Supporting Information

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Regio- and stereoselective hydrohalogenation of ynamide components in 1,3-butadiynes with *in situ* generated HX

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Contents

a) **General Information**: All reactions sensitive to air or moisture were carried out under argon atmosphere and anhydrous conditions unless otherwise noted. Dry solvents were purchased from Wako Pure Chemicals., LTD. and used without further purification and dehydration. All reagents were purchased and used without further purification. Column chromatography was carried out with silica gel, Silica Gel 60 N that is purchased from Kanto Chemical Co., Inc. Mass spectra were reported on a JEOL GC-mate II (for EI). Elemental analyses were performed at A RABBIT SCIENCE JAPAN Cp., LTD. (http://www.rabbit-sc.jp/). ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER-SPECTRON-400 with a 5 mm QNP probe at 400 MHz and 100 MHz, respectively. Chemical shifts are reported in δ (ppm) with reference to residual solvent signals [1H NMR: $CHCl_3$ (7.26); ^{13}C NMR: $CDCl_3$ (77.0)]. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

b) **General Procedure for Hydrohalogenation of *N*,*N*'-(buta-1,3-diyne-1,4-diyl)bis(4-methyl-*N*-phenylbenzenesulfonamide),**

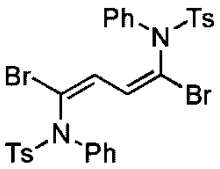
for Table 1, entry 10: To a solution of **1** (2.0 mmol) in anhydrous CH_2Cl_2 (80 mL) at -78 ºC was added TMSBr (6.4 mL of 1 M in CH2Cl2) dropwise over 12 min, and the mixture was stirred for 10 min. Then, H_2O (80 mmol) was added, and the cooling-bath was removed to warm to room temperature. After additional stirring for 50 min, the reaction was quenched at 0 ºC with saturated aqueous sodium thiosulfate (26 mL), and stirred for 10 min, and allowed to warm to ambient temperature. The organic phases were washed with brine (50 mL), and then dried over Na_2SO_4, and concentrated to give a crude product. Purification by silica gel column chromatography (eluent; hexane/CH_2Cl_2/EtOAc = 70/30/1) afforded 1.1 g of **2** in 79% yield as white solid materials. Analytical data are listed in the section below.

c) **Procedure for Hydrochlorination of *N*,*N*'-(buta-1,3-diyne-1,4-diyl)bis(4-methyl-*N*-phenylbenzenesulfonamide) to yield the chloride 4, for Scheme 3**: To a solution of **1** (200 mg, 0.37 mmol) in anhydrous CH_2Cl_2 (16 mL) and CH_3CN (10 mL) at room temperature was added TMSCl (1.18 mL of 1 M in CH_2Cl_2) dropwise over 7 min, and the mixture was stirred for 10 min. Then, saturated aqueous NH_4Cl (14.8 mmol) was added, and the reaction was performed for 9 h at ambient temperature until the starting **1** was consumed. The reaction was quenched at 0 ºC with saturated aqueous sodium thiosulfate (10 mL), and stirred for 10 min, and allowed to warm to ambient temperature. The organic phases were washed with brine, and then dried over Na_2SO_4, and concentrated to give a crude product. Purification by silica gel column chromatography (eluent; hexane/CH_2Cl_2/EtOAc = 70/30/1) afforded 147 mg of **4** in 65% yield as white solid materials. The recrystallization from ethanol furnished **4** as colorless needles. Analytical data are listed in the section below.

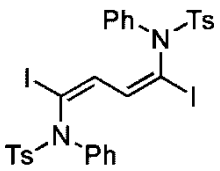
d) **Preparation of 1 M Halotrimethylsilane (TMSX) stock solution in CH_2Cl_2**: 2.6 g of TMSCl (Wako Pure Chemicals, Co., LTD.) was added to 21 mL of dry CH_2Cl_2, and 3.5 of TMSBr (Tokyo Chemical Industry Co., LTD.) were added to 20 mL of dry CH_2Cl_2, and each was used as a 1M TMSX solution. As for TMSI, we purchased the seal-tubed version in neat form from Tokyo Chemical Industry Co., LTD, and it included a portion of Al metal inside the tube for inhibiting the decomposition of TMSI. 5 g of TMSI was added to 25 mL of dried CH_2Cl_2 along with the Al metal as a solid, thus providing colorless 1 M stock solution for our experimental usage. The Al metal would not have a crucial role for the reactivity of the TMSI solution: actually, the reactivity of the freshly prepared TMSI solution was not influenced by with or without the metal. The stock solution in the presence of the Al metal was stable for at least two weeks, although it turned to slightly red colored solution. However, in the case of 1 M toluene solution,

unfortunately, complete decomposition on ^{1}H NMR spectra was observed only in 24 h.

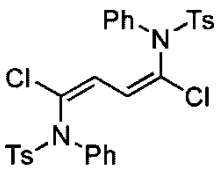
e) **Characterization for novel compounds 2 - 9**:



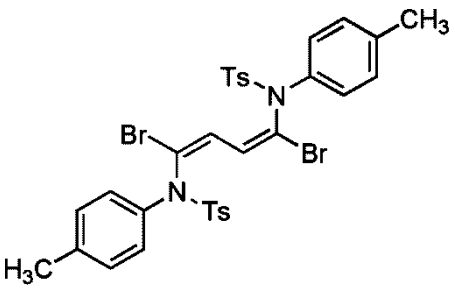
Compound 2: 79% yield (1.10 g); white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 4H), 7.39-7.24 (m, 14H), 6.80 (s, 2H), 2.41 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 138.8, 135.4, 132.5, 130.0, 129.7, 129.1, 129.0, 128.1, 123.5, 22.0; MS (EI) *m/z*: 622 ($[MH\text{-}Br]^+$), 547 ($[M\text{-}Ts]^+$); IR (neat): 3065 (C=C), 3016, 2974, 1739, 1577, 1351 (NSO_2), 1163 (NSO_2), 1086 cm^{-1}; Anal. Calcd for $C_{30}H_{26}Br_2N_2O_4S_2$: C, 51.29; H, 3.73; N, 3.99. Found: C, 51.21; H, 3.83; N, 3.97.



Compound 3: 71% yield (142 mg); beige solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 4H), 7.42-7.27 (m, 14H), 6.99 (s, 2H), 2.40 (s, 6H); ^{13}C NMR (100 MHz, CDCl3) δ 145.3, 141.1, 139.4, 135.4, 130.2, 129.8, 129.1, 129.0, 127.6, 98.9, 22.1; MS (EI) *m/z*: 543 ($[(M\text{-}I_2)H]^+$); IR (neat): 3109 (C=C), 1609, 1593, 1560, 1487, 1346 (NSO_2), 1161 (NSO_2) cm^{-1}; Anal. Calcd for $C_{30}H_{26}I_2N_2O_4S_2$: C, 45.24; H, 3.29; N, 3.52. Found: C, 45.23; H, 3.30; N, 3.58.

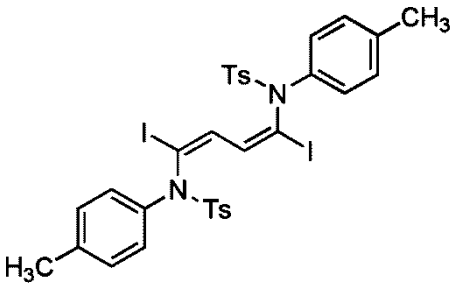


Compound 4: 65% yield (147 mg); white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.4 Hz, 4H), 7.37-7.34 (m, 6H), 7.31-7.27 (m, 4H), 7.23 (d, *J* = 8.4 Hz, 4H), 6.69 (s, 2H), 2.41 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 138.6, 135.5, 132.5, 129.9, 129.7, 129.0, 128.8, 128.1, 127.7, 21.9. MS (FAB) *m/z*: 613 ($[MH]^+$), 537 ($[M\text{-}Ph]^+$), 457 ($[M\text{-}Ts]^+$); IR (neat): 3071, 2924, 1584, 1489, 1359, 1160, 1087 cm^{-1}; Anal. Calcd for $C_{30}H_{26}Cl_2N_2O_4S_2$: C, 58.72; H, 4.27; N, 4.57. Found: C, 58.59; H, 4.08; N, 4.51.

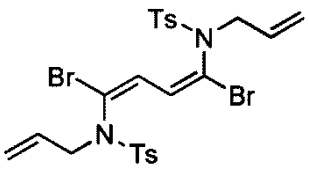


Compound 5a: 79% yield (290 mg); pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz 4H), 7.25 (d, *J* = 8.3 Hz, 4H), 7.16 (s, 8H), 6.76 (s, 2H), 2.41 (s, 6H), 2.3 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 139.4, 136.1, 135.5, 132.3, 130.4, 129.9, 129.0, 128.1, 123.7, 22.0, 21.5; MS (FAB) *m/z*: 728 (M^+); IR (neat): 2924, 1581, 1504, 1358, 1165, 1080 cm^{-1}; Anal. Calcd for $C_{32}H_{30}Br_2N_2O_4S_2$: C, 52.61; H, 4.14; N, 3.83. Found:

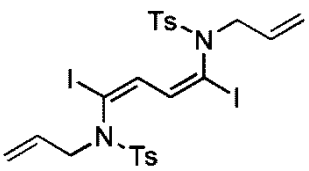
C, 52.78; H, 4.05; N, 3.77.



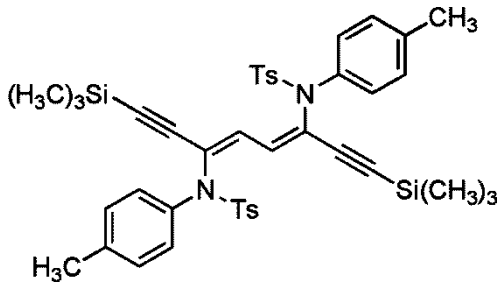
Compound 5b: 69% yield (143 mg); pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.2 Hz, 4H), 7.27 (d, *J* = 8.2 Hz, 4H), 7.19 (d, *J* = 8.4 Hz, 4H), 7.14 (d, *J* = 8.4 Hz, 4H), 6.94 (s, 2H), 2.41 (s, 6H), 2.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 140.8, 139.2, 136.6, 135.4, 130.4, 130.1, 129.1, 127.6, 99.2, 22.1, 21.5; MS (FAB) *m/z*: 824 (M^+), 386 ([M-$(CH_3C_6H_4SO_2)_2$-I]$^+$); IR (neat): 3059, 2924, 1589, 1504, 1338, 1161, 1061 (NSO2) cm^{-1}; Anal. Calcd for $C_{32}H_{30}I_2N_2O_4S_2$: C, 46.61; H, 3.67; N, 3.40. Found: C, 46.73; H, 3.53; N, 3.51



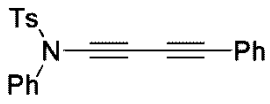
Compound 6a: 74% yield (140 mg); white solid; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.85-7.79 (br, 4H), 7.50-7.48 (br, 4H), 6.73 (s, 2H), 5.85-5.73 (br, 2H), 5.37-5.20 (br, 4H), 4.39-4.34 (br, 2H), 3.56-3.50 (br, 2H), 2.47 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 134.5, 134.2, 130.0 (four peaks are overlapped), 128.9, 52.3, 21.9; MS (FAB) *m/z*: 631 ([MH]$^+$), 551 ([MH-Br]$^+$), 475 ([M-Ts]$^+$), 395 ([M-Ts-Br]$^+$); IR (neat): 3066, 2920, 1584, 1357, 1272, 1164 cm^{-1}; Anal. Calcd for $C_{24}H_{26}Br_2N_2O_4S_2$: C, 45.73; H, 4.16; N, 4.44. Found: C, 45.68; H, 4.18; N, 4.29.



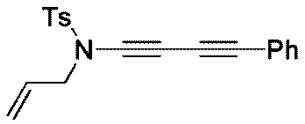
Compound 6b: 70% yield (152 mg); pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.71 (m, 4H), 7.38-7.33 (br, 4H), 7.09 (brs, 2H), 5.78-5.61 (br, 2H), 5.37-5.17 (m, 4H), 4.39-4.25 (br, 2H), 3.23-3.14 (m, 2H), 2.46 (brs, 6H); ^{13}C NMR (100 MHz, CDCl3) δ 145.1, 143.04, 142.97, 133.88, 133.84, 131.1, 130.7, 130.0, 129.3, 129.1, 121.3, 120.9, 100.4, 99.9, 54.2, 53.9, 22.0; MS (FAB) *m/z*: 725 ([MH]$^+$), 569 ([M-Ts]$^+$), 415 ([MH-Ts-Ts]$^+$); IR (neat): 3088, 2898, 2854, 1596, 1576, 1362, 1278, 1165 cm^{-1}; Anal. Calcd for $C_{24}H_{26}I_2N_2O_4S_2$: C, 39.79; H, 3.62; N, 3.87. Found: C, 39.86; H, 3.80; N, 3.96.



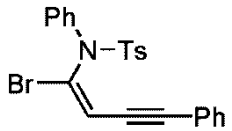
Compound 7: 69% yield (105 mg); orange solid materials; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.3 Hz 4H), 7.30 (s, 2H), 7.22 (d, *J* = 8.3 Hz 4H), 7.20 (d, *J* = 8.5 Hz 4H), 7.09 (d, *J* = 8.5 Hz 4H), 2.41 (s, 6H), 2.33 (s, 6H), 0.11 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 138.5, 137.4, 136.3, 134.5, 130.0, 129.4, 129.1, 128.4, 123.8, 103.1, 100.3, 21.9, 21.4, -0.2; MS (FAB) *m/z*: 608 ($[M\text{-}CH_3C_6H_5SO_2\text{-}H]^+$); IR (neat): 2958, 2137, 1504, 1350, 1161, 845 cm^{-1}; Anal. Calcd for $C_{42}H_{48}I_2N_2O_4S_2Si_2$: C, 65.93; H, 6.32; N, 3.66. Found: C, 65.94; H, 6.37; N, 3.51.



