Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers

Copper-Mediated Efficient Three-component Synthesis of 1,2,4-Triazoles from Amines and Nitriles

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Supporting Information

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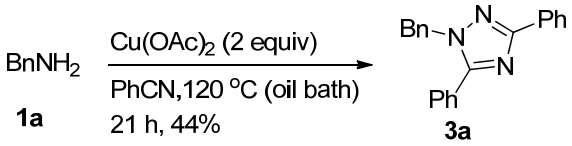
General Information: All reactions were carried out in oven-dried Schlenk tubes. PhCN was dried over calcium hydride before distillation. All the temperatures are referred to the bath temperature. All ^{1}H NMR experiments were measured in relative to the signal of tetramethylsilane (0 ppm) in $CDCl_3$ and ^{13}C NMR experiments were measured in relative to the signal of residual chloroform (77.00 ppm) in $CDCl_3$. ^{19}F NMR experiments were measured with trifluoroacetic acid (-77.00 ppm) or $CFCl_3$ (0 ppm) as the external reference. IR spectra were recorded on the Bruker Tensor 27 infrared spectrometer with the major peaks listed. Melting points were measured without correction. Copper(II) acetate anhydrous (98.5%) was purchased from J&K, other common reagents were purchased from commercial sources and used without further purification unless noted otherwise. Column chromatography was performed using silica gel (H) eluting with ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates.

Microwave irradiation experiments

For reactions run in sealed microwave vials, oven-dried 5 mL vials containing a Teflon-coated stirring bar and sealed with a Teflon-lined septum were used. All microwave irradiation experiments were carried out with a MILESTONE S.r.l (MicroSYNTH 131718)® microwave reactor, operating at a frequency of 50 Hz with continuous irradiation power from 0 to 800 W utilizing the standard absorbance level of 800 W maximum power. The instrument was used in the standard configuration as delivered, including proprietary software. The temperature was measured with an IR

sensor on the outer surface of the process vial. After irradiation, reaction vessels were cooled rapidly to ambient temperature by gas jet cooling.

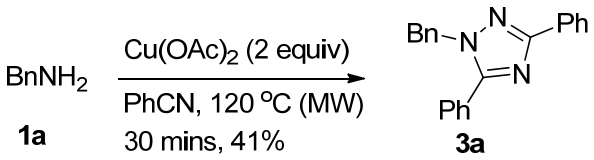
1. 1-Benzyl-3,5-diphenyl-1*H*-1,2,4-triazole (3a) (cb-5-117, 11-94, 9-112)



Method A: To a dried Schlenk tube were added $Cu(OAc)_2$ (367.9 mg, 2 mmol), $BnNH_2$ (108.6 mg, 1 mmol)/PhCN (2 mL) sequentially at room temperature. After stirring at 120 ^oC (oil bath) for 21 h, the resulting mixture was cooled to room temperature, diluted with 50 mL of Et_2O, filtered through a short pad of silica gel and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 40/1 to 10/1) to afford **3a** (139.7 mg, 44%): solid; ^1H NMR (300 MHz, $CDCl_3$) δ 8.25-8.14 (m, 2 H, ArH), 7.66-7.57 (m, 2 H, ArH), 7.52-7.16 (m, 11 H, ArH), 5.40 (s, 2 H, CH_2).

Gram-scale synthesis of 3a:

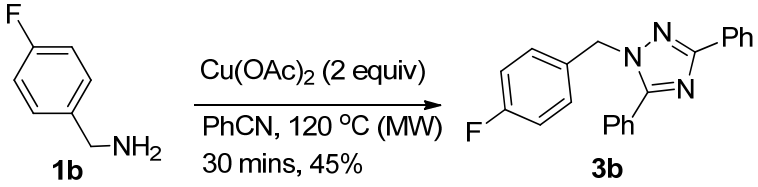
To a dried three-necked flask were added $Cu(OAc)_2$ (3.6321 g, 20 mmol), $BnNH_2$ (1.0704 g, 10 mmol)/PhCN (20 mL) sequentially at room temperature. After stirring at 120 ^oC (oil bath) for 48 h, the resulting mixture was cooled to room temperature, diluted with 50 mL of Et_2O, filtered through a short pad of silica gel and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 30/1 to 15/1) to afford 3a (1.3062 g, 42%): solid; 1H NMR (300 MHz, CDCl3) δ 8.27-8.14 (m, 2 H, ArH), 7.64-7.52 (m, 2 H, ArH), 7.51-7.27 (m, 9 H, ArH), 7.25-7.16 (m, 2 H, ArH), 5.46 (s, 2 H, CH2).



Method B: To a dried MW tube were added $Cu(OAc)_2$ (363.9 mg, 2 mmol), $BnNH_2$ (106.8 mg, 1 mmol)/PhCN (5 mL) sequentially at room temperature. The tube was sealed and irradiated in a microwave reactor (120 ^oC, 30 minutes, maximum power 800 W). Then, the resulting mixture was cooled to room temperature with a stream of air, diluted with 50 mL of Et_2O, filtered through a short pad of silica gel and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10/1) to afford **3a**[1] (127.0 mg, 41%): solid; m.p. 99-100 ^oC (hexane/Et_2O) (lit. m.p. 98.5-99.5 ^oC); ^1H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 7.2 Hz, 2 H, ArH), 7.62-7.51 (m, 2 H, ArH), 7.48-7.13 (m, 11 H, ArH), 5.39 (s, 2 H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 156.0, 135.9, 130.9, 130.0, 129.0, 128.70, 128.67, 128.6, 128.4, 127.9, 127.8, 126.6, 126.3, 52.6. IR (neat) 1519, 1497, 1476, 1463, 1443, 1406, 1353 cm^{-1}; MS (EI) (*m/z*) 312 ($(M+1)^+$, 5.71), 311 (M^+, 27.09), 91 (100).

The following compounds were prepared according to **Method A or B** in main text.

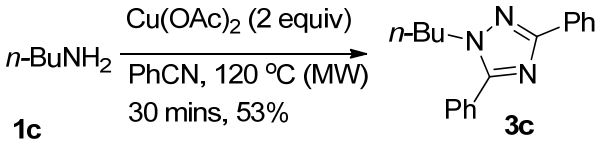
2. 1-(4-Fluorobenzyl)-3,5-diphenyl-1*H*-1,2,4-triazole (3b) (cb-9-144)



Method B: The reaction of $Cu(OAc)_2$ (362.4 mg, 2 mmol), 4-fluorobenzylamine (129.7 mg, 97% purity, 1 mmol), and PhCN (5 mL) afforded **3b** (150.3 mg, 45%)

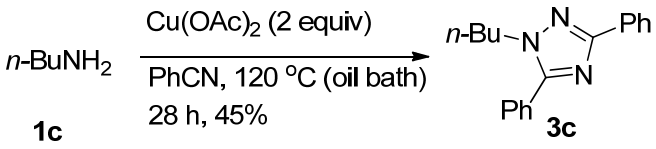
(eluent: petroleum ether/ethyl acetate = 10/1): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24-8.16 (m, 2 H, ArH), 7.64-7.52 (m, 2 H, ArH), 7.50-7.33 (m, 6 H, ArH), 7.20-7.10 (m, 2 H, ArH), 7.05-6.92 (m, 2 H, ArH), 5.37 (s, 2 H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.2 (d, *J* = 245.9 Hz), 161.5, 155.9, 131.6 (d, *J* = 3.5 Hz), 130.8, 130.2, 129.2, 128.8, 128.63, 128.61 (d, *J* = 8.1 Hz), 128.45, 127.8, 126.3, 115.7 (d, *J* = 20.9 Hz), 51.9; ^{19}F NMR ($CDCl_3$, 282 MHz) -113.9; IR (neat) 1605, 1509, 1478, 1458, 1446, 1405, 1353, 1222, 1156, 1141, 1016 cm^{-1}; MS (EI) (*m/z*) 330 ($(M+1)^+$, 11.24), 329 (M^+, 49.41), 109 (100); HRMS calcd for $C_{21}H_{16}N_3F$ (M^+): 329.1328, found: 329.1329.

3. 1-Butyl-3,5-diphenyl-1*H*-1,2,4-triazole (3c) (cb-9-114, 9-117)



1c **3c**

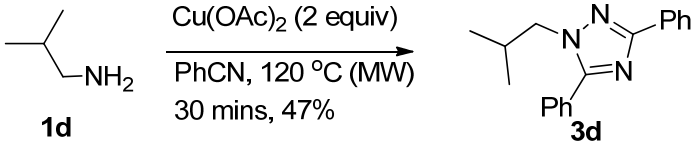
Method B: The reaction of $Cu(OAc)_2$ (363.9 mg, 2 mmol), *n*-$BuNH_2$ (73.1 mg, 1 mmol), and PhCN (5 mL) afforded **3c** (147.8 mg, 53%) (eluent: petroleum ether/ethyl acetate = 10/1): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.2 Hz, 2 H, ArH), 7.66-7.61 (m, 2 H, ArH), 7.60-7.24 (m, 6 H, ArH), 4.18 (t, *J* = 7.2 Hz, 2 H, NCH_2), 2.00-1.83 (m, 2 H, CH_2), 1.40-1.21 (m, 2 H, CH_2), 0.86 (t, *J* = 7.2 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.0, 155.3, 131.1, 129.8, 128.8, 128.6, 128.3, 126.2, 48.8, 31.9, 19.5, 13.3; IR (neat) 3068, 2959, 2933, 2873, 1519, 1476, 1463, 1442, 1410, 1354, 1132, 1019 cm^{-1}; MS (EI) (*m/z*) 278 ($(M+1)^+$, 11.49), 277 (M^+, 55.63), 234 (100); HRMS calcd for $C_{18}H_{19}N_3$ (M^+): 277.1579, found: 277.1578.



1c 3c

Method A: The reaction of $Cu(OAc)_2$ (363.2 mg, 2 mmol), *n*-$BuNH_2$ (74.0 mg, 1 mmol), and PhCN (2 mL) afforded **3c** (125.3 mg, 45%) (eluent: petroleum ether/ethyl acetate = 10/1): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.5 Hz, 2 H, ArH), 7.66-7.60 (m, 2 H, ArH), 7.59-7.30 (m, 6 H, ArH), 4.20 (t, *J* = 7.2 Hz, 2 H, NCH_2), 2.00-1.80 (m, 2 H, CH_2), 1.40-1.21 (m, 2 H, CH_2), 0.87 (t, *J* = 7.2 Hz, 3 H, CH_3).

