Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Electronic Supplementary Information for

Functionalization of Heteroaromatic *N*-Oxides Using Organic Superbase Catalyst

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General Comments.

Reactions were carried out under Ar atmosphere using dry solvents. Melting points (mp) were determined with a Yazawa micro melting point apparatus and uncorrected. Infrared (IR) data were recorded on SensIR ATR (Attenuated Total Reflectance) FT-IR. The spectra were acquired in 32 scans per spectrum at a resolution of four using system ReactIR™ 2.20 software. Absorbance frequencies are reported in reciprocal centimeters (cm^{-1}). NMR data were recorded on either a JEOL AL400 spectrometer (395.75 MHz for ^{1}H, 99.50 MHz for ^{13}C). Chemical shifts are expressed in δ (parts per million, ppm) values, and coupling constants (*J*) are expressed in hertz (Hz). ^{1}H NMR spectra were referenced to a tetramethylsilane (TMS) as an internal standard or to a solvent signal ($CDCl_3$: 7.26 ppm). ^{13}C NMR spectra were referenced to a solvent signal ($CDCl_3$: 77.0 ppm). The following abbreviations are used: s = singlet, d = doublet, m = multiplet. Low and high mass spectra (LRMS and HRMS) were obtained from Mass Spectrometry Resource, Graduate School of Pharmaceutical Sciences, Tohoku University, on a JEOL JMS-DX 303 and JMS-700 respectively. Elemental analyses (*Anal.*) were performed on Yanaco CHN CORDER MT-6 at Central Analytical Center, Graduate School of Pharmaceutical Sciences, Tohoku University.

Materials.

Unless otherwise noted, commercially available materials were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used after appropriate purification (distillation or recrystallization) or as received. Flash column chromatographies were performed with Kanto silica gel 60 N (spherical, neutral, 70−230 mesh). Thin-layer chromatographies were carried out on precoated plates of silica gel (Merck Silica gel 60 F_{254}).

Procedure for preparation of alkynylsilanes.[1]

Under argon atmosphere, aldehyde (20 mmol) was added to a mixture of carbontetrabromide (13.3 g, 40 mmol) and triphenylphosphine (21.0 g, 80 mmol) in dry CH_2Cl_2 (100 mL) at 0 ºC, and the mixture was stirred for 5 min. at 0 ºC. After the reaction, CH_2Cl_2 was evaporated, $CHCl_3$ was added to the residue, and the insoluble materials were filtered through a Celite plug. The solution was concentrated *in vacuo*. The crude material was purified by SiO_2 column chromatography (eluting with hexane/ethyl acetate = 19:1) to give dibromoethene.

Under argon atmosphere, *n*-BuLi (9.0 mL, 2.64 M in hexane, 24 mmol) was added to a mixture of dibromoethene (10 mmol) and dry THF (100 mL) at −78 ºC and the mixture was stirred for 1 h at −78 ºC. trimethylsilyl chloride (1.3 g, 12 mmol) was added to the mixture at −78 ºC and the mixture was stirred for 1 h at −78 ºC. After the reaction, saturated aq. NH_4Cl and H_2O were added to the mixture. The mixture was extracted with Et_2O (50 mL x 3). The solution was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified by SiO_2 column chromatography (eluting with hexane/ethyl acetate = 19:1).

1,1'-Dibromo-2-(4-methoxyphenyl)ethene.[2]

Yellow oil (5.14 g, 88 %).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 3.74 (s, 3H), 6.83 (d, *J* = 8.7 Hz 2H), 7.34 (s, 1H), 7.45 (d, *J* = 8.7 Hz, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 55.1, 87.0, 113.6, 127.5, 129.7, 136.1, 159.4.

LRMS (EI) *m/z*: 290 (M^+), 292 (M^++2), 294 (M^++4).

HRMS: Calcd. For. $C_9H_8Br_2O$: 289.8942. Found: 289.8923.

IR (neat): 2933, 2837, 1734, 1603, 1507, 1245, 1176, 1027, 868, 802 cm^{-1}.

1,1'-Dibromo-2-(4-chlorophenyl)ethene.[3]

Yellow oil (5.75 g, 97 %).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.33 (d, *J* = 8.7 Hz, 2H), 7.43 (s, 1H), 7.46 (d, *J* = 8.7 Hz, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 90.4, 128.6, 129.6, 133.6, 134.3, 135.6.

LRMS (EI) *m/z*: 294 (M^+), 296 (M^++2), 298 (M^++4), 300 (M^++6).

HRMS: Calcd. For. $C_8H_5Br_2Cl$: 293.8446. Found: 293.8436.

IR (neat): 3008, 1734, 1487, 1241, 1097, 1013, 874, 808, 782 cm^{-1}.

(4-Methoxyphenylethynyl)-trimethylsilane.[4]

Yellow oil (2.02 g, 99 %).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.23 (s, 9H), 3.80 (s, 3H), 6.81 (d, *J* = 8.8 Hz, 2H), 7.39 (d, *J* = 8.8 Hz, 2H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm): 0.04, 55.2, 92.4, 105.2, 113.8, 115.3, 133.4, 159.7.

LRMS (EI) *m/z*: 204 (M^+).

HRMS: Calcd. For. $C_{12}H_{16}OSi$: 204.0970. Found: 209.0965.

IR (neat): 2597, 2154, 1605, 1506, 1245, 861, 829, 754 cm^{-1}.

(4-Chlorophenylethynyl)-trimethylsilane.[4]

Recrystallized from ethanol, colorless prism (1.88 g, 90 %), mp: 43–45 ºC.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.24 (s, 9H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm): –0.12, 95.3, 103.8, 121.6, 128.5, 133.2, 134.5.

LRMS (EI) *m/z*: 208 (M^+), 210 (M^++2).

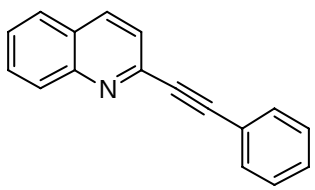
HRMS: Calcd. For. $C_{11}H_{13}ClSi$: 208.0475. Found: 208.0498.

IR (neat): 2958, 2159, 1487, 1249, 1090, 1015, 825, 758, 684 cm^{-1}.

Procedure for the reaction of quinoline *N*-oxide with organosilicon nucleophiles (Scheme1, 2).

Under argon atmosphere, P4-^{t}Bu base (0.03 mL 1.0 M in hexane, 0.03 mmol, or 0.06 mL 1.0 M in hexane, 0.06 mmol) was added to a mixture of quinoline *N*-oxide (43.5 mg, 0.30 mmol) and organosilicon nucleophile (0.54 mmol) in dry solvent (1.0 mL) and the mixture was stirred for 1–17 h at room temperature. After the reaction, saturated aq. NH_4Cl and H_2O were added to the mixture. The mixture was extracted with AcOEt (20 mL x 3). The combined organic layers were then washed with saturated aq. NaCl (50 mL). The solution was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified by SiO_2 column chromatography.