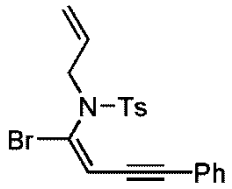
Compound 8a: 58% yield (430 mg); white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.4 Hz 2H), 7.48 (dd, *J* = 7.9, 1.9 Hz, 2H), 7.36-7.30 (m, 8H), 7.25-7.23 (m, 2H), 2.45 (s,3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 138.3, 133.2, 132.6, 130.1, 129.6, 129.3, 129.0, 128.7, 128.4, 126.6, 122.2, 81.8, 74.7, 73.7, 58.0, 22.0. MS (FAB) *m/z*: 371 (M^+); IR (neat) 2961, 2154, 1917, 1596, 1488, 1349 (NSO_2), 1166 (NSO_2) cm^{-1}; Anal. Calcd for $C_{23}H_{17}NO_2S$: C, 74.37; H, 4.61; N, 3.77. Found: C, 74.35; H, 4.60; N, 3.89.



Compound 8b: 66% yield (411 mg); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.4 Hz, 2H), 7.47 (dd, *J* = 7.7, 1.5 Hz, 2H), 7.39-7.29 (m, 5H), 5.74 (dddd, *J* = 16.9, 10.3, 6.3, 6.3 Hz, 1H), 5.31-5.24 (m, 2H), 4.02 (ddd, *J* = 6.3, 1.2, 1.2 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 134.9, 132.7, 130.6, 130.3, 129.3, 129.0, 128.7, 128.0, 122.3, 121.0, 81.4, 74.2, 73.8, 58.7, 22.0. MS (FAB) *m/z*: 355 (M^+), 188 ([M-Ts]+); IR (neat) 3062, 2927, 2225, 2156, 1593, 1493, 1365, 1165 cm^{-1}; Anal. Calcd for $C_{20}H_{17}NO_2S$: C, 71.62; H, 5.11; N, 4.18. Found: C, 71.59; H, 5.04; N, 4.20.

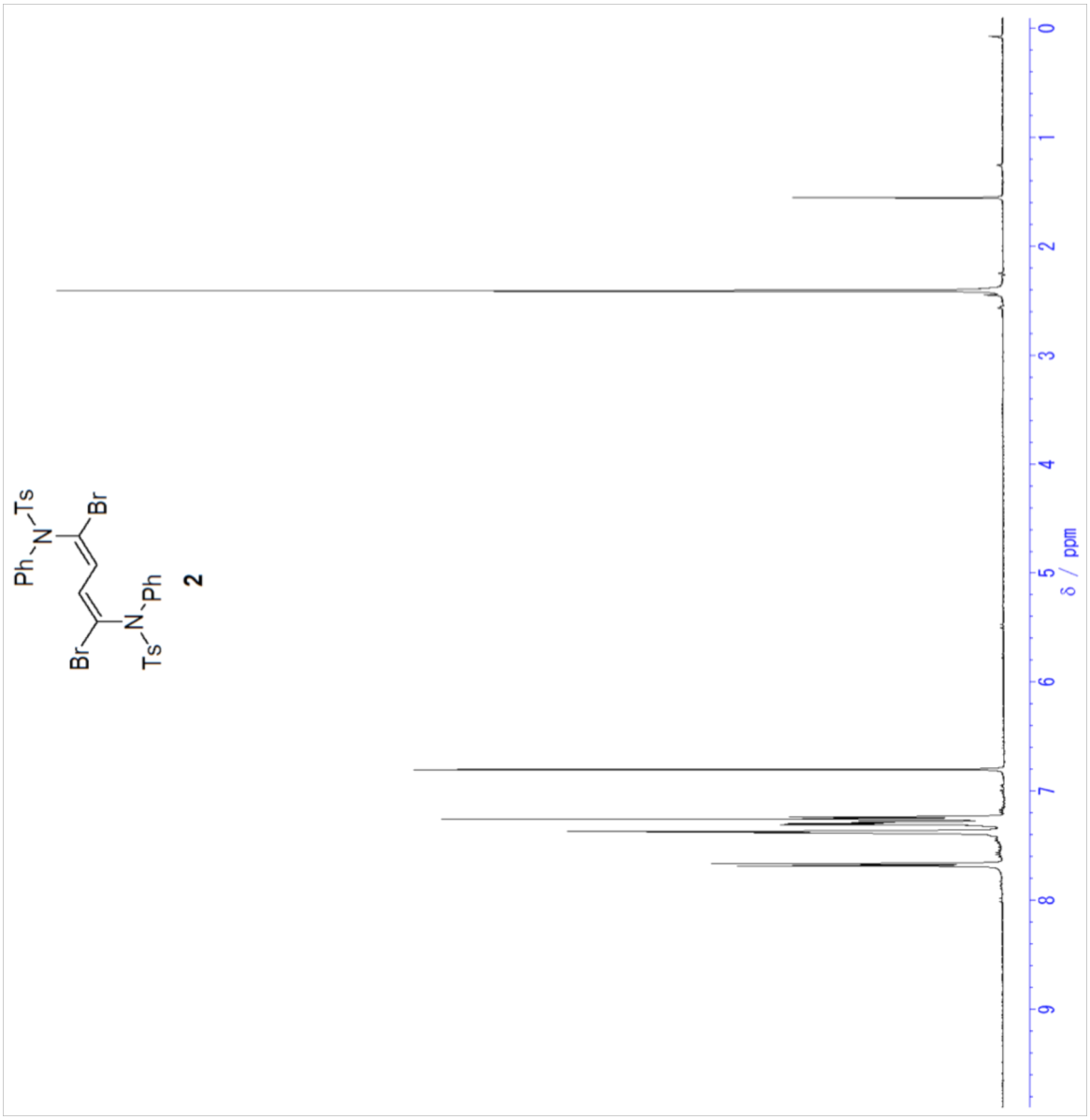


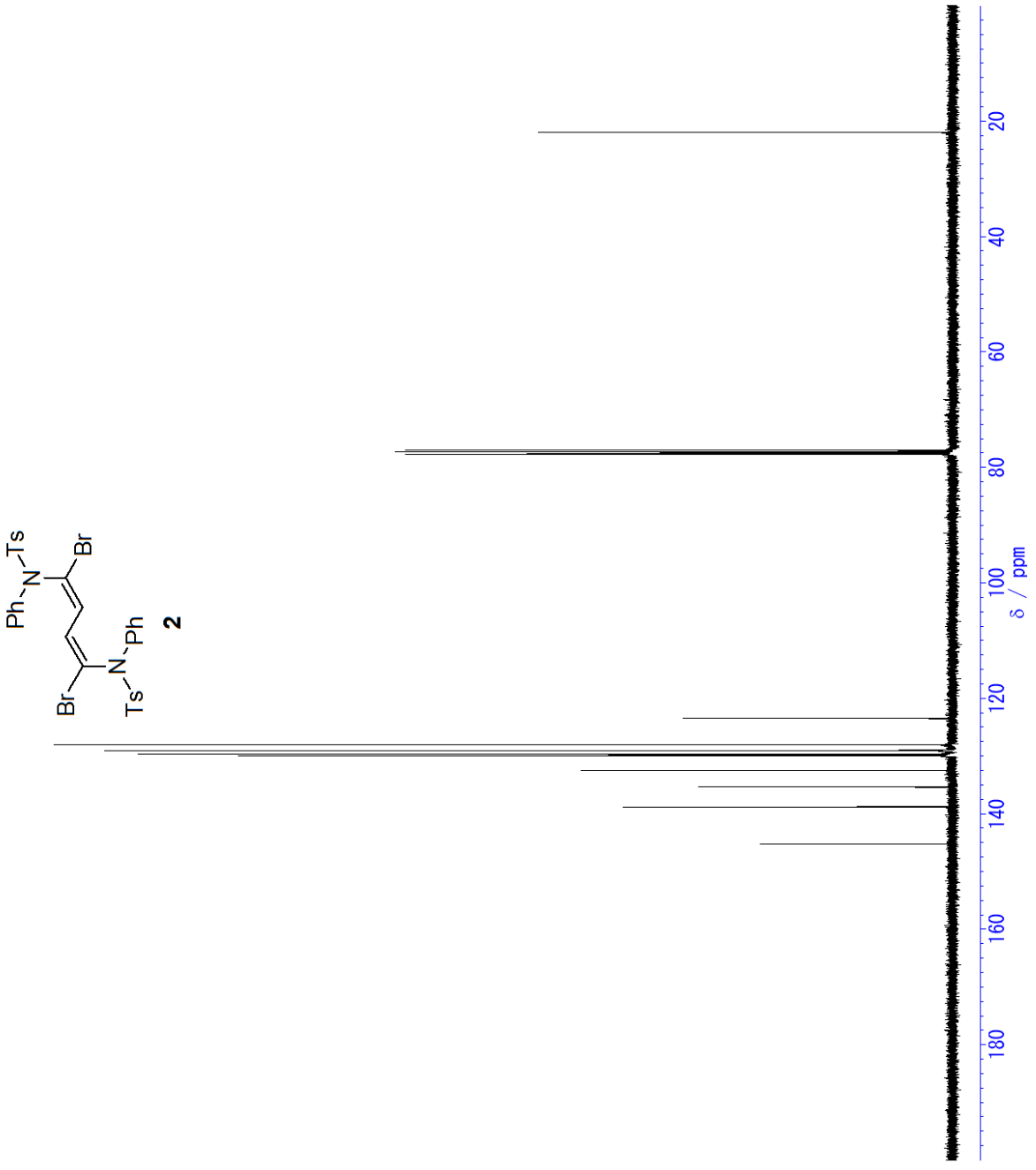
Compound 9a: 99% yield (157 mg); pale yellow viscous materials; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.4 Hz 2H), 7.47-7.42 (m, 4H), 7.38-7.31 (m, 6H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.34 (s, 1H), 2.34 (s, 1H); $_{13}$C NMR (100 MHz, $CDCl_3$) δ 144.7, 138.9, 136.3, 132.1, 129.7, 129.6, 129.3, 129.2, 129.0, 128.9, 128.7, 122.8, 119.4, 96.8, 85.3, 21.9; MS (FAB) *m/z*: 451 (M^+); IR (neat) 3044, 2925, 2522, 2158, 2027, 1588, 1488, 1360, 1165, 1083 cm^{-1}; Anal. Calcd for $C_{23}H_{18}BrNO_2S$: C, 61.07; H, 4.01; N, 3.10. Found: C, 60.82; H, 3.85; N, 3.02.



Compound 9b: 99% yield (143 mg); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 2H), 7.42 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.35-7.25 (m, 5H), 6.33 (s, 1H), 5.84 (dddd, *J* = 16.4, 10.2, 6.5, 6.5 Hz, 1H), 5.33 (dd, *J* = 16.4, 1.2 Hz, 1H), 5.21 (dd, *J* = 10.2, 1.2 Hz, 1H), 3.94 (brs, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 135.8, 132.1, 131.5, 130.0, 129.2, 129.1, 128.7, 128.6, 122.9, 120.4, 120.2, 96.7, 85.2, 52.5, 21.9; MS (FAB) *m/z*: 415 (M^+); IR (neat) 3047, 2920, 2202, 1593, 1354, 1161 cm^{-1}; Anal. Calcd for $C_{20}H_{18}BrNO_2S$: C, 57.70; H, 4.36; N, 3.36. Found: C, 57.71; H, 4.44; N, 3.35.

f) **^{1}H NMR and ^{13}C NMR spectra for compounds 2 - 9**:

