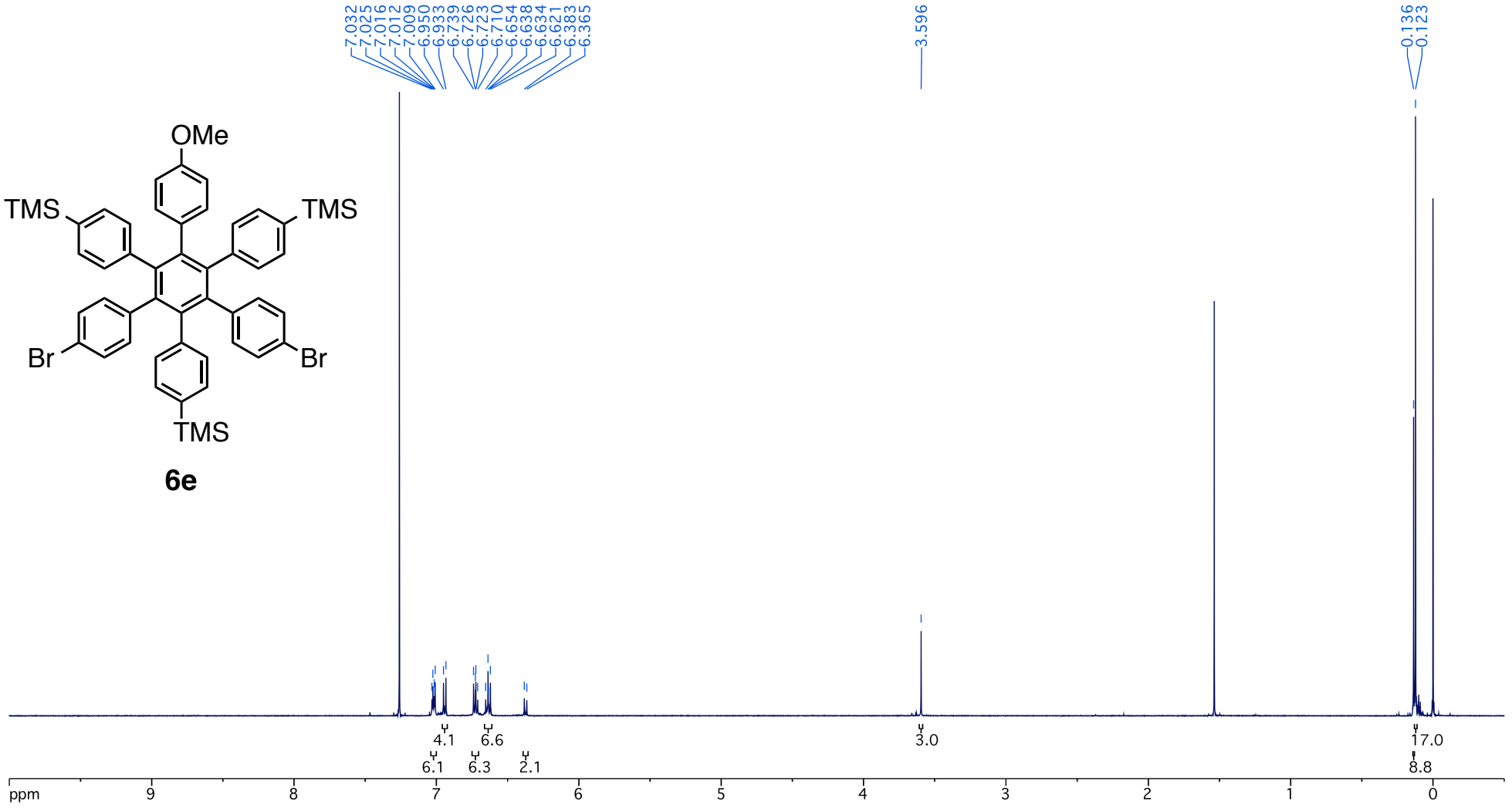
6d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7.016
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7.009
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6.739
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6.723
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6.654
6.638
6.634
6.621
6.383
6.365
3.596
0.136
0.123
OMe