2-(Phenylethynyl)quinoline (3)[5]



Purification by SiO_2 column chromatography (eluting with hexane/ethyl acetate = 19:1), orange oil (59.8

mg, 87%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.26–7.40 (m, 3H), 7.53–7.57 (m, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.66–7.68 (m, 2H), 7.72–7.75 (m, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 8.12–8.15 (m, 2H).

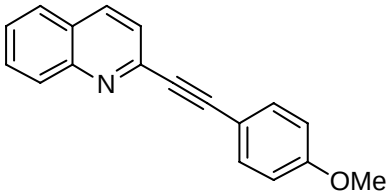
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 89.3, 89.9, 122.1, 124.3, 127.0, 127.0, 127.4, 128.3, 129.1, 129.2, 130.0, 132.2, 136.0, 143.5, 148.2.

LRMS (EI) *m/z*: 229 (M^+).

HRMS: Calcd. For. $C_{17}H_{11}N$: 229.0891. Found: 229.0875.

IR (neat): 3056, 2219, 1734, 1592, 1499, 1424, 1309, 1240, 1159, 1113, 1045, 827, 752, 689 cm^{-1}.

2-(4-Methoxyphenylethynyl)quinoline (4)



Purification by SiO_2 column chromatography (eluting with hexane/ethyl acetate = 7:3),

recrystallized from ethanol, colorless needles (46.7 mg, 60 %), mp: 145–147 ºC.

Anal. Calcd. For $C_{18}H_{13}NO$: C, 83.37; H, 5.05; N, 5.40. Found: C, 83.14; H, 5.35; N, 5.25.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 3.85 (s, 3H), 6.90 (d, *J* = 8.7 Hz, 2H), 7.52–7.62 (m, 4H), 7.71–7.75 (m, 1H), 7.80 (d, *J* = 7.3 Hz, 1H), 8.13 (d, *J* = 8.7 Hz, 2H).

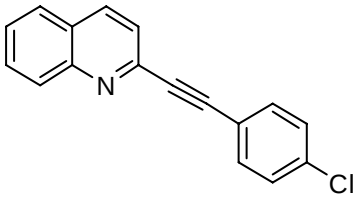
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 55.3, 88.4, 90.3, 114.1, 114.1, 124.2, 126.8, 126.9, 127.4, 129.2, 129.9, 133.8, 136.0, 143.9, 148.2, 160.3.

LRMS (EI) *m/z*: 259 (M^+).

HRMS: Calcd. For. $C_{18}H_{13}NO$: 259.0997. Found: 259.0997.

IR (neat): 3063, 1499, 1420, 1079, 1009, 830, 822, 788, 751 cm^{-1}.

2-(4-Chlorophenylethynyl)quinoline (5)



Purification by SiO_2 column chromatography (eluting with hexane/ethyl acetate = 9:1),

recrystallized from ethanol, orange needles (38.0 mg, 48 %), mp: 122–123 ºC.

Anal. Calcd. For $C_{17}H_{10}NCl$: C, 77.42; H, 3.82; N, 5.31. Found: C, 77.26; H, 4.08; N, 5.17.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.53–7.61 (m, 6H), 7.73–7.77 (m, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 8.12–8.17 (m, 2H).

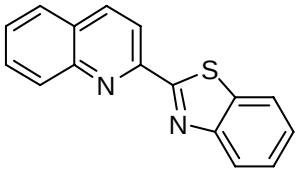
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm): 88.6, 90.2, 120.7, 124.3, 127.2, 127.2, 127.5, 128.8, 129.4, 130.1, 133.4, 135.3, 136.2, 143.3, 148.3.

LRMS (EI) *m/z*: 263 (M^+), 265 (M^++2).

HRMS: Calcd. For. $C_{17}H_{10}NCl$: 263.0502. Found: 263.0501.

IR (neat): 3007, 2197, 1590, 1509, 1252, 1154, 828, 757 cm^{-1}.

2-(2-Benzothiazolyl)quinoline (6)



Purification by SiO_2 column chromatography (eluting with hexane/ethyl acetate = 19:1), recrystallized from ethanol, yellow needles (76.3 mg, 97 %), mp: 185–186 ºC.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.42–7.46 (m, 1H), 7.50–7.54 (m, 1H), 7.57–7.61 (m, 1H), 7.75–7.79 (m, 1H), 7.87 (d, *J* = 8.6 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 8.6 Hz, 1H), 8.30 (d, *J* = 8.6 Hz, 1H), 8.49 (d, *J* = 8.5 Hz, 1H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm): 118.3, 122.0, 123.8, 125.8, 126.2, 127.5, 127.7, 129.0, 129.7, 130.1, 136.5, 136.9, 147.9, 151.3, 154.4, 169.8.

LRMS (EI) *m/z*: 262 (M^+).

HRMS: Calcd. For. $C_{16}H_{10}N_2S$: 262.0565 Found: 262.0550.

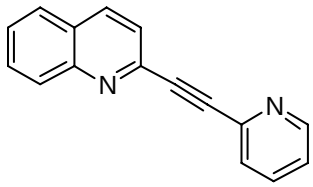
IR (neat): 1595, 1590, 1499, 1452, 1426, 1325, 1308, 1117, 995, 936, 836, 760, 751, 725, 697 cm^{-1}.

Procedure for the reaction of quinoline *N*-oxide with *H*-nucleophiles using organosilicon additive (Table 1, Scheme 3).

Under argon atmosphere, P4-^{t}Bu base (0.03 mL 1.0 M in hexane, 0.03 mmol, or 0.06 mL 1.0 M in hexane, 0.06 mmol) was added to a mixture of quinoline *N*-oxide (43.5 mg, 0.30 mmol), organosilicon additive (0.75 mmol) and *H*-nucleophile (0.45 mmol) in dry solvent (1.0 mL) at room temperature and the mixture was stirred for 24 h at room temperature. After the reaction, saturated aq. NH_4Cl and H_2O were added to the mixture. The mixture was extracted with AcOEt (20 mL x 3). The combined organic layers were then washed with saturated aq. NaCl (50 mL). The solution was dried over $MgSO_4$, filtered, and concentrated

in vacuo. The crude material was purified by SiO_2 column chromatography.

2-(2- Pyridylethynyl)quinoline (7)



Purification by SiO_2 column chromatography (eluting with hexane/ethyl acetate = 1:1), brown oil (42.1 mg, 61 %).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.31–7.33 (m, 1H), 7.56–7.60 (m, 1H), 7.70–7.78 (m, 4H), 7.83 (d, *J* = 8.3 Hz, 1H), 8.15 (d, *J* = 8.3 Hz, 1H), 8.18 (d, *J* = 8.8 Hz, 1H), 8.68 (d, *J* = 4.9 Hz, 1H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm): 88.3, 88.4, 123.5, 124.5, 127.3, 127.4, 127.5, 127.9, 128.8, 129.4, 130.1, 136.2, 142.6, 142.8, 148.2, 150.2.

LRMS (EI) *m/z*: 230 (M^+).

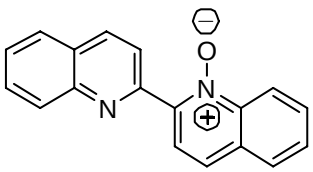
HRMS: Calcd. For. $C_{16}H_{10}N_2$: 230.0844. Found: 230.0839.