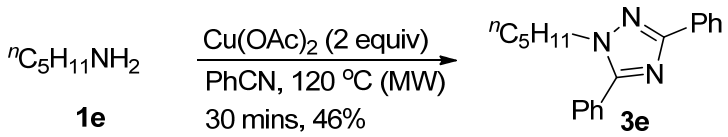
4. 1-Isobutyl-3,5-diphenyl-1*H*-1,2,4-triazole (3d) (cb-11-146)



1d 3d

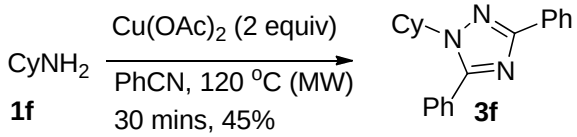
Method B: The reaction of $Cu(OAc)_2$ (362.5 mg, 2 mmol), isobutylNH_2 (74.1 mg, 1 mmol), and PhCN (5 mL) afforded **3d** (132.4 mg, 47%) (eluent: petroleum ether/ethyl acetate = 10/1): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.2 Hz, 2 H, ArH), 7.68-7.57 (m, 2 H, ArH), 7.55-7.30 (m, 6 H, ArH), 4.02 (d, *J* = 7.2 Hz, 2 H, NCH_2), 2.45-2.25 (m, 1 H, CH), 0.86 (d, *J* = 6.6 Hz, 6 H, $(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.0, 156.0, 131.1, 129.8, 128.9, 128.7, 128.5, 128.4, 126.3, 56.2, 29.2, 19.7; IR (neat) 1519, 1476, 1462, 1441, 1409, 1390, 1354, 1284, 1193, 1173, 1132, 1098, 1070, 1040, 1027, 1018 cm^{-1}; MS (EI) (*m/z*) 278 ($(M+1)^+$, 14.65), 277 (M^+, 67.21), 104 (100); HRMS calcd for $C_{18}H_{19}N_3$ (M^+): 277.1579, found: 277.1577.

5. 1-Pentyl-3,5-diphenyl-1*H*-1,2,4-triazole (3e) (cb-9-140)



Method B: The reaction of $Cu(OAc)_2$ (363.3 mg, 2 mmol), $^nC_5H_{11}NH_2$ (88.1 mg, 1 mmol), and PhCN (5 mL) afforded **3e** (135.1 mg, 46%) (eluent: petroleum ether/ethyl acetate = 15/1): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.5 Hz, 2 H, ArH), 7.72-7.60 (m, 2 H, ArH), 7.55-7.30 (m, 6 H, ArH), 4.19 (t, *J* = 7.4 Hz, 2 H, NCH_2), 2.00-1.82 (m, 2 H, CH_2), 1.38-1.20 (m, 4 H, -$(CH_2)_2$-), 0.85 (t, *J* = 5.9 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.1, 155.4, 131.1, 129.9, 128.9, 128.7, 128.4, 126.3, 49.2, 29.7, 28.5, 22.0, 13.8; IR (neat) 2958, 2926, 2856, 1476, 1463, 1441, 1408, 1355 cm^{-1}; MS (EI) (*m/z*) 292 ($(M+1)^+$, 12.96), 291 (M^+, 59.60), 234 (100); HRMS calcd for $C_{19}H_{21}N_3$ (M^+): 291.1735, found: 291.1734.

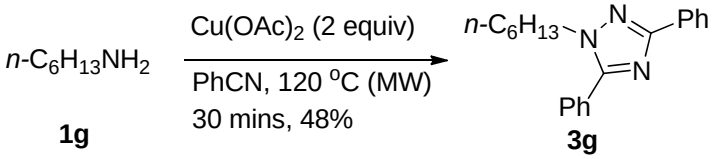
6. 1-Cyclohexyl-3,5-diphenyl-1*H*-1,2,4-triazole (3f) (cb-9-122)



Method B: The reaction of $Cu(OAc)_2$ (363.1 mg, 2 mmol), $CyNH_2$ (99.4 mg, 1 mmol), and PhCN (5 mL) afforded **3f**[2] (137.7 mg, 45%) (eluent: petroleum ether/ethyl acetate = 10/1): solid, 107-108 °C (petroleum ether /Et_2O) (lit. m.p. 106-107 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.8 Hz, 2 H, ArH), 7.68-7.57 (m, 2 H, ArH), 7.56-7.47 (m, 3 H, ArH), 7.46-7.30 (m, 3 H, ArH), 4.22 (tt, *J* = 11.4, 4.1 Hz, 1 H, NCH_2), 2.23-2.02 (m, 2 H, CH_2), 2.02-1.80 (m, 4 H, -$(CH_2)_2$-), 1.78-1.61 (m, 1 H, one proton in CH_2), 1.40-1.20 (m, 3 H, three proton in $(CH_2)_2$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.9, 154.6, 131.4, 129.8, 128.9, 128.8, 128.7, 128.4, 126.3,

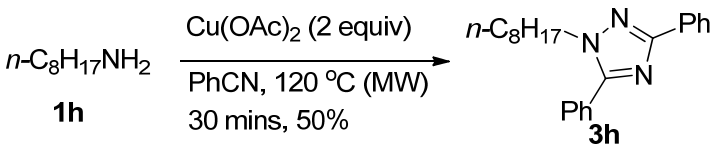
58.0, 33.1, 25.4, 24.9; IR (neat) 2955, 2941, 2853, 1515, 1476, 1455, 1438, 1402, 1380, 1350, 1326, 1300, 1263, 1174, 1131, 1071, 1025, 1019 cm^{-1}; MS (EI) (*m/z*) 304 ($(M+1)^+$, 8.77), 303 (M^+, 36.94), 221 (100).

7. 1-Hexyl-3,5-diphenyl-1*H*-1,2,4-triazole (3g) (cb-9-130)



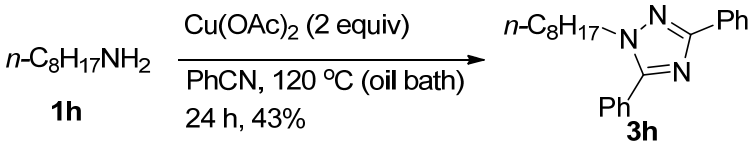
Method B: The reaction of $Cu(OAc)_2$ (363.5 mg, 2 mmol), *n*-$C_6H_{13}NH_2$ (102.0 mg, 1 mmol), and PhCN (5 mL) afforded **3g** (146.1 mg, 48%) (eluent: petroleum ether/ethyl acetate = 10/1): oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.2 Hz, 2 H, ArH), 7.70-7.63 (m, 2 H, ArH), 7.59-7.50 (m, 3 H, ArH), 7.49-7.35 (m, 3 H, ArH), 4.21 (t, *J* = 7.4 Hz, 2 H, NCH_2), 2.00-1.87 (m, 2 H, CH_2), 1.36-1.20 (m, 6 H, -$(CH_2)_3$-), 0.85 (t, *J* = 6.8 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.1, 155.4, 131.2, 129.9, 128.9, 128.8, 128.4, 126.3, 49.2, 31.1, 30.0, 26.1, 22.4, 13.9; IR (neat) 3068, 2954, 2928, 2857, 1519, 1476, 1463, 1441, 1409, 1377, 1353, 1302, 1283, 1173, 1132, 1102, 1070, 1018 cm^{-1}; MS (EI) (*m/z*) 306 ($(M+1)^+$, 11.44), 305 (M^+, 50.21), 234 (100); HRMS calcd for $C_{20}H_{23}N_3$ (M^+): 305.1892, found: 305.1893.

8. 1-Octyl-3,5-diphenyl-1*H*-1,2,4-triazole (3h) (cb-9-141, cb-9-150)



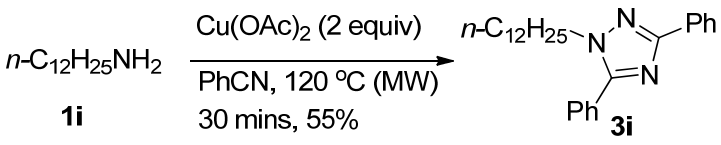
Method B: The reaction of $Cu(OAc)_2$ (363.8 mg, 2 mmol), *n*-$C_8H_{17}NH_2$ (128.5 mg, 1 mmol), and PhCN (5 mL) afford **3h**[3] (166.9 mg, 50%) (eluent: petroleum ether/ethyl acetate = 15/1): oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.8 Hz, 2

H, ArH), 7.67-7.60 (m, 2 H, ArH), 7.53-7.30 (m, 6 H, ArH), 4.19 (t, J = 7.4 Hz, 2 H, NCH_2), 2.00-1.83 (m, 2 H, CH_2), 1.38-1.07 (m, 10 H, -$(CH_2)_5$-), 0.85 (t, J = 6.5 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.0, 155.4, 131.1, 129.8, 128.9, 128.7, 128.4, 126.2, 49.1, 31.6, 30.0, 28.9, 28.8, 26.3, 22.5, 13.9; IR (neat) 2926, 2855, 1519, 1476, 1442, 1354, 1133, 1071 cm^{-1}; MS (EI) (*m/z*) 334 ($(M+1)^+$, 3.84), 333 (M^+, 17.96), 221 (100).



Method A: The reaction of $Cu(OAc)_2$ (363.4 mg, 2 mmol), *n*-$C_8H_{17}NH_2$ (128.9 mg, 1 mmol), and PhCN (2 mL) afforded **3h** (143.6 mg, 43%) (eluent: petroleum ether/ethyl acetate = 10/1): oil; ^1H NMR (300 MHz, $CDCl_3$) δ 8.22-8.14 (m, 2 H, ArH), 7.69-7.60 (m, 2 H, ArH), 7.55-7.30 (m, 6 H, ArH), 4.20 (t, J = 7.4 Hz, 2 H, NCH_2), 2.00-1.84 (m, 2 H, CH_2), 1.38-1.15 (m, 10 H, -$(CH_2)_5$-), 0.86 (t, J = 6.8 Hz, 3 H, CH_3)

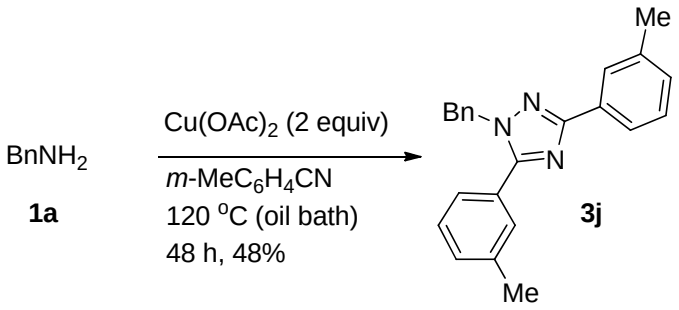
9. 1-Dodecyl-3,5-diphenyl-1*H*-1,2,4-triazole (3i) (cb-9-131)