TMS
TMS
Br
Br
TMS
6e
4.1
6.6
3.0
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6.3
2.1
8.8
ppm
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7
6
5
4
3
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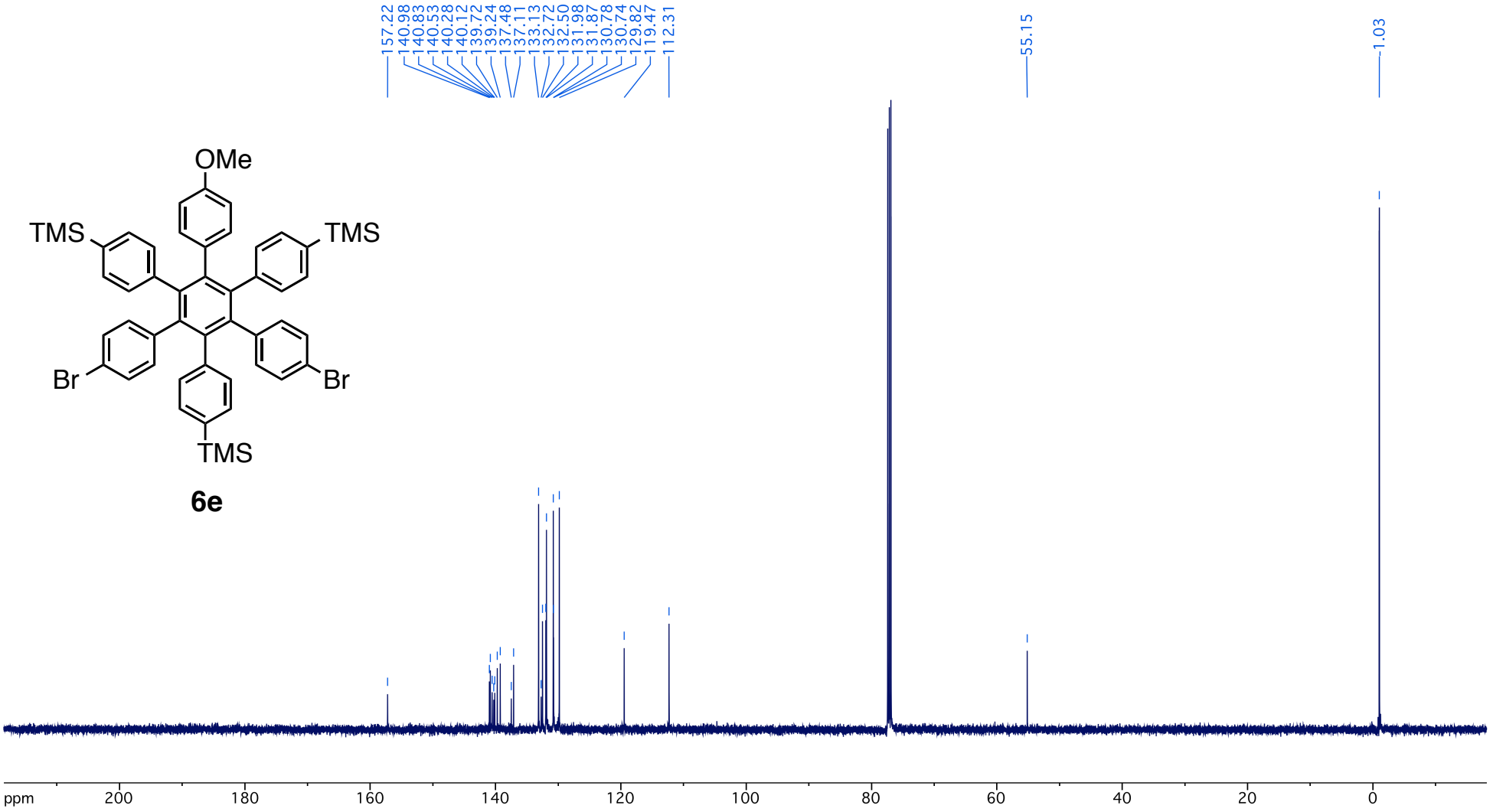
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140.12
139.72
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133.13
132.72