IR (neat): 3053, 2926, 1718, 1577, 1465, 1280, 1115, 828, 752 cm^{-1}.

Procedure for the dimerization of quinoline *N*-oxide (Scheme 5).

Under argon atmosphere, P4-^{t}Bu base (0.03 mL 1.0 M in hexane, 0.03 mmol) was added to a mixture of quinoline *N*-oxide (43.5 mg, 0.30 mmol) and trimethylsilyl diethylamine (78.5 mg, 0.54 mmol) in dry DMF (1.0 mL) and the mixture was stirred for 24 h at room temperature. After the reaction, saturated aq. NH_4Cl and H_2O were added to the mixture. The mixture was extracted with AcOEt (20 mL x 3). The combined organic layers were then washed with saturated aq. NaCl (50 mL). The solution was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude material was purified by SiO_2 column chromatography (eluting with hexane/ethyl acetate = 1:1).

Biquinoline *N*-oxide (8)[6]



Recrystallized from ethanol, brown needles (16.3 mg, 40 %), mp: 172–173 ºC.

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.60 (m, 1H), 7.68 (m, 1H), 7.75 (m, 1H), 7.84 (d, *J* = 7.6 Hz,

1H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.90 (m, 2H), 8.19 (d, *J* = 8.3 Hz, 1H), 8.31 (d, *J* = 2.7 Hz, 2H), 8.90 (d, *J* = 8.8 Hz, 1H), 8.95 (d, *J* = 8.8 Hz, 1H).

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm): 120.2, 122.9, 123.7, 125.4, 127.4, 127.5, 128.1, 128.2, 128.9, 129.6, 129.8, 130.3, 130.5, 135.6, 142.3, 143.9, 148.1, 151.5.

LRMS (EI) *m/z*: 272 (M^+).

HRMS: Calcd. For. $C_{18}H_{12}N_2O$: 272.0950. Found: 272.0943.

IR (neat): 3108, 3054, 2920, 1559, 1363, 1123, 877, 834, 765, 744, 730 cm^{-1}.

References

[1] E. J. Corey, P. L. Fuchs, *Tetrahedron Lett.,* 1972, **36**, 3769.

[2] A. Rosiak, W. Frey, J. Christoffers, *Eur. J. Org. Chem.,* 2006, 4044.

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[5] E. A. Reddy, D. K. Barange, A. Islam, A. Mukkanti, M. Pal, *Tetrahedron,* 2008, **64**, 7143.

[6] R. P. Thummel, F. Lefoulon, *J. Org. Chem.,* 1985, **50**, 666.

^{1}H and ^{13}C NMR spectra of the products

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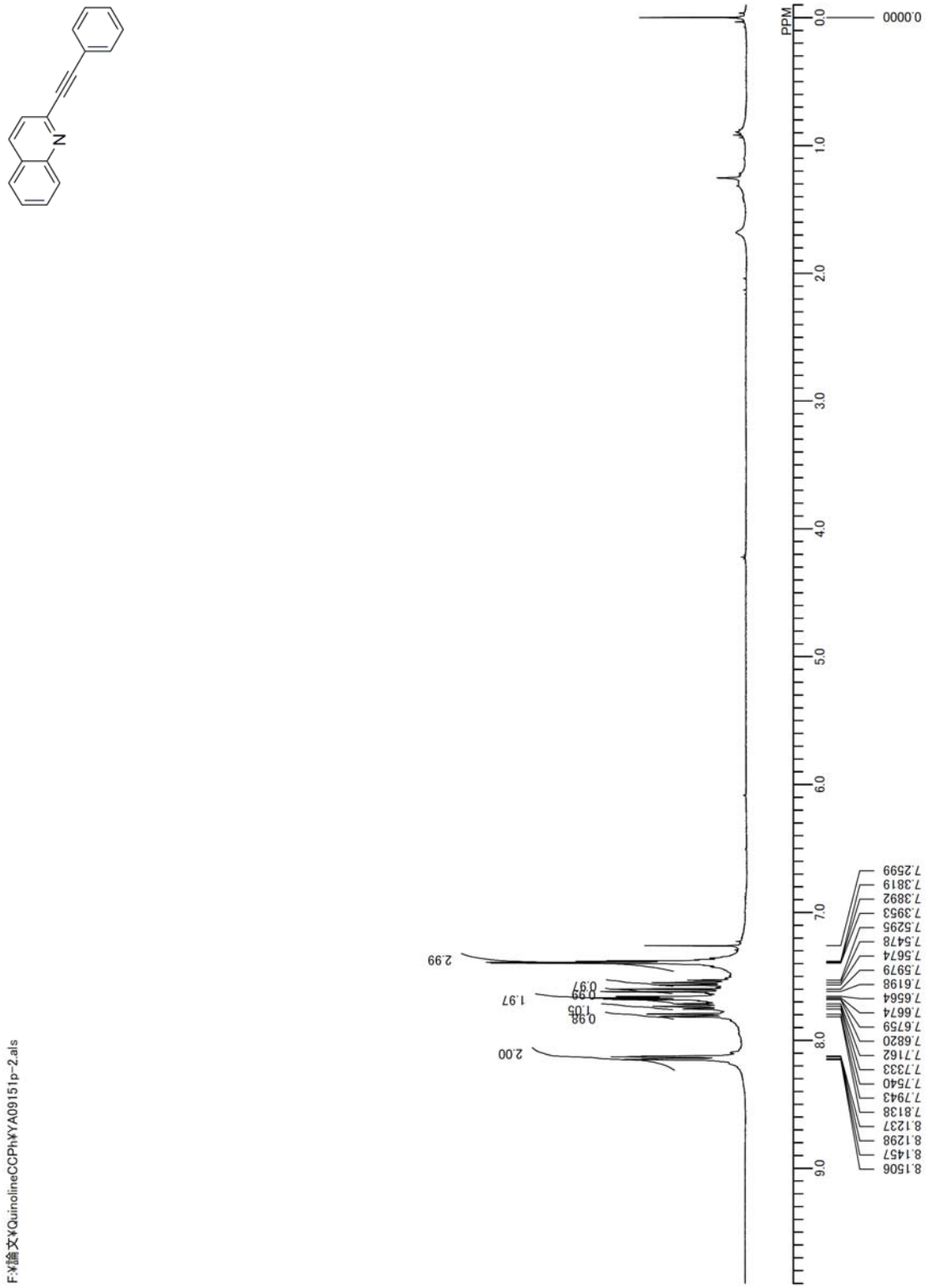

