Supporting Information

Elucidation of reaction process through beta-halogen elimination

in CuCN-mediated cyanation of (*E*)-1-bromo-2-iodoalkene.

Naoki Endo, Mao Kanaura, & Tetsuo Iwasawa*

Department of Materials Chemistry, Faculty of Science and Technology,

Ryukoku University, Seta, Otsu, 520-2194, Japan

iwasawa@rins.ryukoku.ac.jp

Contents

1. General Information.

All reactions sensitive to air or moisture were carried out under an argon atmosphere and anhydrous conditions unless otherwise noted. Dry solvents were purchased and used without further purification and dehydration. All reagents were purchased and used without further purification. Analytical thin layer chromatography was carried out on Merck silica $60F_{254}$. Column chromatography was carried out with silica gel 60 $_N$ (Kanto Chemical Co.). HRMS were reported on the basis of TOF (time of flight)-MS (LCMS-IT-TOF; Shimadzu), and EB (double-focusing)-MS. ^1H and ^{13}C NMR spectra were recorded with a 5 mm QNP probe at 400 MHz and 100 MHz, respectively. Chemical shifts are reported in d (ppm) with reference to residual solvent signals [^1H NMR: $CHCl_3$ (7.26), C_7H_8 (2.08), C_6H_6 (7.16), CH_2Cl_2 (5.32); ^{13}C NMR: $CDCl_3$ (77.0)]. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

2. Procedure for preparation of (*E*)-2-(Bromo(phenyl)methylene)butanenitrile (2), for Scheme 2.

To the mixture of (*E*)-(1-bromo-2-iodobut-1-en-1-yl)benzene **1** (169 mg, 0.5 mmol) and DMF (1 mL) was added CuCN (50 mg, 1.1 mmol). After stirring at 70 ºC for 22 h, the reaction mixture was allowed to cool to room temperature. The mixture was diluted with 10 mL of CH_2Cl_2, and transferred into the 50 mL flask, and quenched with 5 mL of 3 M aq.NH_3. After stirring for 10 min, the mixture was transferred into a separatory funnel, and the organic phase was washed with water (10 mL x 3) and brine (10 mL), and dried over Na_2SO_4, and filtered, and concentrated *in vacuo* to give a crude product of yellowish brown oil. The reaction was amenable to scale up in 1 and 2 mmol, and the reproducibility

was confirmed. Purification of these combined crude products with silica gel column chromatography (hexane/toluene=2/1) afforded **2** in 27% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) 7.56-7.53 (m, 2H), 7.42-7.41 (m, 3H), 2.16 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 141.4, 138.3, 130.6, 129.0, 128.6, 117.2, 117.0, 29.3, 11.9 ppm. MS (DI) m/z: 237 (M^+), 235 (M^+), 156 ([M - Br]$^+$). IR (neat): 2976, 2936, 2875, 2212 (CN), 1590, 1575, 1443, 1226, 875 cm^{-1}. Anal. Calcd for $C_{11}H_{10}BrN$: C, 55.96; H, 4.27; N, 5.93. Found: C, 55.73; H, 4.01; N, 5.68.

Procedure for preparation of (*E*)-3-bromo-2-phenylpent-2-enenitrile (3), for Scheme 2.

To the mixture of (*E*)-(1-bromo-2-iodobut-1-en-1-yl)benzene **1** (169 mg, 0.5 mmol) and Ph_3P=O (278 mg, 1 mmol), and toluene (1 mL) was added CuCN (50 mg, 1.1 mmol). After stirring at 130 ºC for 8 h, the reaction mixture was allowed to cool to room temperature. The mixture was diluted with 10 mL of CH_2Cl_2, and transferred into the 50 mL flask, and quenched with 5 mL of 3 M aq.NH_3. After stirring for 10 min, the mixture was transferred into a separatory funnel, and the organic phase was washed with water (10 mL x 3) and brine (10 mL), and dried over Na_2SO_4, and filtered, and concentrated *in vacuo* to give a crude product of dark yellow oil. The reaction was amenable to scale up in 1 and 2 mmol, and the reproducibility was confirmed. Purification of these combined crude products with silica gel column chromatography (hexane/toluene=2/1) afforded **3** in 36% yield as a yellow oil. Rf values of **2** and **3** indicated 0.44 and 0.41 for hexane/EtOAc (19/1), respectively. ^{1}H NMR (400 MHz, $CDCl_3$) 7.46-7.38 (m, 5H), 3.05 (q, *J* = 7.4 Hz, 2H), 1.33 (t, *J* = 7.4 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 149.8, 134.0, 129.3, 129.1, 128.7, 116.6, 114.3, 35.6, 13.4 ppm. MS (DI) m/z: 237 (M^+), 235 (M^+), 156 ([M - Br]$^+$). IR (neat): 2979, 2937, 2212 (CN), 1593, 1455, 1444, 1130, 909, 830, 747 cm^{-1}. Anal. Calcd for $C_{11}H_{10}BrN$: C, 55.96; H, 4.27; N, 5.93. Found: C, 55.73; H, 4.01; N, 5.68.

3. Procedure for preparation of (*E*)-2-(phenyl(pyren-1-yl)methylene)butanenitrile (6) and (*E*)-2-phenyl-3-(pyren-1-yl)pent-2-enenitrile (7), for Scheme 3.

To **2** or **3** (118 mg, 0.5 mmol) in DMF (2 mL) was added 1-Pyreneboronic acid (185 mg, 0.75 mmol) and K_2CO_3 (138 mg, 1 mmol) and $Pd(PPh_3)_4$ (58 mg, 0.05 mmol). After stirring at 90 ^oC for 10 h, the reaction mixture was allowed to cool to ambient temperature. The mixture was diluted with EtOAc (6 mL), and filtered through a pad of celite and frolisil, and the filtrate was evaporated off. The resultant residue in EtOAc was washed with water (20 mL), and the aqueous phase was extracted with EtOAc (10 mL x 3). The combined organic layers were washed with brine (20 mL), and dried over Na_2SO_4, and concentrated in vacuoto give a crude product as a brown solid. Purification with silica gel column chromatography (toluene/hexane=2/1) afforded 157 mg of **6** as a yellowish white solid in 88% yield or 103 mg of **7** as a yellow solid in 58% yield. Data for **6**: ^1H NMR (400 MHz, $CDCl_3$) 8.25-8.20 (m, 3H), 8.15-7.99 (m, 5H), 7.76 (d, J = 7.8 Hz, 1H), 7.54-7.52 (m, 2H), 7.33-7.32 (m, 3H), 2.13 (q, J = 7.4 Hz, 2H), 1.12 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 155.5, 139.7, 133.7, 131.7, 131.6, 131.1, 129.7, 129.1, 129.0, 128.8, 128.6, 128.5, 127.5, 126.72, 126.66, 126.1, 125.9, 125.2, 125.1, 124.9, 124.5, 119.9, 115.6, 26.8, 13.2 ppm; MS (LCMS-IT-TOF) m/z: 380 ($[MNa]^+$); IR (neat): 3045, 2965, 2930, 2871, 2208 (CN), 1600 1488, 1180, 843 cm^{-1}; HRMS (LCMS-IT-TOF) calcd for $C_{27}H_{19}NNa$: 380.1415 $[MNa]^+$, Found 380.1405. Data for **7**: ^1H NMR (400 MHz, $CDCl_3$) 8.22-8.17 (m, 2H), 8.10-7.94 (m, 6H), 7.64 (d, J = 7.9 Hz, 1H), 7.04-7.02 (m, 2H), 6.97-6.88 (m, 3H), 3.28 (dq, J = 7.5, 7.5 Hz, 1H), 3.16 (dq, J = 7.5, 7.5 Hz, 1H), 1.10 (t, J = 7.5 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 161.2, 133.8, 133.2, 131.42, 131.38, 130.8, 128.8, 128.6, 128.3, 128.21, 128.18, 128.16, 127.5, 126.5, 126.1, 125.9, 125.7, 125.0, 124.9, 124.8, 124.2, 118.9, 114.2, 34.1, 12.8 ppm; MS (LCMS-IT-TOF) m/z: 380 ($[MNa]^+$); IR (neat): 3045, 2979, 2939, 2206 (CN), 1597, 1443, 1192 cm^{-1}; HRMS (LCMS-IT-TOF) calcd for

$C_{27}H_{19}NNa$: 380.1415 $[MH]^+$, Found 380.1406; Anal. Calcd for $C_{27}H_{19}N$: C, 90.72; H, 5.36; N, 3.92. Found: C, 90.72; H, 5.43; N, 3.90.

4. Characterization of 2-ethyl-3-phenylfumaronitrile (4), for Scheme 2 and Table 2.

^1H NMR (400 MHz, $CDCl_3$) 7.76-7.71 (m, 2H), 7.53-7.47 (m, 3H), 2.82 (q, *J* = 7.6 Hz, 2H), 1.37 (t, *J* = 7.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 131.7, 131.2, 129.5, 128.6, 128.5, 127.4, 116.6, 115.6, 29.4, 12.8 ppm; MS (DI) m/z: 182 (M^+); IR (neat): 2979, 2939, 2878, 2224 (CN), 1496, 1441 cm^{-1}; Anal. Calcd for $C_{12}H_{10}N_2$: C, 79.10; H, 5.53; N, 15.37. Found: C, 78.95; H, 5.66; N, 15.2.