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Br
Br
N
Ph
Ts
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80
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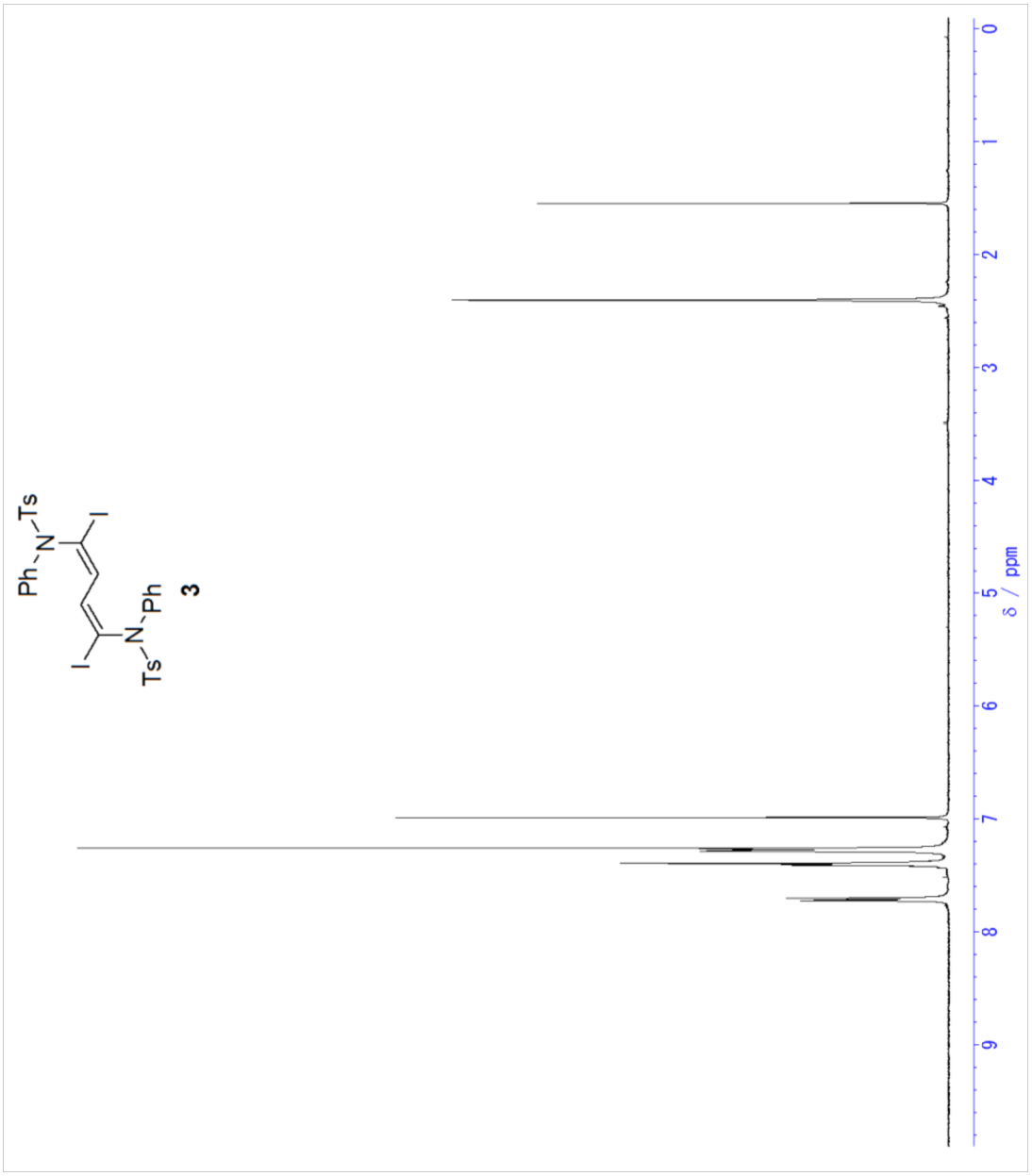
140
160
180
δ / ppm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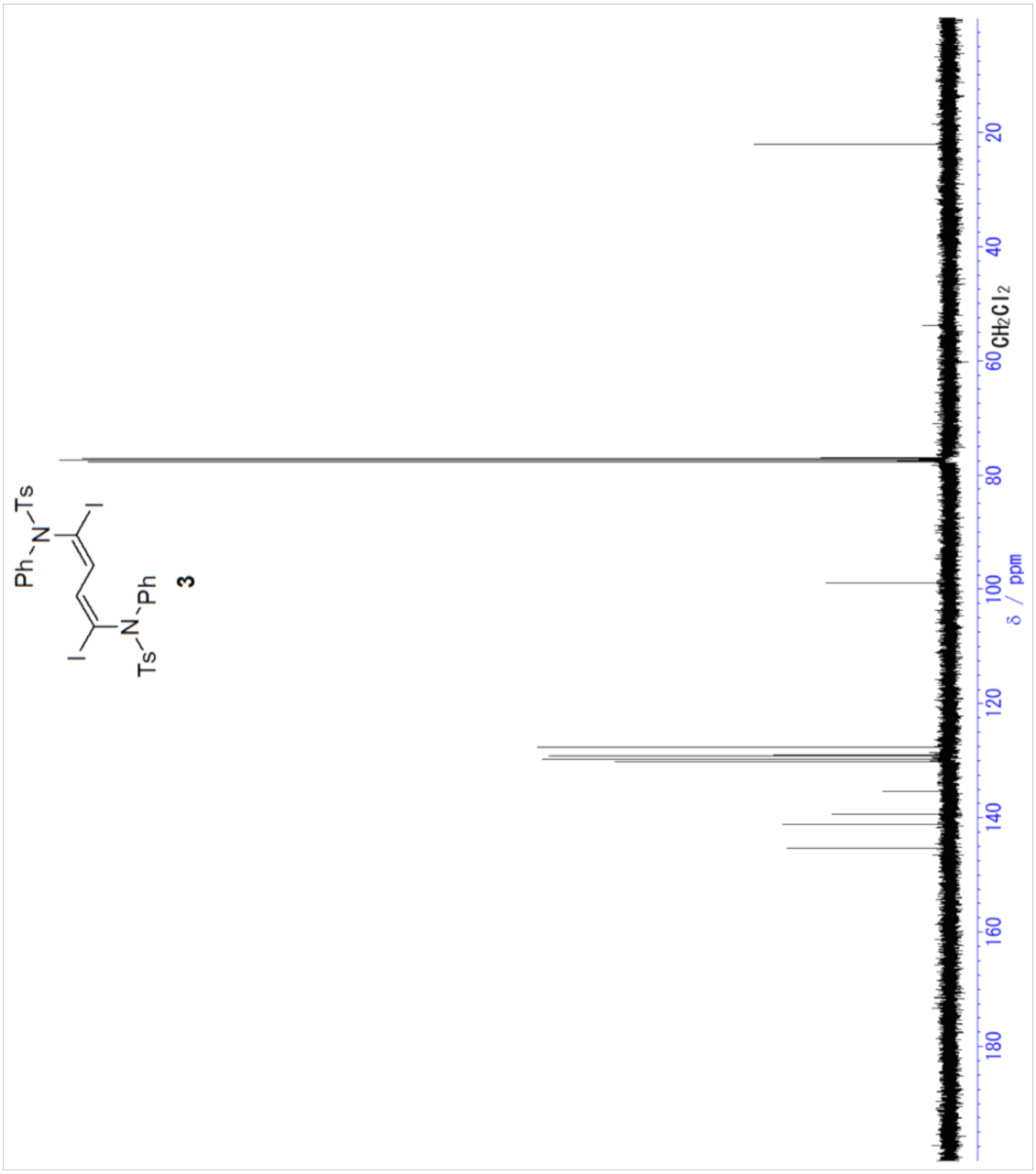
δ / ppm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Ph