132.50
131.98
131.87
130.78
130.74
129.82
119.47
112.31
55.15
1.03
OMe
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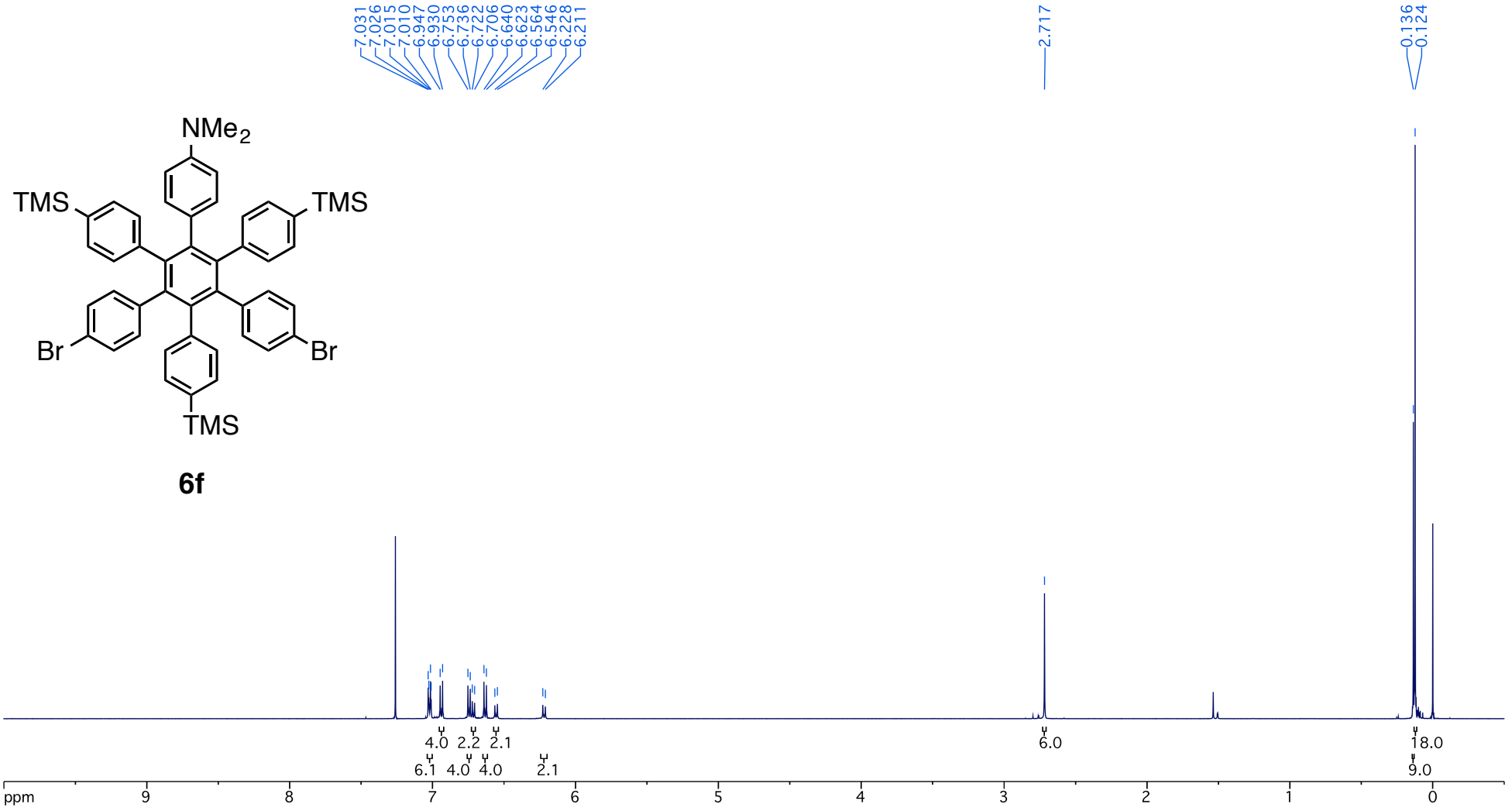
Br
Br
TMS
ppm
200
180
160
140
120
100
80
60
40
20
0

6e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6.930
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6.706
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6.623