5. Procedure for preparation of differentially all-carbon tetrasubstituted acrylonitriles (8)-(11), for Scheme 4.

For **8** and **9** *via* Sonogashira reactions: To **2** or **3** (118 mg, 0.5 mmol) in toluene (1 mL) and Et_3N (1 mL) was added ethynyl benzene (0.11 mL, 1 mmol), and followed by addition of $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol) and PPh_3 (26 mg, 0.1 mmol) and CuI (19 mg, 0.1 mmol) in one-portion. After stirring at 70 ºC for 1.5 h, the reaction mixture was allowed to cool to ambient temperature, and diluted with EtOAc (6 mL), and filtered through a pad of elite and frolisil, and the filtrate was evaporated off. The resultant residue in CH_2Cl_2 was washed with brine (15 mL), and the aqueous phase was extracted with CH_2Cl_2 (10 mL x 3). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4, and concentrated *in vacuo* to give a crude product as a dark brown viscous material. Purification with silica gel column chromatography (hexane/toluene=1/1) afforded 117 mg of **8** as an orange oil in 91% yield or 104 mg of **9** as an orange oil in 81% yield. Data for **8**: ^1H NMR (400 MHz, $CDCl_3$) 7.74-7.72 (m, 2H), 7.51-7.35 (m, 8H), 2.78 (q, *J* = 7.6 Hz, 2H), 1.33 (t, *J* = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 137.3, 136.2, 131.8, 129.7, 129.6, 128.6, 128.5, 128.4, 122.0, 119.7, 118.9, 103.6, 86.5, 27.7, 12.5 ppm. MS (LC-TOF)

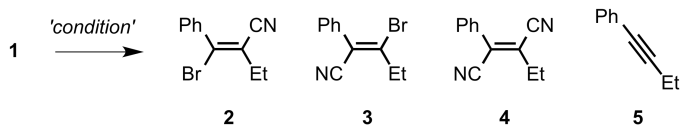
m/z: 258 ([MH]$^+$); IR (neat): 2973, 2934, 2190 (CN), 1559, 1488, 1443, 1335, 754, 689 cm^{-1}. HRMS (LCMS-IT-TOF) calcd for $C_{19}H_{15}NH$: 258.1277 [MH]$^+$, Found 258.1267. Data for **9**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.86-7.83 (m, 2H), 7.46-7.32 (m, 8H), 2.81 (q, *J* = 7.5 Hz, 2H), 1.36 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 140.4, 133.7, 132.0, 129.7, 129.3, 128.7, 128.6, 128.4, 122.1, 118.2, 117.3, 103.5, 87.7, 31.4, 13.2 ppm; MS (LCMS-IT-TOF) m/z: 280 [MNa$^+$]; IR (neat): 3057, 2975, 2934, 2874, 2187, 1557, 1489, 1443, 756, 688 cm^{-1}; HRMS (LCMS-IT-TOF) calcd for $C_{19}H_{15}NNa$: 280.1102 [MNa]$^+$, Found 280.1071.

For **10** and **11** *via* Suzuki-Miyaura reactions: To **2** or **3** (102 mg, 0.43 mmol) in DMF (2 mL) was added *p*-methyl phenylboronic acid (88 mg, 0.65 mmol) and K_2CO_3 (138 mg, 1 mmol) and $Pd(PPh_3)_4$ (46 mg, 0.04 mmol). After stirring at 90 ºC for 22 h, the reaction mixture was allowed to cool to ambient temperature. The mixture was diluted with EtOAc (6 mL), and filtered through a pad of elite and frolisil, and the filtrate was evaporated off. The resultant residue in EtOAc was washed with water (15 mL), and the aqueous phase was extracted with EtOAc (10 mL x 3). The combined organic layers were washed with brine (10 mL), and dried over Na_2SO_4, and concentrated *in vacuo* to give a crude product as a brown oil. Purification with silica gel column chromatography (toluene/hexane=2/1) afforded 94 mg of **10** as an orange oil in 89% yield or 78 mg of **11** as an orange oil in 62% yield. Data for **10**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.36-7.32 (m, 5H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 2.42-2.36 (m, 5H), 1.23 (t, *J* = 7.5 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 156.6, 140.1, 138.8, 136.0, 129.4, 129.14, 129.12, 129.10, 128.3, 119.8, 113.1, 25.9, 21.3, 13.4 ppm. MS (LCMS-IT-TOF) m/z: 248 ([MH]$^+$); IR (neat): 2974, 2919, 2207 (CN), 1608, 1508, 1490, 1443, 699 cm^{-1}; HRMS (LCMS-IT-TOF) calcd for $C_{18}H_{17}NH$: 248.1434 [MH]$^+$, Found 248.1421. Data for **11**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.17-7.09 (m, 5H), 7.03 (d, *J* = 8.3 Hz, 2H), 6.92 (d, *J* = 8.3 Hz, 2H), 2.95 (q, *J* = 7.5 Hz, 2H), 2.30 (s, 3H,) 1.08 (t, *J* = 7.5 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) 161.5, 138.6, 134.9, 134.2,

129.6, 129.3, 128.6, 128.4, 127.9, 119.2, 110.9, 32.4, 21.3, 12.8 ppm. MS (LCMS-IT-TOF) m/z: 248 ($[MH]^+$); IR (neat): 2973, 2930, 2209 (CN), 1609, 1509, 1490, 1444, 817, 764 cm^{-1}; HRMS (LCMS-IT-TOF) calcd for $C_{18}H_{17}NH$: 248.1434 $[MH]^+$, Found 248.1414.

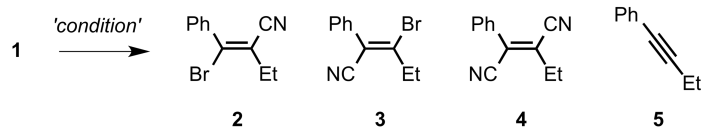
6. Evaluation of reactivity of 1 on vinylic Rosenmund-von Braun reaction (Table 1S)

Table 1S. Evaluation of reaction condition on the cyanation of **1**



2 **3** **4** **5**

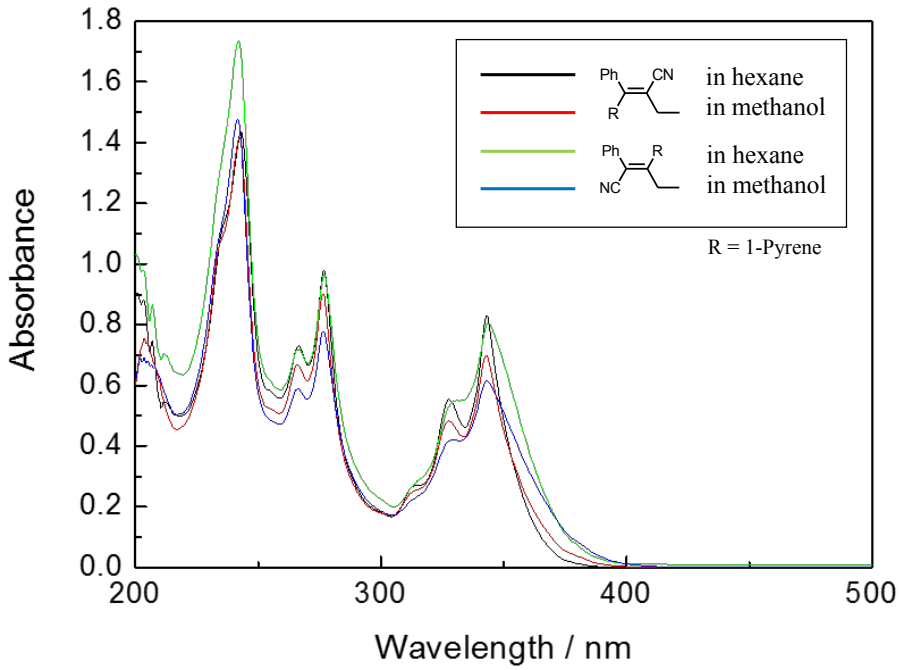
Entry	*'condition'*	NMR yield/% (crude state)				
		1	**2**	**3**	**4**	**5**
1	CuCN (1.1 eq), DMF, 70 ºC, 22 h	0	48	9	24	15
2	CuCN (1.1 eq), DMA, 70 ºC, 22 h	< 16	32	13	15	9
3	CuCN (1.1 eq), DMA, 70 ºC, 4 h	42	32	3	6	10
4	CuCN (1.1 eq), 1,3-dimethyl-2-imidazolidinone, 70 ºC, 8 h	24	40	19	13	7
5	CuCN (1.1 eq), *N*-methylpyrrolidone, 70 ºC, 17 h	12	32	11	15	26
6	CuCN (1.1 eq), 2-Pyrrolidone, 70 ºC, 4 h	54	8	0	0	16
7	CuCN (1.1 eq), DMF (12 eq) toluene, 70 ºC, 4 h	100	0	0	0	0
8	CuCN (1.1 eq), DMF (11 eq) toluene, 110 ºC, 18 h	0	24	54	22	3
9	CuCN (1.1 eq), DMF (13 eq) THF, 70 ºC, 63 h	~ 0	34	13	26	1
10	CuCN (1.1 eq), DMSO, 70 ºC, 7.5 h	~ 0	20	2	4	40
11	CuCN (1.1 eq), DMSO (6.6 eq) toluene, 70 ºC, 60 h	< 24	20	6	5	17
12	CuCN (1.1 eq), DMSO (11 eq) toluene, 70 ºC, 60 h	< 26	22	3	3	24
13	CuCN (1.1 eq), Methyl phenyl sulfoxide (10 eq) toluene, 110 ºC, 5 h	~ 0	20	44	11	3
14	CuCN (1.1 eq), Diphenyl sulfoxide (10 eq) toluene, 110 ºC, 19 h	~ 0	16	42	7	6
15	CuCN (1.1 eq), Diphenyl sulfite, 110 ºC, 5 h	100	0	0	0	0