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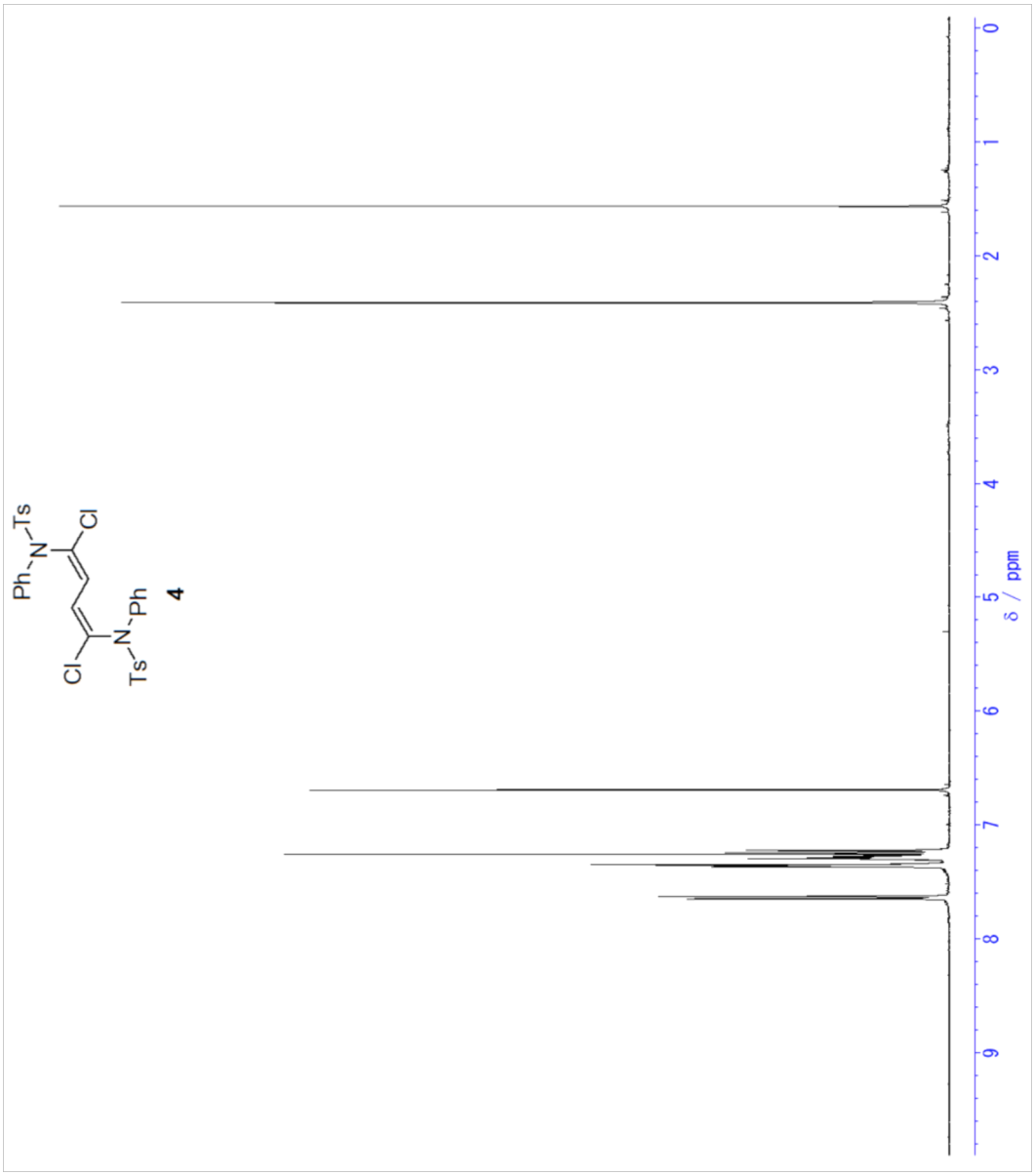
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Cl
Cl
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Ts
Ph
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δ / ppm
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3
4
5
6
7
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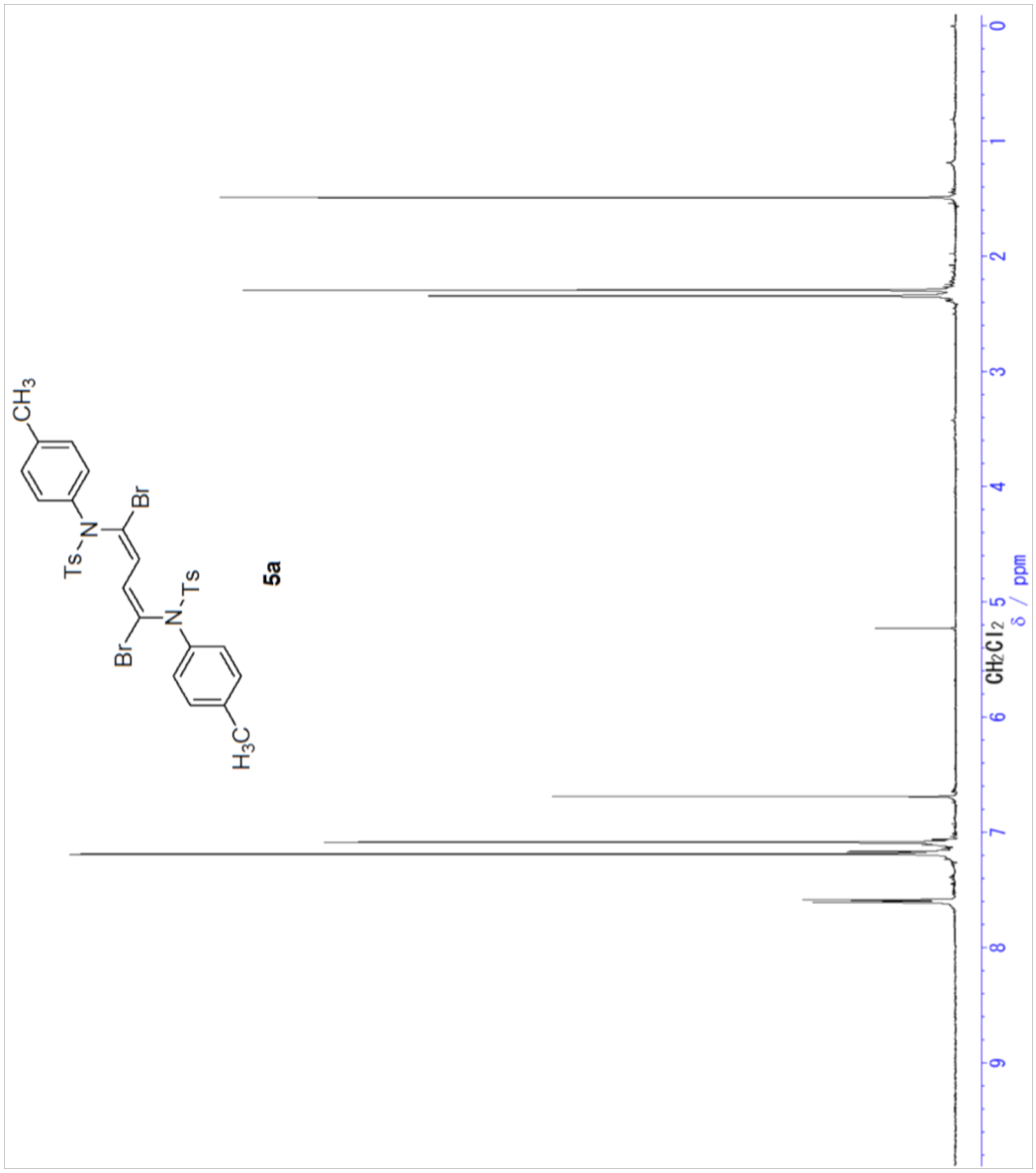