6.564
6.546
6.228
6.211
2.717
0.136
0.124
NMe2
TMS
TMS
Br
Br
TMS
4.0
2.2
2.1
6.1
4.0
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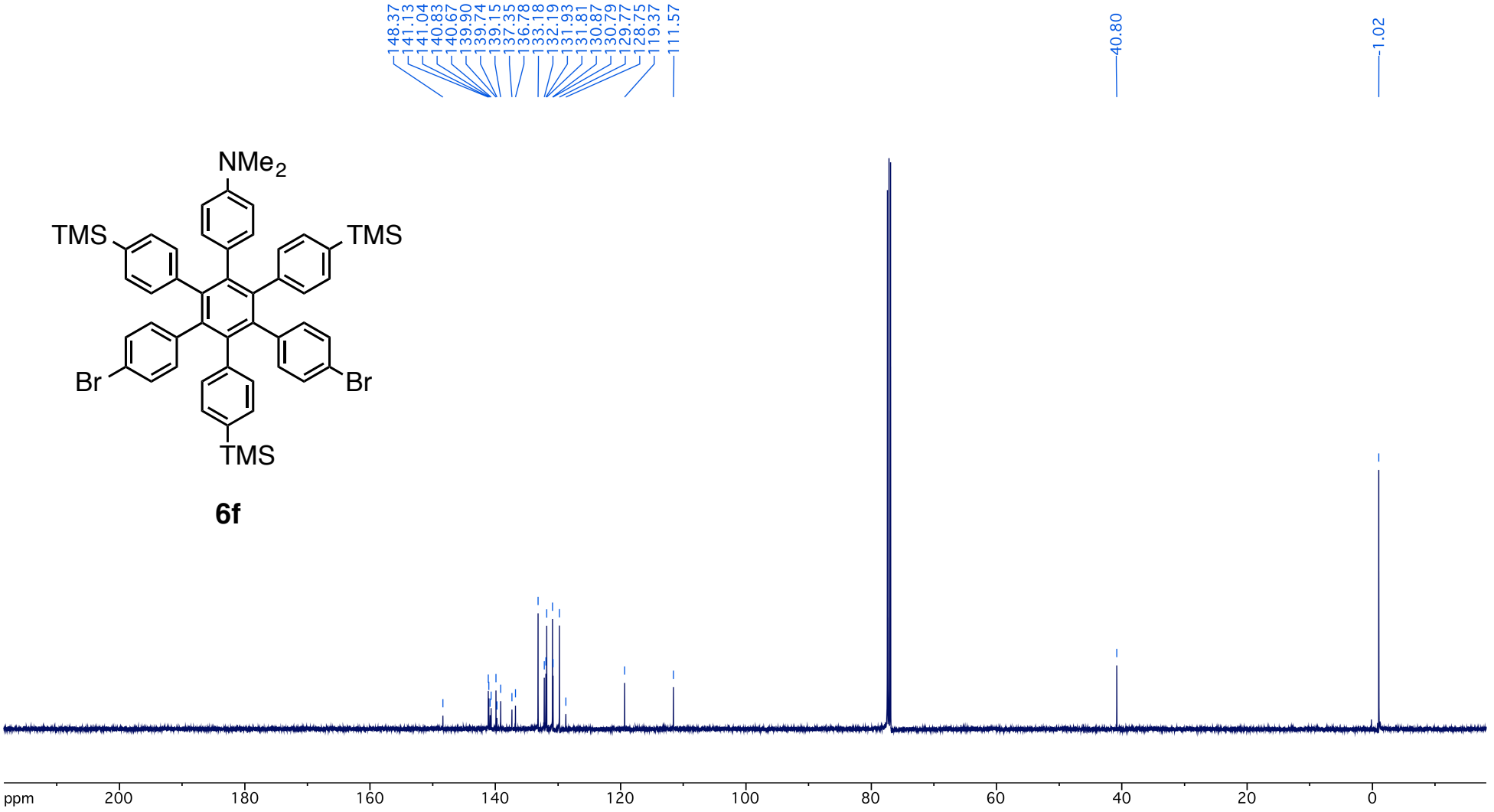
8
7
6
5
4
3
2
1
0

6f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131.93
131.81
130.87
130.79
129.77
128.75
119.37
111.57
40.80
1.02
NMe2
TMS
TMS
Br
Br
TMS
6f
ppm
200
180
160
140
120
100
80
60
40
20
0