Entry	*'condition'*	NMR yield/% (crude state)				
		1	**2**	**3**	**4**	**5**
16	CuCN (1.1 eq), PPh_3 (2.2 eq) DMF, 70 ºC, 3 h	~ 0	0	0	0	~ 100
17	CuCN (1.1 eq), $Ph_3P{=}O$ (2.0 eq) toluene, 130 ºC, 8 h	~ 0	20	49	18	3
18	CuCN (1.1 eq), HMPA (2.0 eq) toluene, 70 ºC, 22 h	< 24	32	24	12	4
19	CuCN (1.1 eq), HMPA (2.0 eq) toluene, 90 ºC, 22 h	< 28	34	24	9	3
20	CuCN (1.1 eq), Pyridine, 70 ºC, 4.5 h	4	3	0	0	52
21	CuCN (1.1 eq), Pyridine N-Oxide (2.0 eq) toluene, 70 ºC, 17 h	~ 0	3	0	0	48
22	CuCN (1.1 eq), Pyridine N-Oxide (2.0 eq) toluene, 110 ºC, 17 h	~ 0	13	13	5	28
23	CuCN (1.1 eq), L-Proline (1.0 eq) DMF, 80 ºC, 1.5 h	12	20	1	2	34
24	CuCN (1.1 eq), TMEDA (1.5 eq) toluene, 70 ºC, 4 h	100	0	0	0	0
25	CuCN (1.1 eq), $[(CH_3)_2NCH_2CH_2]_2NCH_3$ (1.2 eq) toluene, 70 ºC, 4 h	100	0	0	0	0
26	CuCN (1.1 eq), $[(CH_3)_2CH]_2NH$ (1.5 eq) toluene, 70 ºC, 4 h	100	0	0	0	0
27	CuCN (1.1 eq), toluene, 70 ºC, 5 h	100	0	0	0	0
28	CuCN (1.1 eq), CH_3CN, 70 ºC, 2 h	100	0	0	0	0
29	CuCN (1.1 eq), EtOAc, 70 ºC, 2 h	100	0	0	0	0

7. UV-Vis absorption of pyrene derivatives 6 and 7 (Figure 1S).

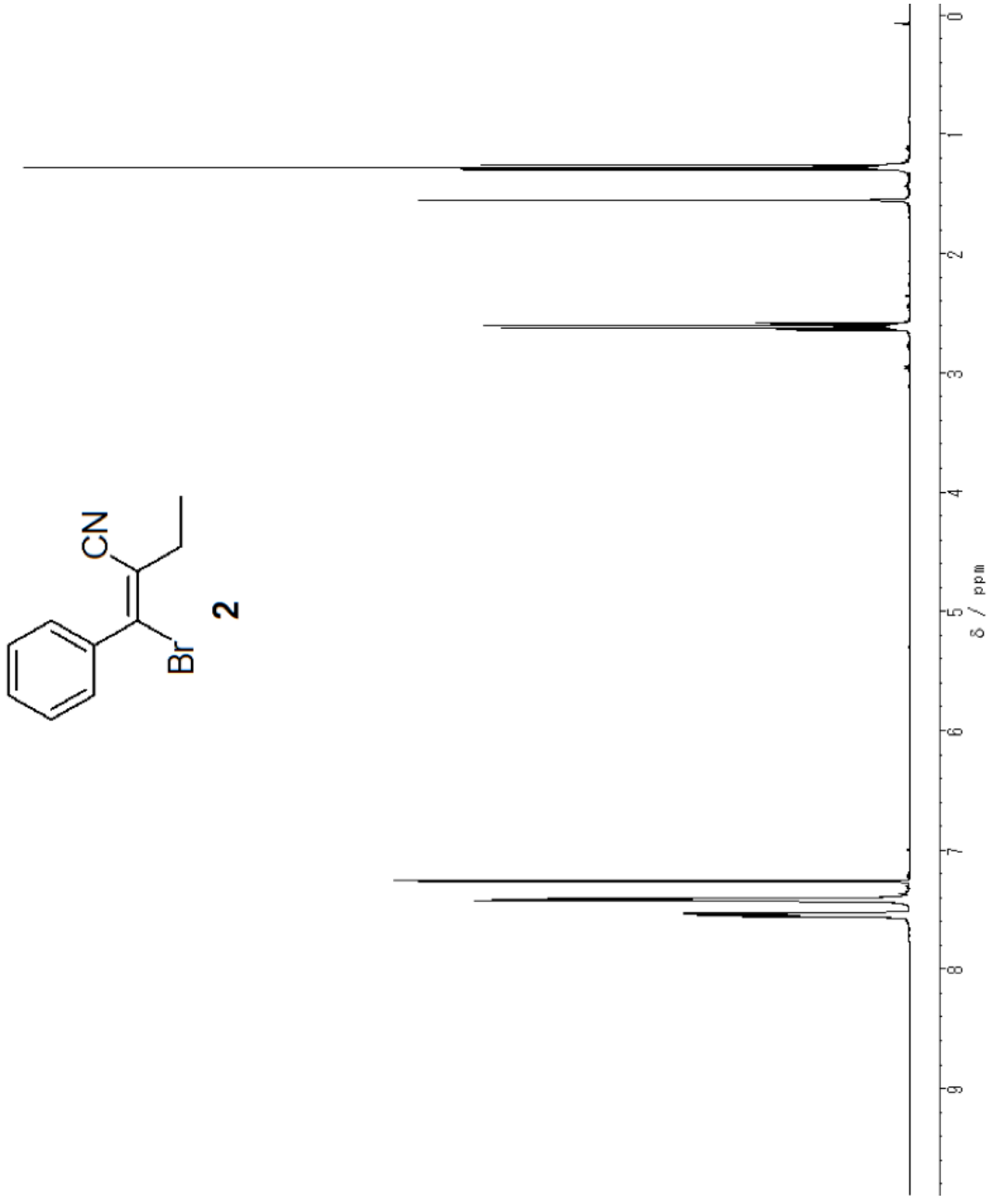
Figure 1S. UV-Vis absorption of pyrene derivatives **6** and **7**.



8. The ^{1}H and ^{13}C NMR spectra of all new compounds **2**, **3**, **4**, **6**, **7**, **8**, **9**, **10**, **11**.