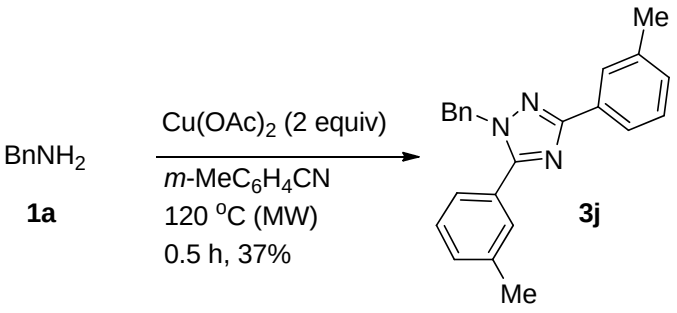
Method B: The reaction of $Cu(OAc)_2$ (363.4 mg, 2 mmol), *n*-$C_{12}H_{25}NH_2$ (185.7 mg, 1 mmol), and PhCN (5 mL) afforded **3i** (214.7 mg, 55%) (eluent: petroleum ether/ethyl acetate = 10/1): oil; ^1H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, J = 7.5 Hz, 2 H, ArH), 7.72-7.60 (m, 2 H, ArH), 7.58-7.30 (m, 6 H, ArH), 4.20 (t, J = 7.2 Hz, 2 H, NCH_2), 2.00-1.82 (m, 2 H, CH_2), 1.38-1.12 (m, 18 H, -$(CH_2)_9$-), 0.88 (t, J = 6.0 Hz, 3

H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.1, 155.5, 131.2, 129.9, 128.9, 128.81, 128.79, 128.4, 126.3, 49.2, 31.8, 30.1, 29.5, 29.4, 29.34, 29.27, 28.9, 26.4, 22.6, 14.1; IR (neat) 2924, 2853, 1464, 1442, 1354, 1018 cm^{-1}; MS (EI) (*m/z*) 390 ($(M+1)^+$, 5.76), 389 (M^+, 19.41), 221 (100); HRMS calcd for $C_{26}H_{35}N_3$ (M^+): 389.2831, found: 389.2832.

10. 1-Benzyl-3,5-di(*m*-tolyl)-1*H*-1,2,4-triazole (3j) (cb-11-68, kjq-2-55)

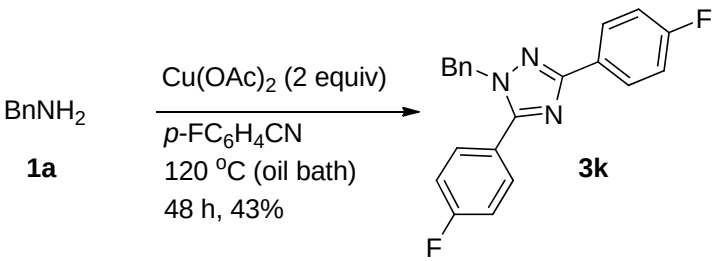


Method A: The reaction of $Cu(OAc)_2$ (363.4 mg, 2 mmol), $BnNH_2$ (107.1 mg, 1 mmol), and *m*-MeC_6H_4CN (2 mL) afforded **3j** (163.8 mg, 48%) (eluent: petroleum ether/ethyl acetate = 15/1): oil; ^1H NMR (300 MHz, $CDCl_3$) δ 8.10-7.95 (m, 2 H, ArH), 7.46 (s, 1 H, ArH), 7.39-7.15 (m, 10 H, ArH), 5.40 (s, 2 H, NCH_2), 2.38 (s, 3 H, Me), 2.33 (s, 3 H, Me); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 156.0, 138.5, 138.0, 136.0, 130.7, 129.8, 129.4, 128.6, 128.5, 128.3, 127.71, 127.67, 126.8, 126.6, 125.4, 123.4, 52.5, 21.19, 21.14; IR (neat) 1611, 1592, 1512, 1496, 1452, 1433, 1358, 1339, 1301, 1262, 1143 cm^{-1}; MS (EI) (*m/z*) 340 ($(M+1)^+$, 23.42), 339 (M^+, 94.69), 91 (100); HRMS calcd for $C_{23}H_{21}N_3$ (M^+): 339.1735, found: 339.1736.



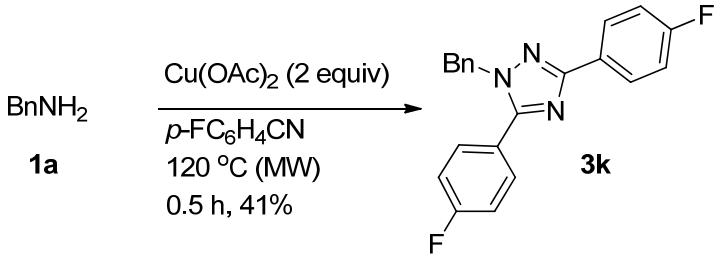
Method B: The reaction of $Cu(OAc)_2$ (362.7 mg, 2 mmol), $BnNH_2$ (107.4 mg, 1 mmol), and *m*-MeC_6H_4CN (5 mL) afforded **3j** (126.9 mg, 37%) (eluent: petroleum ether/ethyl acetate = 15/1): oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1 H, ArH), 7.99 (d, *J* = 7.6 Hz, 1 H, ArH), 7.47 (s, 1 H, ArH), 7.39-7.27 (m, 7 H, ArH), 7.24-7.19 (m, 3 H, ArH), 5.45 (s, 2 H, NCH_2), 2.42 (s, 3 H, Me), 2.38 (s, 3 H, Me).

11. 1-Benzyl-3,5-bis(4-fluorophenyl)-1*H*-1,2,4-triazole (3k) (cb-12-66, kjq-2-56)



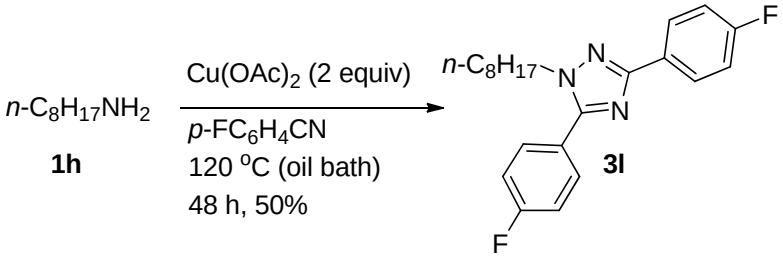
Method A: The reaction of $Cu(OAc)_2$ (363.1 mg, 2 mmol), $BnNH_2$ (107.0 mg, 1 mmol), and *p*-FC_6H_4CN (2 mL) afforded **3k** (150.1 mg, 43%) (eluent: petroleum ether/ethyl acetate = 30/1 to 15/1 for twice): solid, 165-166 °C (Et_2O/petroleum ether); ^1H NMR (300 MHz, $CDCl_3$) δ 8.20-8.11 (m, 2 H, ArH), 7.66-7.56 (m, 2 H, ArH), 7.40-7.28 (m, 3 H, ArH), 7.24-7.05 (m, 6 H, ArH), 5.42 (s, 2 H, NCH_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.8 (d, *J* = 249.9 Hz), 163.5 (d, *J* = 247.1 Hz), 160.8, 155.2, 135.8, 130.8 (d, *J* = 9.2 Hz), 129.0, 128.3 (d, *J* = 8.0 Hz), 128.1, 127.1 (d, *J* = 3.0 Hz), 126.7, 124.0 (d, *J* = 3.2 Hz), 116.1 (d, *J* = 22.0 Hz), 115.5 (d, *J* = 21.2 Hz), 52.8; ^{19}F NMR ($CDCl_3$, 282 MHz) –109.4, -112.1; IR (neat) 1600, 1543, 1527, 1494,

1474, 1456, 1439, 1426, 1363, 1339, 1318, 1290, 1237, 1215, 1157, 1126, 1096, 1077, 1030, 1014 cm^{-1}; MS (EI) (*m/z*) 347 ($(M)^+$, 41.56), 91 (100); elemental analysis calcd (%) for $C_{21}H_{15}N_3F_2$: C 72.61, H 4.35, N 12.10; found: C 72.63, H 4.47, N 11.97.



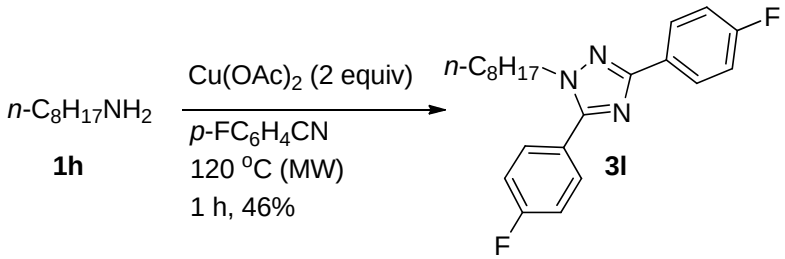
Method B: The reaction of $Cu(OAc)_2$ (363.5 mg, 2 mmol), $BnNH_2$ (107.1 mg, 1 mmol), and *p*-FC_6H_4CN (5 mL) afforded **3k** (142.4 mg, 41%) (eluent: petroleum ether to petroleum ether/ethyl acetate = 30/1): solid; ^1H NMR (400 MHz, $CDCl_3$) δ 8.23-8.10 (m, 2 H, ArH), 7.65-7.55 (m, 2 H, ArH), 7.41-7.29 (m, 3 H, ArH), 7.24-7.05 (m, 6 H, ArH), 5.43 (s, 2 H, NCH_2).