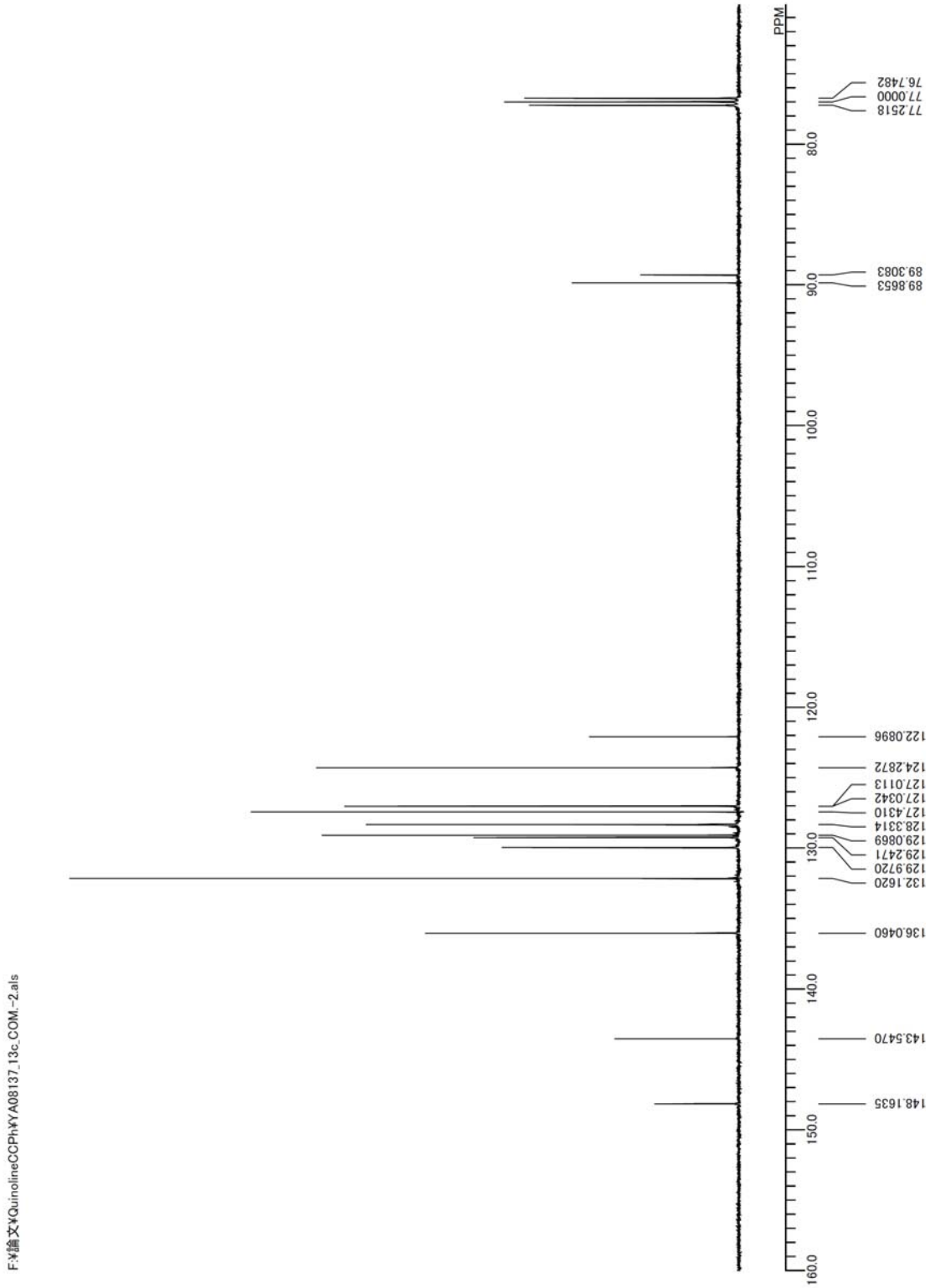
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