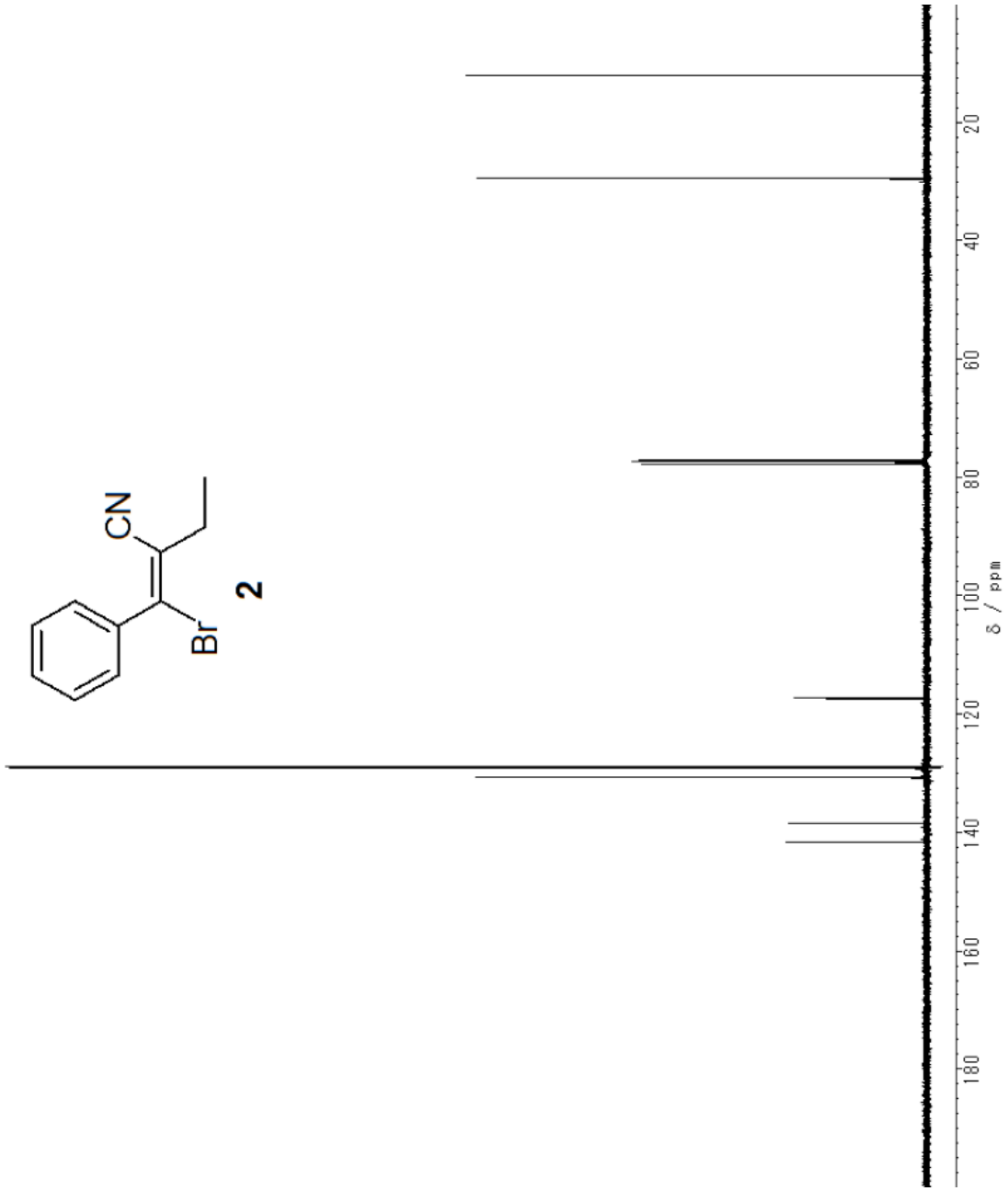
Compound 2

^{1}H NMR spectrum in $CDCl_3$

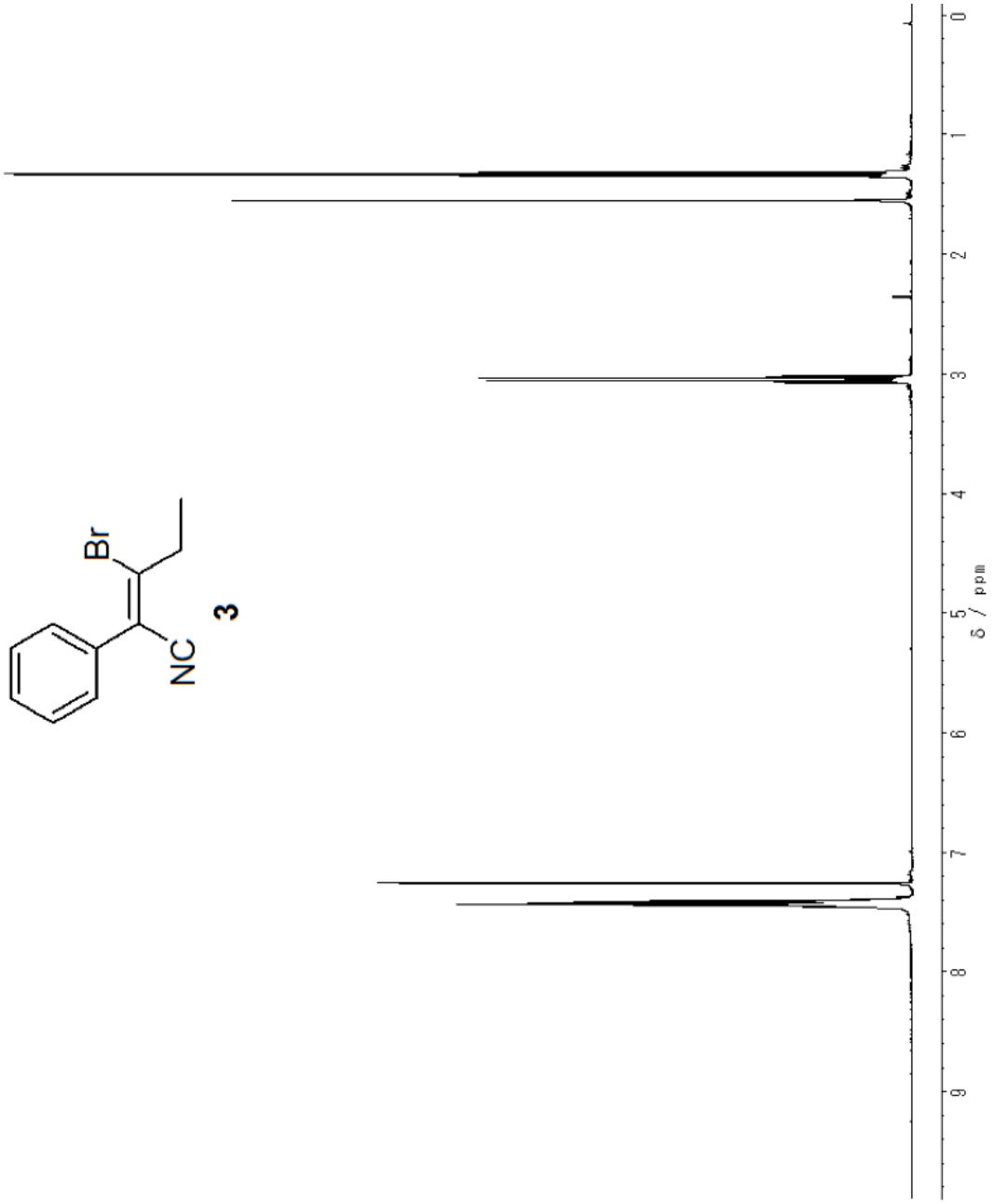


Compound 2

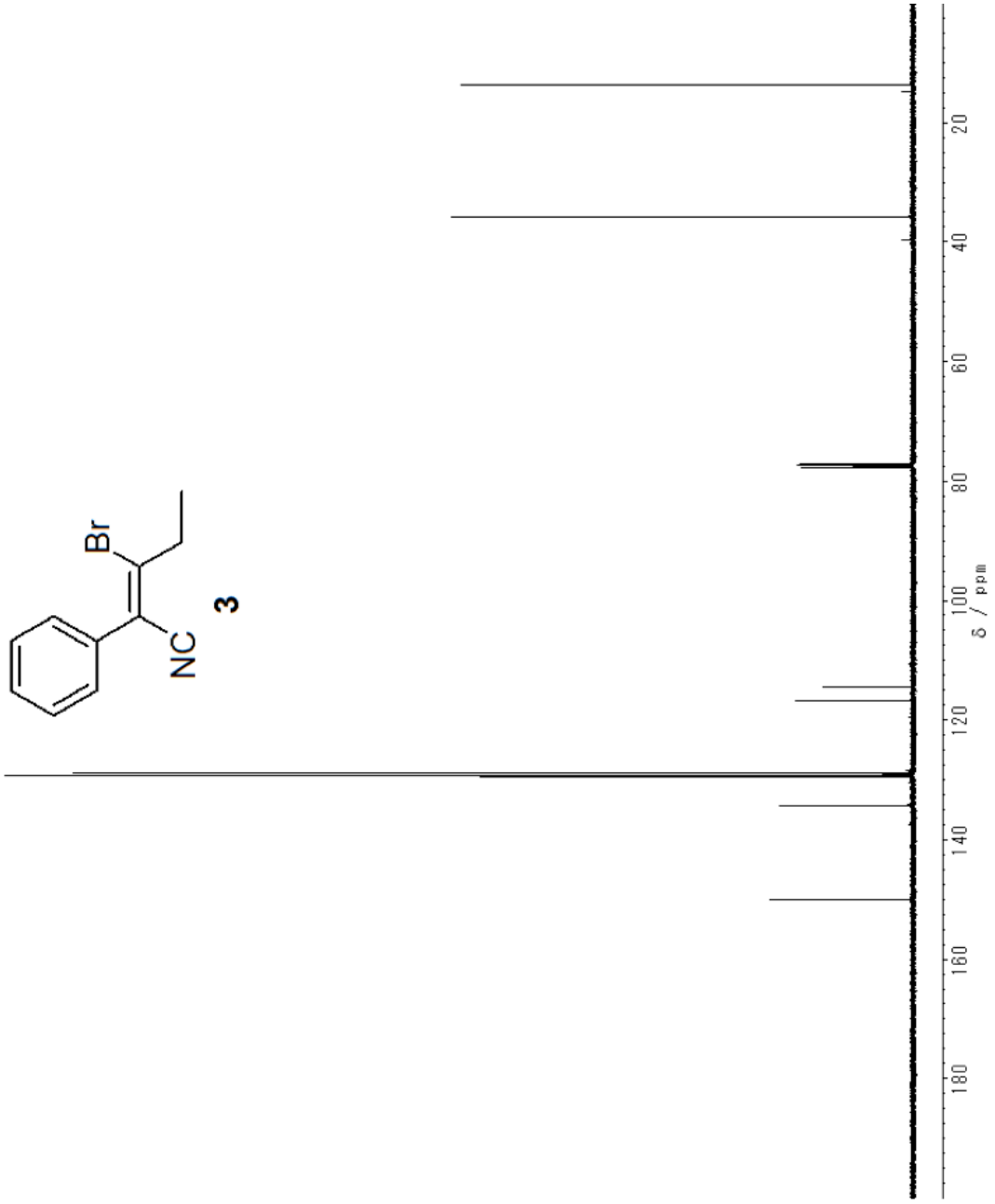
^{13}C NMR spectrum in $CDCl_3$



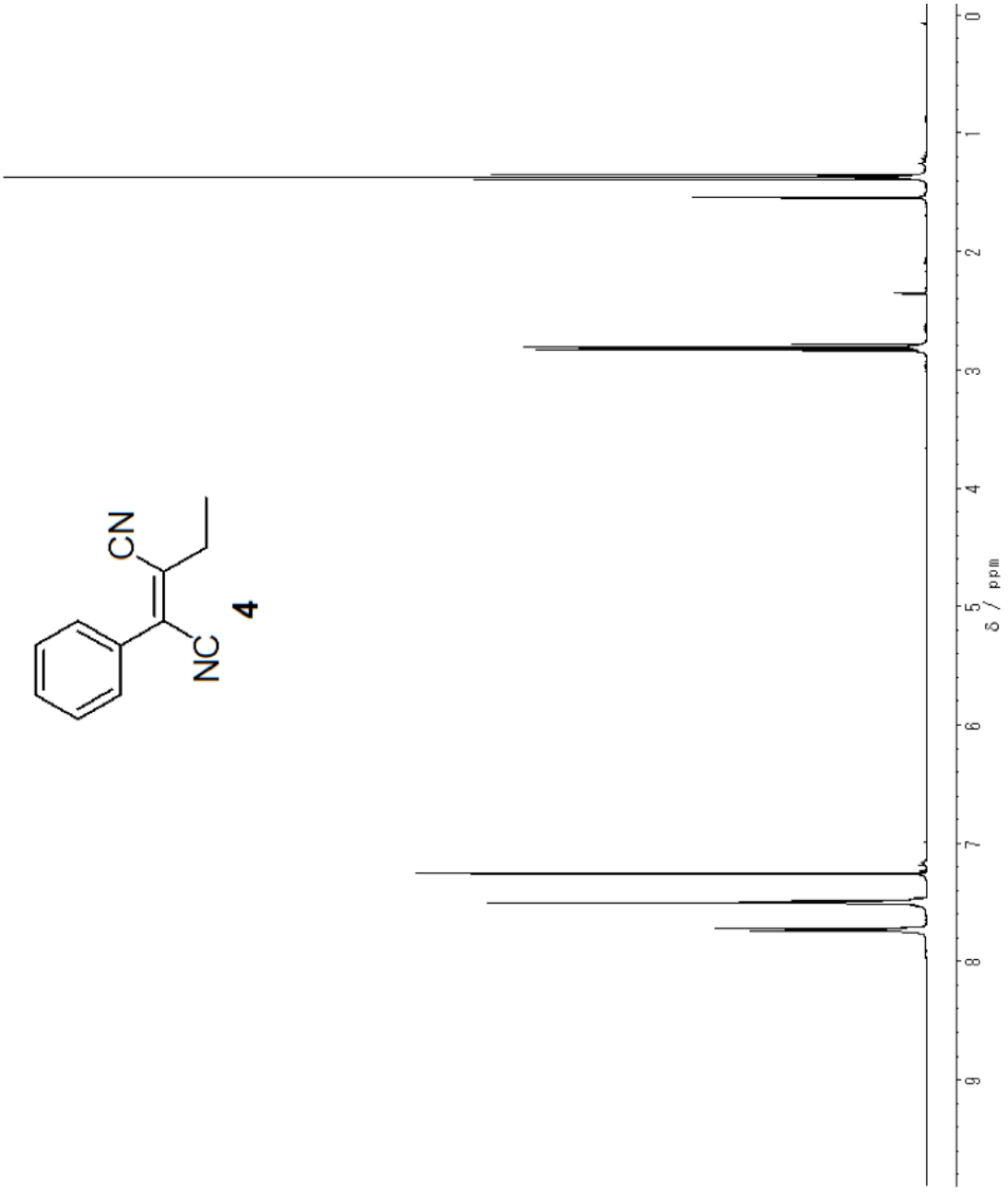