δ / ppm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δ / ppm
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3
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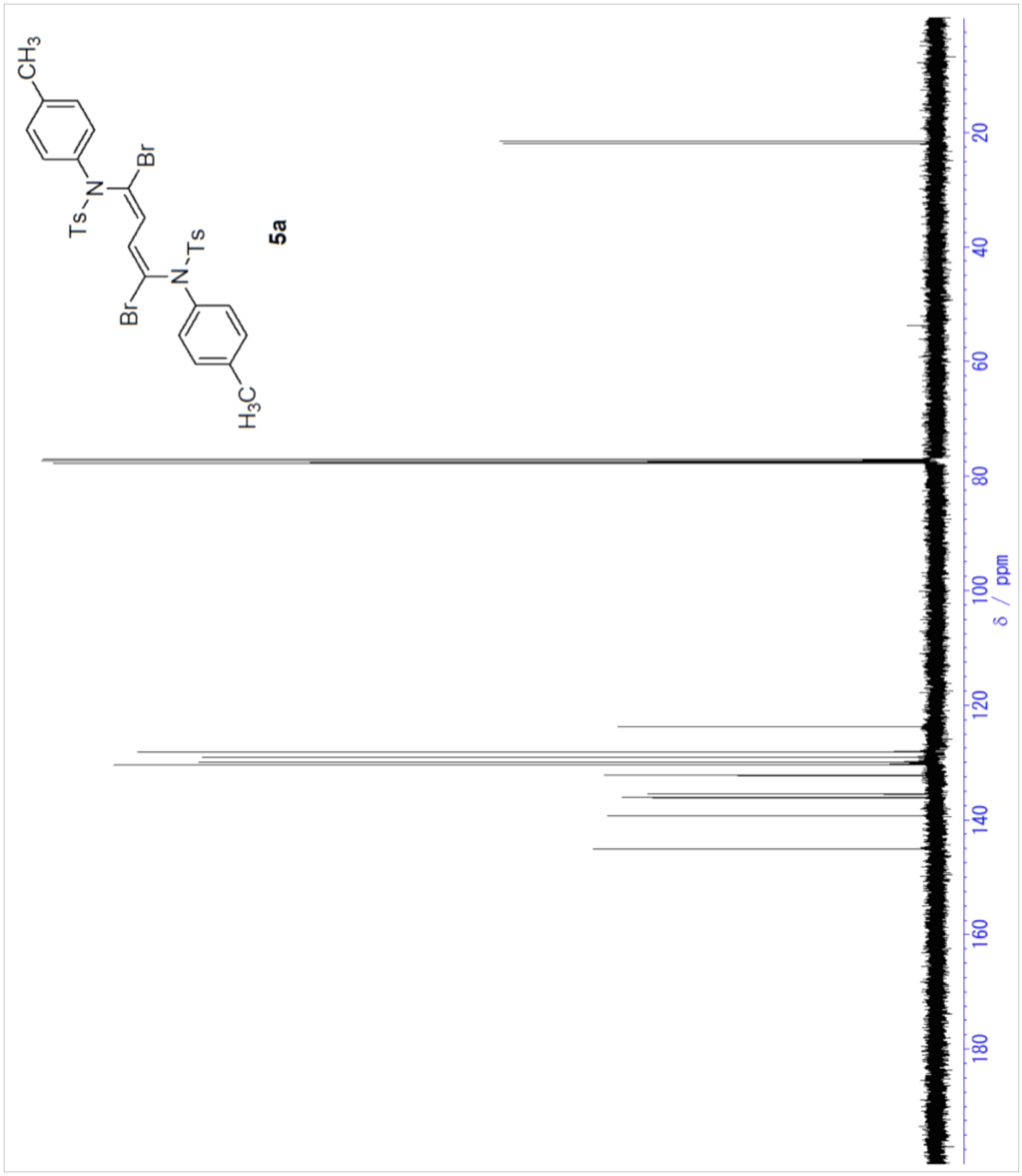
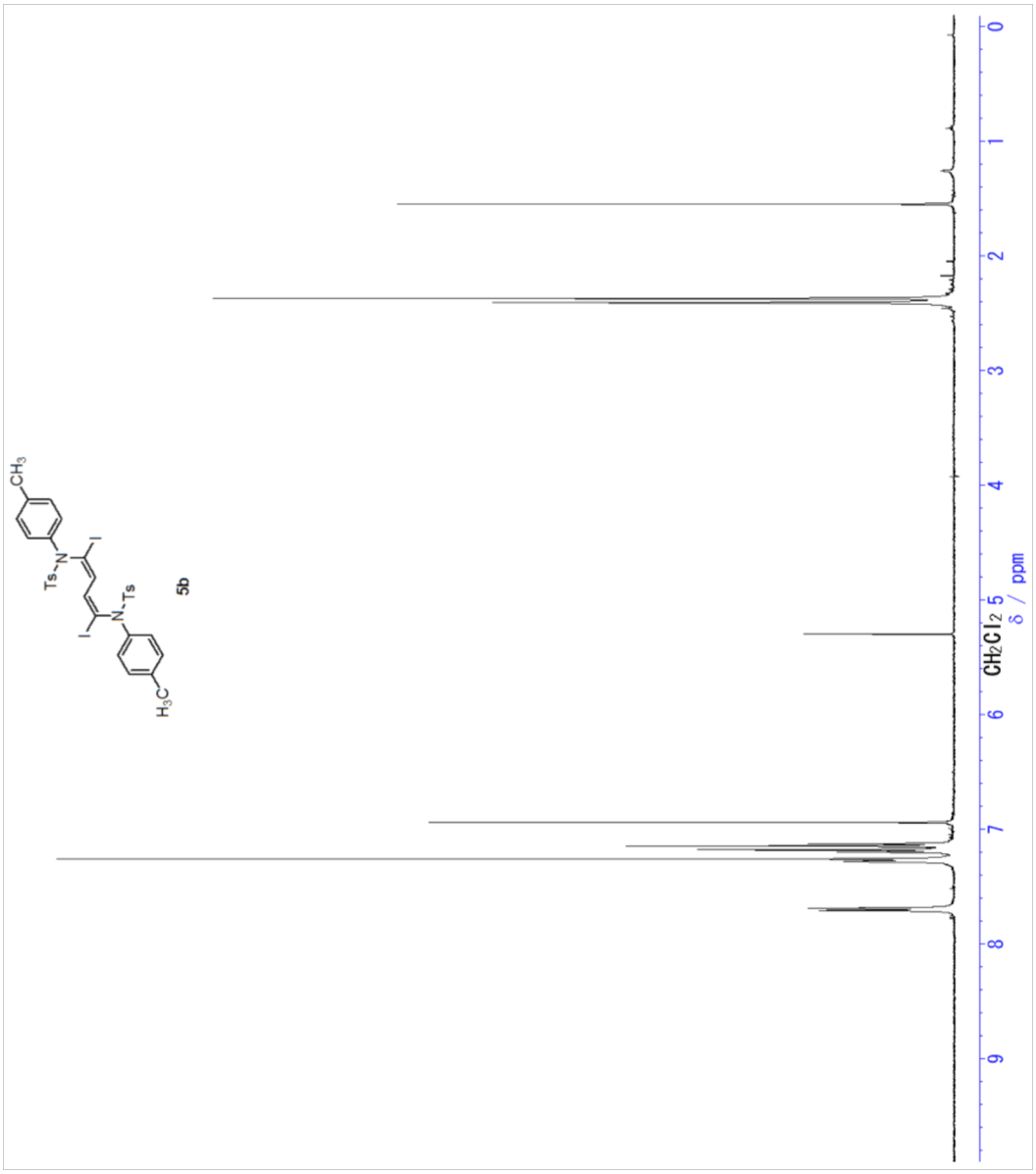
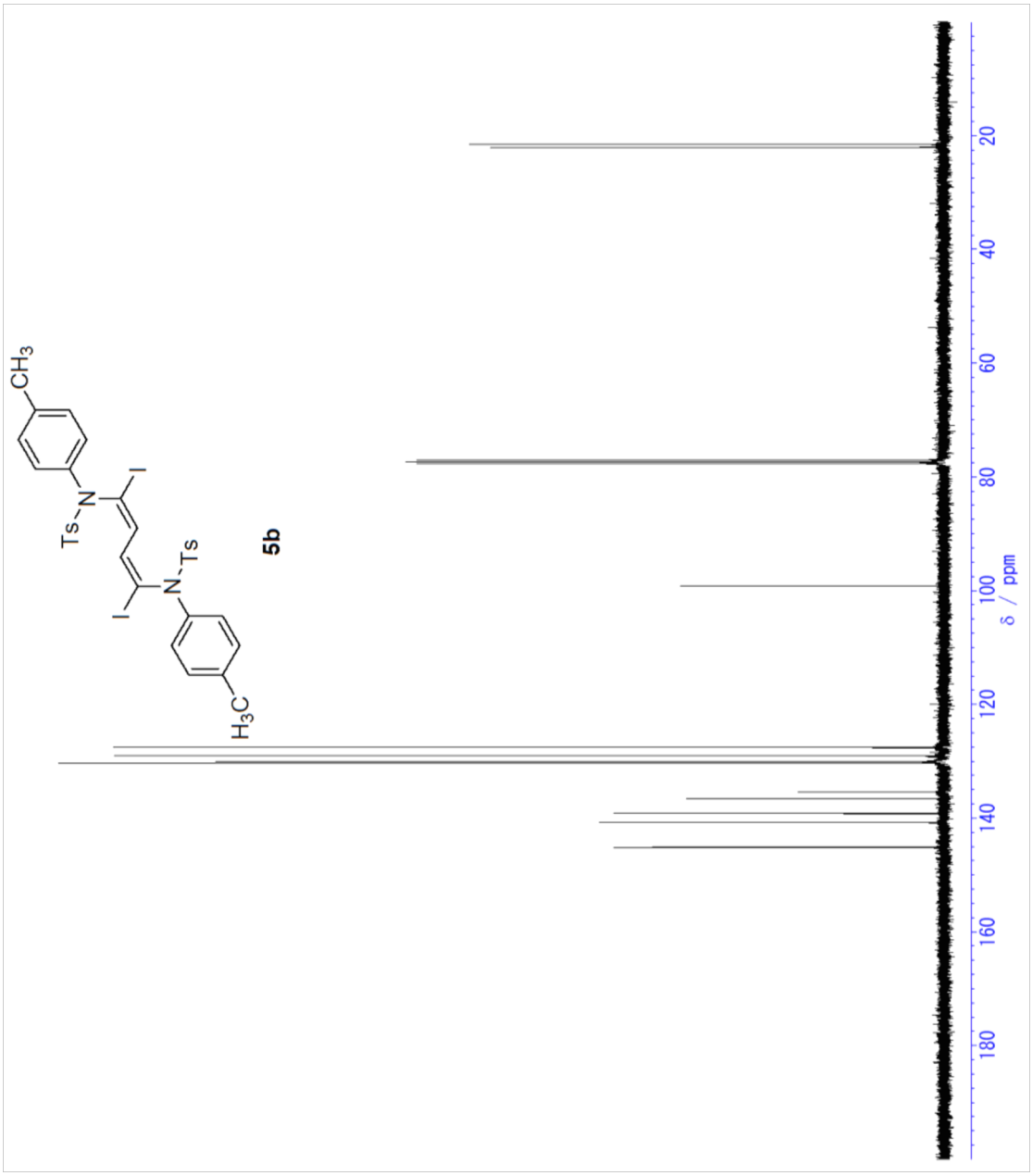
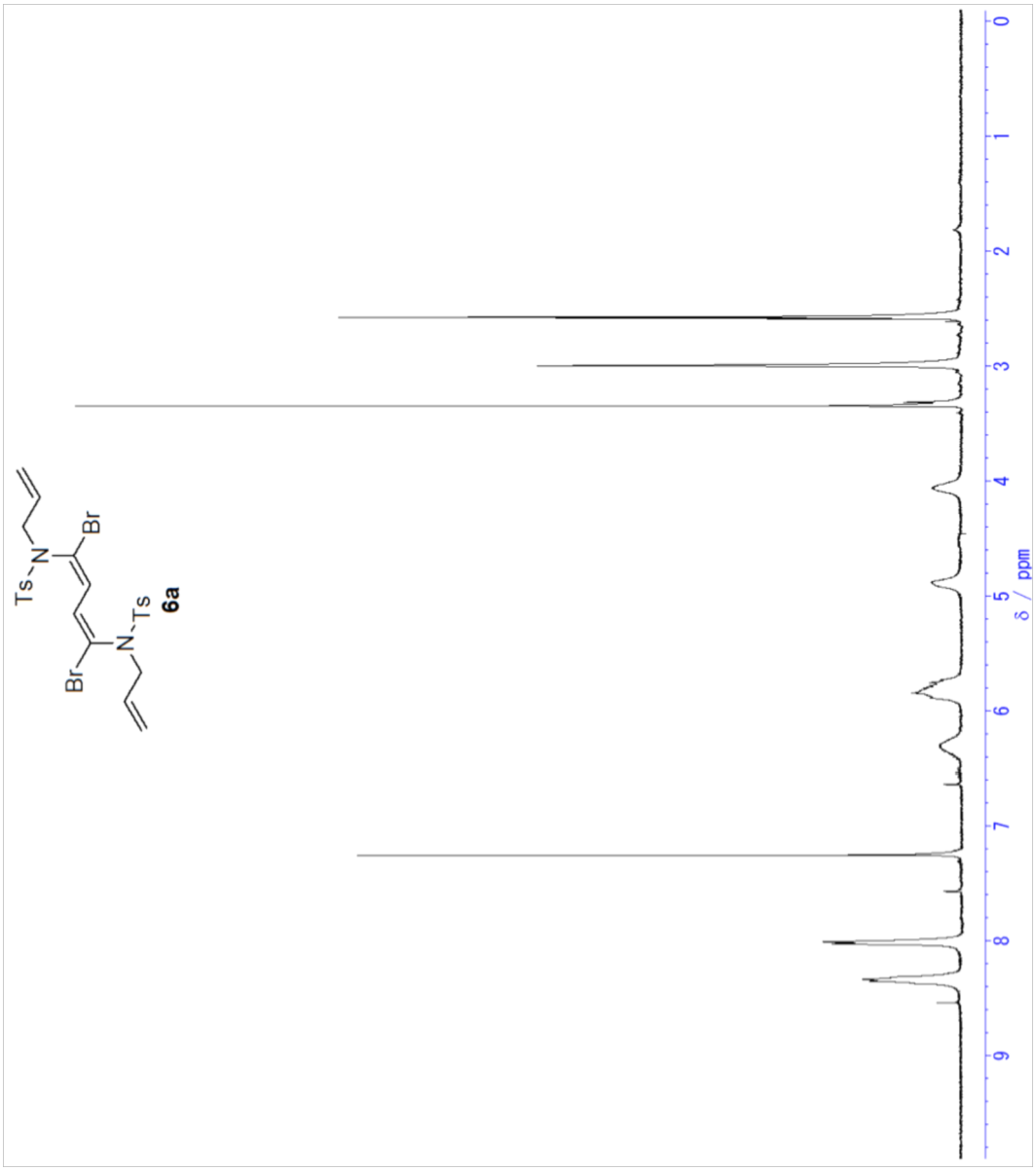
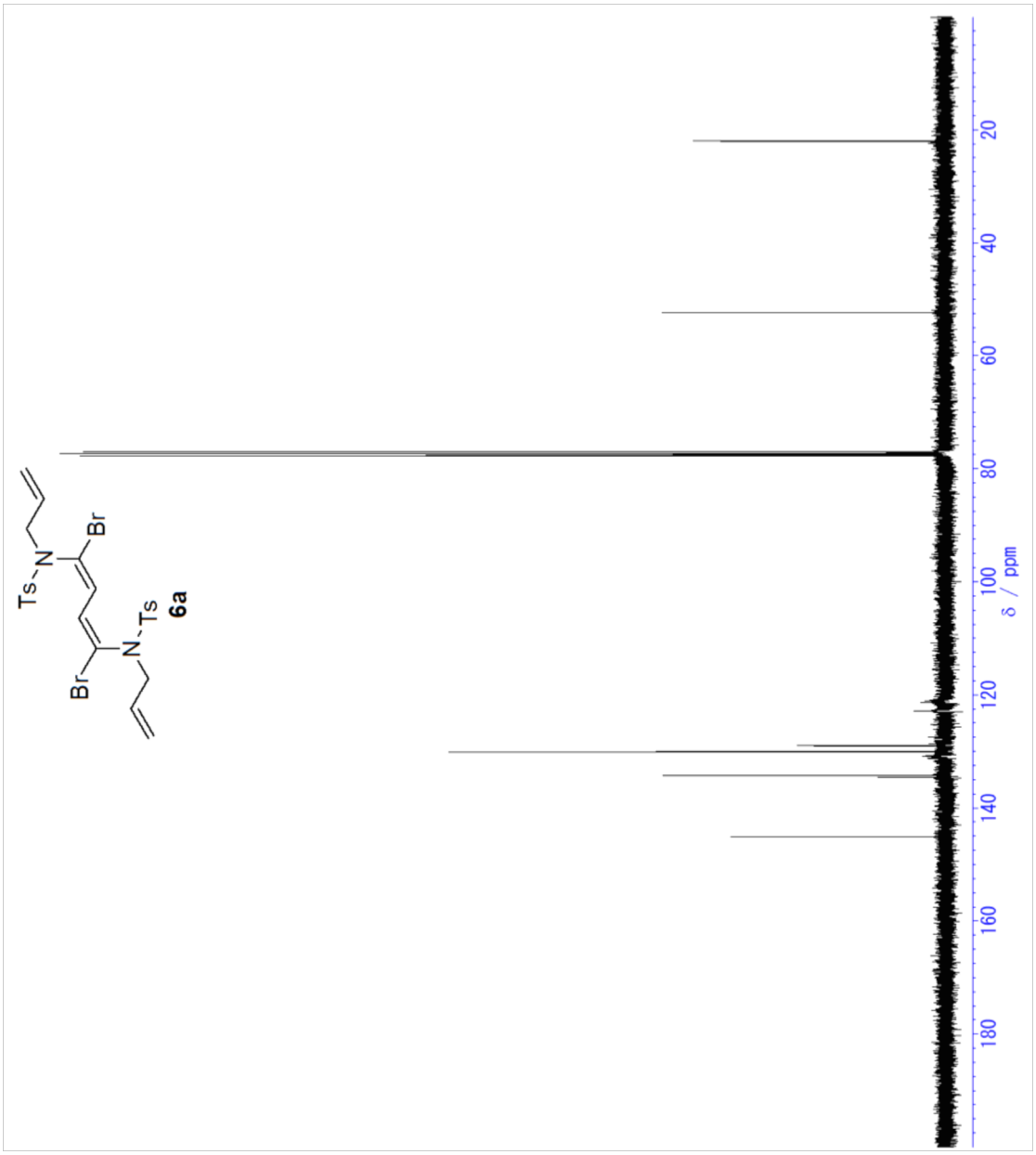
6
7
8
9