12. 1-Octyl-3,5-bis(4-fluorophenyl)-1*H*-1,2,4-triazole (3l) (cb-12-68, kjq-2-58)



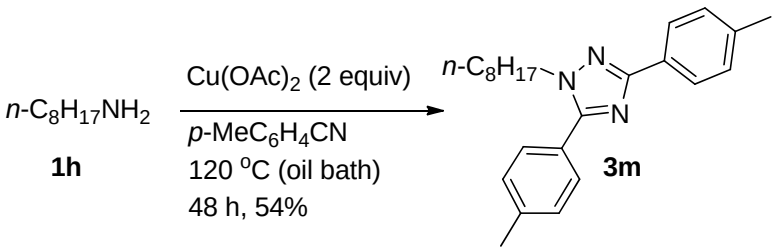
Method A: The reaction of $Cu(OAc)_2$ (363.2 mg, 2 mmol), *n*-$C_8H_{17}NH_2$ (129.1 mg, 1 mmol), and *p*-FC_6H_4CN (2 mL) afforded **3l** (186.4 mg, 50%) (eluent: petroleum ether/ethyl acetate = 30/1 to 15/1 for twice): solid, 56-58 °C (petroleum ether/Et_2O); ^1H NMR (300 MHz, $CDCl_3$) δ 8.20-8.10 (m, 2 H, ArH), 7.69-7.58 (m, 2 H, ArH), 7.26-7.06 (m, 4 H, ArH), 4.16 (t, *J* = 7.5 Hz, 2 H, NCH_2), 2.00-1.85 (m, 2 H, CH_2), 1.40-1.12 (m, 10 H, $(CH_2)_5$), 0.86 (t, *J* = 6.9 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$,

75 MHz) δ 163.6 (d, J = 249.2 Hz), 163.3 (d, J = 246.4 Hz), 160.3, 154.5, 130.8 (d, J = 8.4 Hz), 128.1 (d, J = 8.2 Hz), 127.3 (d, J = 2.8 Hz), 124.4 (d, J = 4.0 Hz), 116.0 (d, J = 21.3 Hz), 115.4 (d, J = 21.7 Hz), 49.2, 31.6, 29.9, 28.9, 28.8, 26.3, 22.5, 13.9; ^{19}F NMR ($CDCl_3$, 282 MHz) –109.8, -112.4; IR (neat) 2948, 2922, 2869, 2851, 1603, 1543, 1529, 1479, 1467, 1428, 1416, 1377, 1347, 1311, 1285, 1224, 1211, 1163, 1151, 1130, 1099, 1090, 1033 cm^{-1}; MS (EI) (*m/z*) 370 ((M+1)$^+$, 9.85), 369 (M$^+$, 41.03), 257 (100); elemental analysis calcd (%) for $C_{22}H_{25}F_2N_3$: C 71.52, H 6.82, N 11.37; found: C 71.49, H 6.75, N 11.27.

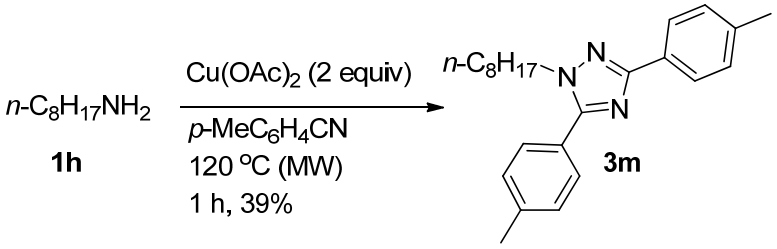


Method B: The reaction of $Cu(OAc)_2$ (362.6 mg, 2 mmol), *n*-$C_8H_{17}NH_2$ (128.6 mg, 1 mmol), and *p*-FC_6H_4CN (5 mL) afforded **3l** (168.4 mg, 46%) (eluent: petroleum ether/ethyl acetate = 100/1 to 20/1 for the first round, petroleum ether/ethyl acetate = 30/1 to 15/1 for the second round): solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-8.09 (m, 2 H, ArH), 7.70-7.60 (m, 2 H, ArH), 7.22 (t, J = 8.6 Hz, 2 H, ArH), 7.12 (t, J = 8.8 Hz, 2 H, ArH), 4.18 (t, J = 7.4 Hz, 2 H, NCH_2), 1.97-1.86 (m, 2 H, CH_2), 1.34-1.15 (m, 10 H, $(CH_2)_5$), 0.86 (t, J = 7.0 Hz, 3 H, CH_3).

13. 1-Octyl-3,5-di(*p*-toyl)-1*H*-1,2,4-triazole (3m) (cb-12-67, kjq-2-59)



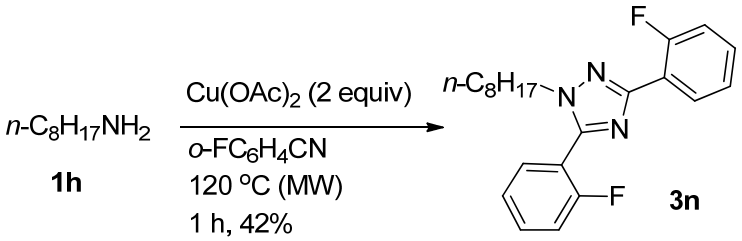
Method A: The reaction of $Cu(OAc)_2$ (363.4 mg, 2 mmol), *n*-$C_8H_{17}NH_2$ (128.7 mg, 1 mmol), and *p*-MeC_6H_4CN (2 mL) afforded **3m** (193.2 mg, 54%) (eluent: petroleum ether/ethyl acetate = 15/1): solid, 81-82 °C (*n*-hexane/Et_2O); ^1H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.1 Hz, 2 H, ArH), 7.54 (d, *J* = 8.4 Hz, 2 H, ArH), 7.30 (d, *J* = 7.8 Hz, 2 H, ArH), 7.23 (d, *J* = 8.1 Hz, 2 H, ArH), 4.17 (t, *J* = 7.4 Hz, 2 H, NCH_2), 2.41 (s, 3 H, $ArCH_3$), 2.37 (s, 3 H, $ArCH_3$), 2.00-1.84 (m, 2 H, CH_2), 1.35-1.11 (m, 10 H, $(CH_2)_5$), 0.86 (t, *J* = 6.9 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.0, 155.4, 139.9, 138.7, 129.4, 129.1, 128.6, 128.4, 126.2, 125.5, 49.1, 31.6, 30.0, 29.0, 28.9, 26.3, 22.5, 21.3, 14.0; IR (neat) 2953, 2929, 2867, 2851, 1615，1467, 1426, 1413, 1393, 1373, 1346, 1316, 1299, 1280, 1237, 1207, 1178, 1130, 1110, 1034, 1017 cm^{-1}; MS (EI) (*m/z*) 362 ($(M+1)^+$, 17.39), 361 (M^+, 68.22), 262 (100); elemental analysis calcd (%) for $C_{24}H_{31}N_3$: C 79.73, H 8.64, N 11.62 ; found: C 79.40, H 8.61, N 11.49.



Method B: The reaction of $Cu(OAc)_2$ (364.4 mg, 2 mmol), *n*-$C_8H_{17}NH_2$ (128.8 mg, 1 mmol), and *p*-MeC_6H_4CN (5 mL) afforded **3m** (141.1 mg, 39%) (eluent: petroleum ether/ethyl acetate = 15/1): solid; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J*

= 8.0 Hz, 2 H, ArH), 7.55 (d, *J* = 8.4 Hz, 2 H, ArH), 7.31 (d, *J* = 8.4 Hz, 2 H, ArH), 7.24 (d, *J* = 8.0 Hz, 2 H, ArH), 4.19 (t, *J* = 7.4 Hz, 2 H, NCH_2), 2.43 (s, 3 H, $ArCH_3$), 2.39 (s, 3 H, $ArCH_3$), 1.96-1.86 (m, 2 H, CH_2), 1.34-1.15 (m, 10 H, $(CH_2)_5$), 0.86 (t, *J* = 7.0 Hz, 3 H, CH_3).

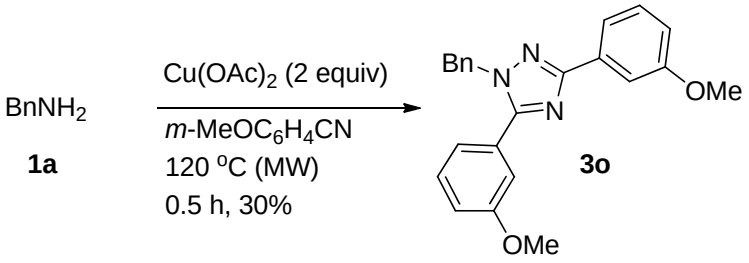
14. 1-Octyl-3,5-bis(2-fluorophenyl)-1*H*-1,2,4-triazole (3n) (kjq-2-103)



Method B: The reaction of $Cu(OAc)_2$ (363.1 mg, 2 mmol), *n*-$C_8H_{17}NH_2$ (128.6 mg, 1 mmol), and *o*-FC_6H_4CN (5 mL) afforded **3n** (154.0 mg, 42%) (eluent: petroleum ether/ethyl acetate = 30/1 to 15/1): oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (td, *J* = 7.6, 1.9 Hz, 1 H, ArH), 7.61 (td, *J* = 7.2, 1.5 Hz, 1 H, ArH), 7.56-7.49 (m, 1 H, ArH), 7.41-7.27 (m, 2 H, ArH), 7.27-7.15 (m, 3 H, ArH), 4.13 (t, *J* = 7.4 Hz, 2 H, NCH_2), 1.95-1.85 (m, 2 H, CH_2), 1.32-1.13 (m, 10 H, $(CH_2)_5$), 0.85 (t, *J* = 7.0 Hz, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 160.3 (d, *J* = 251.9 Hz), 159.7 (d, *J* = 248.9 Hz), 158.2 (d, *J* = 4.7 Hz), 150.4 (d, *J* = 0.9 Hz), 132.4 (d, *J* = 9.0 Hz), 132.0 (d, *J* = 2.1 Hz), 130.5 (d, *J* = 8.7 Hz), 130.2 (d, *J* = 2.9 Hz), 124.7 (d, *J* = 3.8 Hz), 124.0 (d, *J* = 3.2 Hz), 119.1 (d, *J* = 11.7 Hz), 116.6 (d, *J* = 15.0 Hz), 116.4 (d, *J* = 21.6 Hz), 116.2 (d, *J* = 21.1 Hz), 49.4 (d, *J* = 3.3 Hz), 31.6, 29.7, 29.0, 28.9, 26.4, 22.5, 14.0; ^{19}F NMR ($CDCl_3$, 376 MHz) -113.1, -113.3; IR (neat) 2927, 2856, 1622, 1585, 1517, 1483, 1471, 1413, 1344, 1263, 1226, 1157, 1135, 1094, 1034, 1020 cm^{-1}; MS (EI) (*m/z*) 370 ($(M+1)^+$, 6.02), 369 (M^+, 19.67), 257 (100); HRMS calcd for $C_{22}H_{25}F_2N_3$

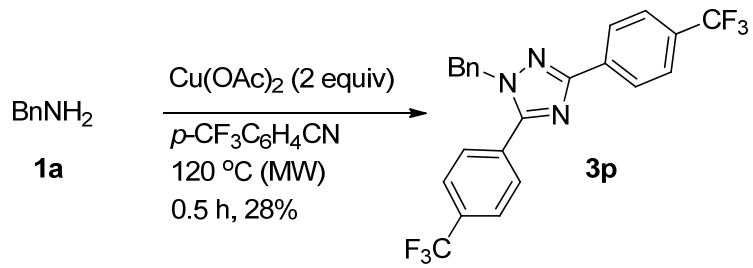
(M^+): 369.2017, found: 369.2013.