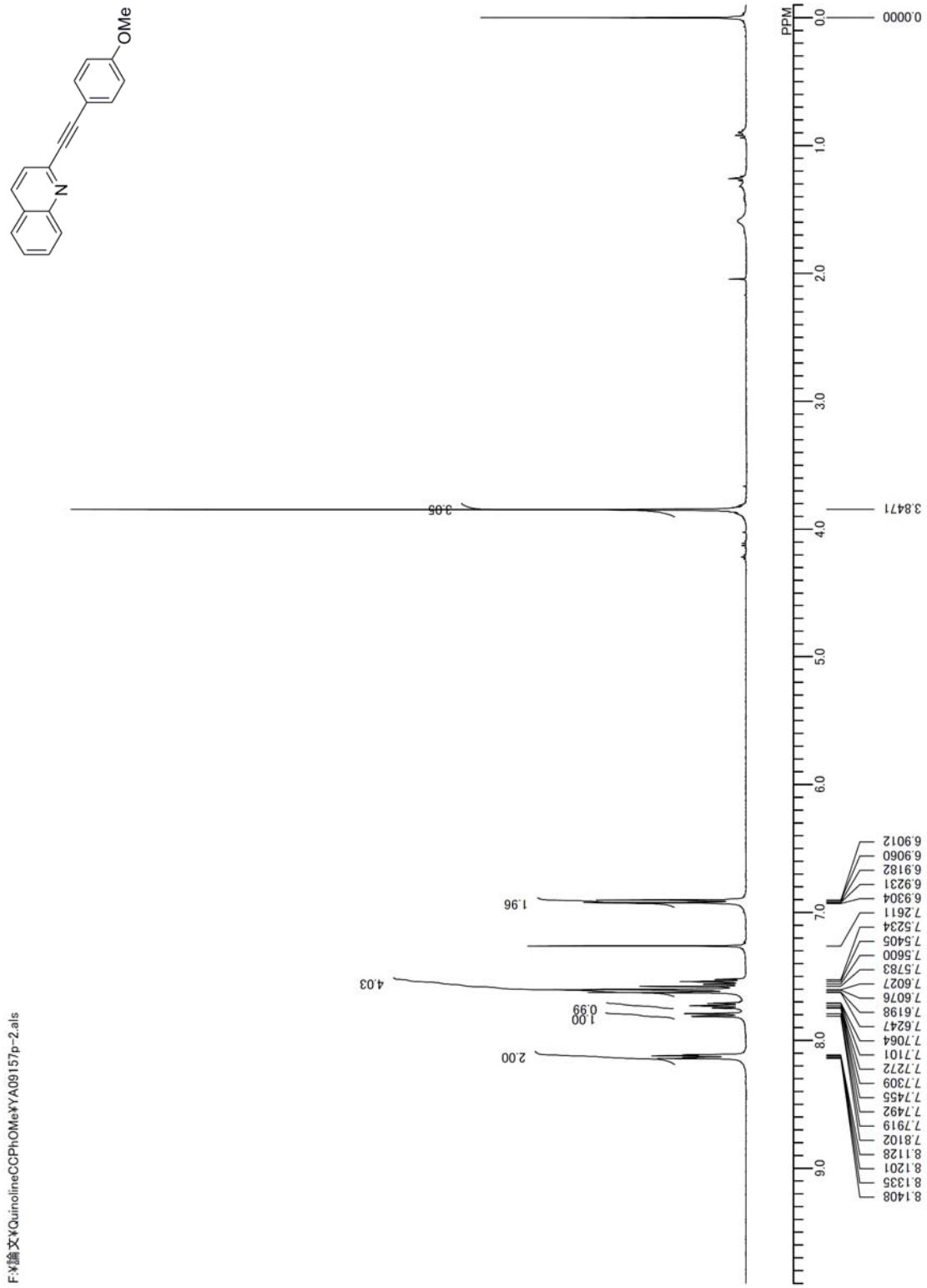
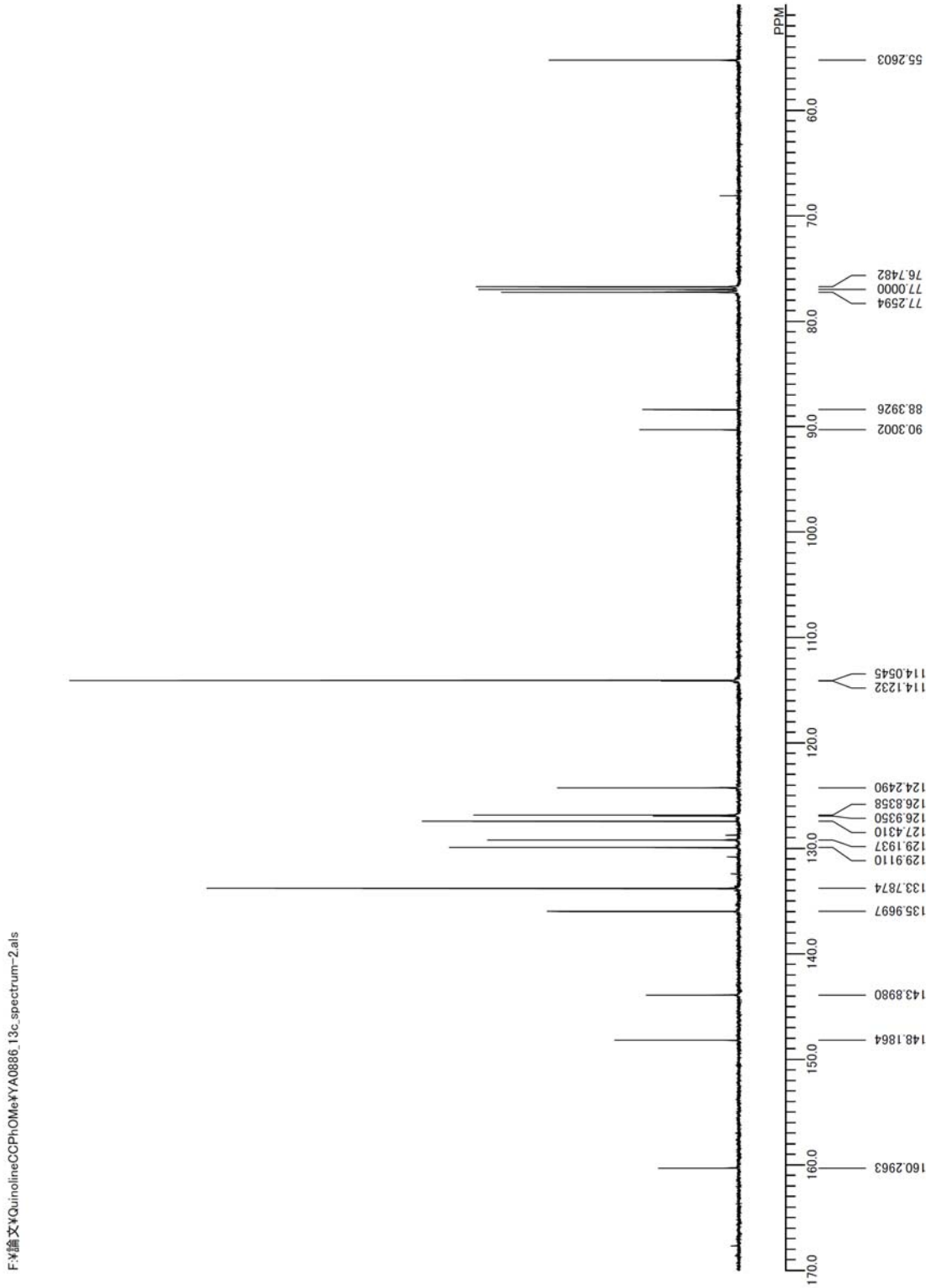
2-(4-Methoxyphenylethynyl)quinoline.