Compound 3
^{1}H NMR spectrum in $CDCl_3$



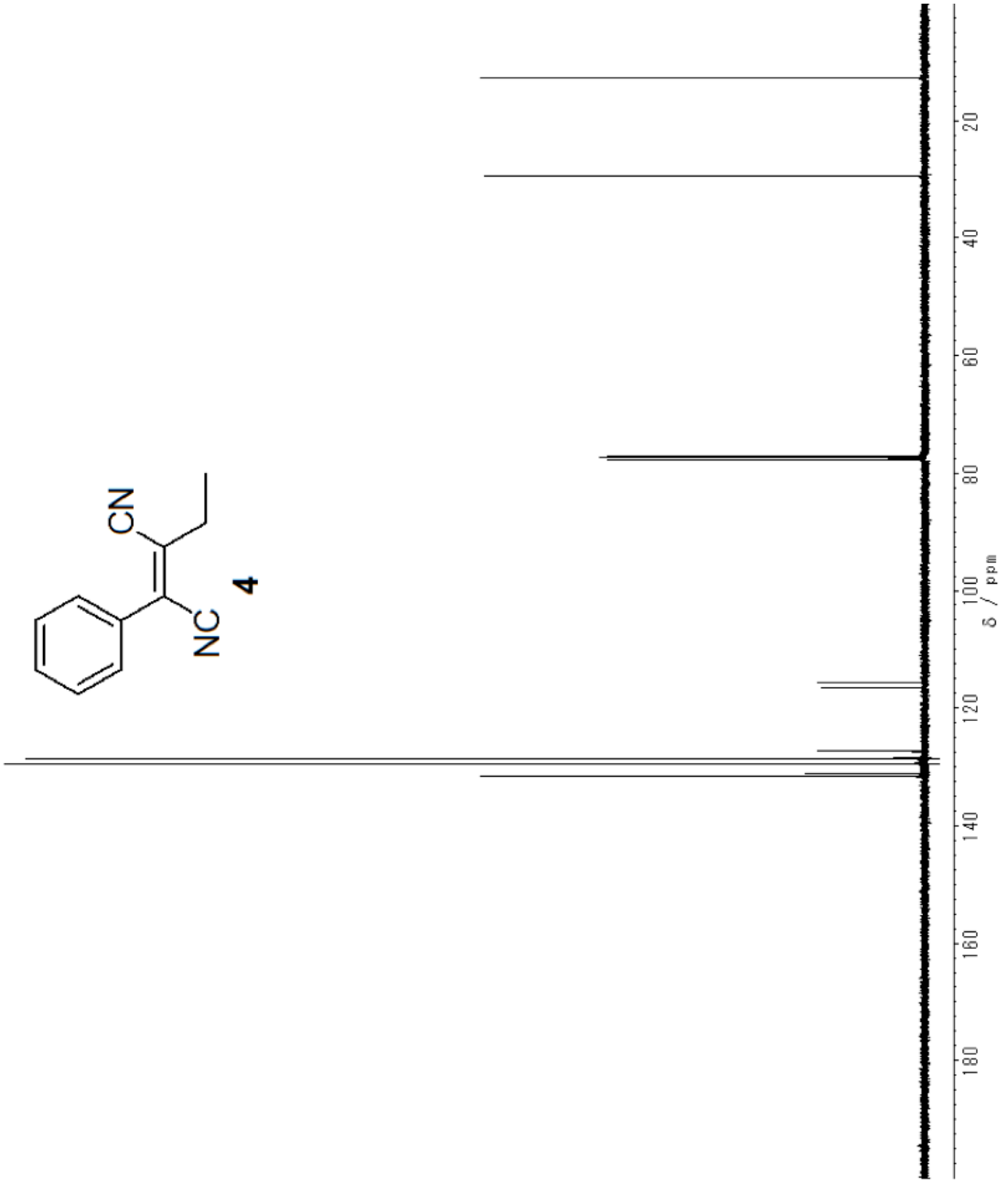
Compound 3
^{13}C NMR spectrum in $CDCl_3$



Compound 4
^{1}H NMR spectrum in $CDCl_3$



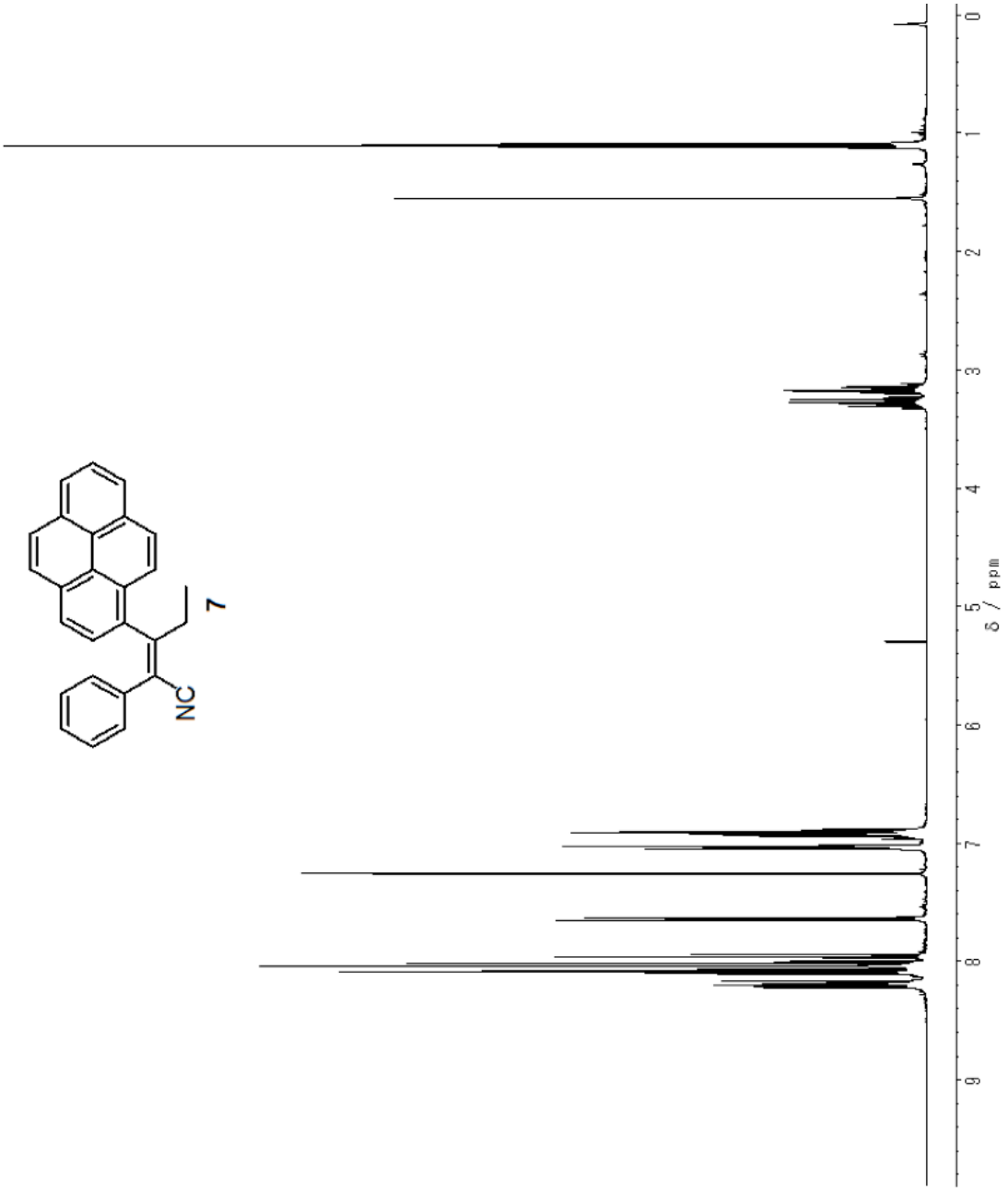
Compound 4
^{13}C NMR spectrum in $CDCl_3$