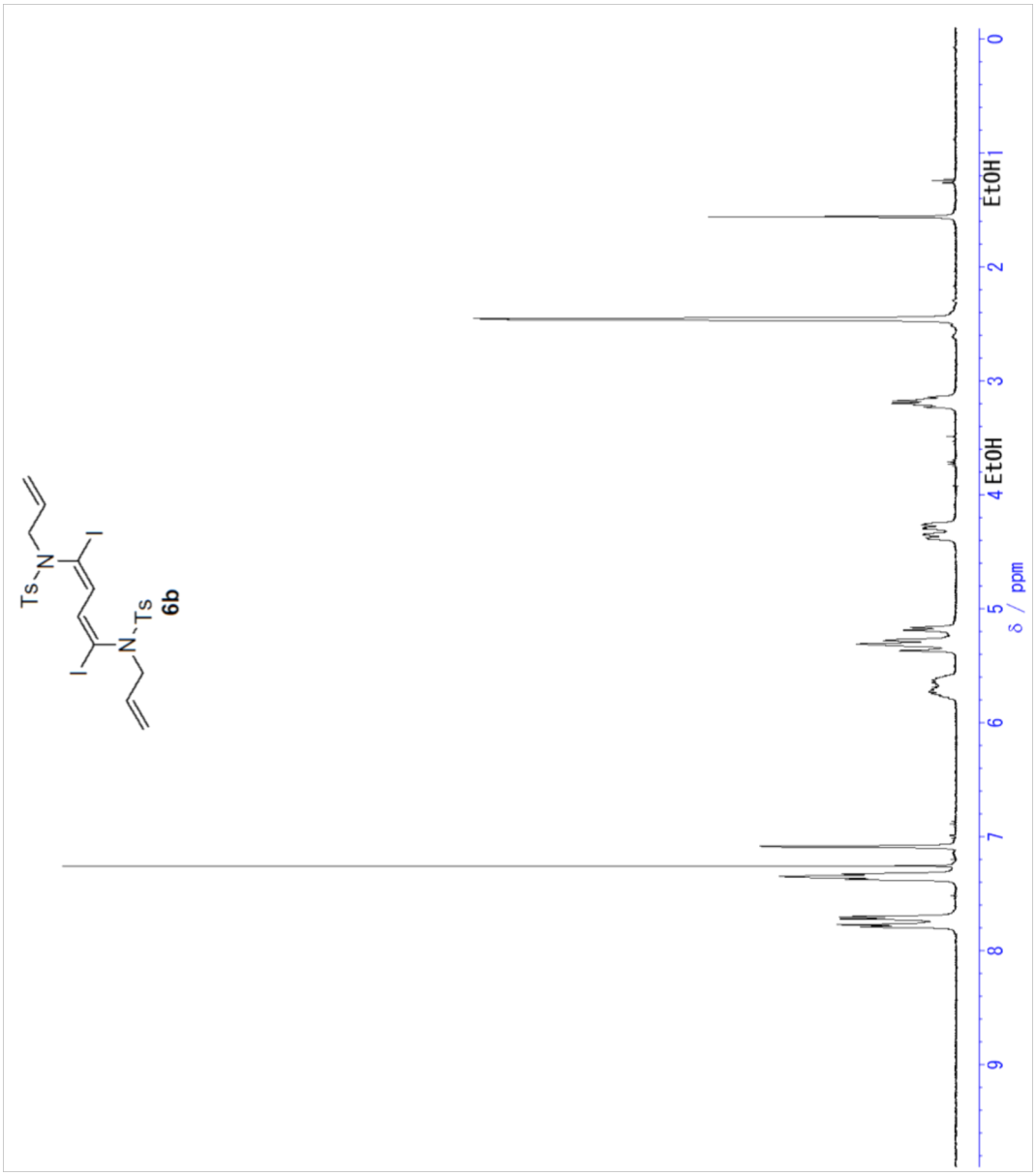

CH3
Br
Ts
N
Br
N
Ts
5a
H3C
20
40
60
80
100
120
140
160
180
δ / ppm

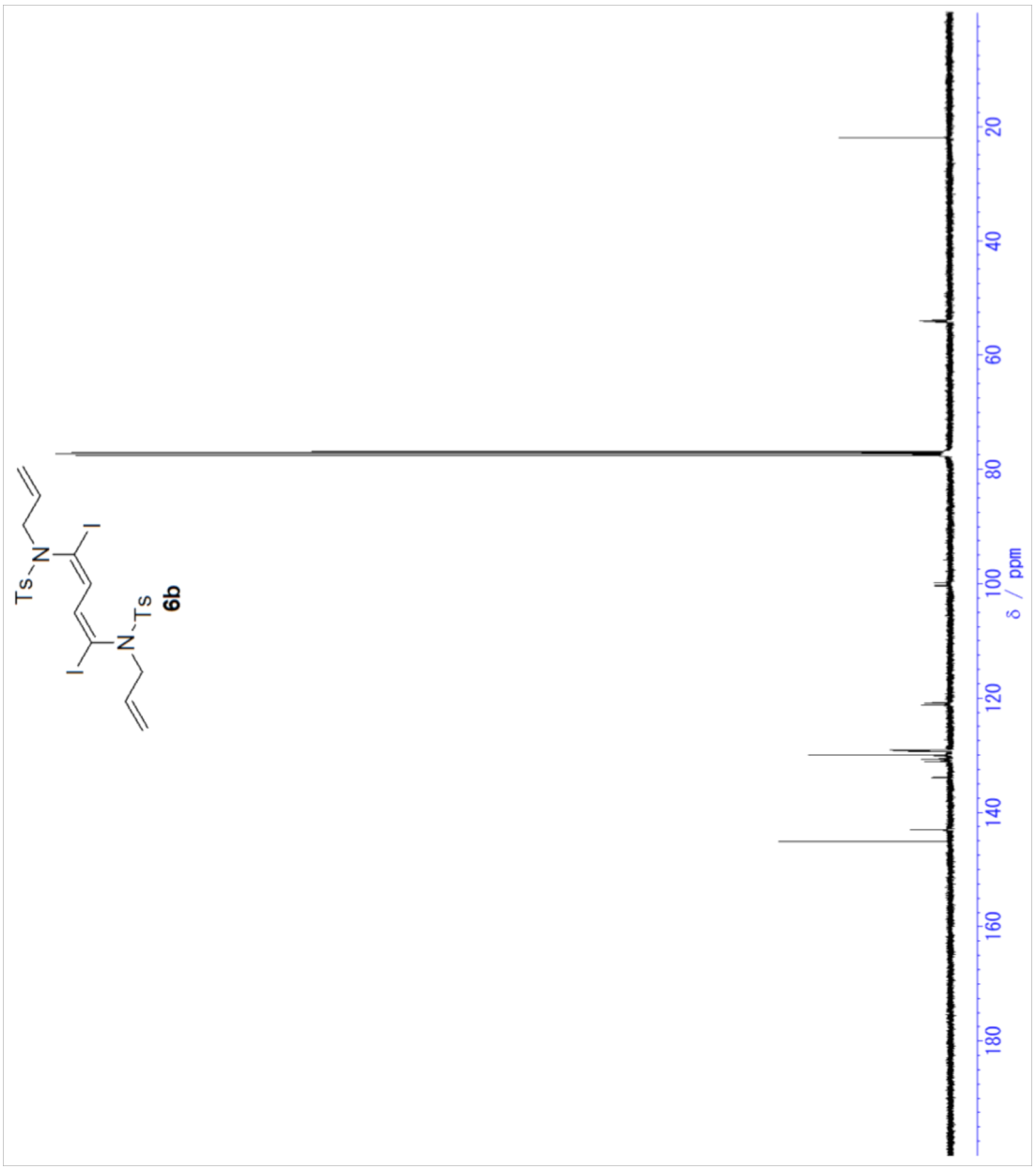

5b
CH2Cl2
δ / ppm

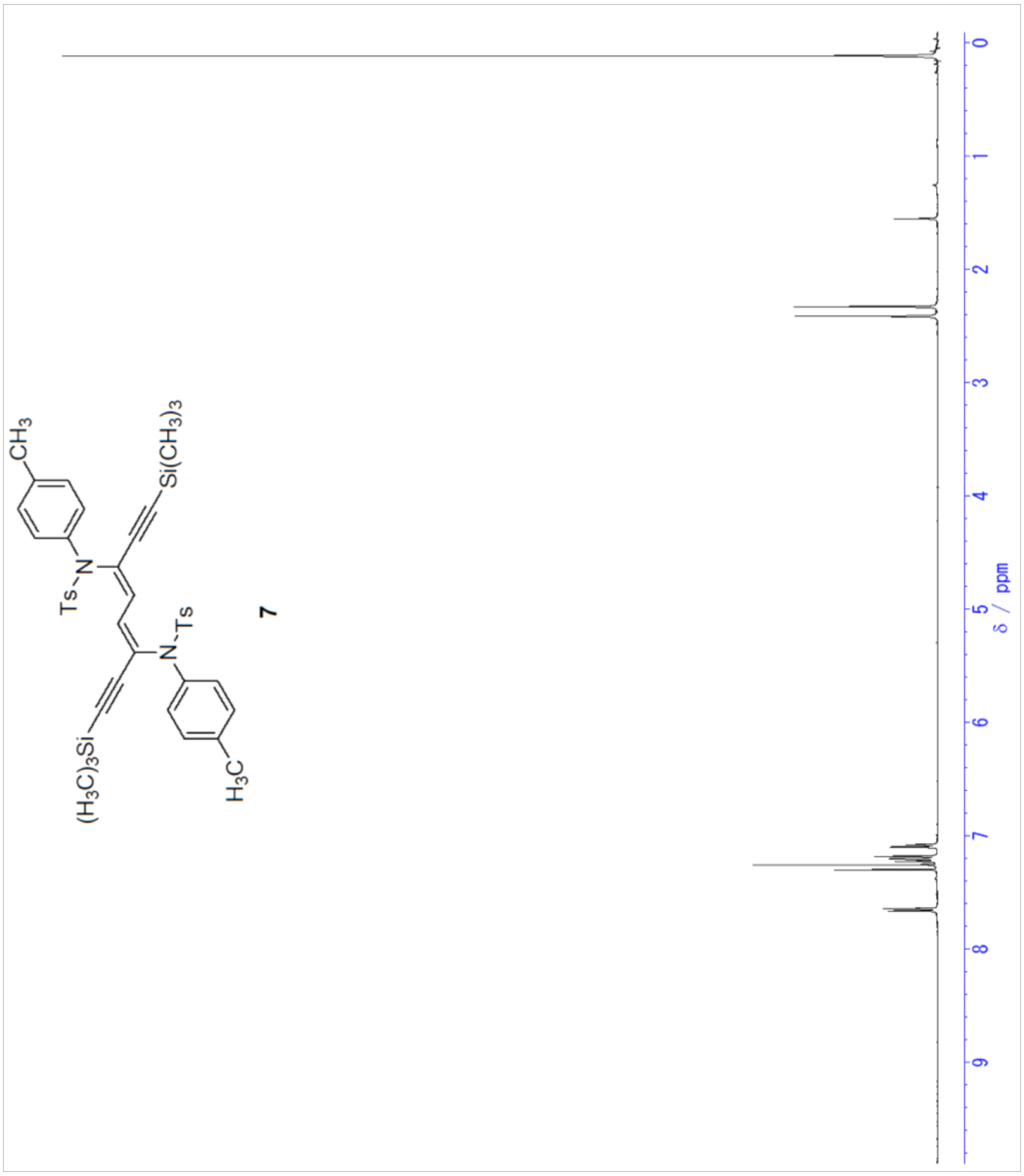

CH3
Ts
N
I
I
N
Ts
H3C
5b
20
40
60
80
100
120
140
160
180
δ / ppm

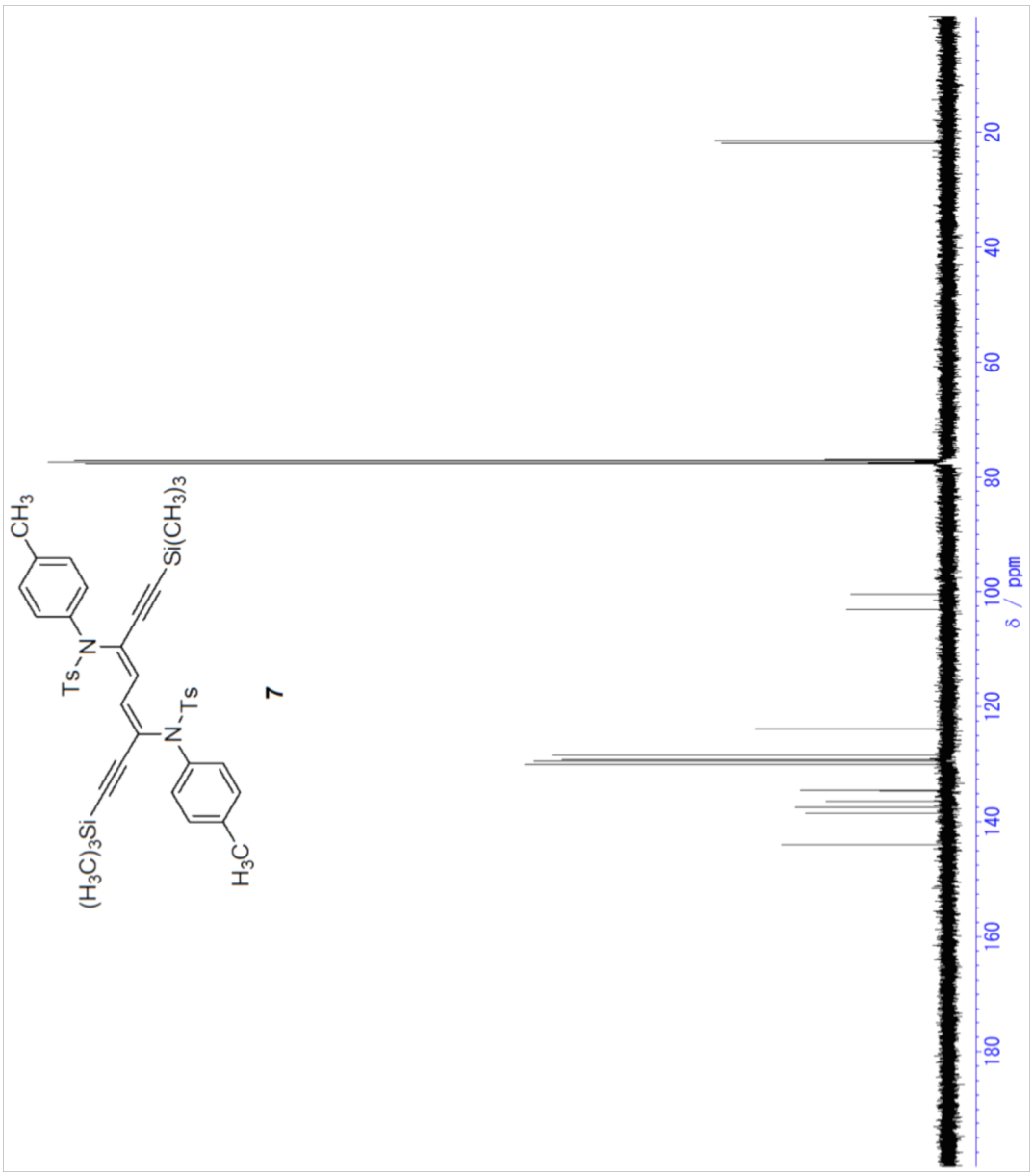

Ts
N
Br
Br
N
Ts
6a
δ / ppm
0
1
2
3
4
5
6
7
8
9

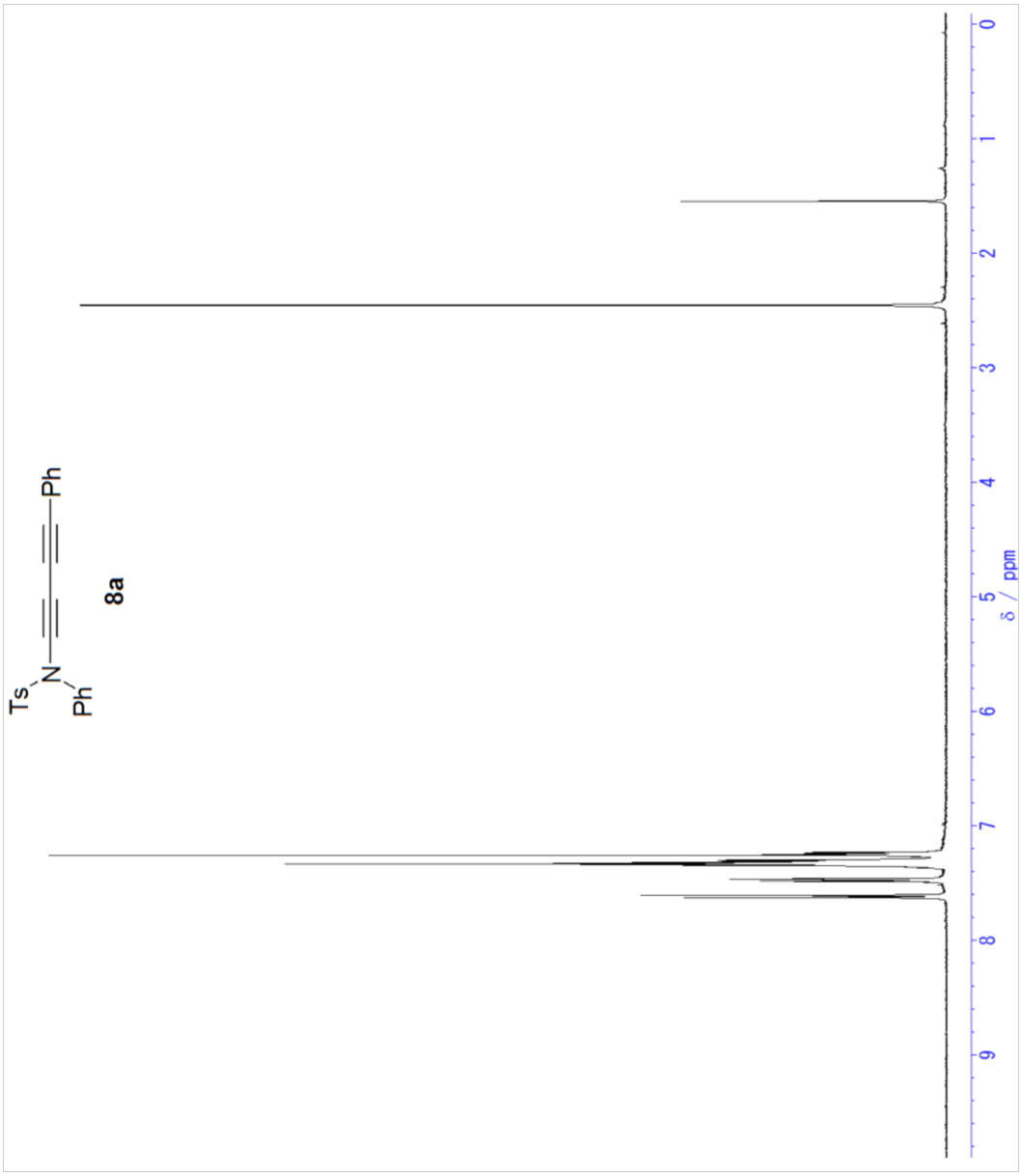

Ts
N
Br
Br
N
Ts
6a
20
40
60
80
100
120
140
160
180
δ / ppm