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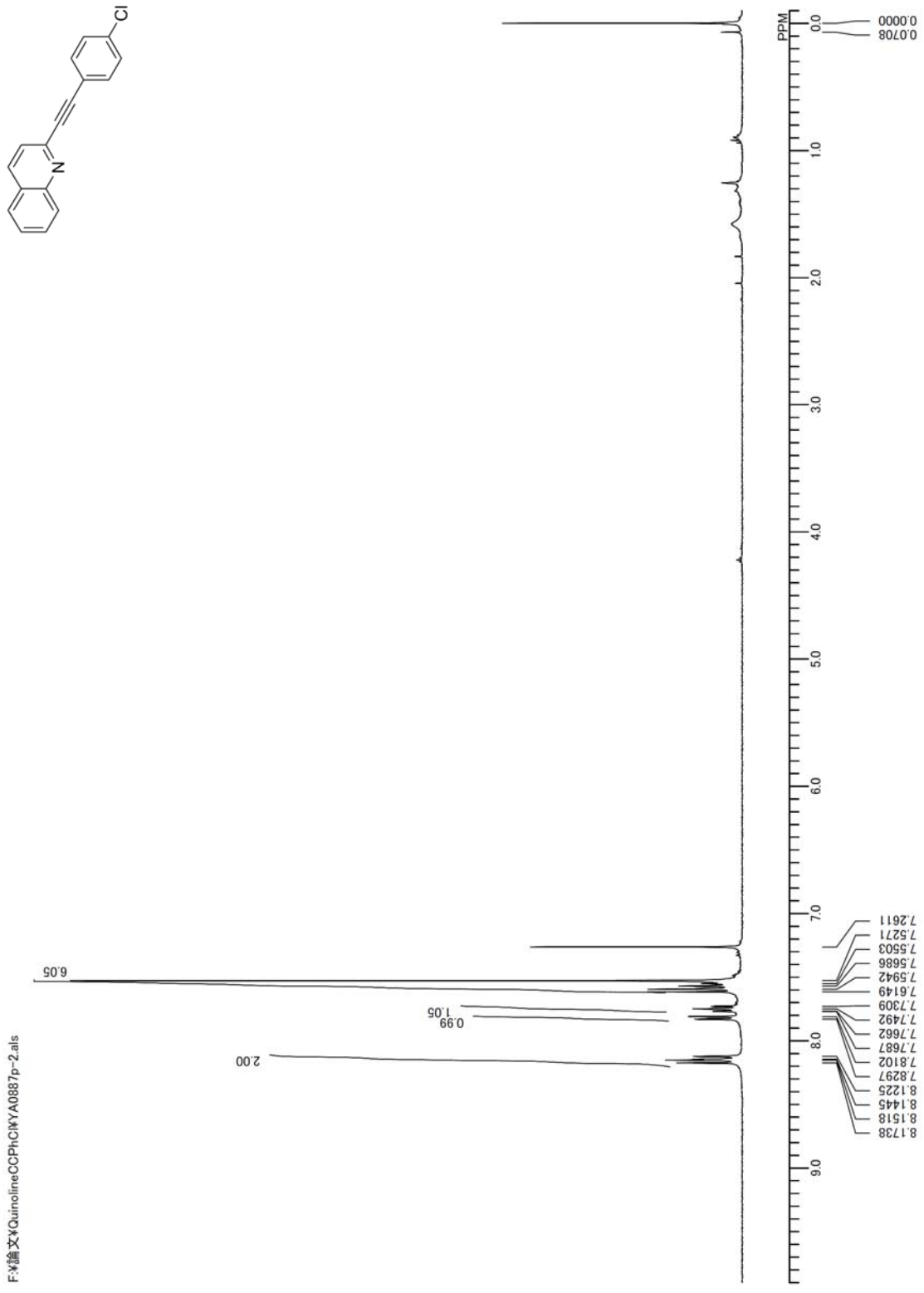
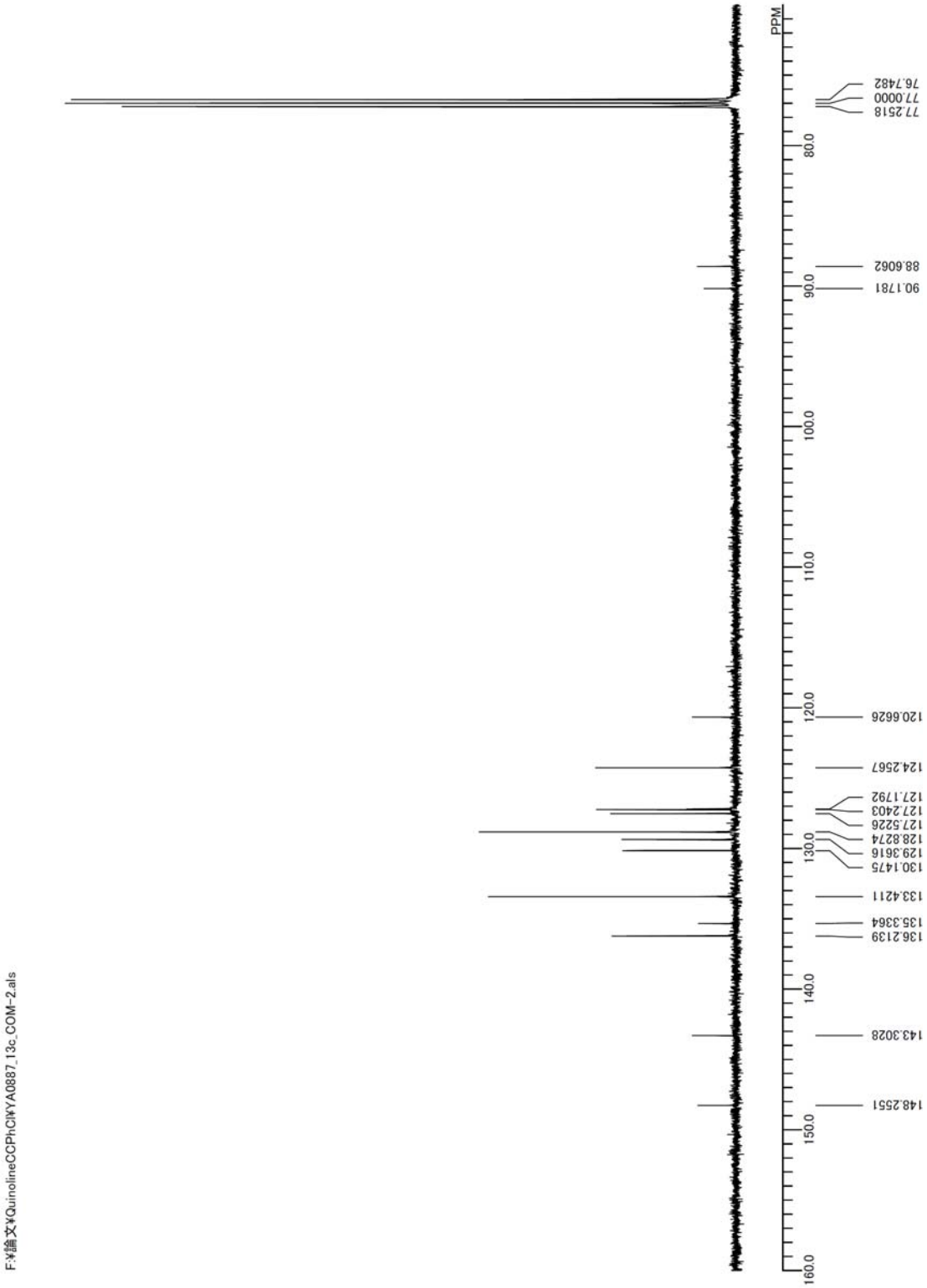
2-(4-Chlorophenylethynyl)quinoline.