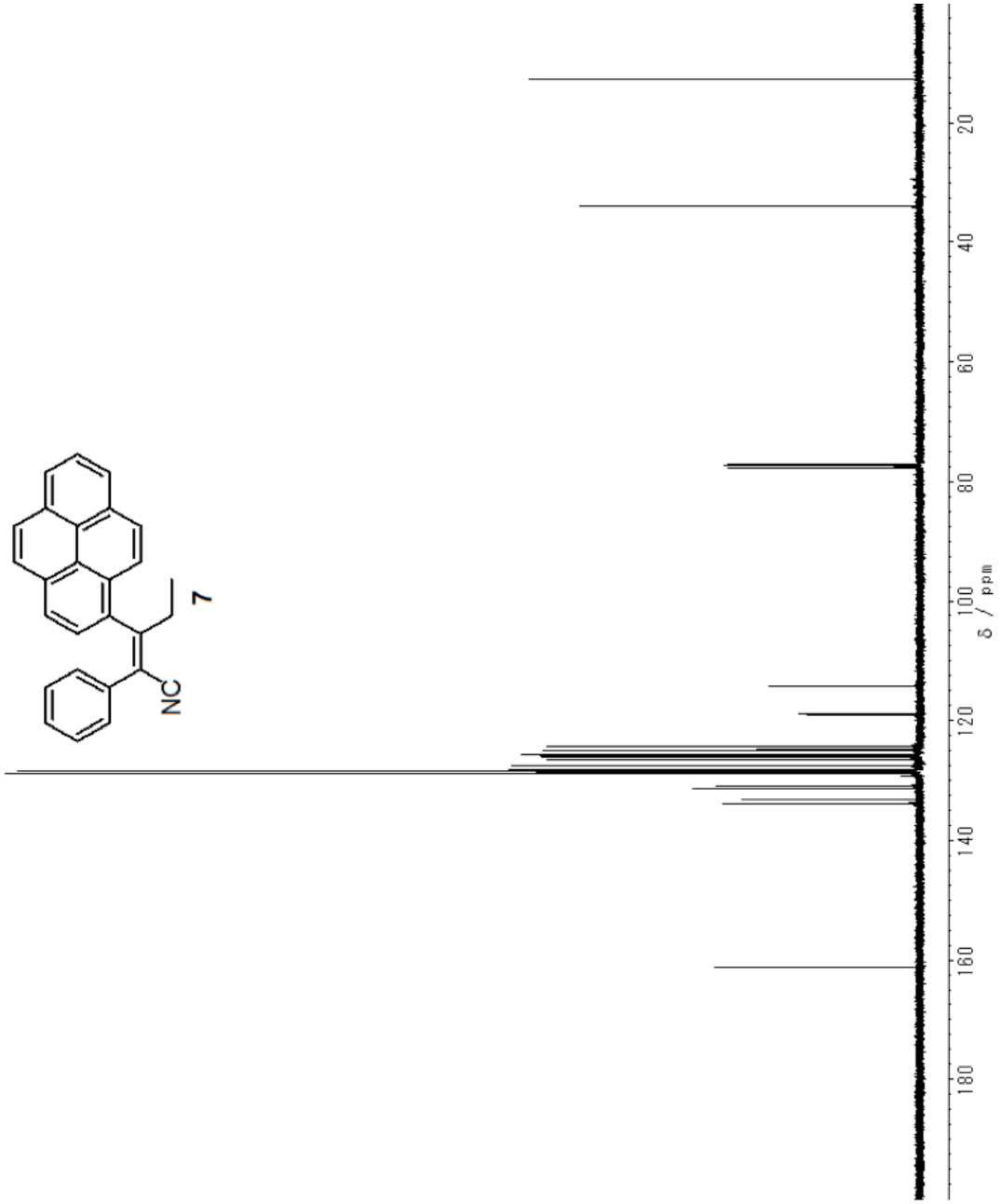
Compound 6
^{1}H NMR spectrum in $CDCl_3$

Compound 6
^{13}C NMR spectrum in $CDCl_3$

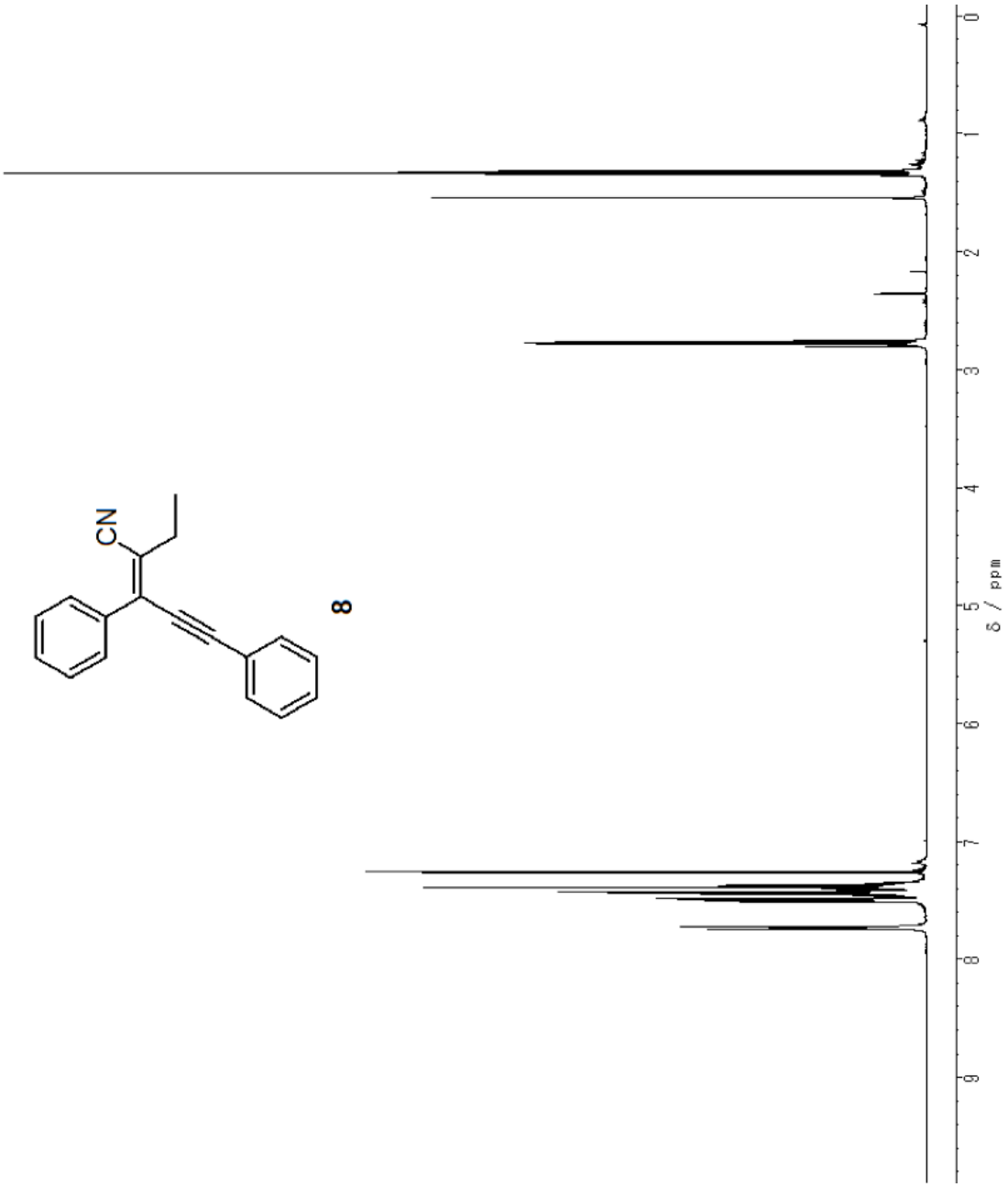
Compound 7
^{1}H NMR spectrum in $CDCl_3$