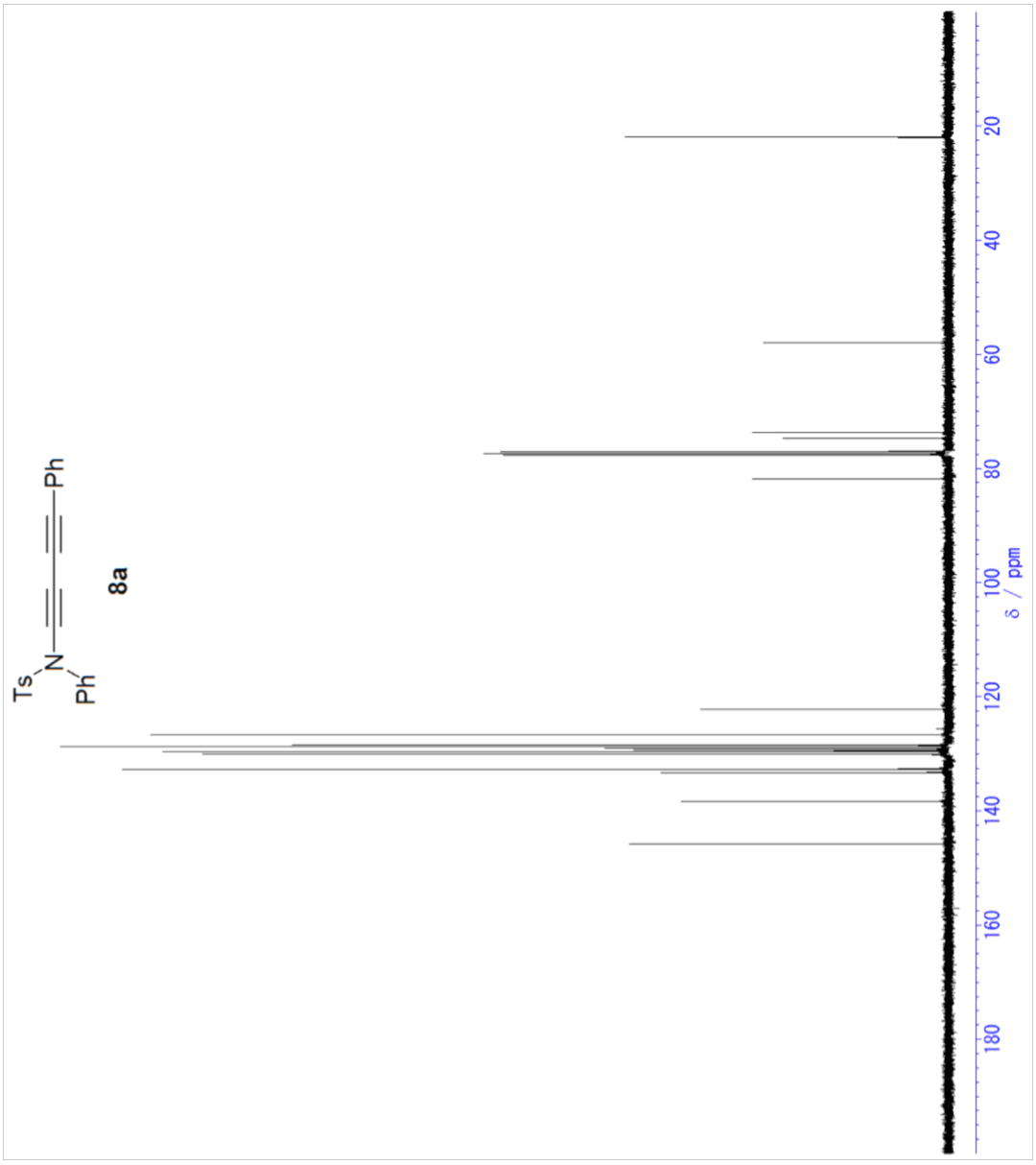

Ts
N
I
I
N
Ts
6b
EtOH
EtOH
δ / ppm
0
1
2
3
4
5
6
7
8
9

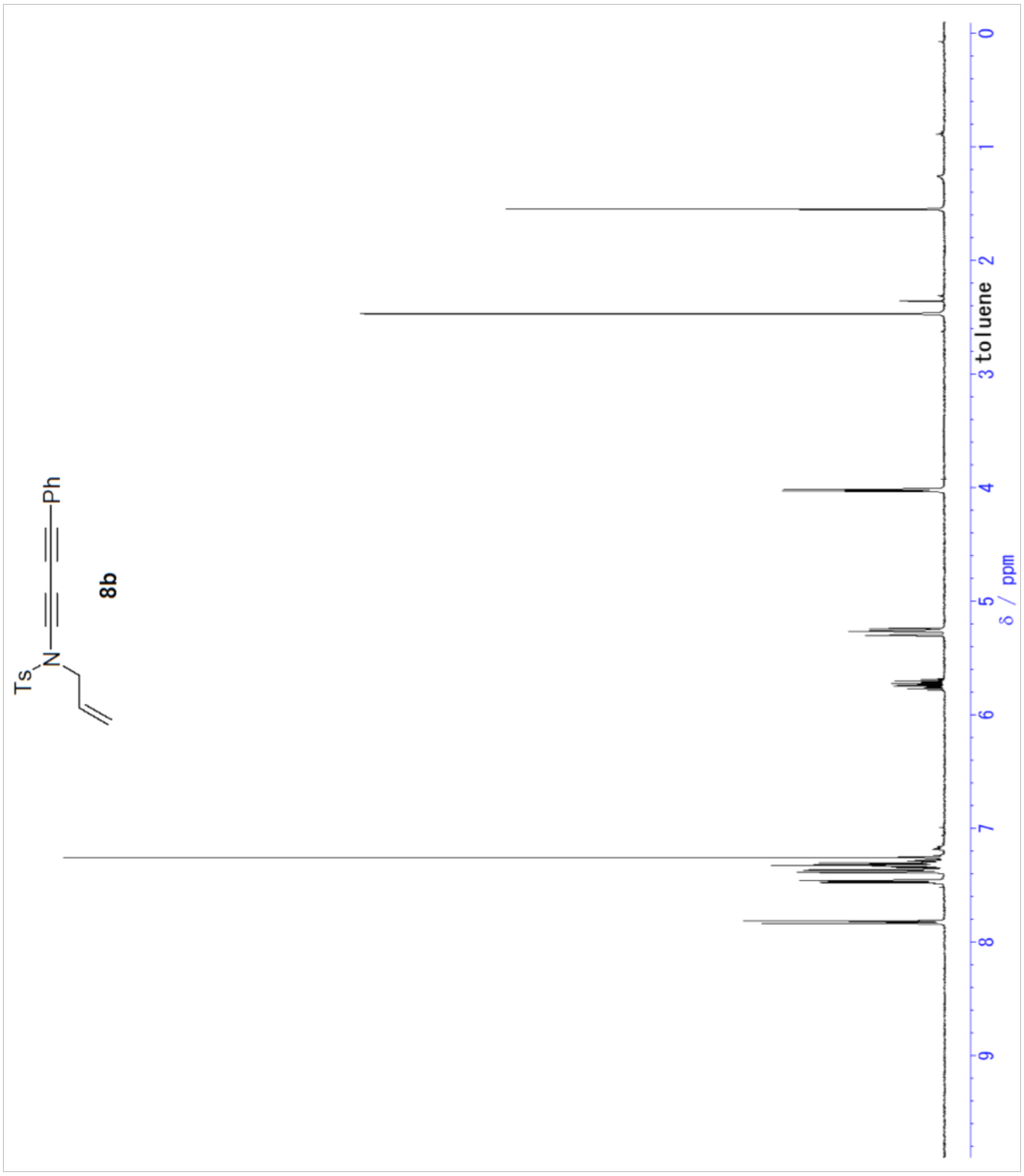

Ts
N
I
N
Ts
I
6b
20
40
60
80
100
120
140
160
180
δ / ppm

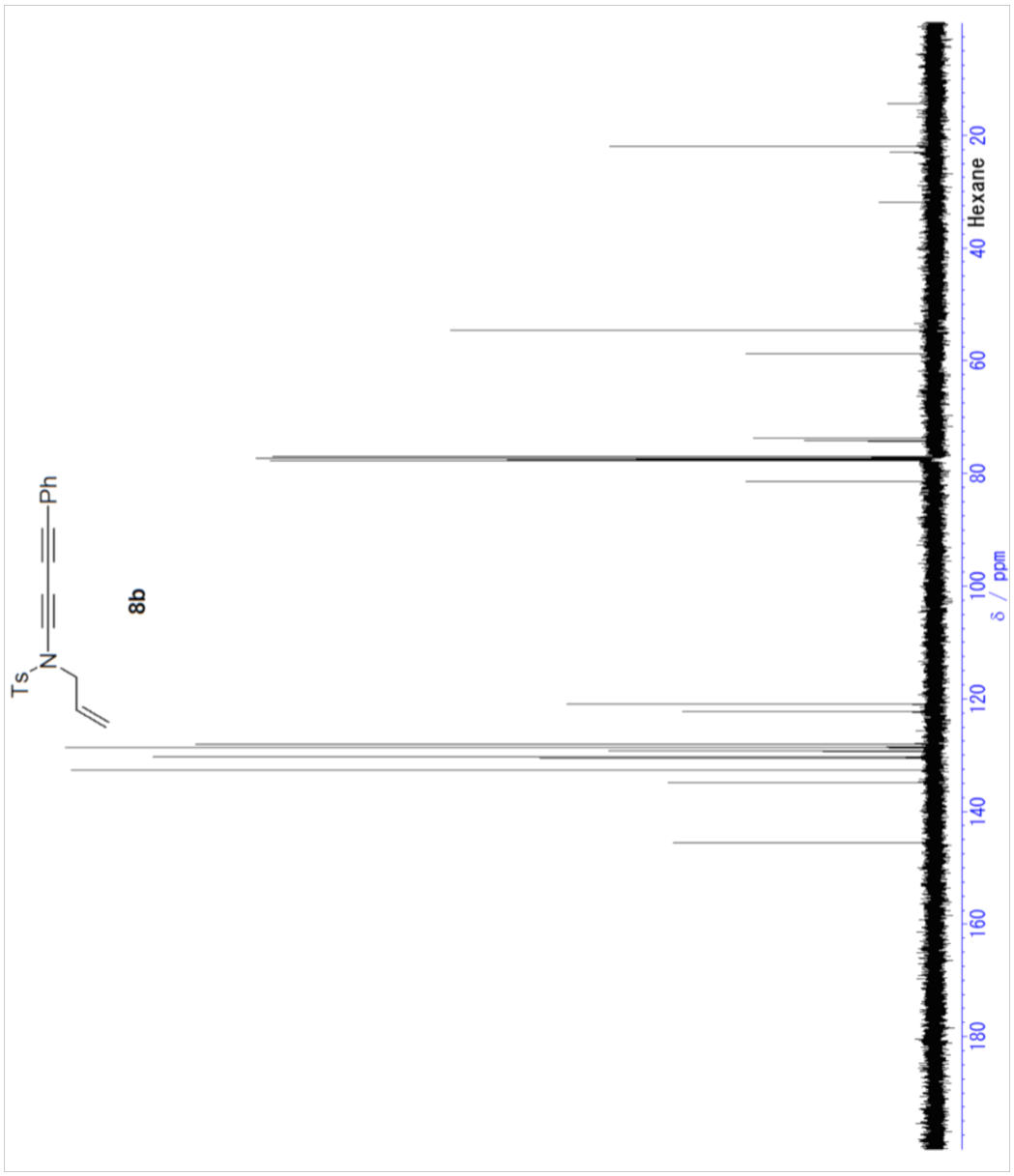

CH3
Ts
N
Si(CH3)3
N
Ts
(H3C)3Si
H3C
7
δ / ppm
0
1
2
3
4
5
6
7
8
9

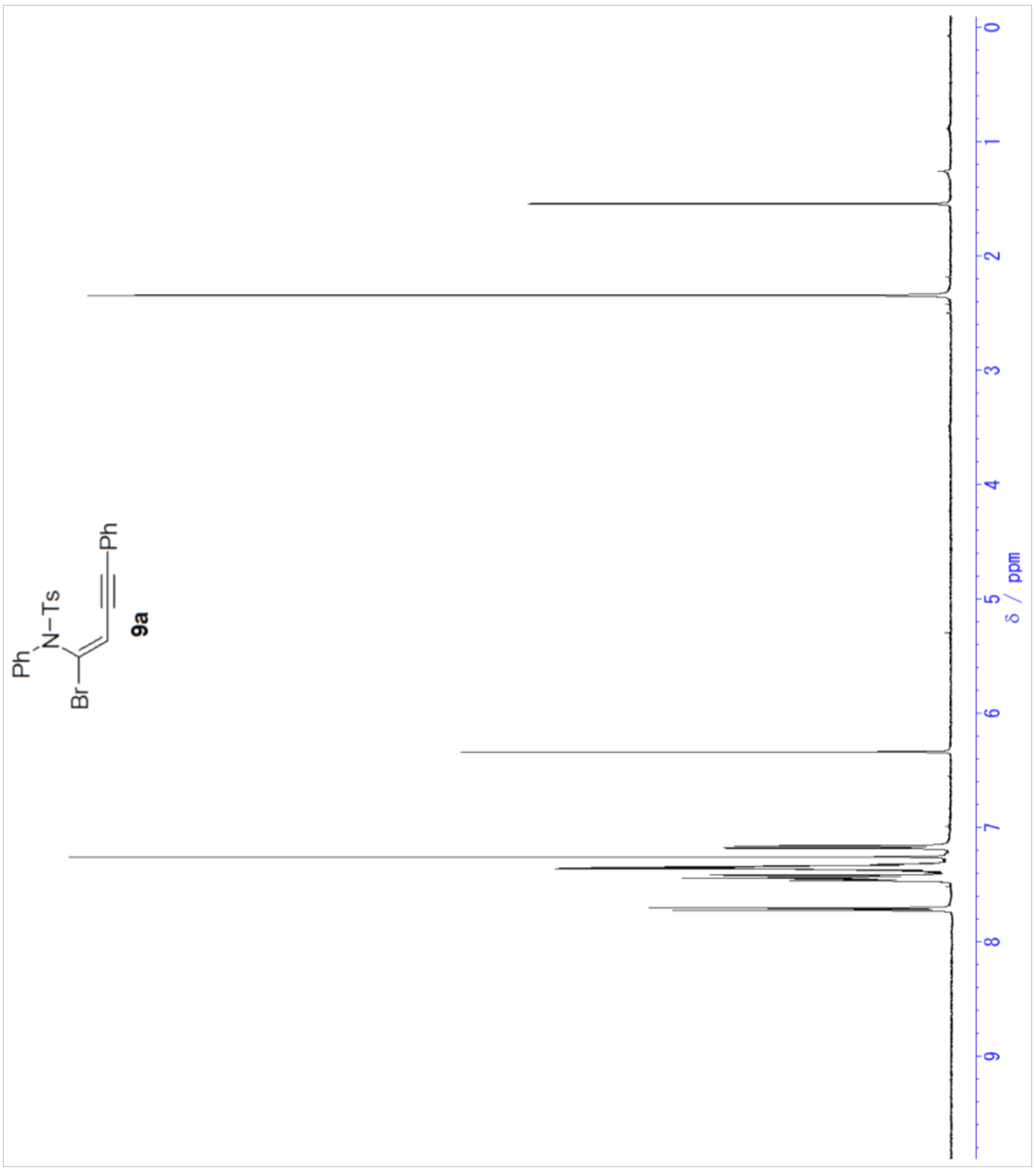

CH3
Ts
N
Si(CH3)3
N
Ts
(H3C)3Si
H3C
7
20
40
60
80
100
120
140
160
180
δ / ppm

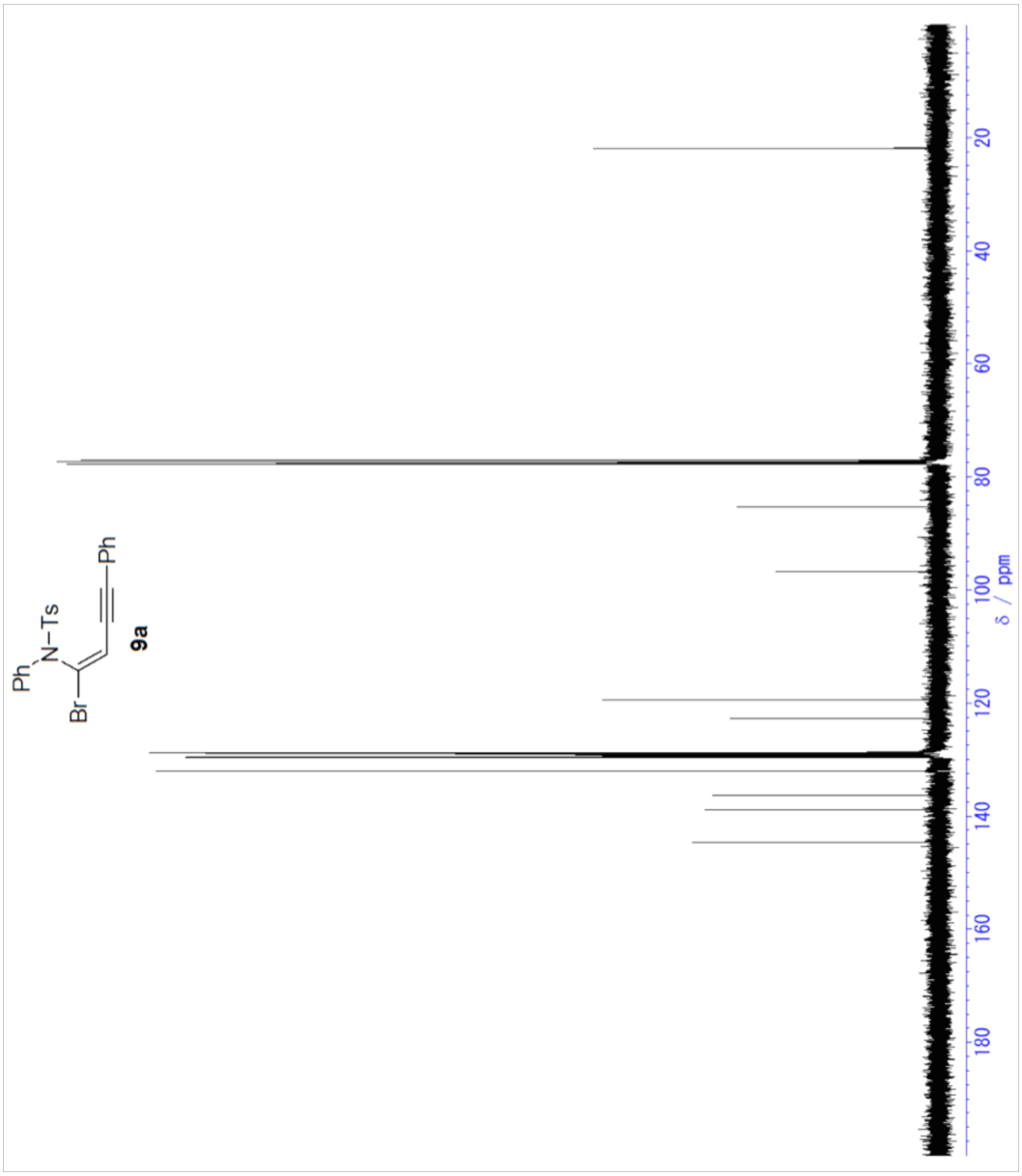

Ts
N
Ph
Ph
8a
δ / ppm