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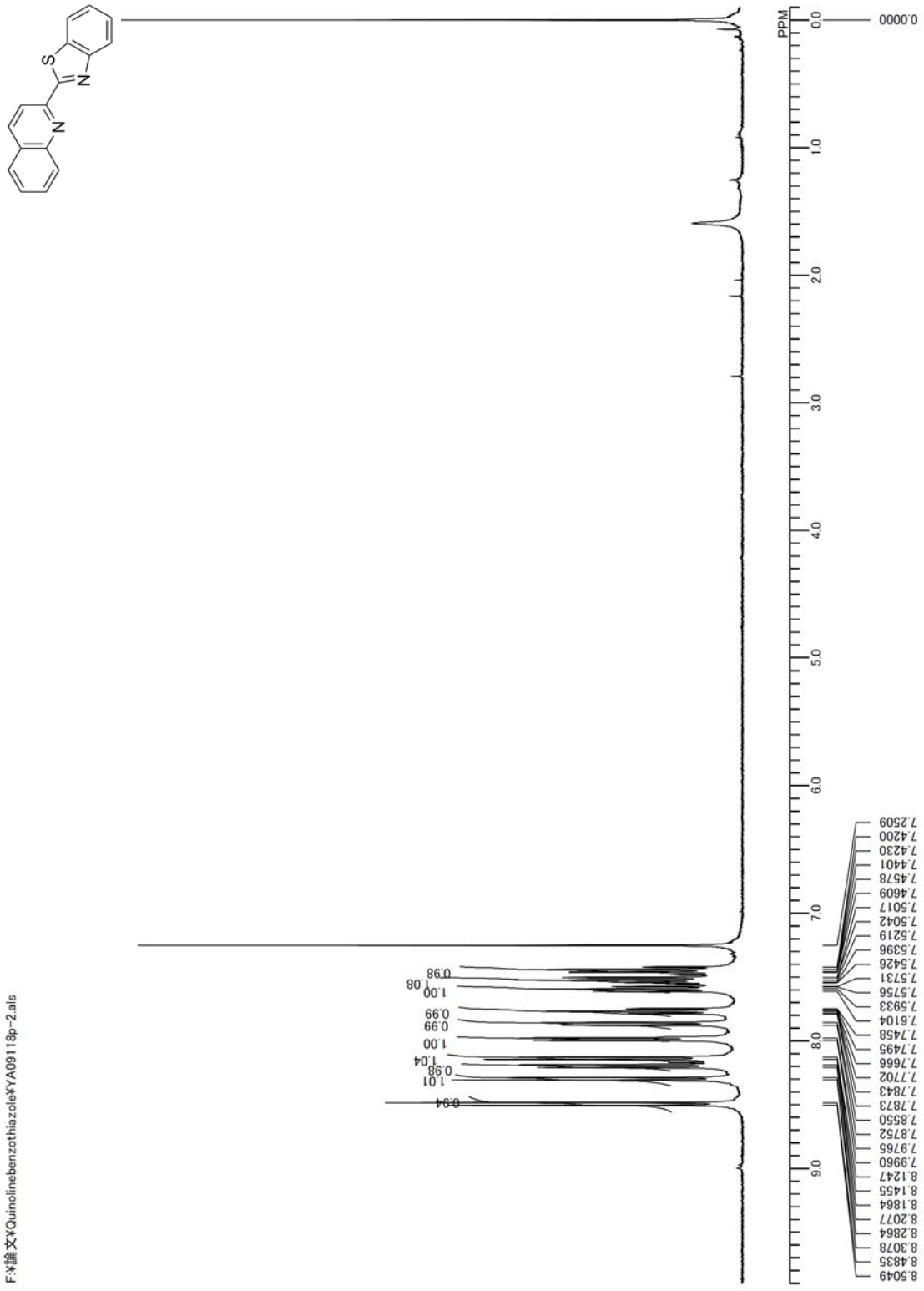
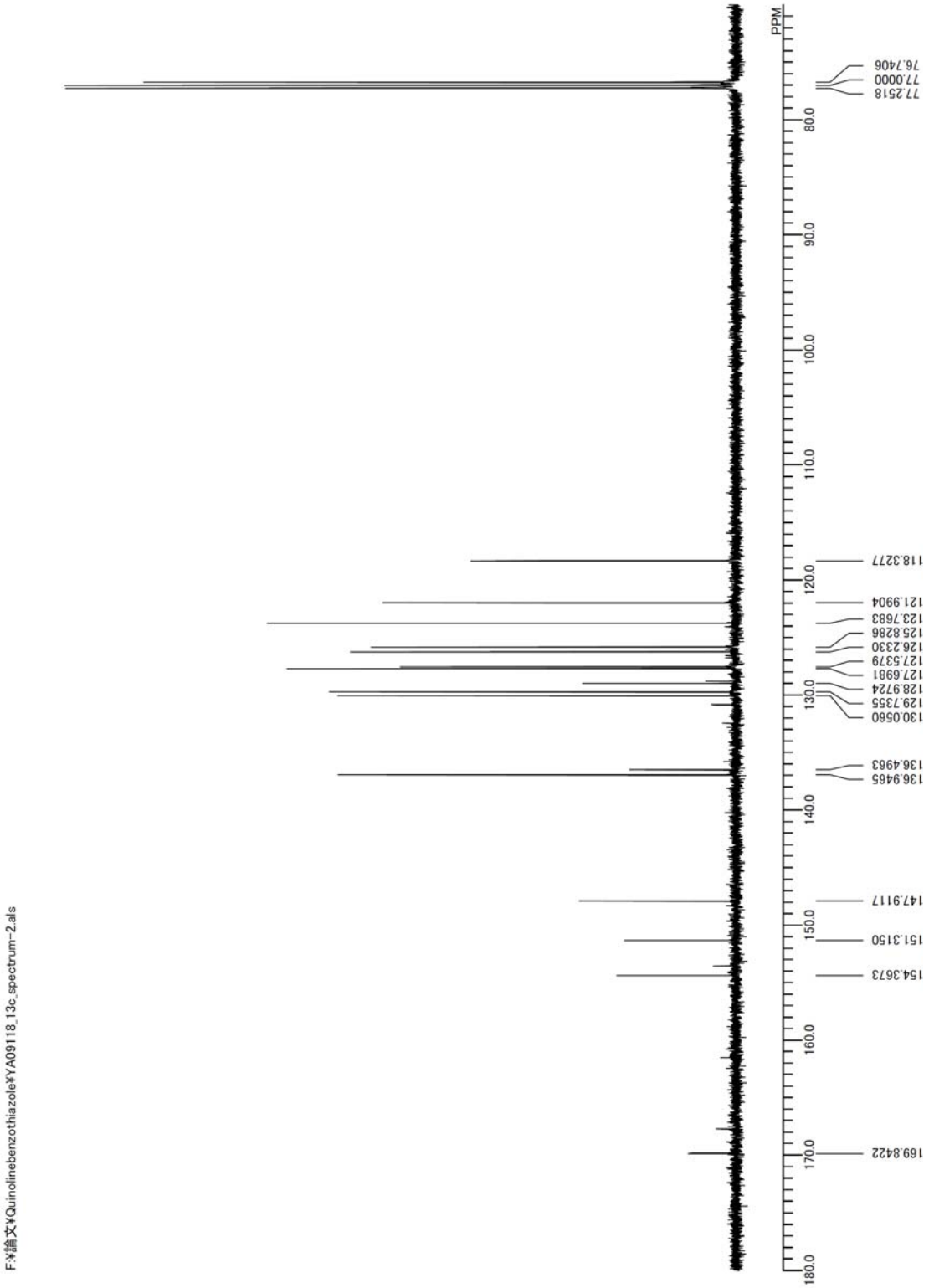
2-(2-Benzothiazolyl)quinoline.