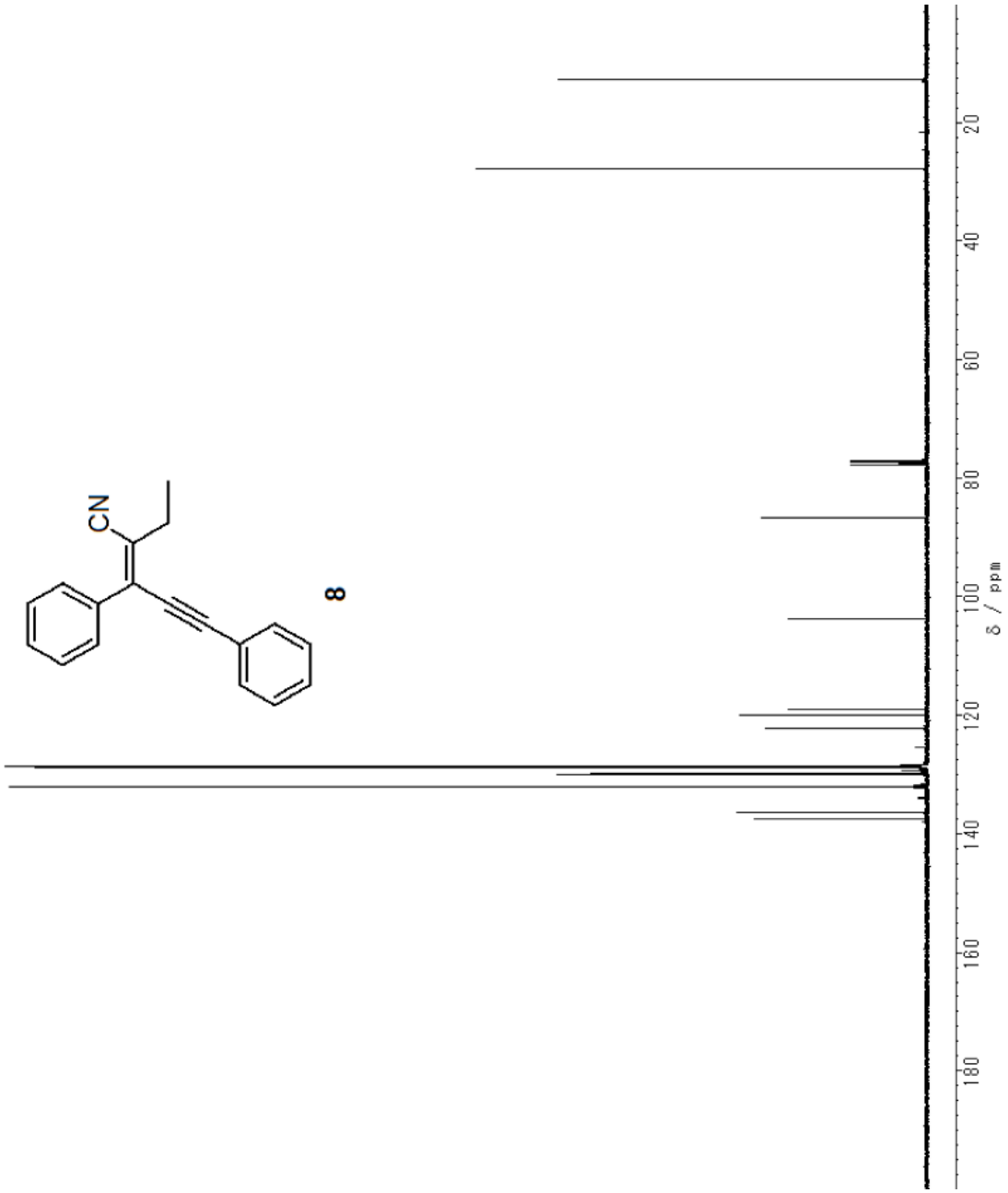
Compound 7
^{13}C NMR spectrum in $CDCl_3$



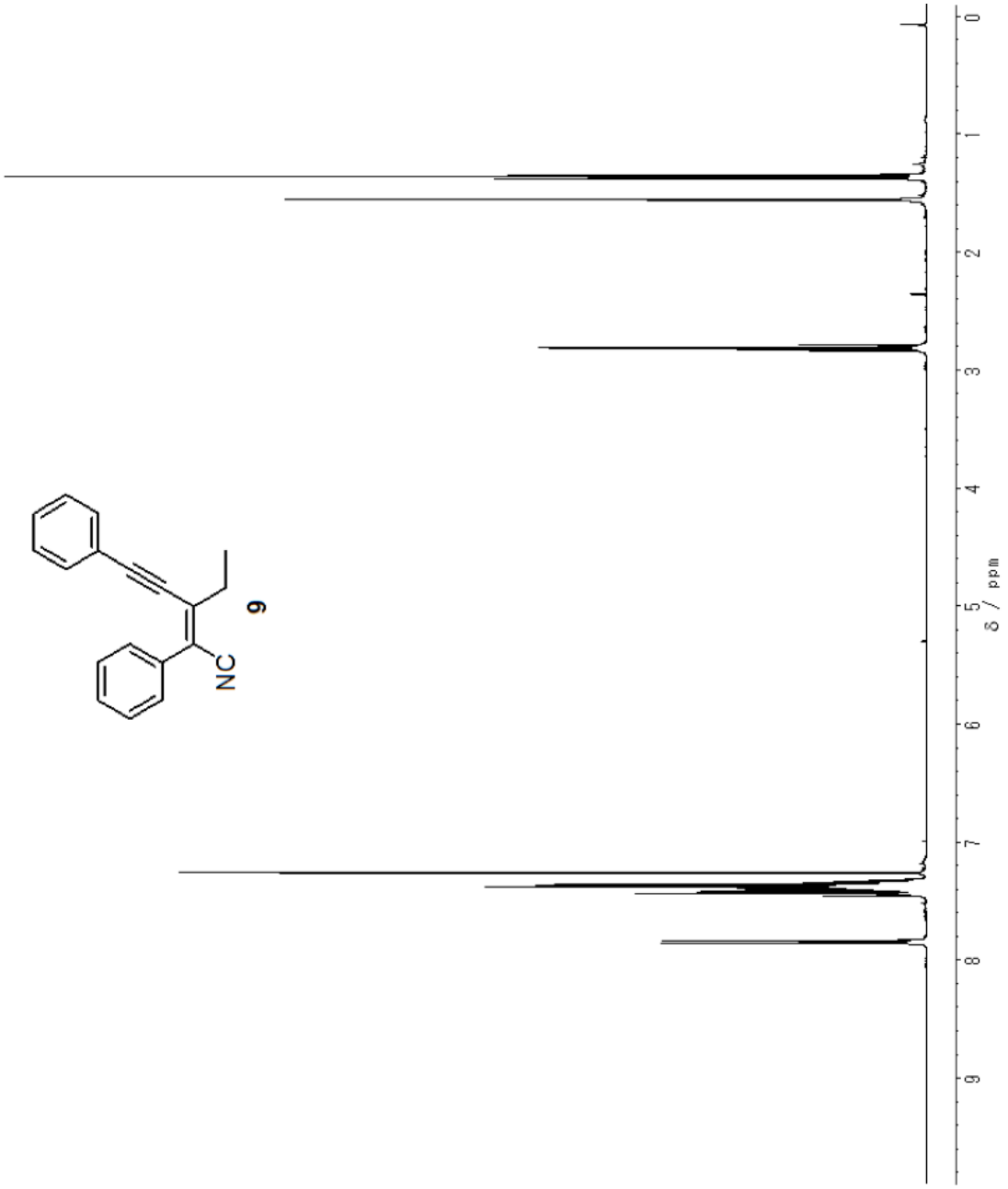
Compound 8
^{1}H NMR spectrum in $CDCl_3$



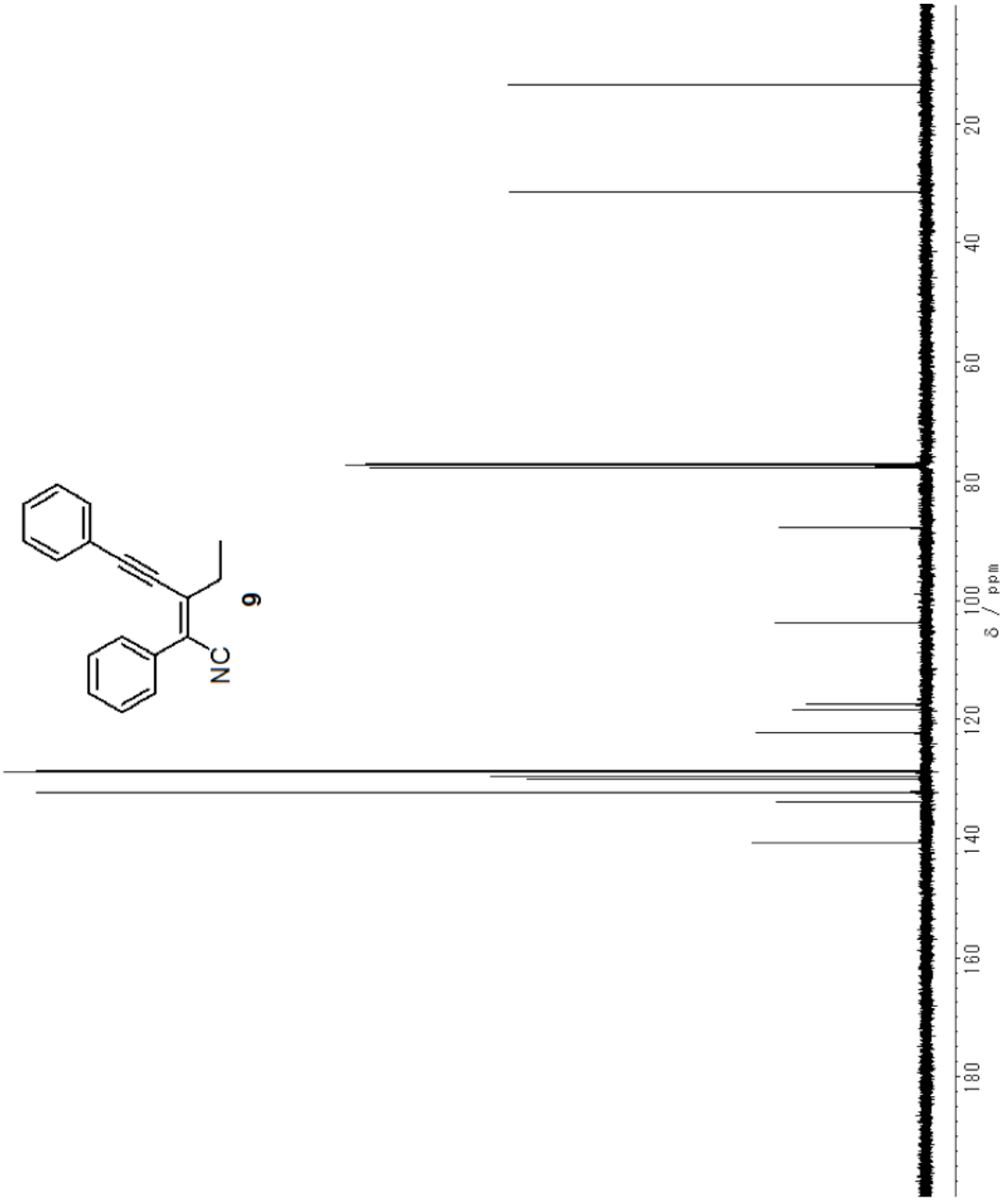
Compound 8
^{13}C NMR spectrum in $CDCl_3$