15. 1-Benzyl-3,5-bis(3-methoxyphenyl)-1*H*-1,2,4-triazole (3o) (kjq-2-67)



Method B: The reaction of $Cu(OAc)_2$ (363.4 mg, 2 mmol), $BnNH_2$ (107.9 mg, 1 mmol), and *m*-$MeOC_6H_4CN$ (5 mL) afforded **3o** (112.8 mg, 30%) (eluent: petroleum ether/ethyl acetate = 50/1 to 10/1 to 5/1): oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.6 Hz, 1 H, ArH), 7.75 (s, 1 H, ArH), 7.38-7.26 (m, 5 H, ArH), 7.24-7.15 (m, 3 H, ArH), 7.15-7.12 (m, 1 H, ArH), 7.01 (dd, *J* = 8.2, 2.2 Hz, 1 H, ArH), 6.96 (dd, *J* = 8.4, 2.4 Hz, 1 H, ArH), 5.46 (s, 2 H, NCH_2), 3.87 (s, 3 H, OMe), 3.74 (s, 3 H, OMe); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.4, 159.8, 159.7, 155.9, 136.1, 132.3, 129.9, 129.6, 129.1, 128.8, 127.9, 126.7, 120.9, 118.9, 116.6, 115.8, 113.7, 110.9, 55.4, 55.3, 52.7; IR (neat) 1584, 1514, 1465, 1433, 1339, 1317, 1283, 1262, 1242, 1222, 1182, 1142, 1113, 1077, 1030 cm^{-1}; MS (EI) (*m/z*) 372 ($(M+1)^+$, 25.21), 371 (M^+, 100); HRMS calcd for $C_{23}H_{21}N_3O_2$ (M^+): 371.1634, found: 371.1638.

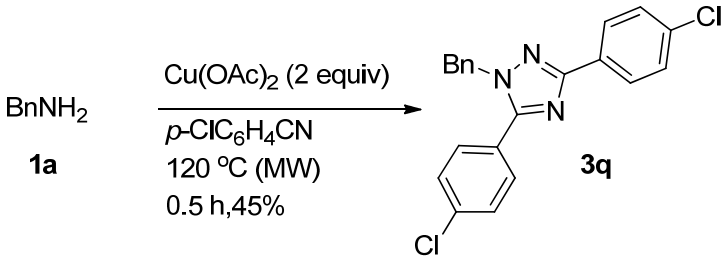
16. 1-Benzyl-3,5-bis(4-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (3p) (kjq-2-65)



Method B: The reaction of $Cu(OAc)_2$ (363.1 mg, 2 mmol), $BnNH_2$ (107.5 mg, 1

mmol), and *p*-$CF_3C_6H_4CN$ (6.3962 g) afforded **3p** (126.5 mg, 28%) (eluent: petroleum ether/ethyl acetate = 100/1 to 20/1): white solid, 151-153 °C (petroleum ether & ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.4 Hz, 2 H, ArH), 7.79-7.69 (m, 6 H, ArH), 7.41-7.31 (m, 3 H, ArH), 7.24-7.19 (m, 2 H, ArH), 5.49 (s, 2 H, NCH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.6, 155.0, 135.4, 134.1, 132.3 (q, *J* = 32.7 Hz), 131.2, 131.1 (q, *J* = 32.0 Hz), 129.2, 129.1, 128.3, 126.68, 126.65, 125.9 (q, *J* = 3.7 Hz), 125.6 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 270.7 Hz), 123.6 (q, *J* = 271.2 Hz), 53.1; ^{19}F NMR ($CDCl_3$, 376 MHz) -63.1, -63.4; IR (neat) 1620, 1535, 1466, 1424, 1359, 1324, 1165, 1105, 1064, 1015 cm^{-1}; MS (EI) (*m/z*) 448 ($(M+1)^+$, 5.15), 447 (M^+, 21.33), 91 (100); elemental analysis calcd (%) for $C_{23}H_{15}N_3F_6$: C 61.75, H 3.38, N 9.39; found: C 61.38, H 3.44, N 9.18.

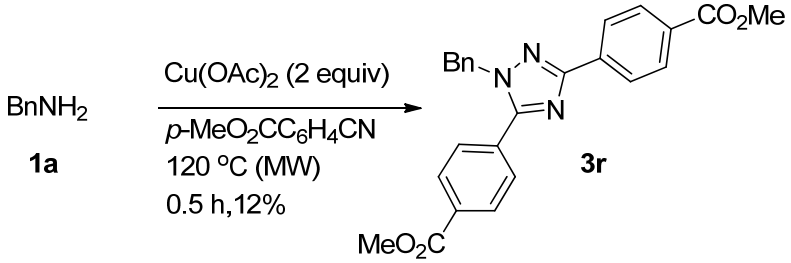
17. 1-Benzyl-3,5-bis(4-chlorophenyl)-1*H*-1,2,4-triazole (3q) (kjq-2-69)



Method B: The reaction of $Cu(OAc)_2$ (364.2 mg, 2 mmol), $BnNH_2$ (106.0 mg, 1 mmol), and *p*-ClC_6H_4CN (5.5560 g) afforded **3q** (170.6 mg, 45%) (eluent: petroleum ether/ethyl acetate = 100/1 to 20/1): white solid, 172-174 °C (petroleum ether & ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 2 H, ArH), 7.55 (d, *J* = 8.0 Hz, 2 H, ArH), 7.50-7.26 (m, 7 H, ArH), 7.20 (d, *J* = 7.2 Hz, 2 H, ArH), 5.44 (s, 2 H, NCH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.7, 155.1, 136.5, 135.6, 135.1, 130.0, 129.3, 129.1, 129.0, 128.7, 128.1, 127.7, 126.6, 126.2, 52.8; IR (neat) 1601,

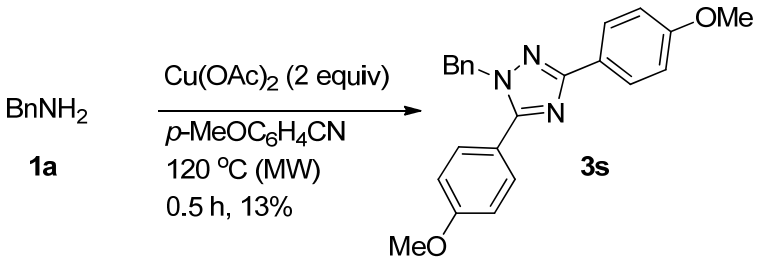
1495, 1470, 1455, 1435, 1422, 1409, 1361, 1342, 1316, 1295, 1275, 1240, 1203, 1172, 1126, 1090, 1033, 1014 cm^{-1}; MS (EI) (*m/z*) 383 (M^+($^{37}Cl^{37}Cl$), 4.33), 381 (M^+($^{37}Cl^{35}Cl$), 23.84), 379 (M^+($^{35}Cl^{35}Cl$), 36.56), 91 (100); elemental analysis calcd (%) for $C_{21}H_{15}N_3Cl_2$: C 66.33, H 3.98, N 11.05; found: C 66.27, H 3.95, N 10.92.

18. Dimethyl 4,4'-(1-benzyl-1*H*-1,2,4-triazole-3,5-diyl)dibenzoate (3r) (kjq-2-70)



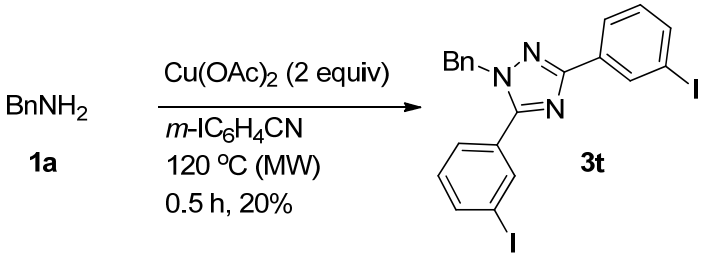
Method B: The reaction of $Cu(OAc)_2$ (364.0 mg, 2 mmol), $BnNH_2$ (107.0 mg, 1 mmol), and *p*-$MeO_2CC_6H_4CN$ (5.8982 g) afforded **3r** (50.5 mg, 12%) (eluent: petroleum ether/ethyl acetate = 50/1 to 5/1 for the first round, petroleum ether/ethyl acetate = 20/1 to 5/1 for the second round): white solid, 157-159 °C (petroleum ether & ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.8 Hz, 2 H, ArH), 8.16-8.10 (m, 4 H, ArH), 7.72 (d, *J* = 8.4 Hz, 2 H, ArH), 7.39-7.29 (m, 3 H, ArH), 7.24-7.18 (m, 2 H, ArH), 5.49 (s, 2 H, NCH_2), 3.95 (s, 3 H, Me), 3.94 (s, 3 H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.8, 166.2, 160.8, 155.3, 135.4, 134.9, 131.8, 131.7, 130.6, 130.0, 129.9, 129.0, 128.8, 128.2, 126.7, 126.3, 53.1, 52.4, 52.1; IR (neat) 1713, 1611, 1577, 1532, 1494, 1476, 1455, 1431, 1362, 1272, 1190, 1135, 1110, 1016 cm^{-1}; MS (EI) (*m/z*) 428 ($(M+1)^+$, 20.76), 427 (M^+, 69.87), 91 (100); elemental analysis calcd (%) for $C_{25}H_{21}N_3O_4$: C 70.25, H 4.95, N 9.83; found: C 70.00, H 5.05, N 9.65.

19. 1-Benzyl-3,5-bis(4-methoxyphenyl)-1*H*-1,2,4-triazole (3s) (kjq-2-71)



Method B: The reaction of $Cu(OAc)_2$ (364.0 mg, 2 mmol), $BnNH_2$ (107.0 mg, 1 mmol), and *p*-$MeOC_6H_4CN$ (5.3978 g) afforded **3s** (47.3 mg, 13%) (eluent: petroleum ether/ethyl acetate = 50/1 to 5/1 for the first round, petroleum ether/ethyl acetate = 20/1 to 5/1 for the second round): white solid, 130-132 °C (petroleum ether & ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.8 Hz, 2 H, ArH), 7.55 (d, *J* = 8.8 Hz, 2 H, ArH), 7.37-7.25 (m, 3 H, ArH), 7.23-7.16 (m, 2 H, ArH), 7.00-6.91 (m, 4 H, ArH), 5.42 (s, 2 H, NCH_2), 3.83 (s, 3 H, Me), 3.82 (s, 3 H, Me); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 161.3, 160.9, 160.4, 155.9, 136.3, 130.2, 128.8, 127.82, 127.81, 126.7, 123.9, 120.4, 114.2, 113.8, 55.3, 55.2, 52.5; IR (neat) 1611, 1580, 1531, 1494, 1478, 1466, 1418, 1345, 1298, 1260, 1246, 1175, 1167, 1144, 1133, 1103, 1026, 1006 cm^{-1}; MS (EI) (*m/z*) 372 ($(M+1)^+$, 24.29), 371 (M^+, 100); elemental analysis calcd (%) for $C_{23}H_{21}N_3O_2$: C 74.37, H 5.70, N 11.31; found: C 74.10, H 5.55, N 11.11.