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110.0
120.0
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150.0
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123.7683
125.8286
126.2330
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127.6981
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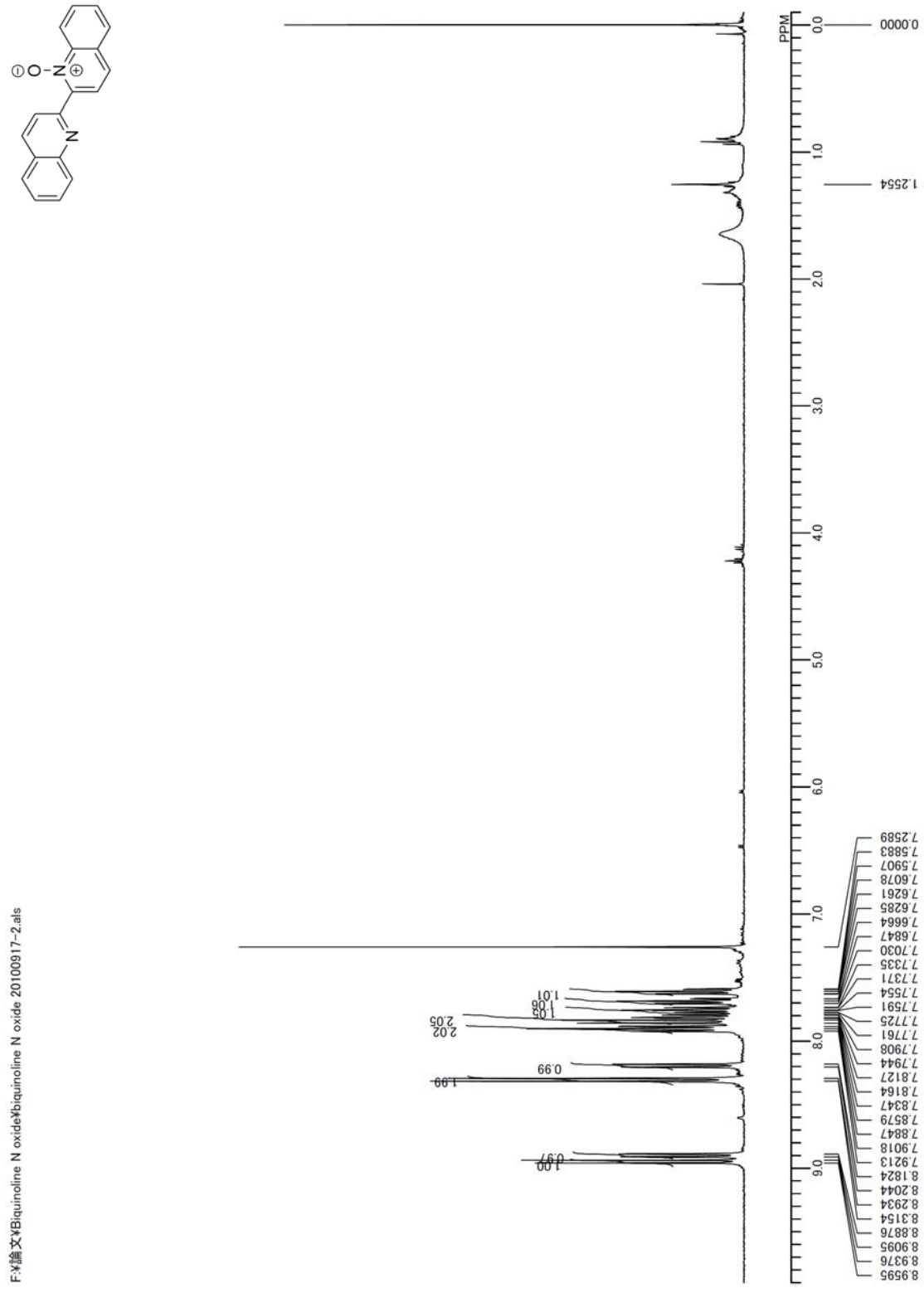
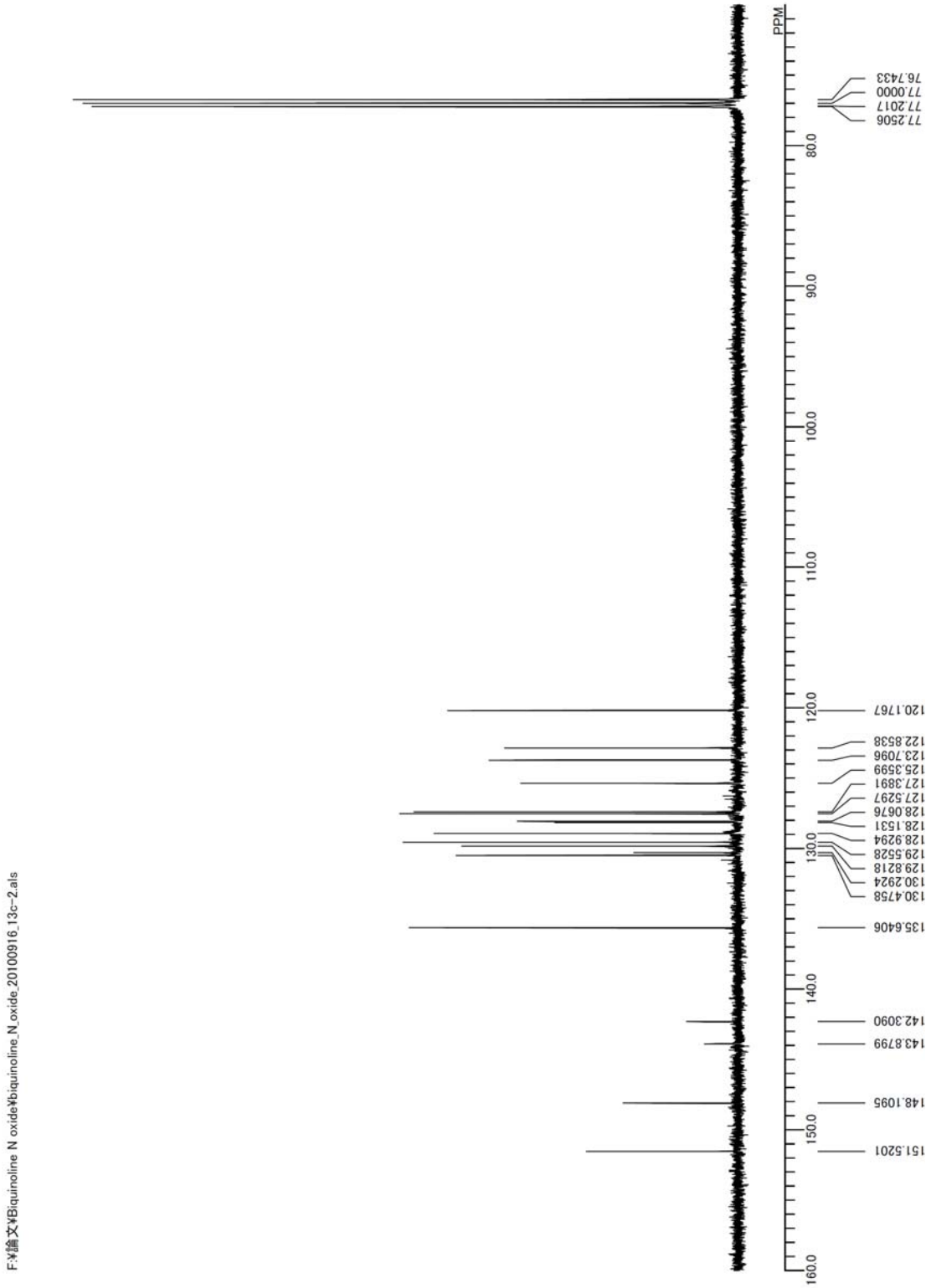
F:¥論文¥Quinolinebenzothiazole¥YA09118_13c_spectrum-2.als

Biquinoline *N*-oxide.




F:¥論文¥Biquinoline N oxide¥biquinoline_N_oxide_20100916_13c~2.als
PPM
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77.2017
77.0000
76.7433
120.1767
122.8538
123.7096
125.3599
127.3891
127.5297
128.0676
128.1531
128.9294
129.5528
129.8218
130.2924
130.4758
135.6406
142.3090
143.8799
148.1095
151.5201