Compound 9
^{1}H NMR spectrum in $CDCl_3$



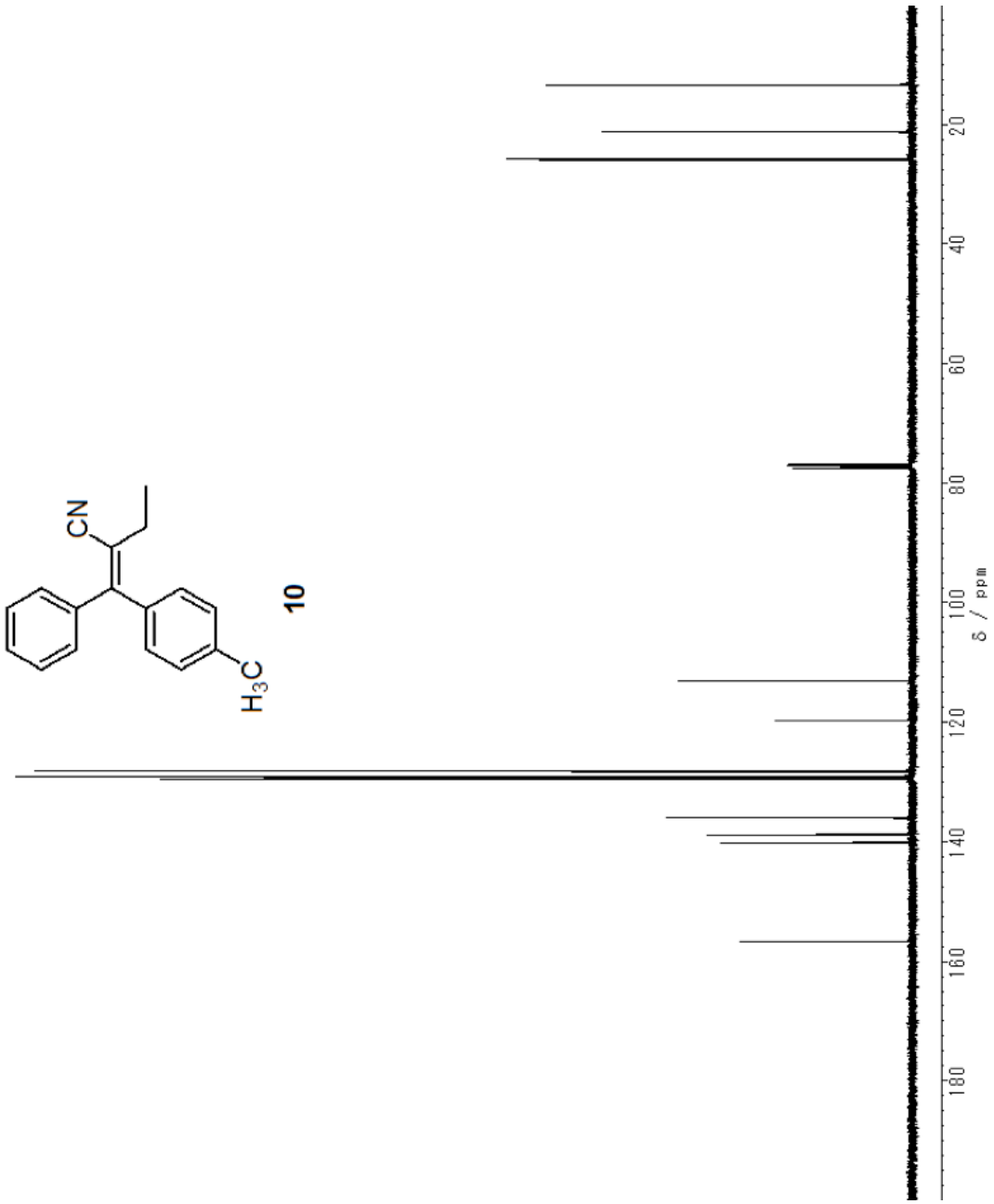
Compound 9
^{13}C NMR spectrum in $CDCl_3$



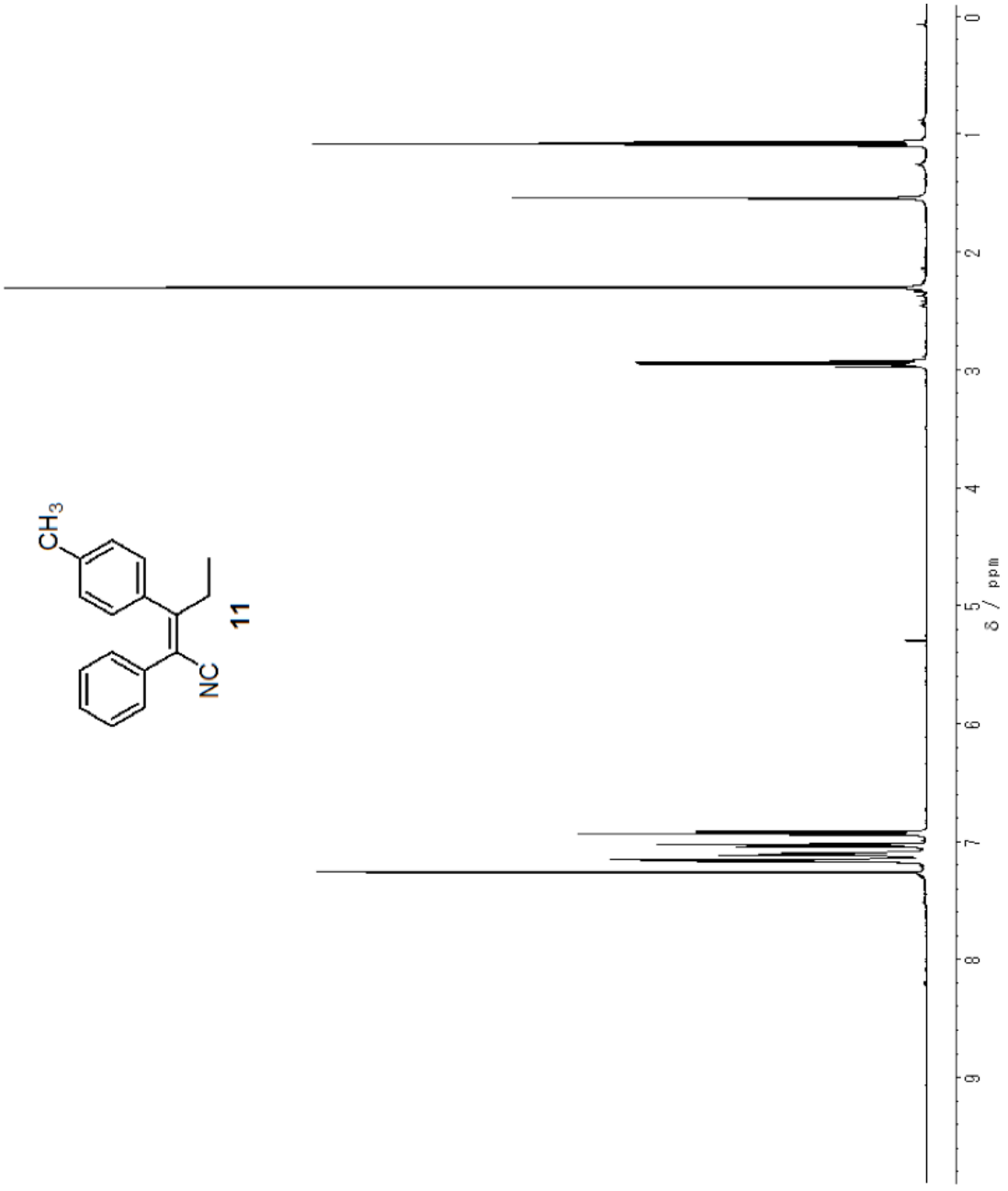
Compound 10
^{1}H NMR spectrum in $CDCl_3$

Compound 10

^{13}C NMR spectrum in $CDCl_3$



Compound 11
^{1}H NMR spectrum in $CDCl_3$



Compound 11
^{13}C NMR spectrum in $CDCl_3$