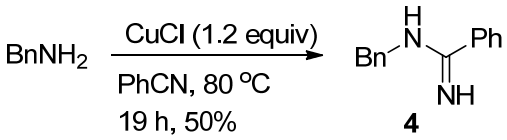
20. 1-Benzyl-3,5-bis(3-iodophenyl)-1*H*-1,2,4-triazole (3t) (kjq-2-73)



Method B: The reaction of $Cu(OAc)_2$ (363.4 mg, 2 mmol), $BnNH_2$ (107.0 mg, 1

mmol), and *m*-IC_6H_4CN (6.0035 g) afforded **3t** (115.0 mg, 20%) (eluent: petroleum ether/ethyl acetate = 100/1 to 20/1): white solid, 117-119 °C (petroleum ether & ethyl ether); ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1 H, ArH), 8.14 (d, *J* = 7.6 Hz, 1 H, ArH), 7.98 (s, 1 H, ArH), 7.83 (d, *J* = 8.0 Hz, 1 H, ArH), 7.74 (d, *J* = 8.0 Hz, 1 H, ArH), 7.54 (d, *J* = 8.0 Hz, 1 H, ArH), 7.43-7.29 (m, 3 H, ArH), 7.28-7.14 (m, 4 H, ArH), 5.43 (s, 2 H, NCH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.1, 154.5, 139.3, 138.2, 137.6, 135.5, 135.1, 132.7, 130.4, 130.3, 129.6, 129.0, 128.3, 127.7, 126.9, 125.6, 94.43, 94.42, 53.0; IR (neat) 1595, 1565, 1505, 1451, 1439, 1425, 1359, 1329, 1306, 1243, 1150, 1132, 1061, 1032 cm^{-1}; MS (EI) (*m/z*) 564 ($(M+1)^+$, 3.92), 563 (M^+, 17.18), 91 (100); elemental analysis calcd (%) for $C_{21}H_{15}N_3I_2$: C 44.79, H 2.68, N 7.46; found: C 44.71, H 2.73, N 7.36.

Synthesis of *N*-benzylbenzimidamide 4[4] (kjq-2-90)



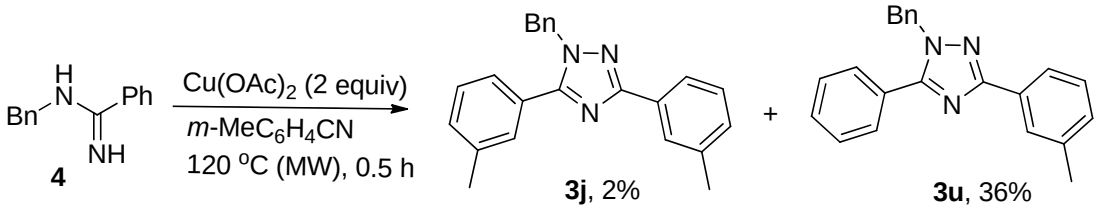
4

To a dried Schlenk tube were added CuCl (1.1911 g, 12 mmol), $BnNH_2$ (1.0724 g, 10 mmol), and PhCN (10 mL) sequentially under Ar atmosphere at room temperature. After being stirred at 80 °C (oil bath) for 19 h, the resulting mixture was cooled to room temperature and poured in 80 mL of Et_2O, followed by the addition of 50 mL of NaOH (2 M, aquous). The resulting mixture was stirred vigorously for 5 min, filtered, extracted with Et_2O (2 x 80 mL), and dried over anhydrous Na_2SO_4. After filtration, a stream of HCl gas was bubbled through the solution forming a solid. The solid was collected by filtration and then dissolved in an aqueous solution of NaOH (1 M). The

resulting mixture was extracted with 3 x 30 mL of Et_2O. Drying over anhydrous Na_2SO_4, filteration, evaporation and column chromatography on silica gel afforded *N*-benzylbenzimidamide **4** (1.0474 g, 50%) (eluent: petroleum ether/ethyl acetate = 3/1 to ethyl acetate/ triethylamine = 30/1): white solid, 79-81 ^oC (petroleum ether & ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 7.60-7.53 (m, 2 H, ArH), 7.43-7.29 (m, 7 H, ArH), 7.29-7.22 (m, 1 H, ArH), 5.94-5.20 (brs, 2 H, 2 x NH), 4.50 (s, 2 H, CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.0, 138.9, 137.4, 129.8, 128.4, 127.5, 126.9, 125.9, 46.6; IR (neat) 3461, 3307, 3175, 3030, 2849, 2813, 1634, 1597, 1563, 1494, 1454, 1443, 1374, 1346, 1155, 1071, 1026 cm^{-1}; MS (EI) (*m/z*) 211 ($(M+1)^+$, 7.10), 210 (M^+, 51.43), 209 (100); elemental analysis calcd (%) for $C_{14}H_{14}N_2$: C 79.97, H 6.71, N 13.32; found: C 79.88, H 6.67, N 13.30.

The reaction of 4 with different nitriles:

1. 1-Benzyl-5-phenyl-3-(*m*-tolyl)-1*H*-1,2,4-triazole (3u) (kjq-2-89)

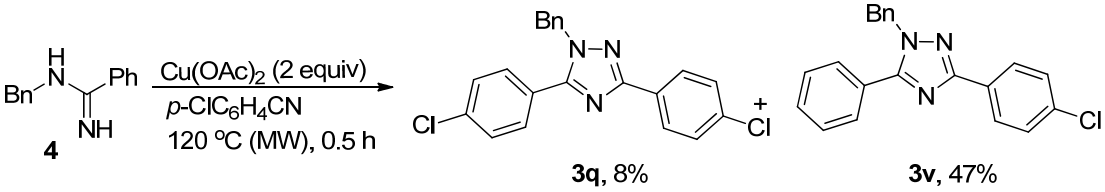


Method B: The reaction of $Cu(OAc)_2$ (365.0 mg, 2 mmol), **4** (210.9 mg, 1 mmol), and *m*-MeC_6H_4CN (5 mL) afforded **3j** (8.3 mg, 2%) and **3u** (117.6 mg, 36%) (eluent: petroleum ether/ethyl acetate = 100/1 to 30/1).

3j: oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1 H, ArH), 7.99 (d, *J* = 8.0 Hz, 1 H, ArH), 7.47 (s, 1 H, ArH), 7.39-7.27 (m, 7 H, ArH), 7.24-7.19 (m, 3 H, ArH), 5.45 (s, 2 H, NCH_2), 2.42 (s, 3 H, Me), 2.38 (s, 3 H, Me).

3u: white solid; 86-88 °C (petroleum ether & ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1 H, ArH), 7.99 (d, *J* = 7.6 Hz, 1 H, ArH), 7.65-7.60 (m, 2 H, ArH), 7.52-7.43 (m, 3 H, ArH), 7.38-7.29 (m, 4 H, ArH), 7.24-7.18 (m, 3 H, ArH), 5.46 (s, 2 H, NCH_2), 2.42 (s, 3 H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.6, 156.0, 138.1, 136.0, 130.8, 130.1, 129.9, 128.80, 128.75, 128.7, 128.4, 127.94, 127.85, 127.0, 126.7, 123.5, 52.6, 21.3; IR (neat) 1605, 1510, 1487, 1451, 1406, 1346, 1301, 1241, 1214, 1179, 1144, 1121, 1077, 1018 cm^{-1}; MS (EI) (*m/z*) 326 ($(M+1)^+$, 26.00), 325 (M^+, 100); elemental analysis calcd (%) for $C_{22}H_{19}N_3$: C 81.20, H 5.89, N 12.91; found: C 81.01, H 6.01, N 12.65.

2. 1-Benzyl-3-(4-chlorophenyl)-5-phenyl-1*H*-1,2,4-triazole (3v) (kjq-2-94)



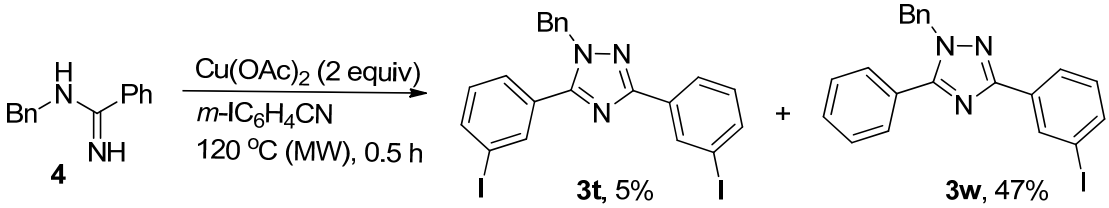
Method B: The reaction of $Cu(OAc)_2$ (362.6 mg, 2 mmol), **4** (211.1 mg, 1 mmol), and *p*-ClC_6H_4CN (5.5022 g) afforded **3q** (30.6 mg, 8%) and **3v** (163.5 mg, 47%) (eluent: petroleum ether/ethyl acetate = 100/1 to 30/1 for the first round, petroleum ether/ethyl acetate = 30/1 for the second round).

3q: white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.0 Hz, 2 H, ArH), 7.55 (d, *J* = 8.4 Hz, 2 H, ArH), 7.48-7.28 (m, 7 H, ArH), 7.19 (d, *J* = 7.2 Hz, 2 H, ArH), 5.43 (s, 2 H, NCH_2).

3v: white solid; 145-147 °C (petroleum ether & ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.4 Hz, 2 H, ArH), 7.65-7.59 (m, 2 H, ArH), 7.53-7.39 (m, 5 H, ArH), 7.39-7.28 (m, 3 H, ArH), 7.24-7.18 (m, 2 H, ArH), 5.45 (s, 2 H, NCH_2); ^{13}C

NMR ($CDCl_3$, 100 MHz) δ 160.5, 156.1, 135.8, 134.9, 130.2, 129.5, 128.80, 128.78, 128.6, 127.9, 127.70, 127.66, 126.7, 52.6; IR (neat) 1601, 1533, 1495, 1467, 1455, 1429, 1417, 1363, 1343, 1318, 1296, 1240, 1203, 1173, 1157, 1126, 1087, 1074, 1018 cm^{-1}; MS (EI) (*m/z*) 347 (M^+(^{37}Cl), 24.67), 345 (M^+(^{35}Cl), 70.06), 91 (100); elemental analysis calcd (%) for $C_{21}H_{16}ClN_3$: C 72.93, H 4.66, N 12.15; found: C 73.08, H 4.99, N 12.00.

3. 1-Benzyl-3-(3-iodophenyl)-5-phenyl-1*H*-1,2,4-triazole (3w) (kjq-2-92)



Method B: The reaction of $Cu(OAc)_2$ (364.3 mg, 2 mmol), **4** (209.5 mg, 1 mmol), and *m*-IC_6H_4CN (5.9982 g) afforded **3t** (28.8 mg, 5%) and **3w** (203.2 mg, 47%) (eluent: petroleum ether/ethyl acetate = 100/1 to 30/1).