0
1
2
3
4
5
6
7
8
9

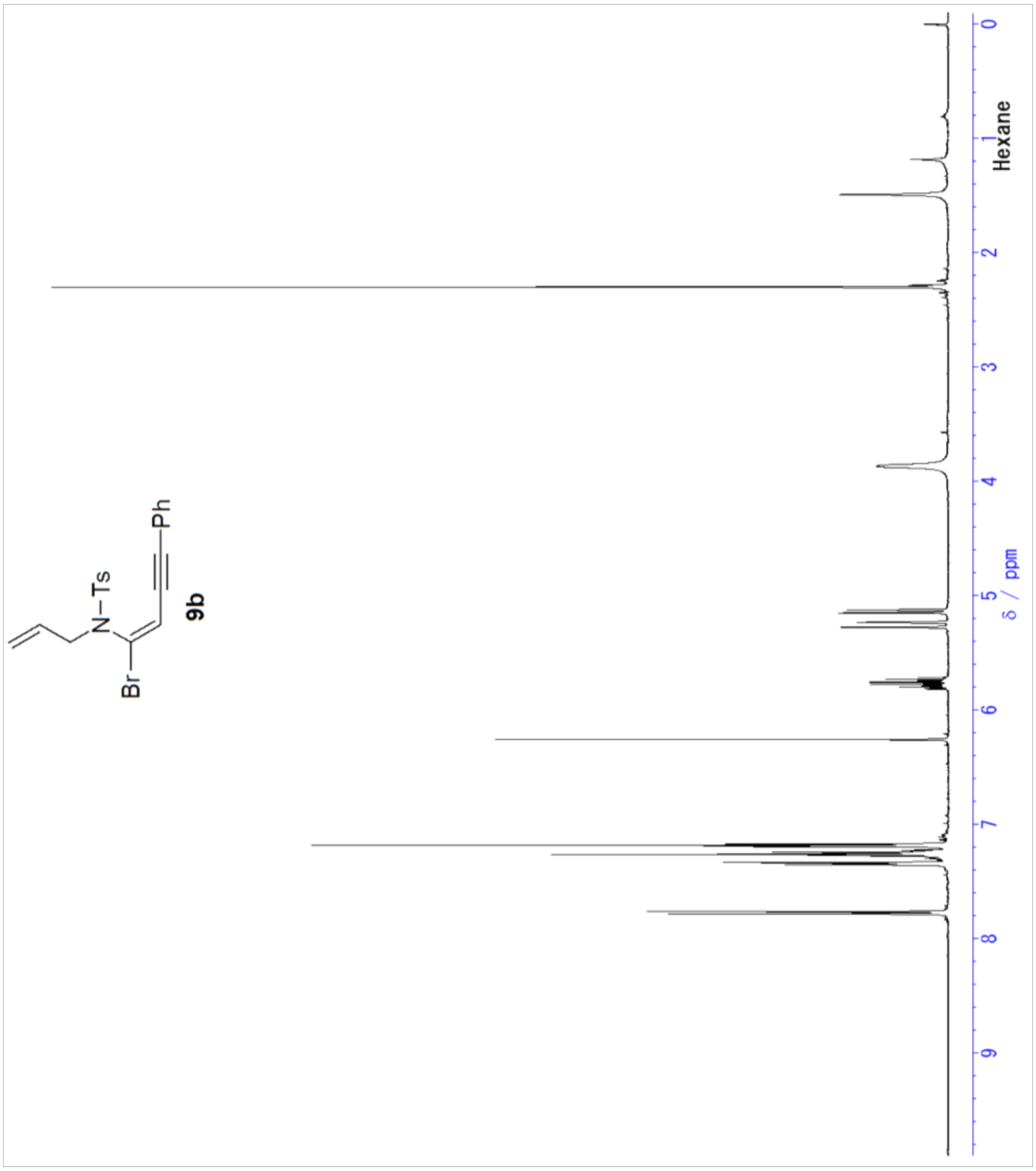

Ts
N
Ph
Ph
8a
20
40
60
80
100
120
140
160
180
δ / ppm

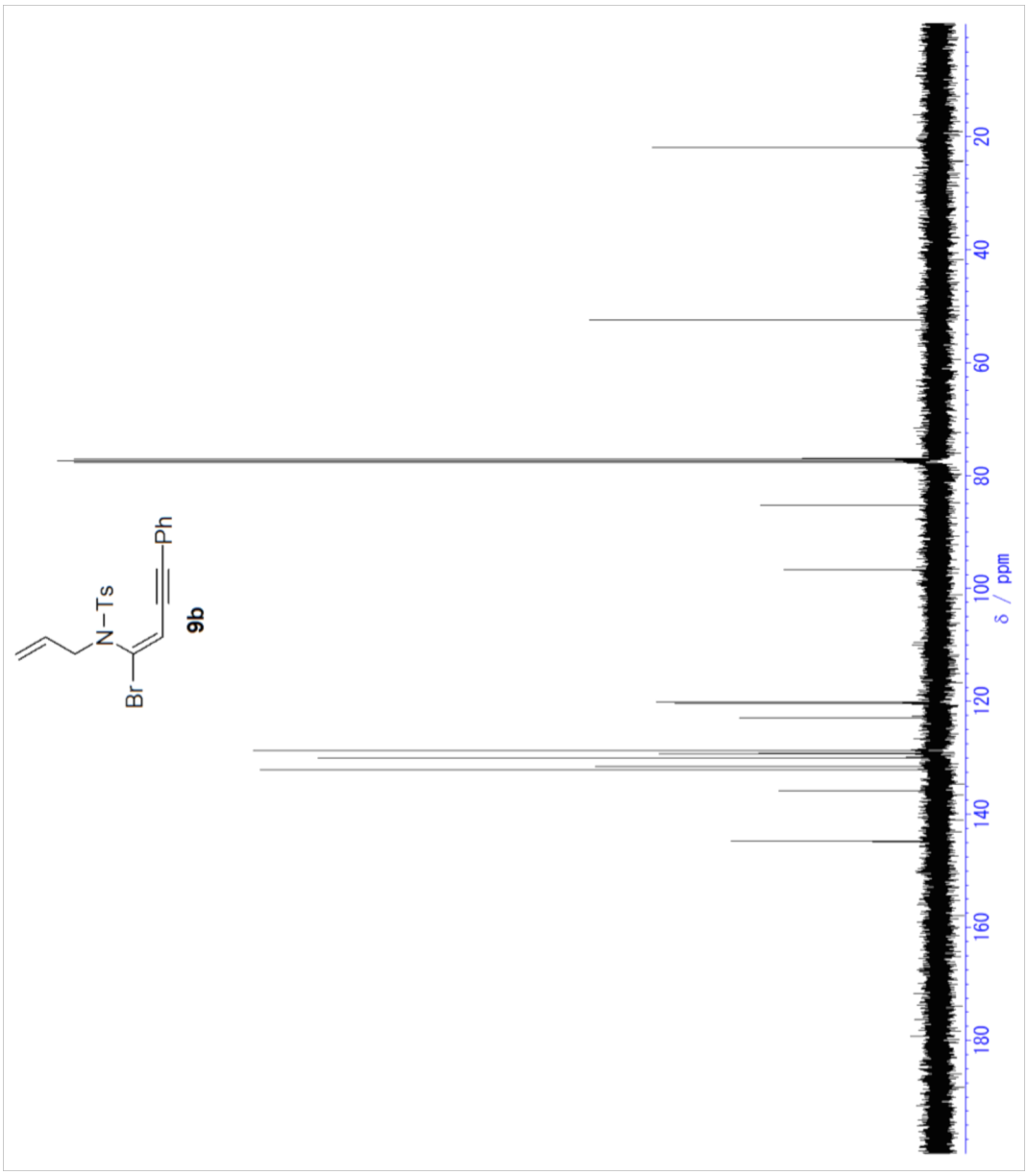

Ts
N
Ph
8b
toluene
δ / ppm
0
1
2
3
4
5
6
7
8
9


Ts
N
Ph
8b
Hexane
δ / ppm
180
160
140
120
100
80
60
40
20


Ph
N–Ts
Br
Ph
9a
δ / ppm
0
1
2
3
4
5
6
7
8
9


Ph
N–Ts
Br
Ph
9a
20
40
60
80
100
120
140
160
180
δ / ppm


N–Ts
Ph
Br
9b
Hexane
δ / ppm
0
1
2
3
4
5
6
7
8
9


Ph
N–Ts
Br
9b
20
40
60
80
100
120
140
160
180
δ / ppm