3t: white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (t, *J* = 1.6 Hz, 1 H, ArH), 8.14 (dt, *J* = 7.6, 1.1 Hz, 1 H, ArH), 7.98 (t, *J* = 1.6 Hz, 1 H, ArH), 7.83 (dt, *J* = 7.8, 1.3 Hz, 1 H, ArH), 7.74 (dt, *J* = 8.0, 1.4 Hz, 1 H, ArH), 7.54 (dt, *J* = 7.8, 1.3 Hz, 1 H, ArH), 7.41-7.30 (m, 3 H, ArH), 7.25-7.15 (m, 4 H, ArH), 5.43 (s, 2 H, NCH_2).

3w: white solid; 142-144 °C (petroleum ether & ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1 H, ArH), 8.16 (d, *J* = 8.0 Hz, 1 H, ArH), 7.73 (d, *J* = 8.0 Hz, 1 H, ArH), 7.65-7.59 (m, 2 H, ArH), 7.54-7.44 (m, 3 H, ArH), 7.39-7.28 (m, 3 H, ArH), 7.23-7.14 (m, 3 H, ArH), 5.46 (s, 2 H, NCH_2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.0, 156.2, 138.0, 135.8, 135.1, 133.0, 130.3, 130.2, 128.9, 128.8, 128.7, 128.0,

127.7, 126.7, 125.5, 94.4, 52.7; IR (neat) 1594, 1565, 1499, 1467, 1452, 1434, 1394, 1358, 1346, 1286, 1261, 1242, 1145, 1061, 1018 cm^{-1}; MS (EI) (*m/z*) 438 ($(M+1)^+$, 23.93), 437 (M^+, 98.71), 91 (100); elemental analysis calcd (%) for $C_{21}H_{16}IN_3$: C 57.68, H 3.69, N 9.61; found: C 57.73, H 3.92, N 9.45.

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2. Boyer, J. H.; Frints, P. J. A. *J. Heterocycl. Chem.* **1970**, *7*, 59-70.

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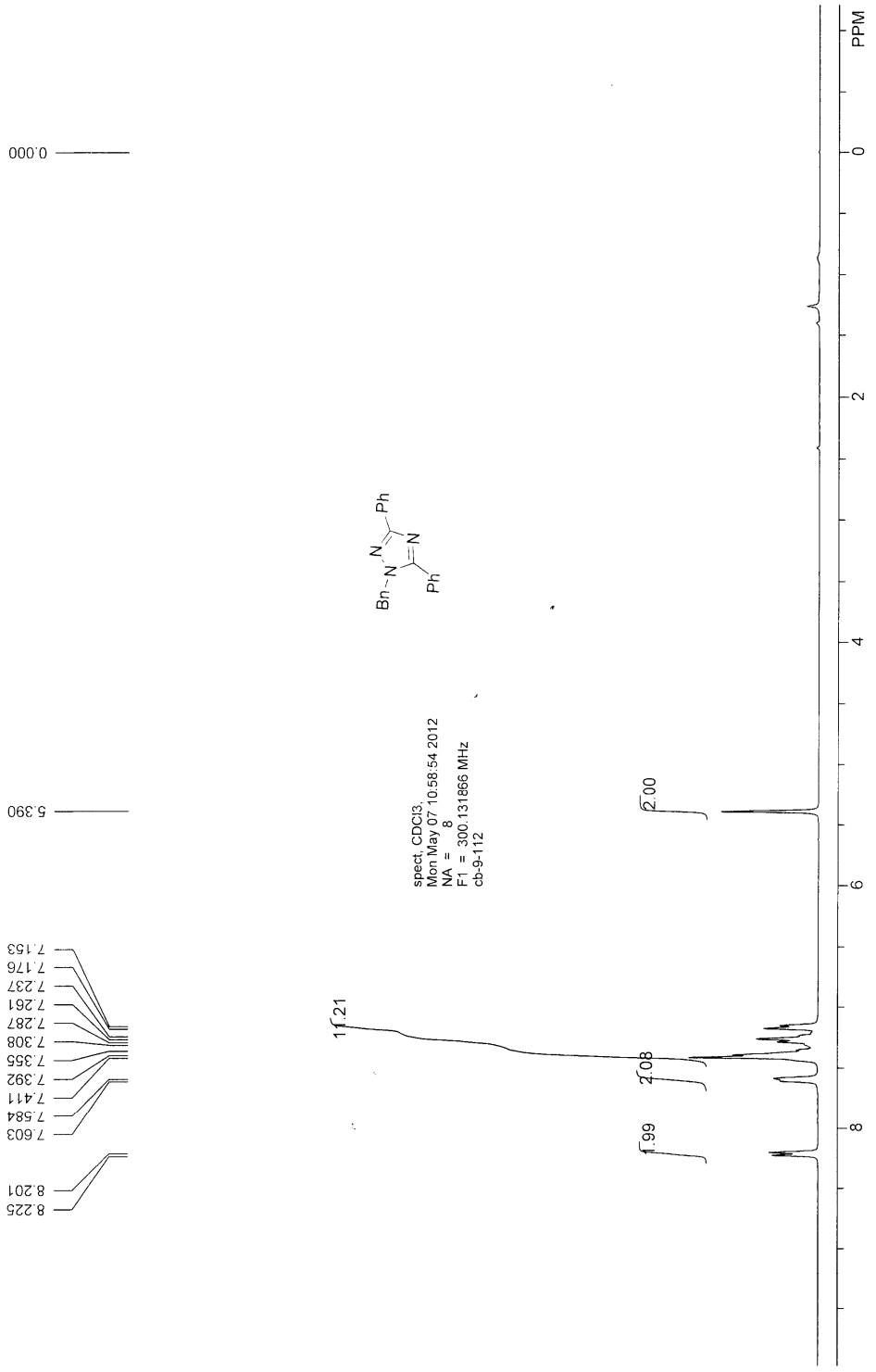

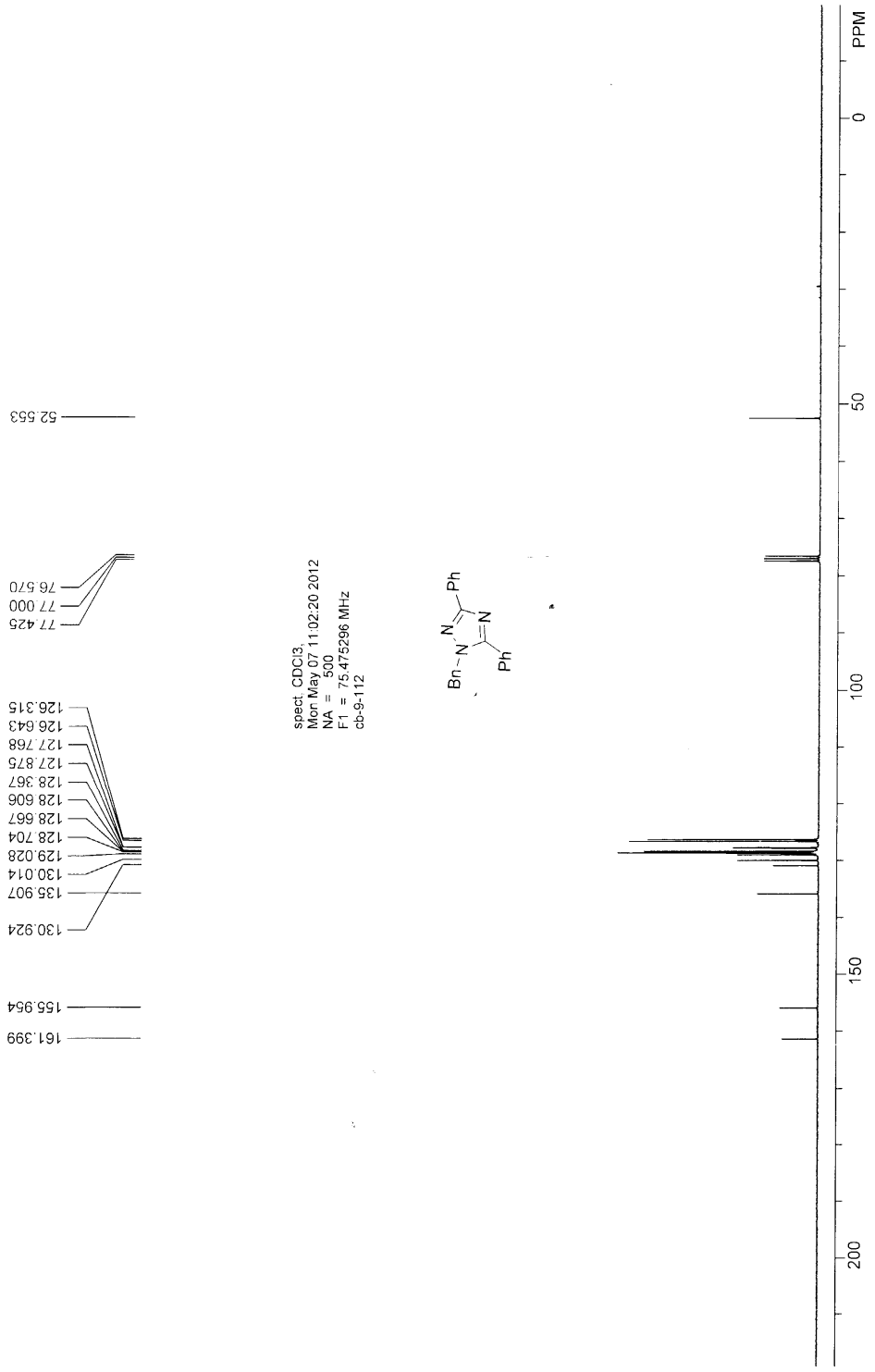

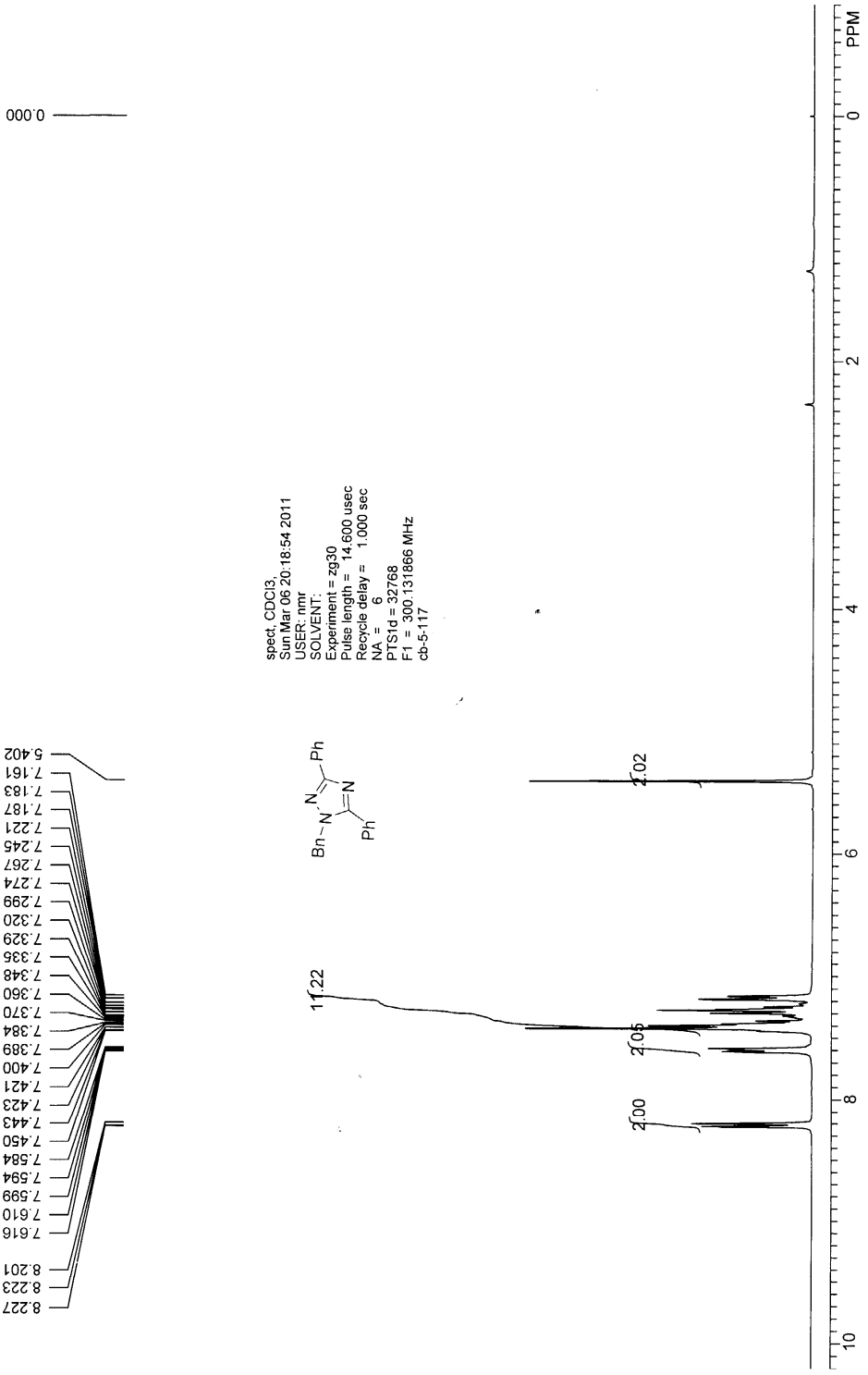

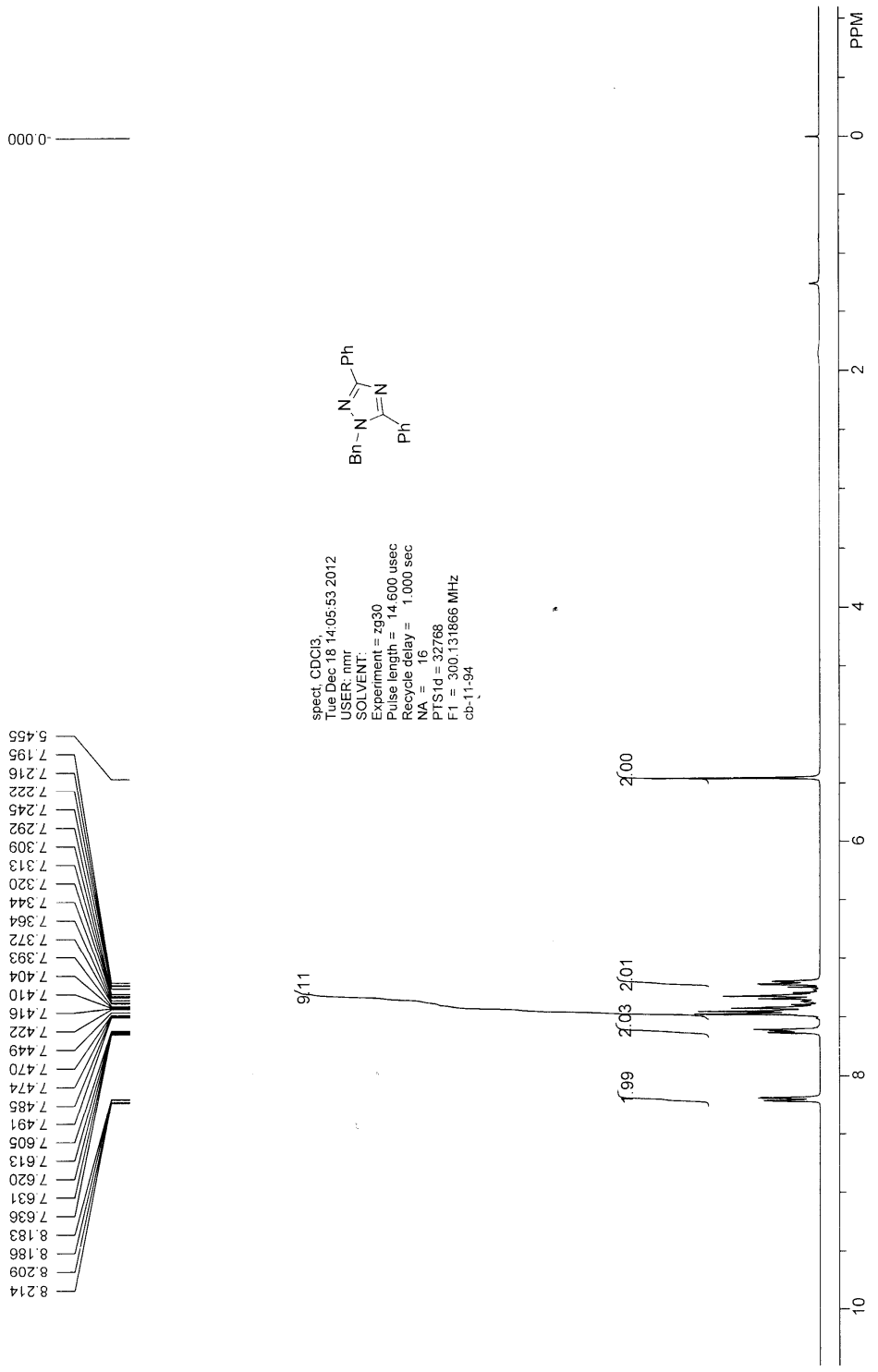

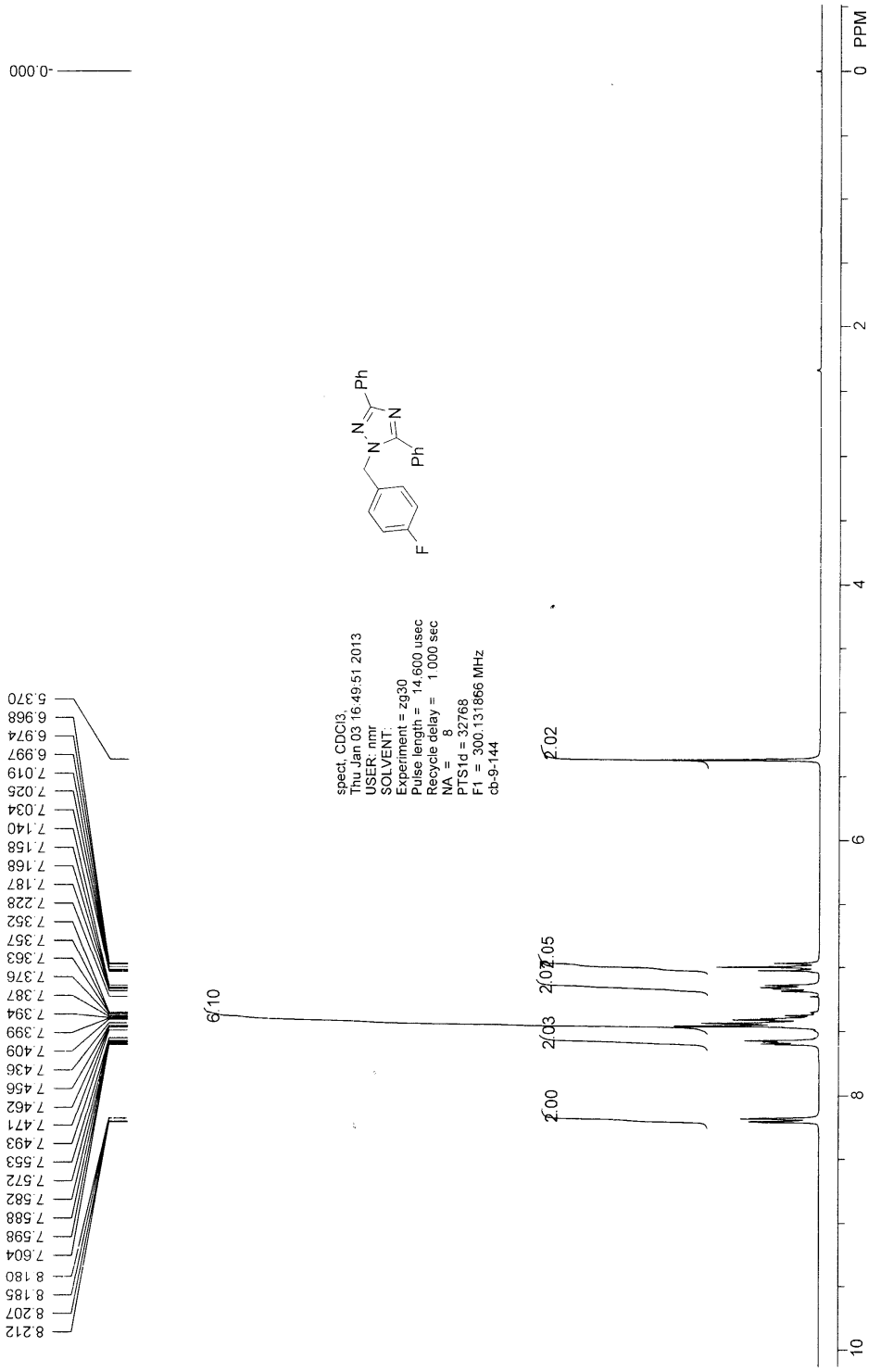

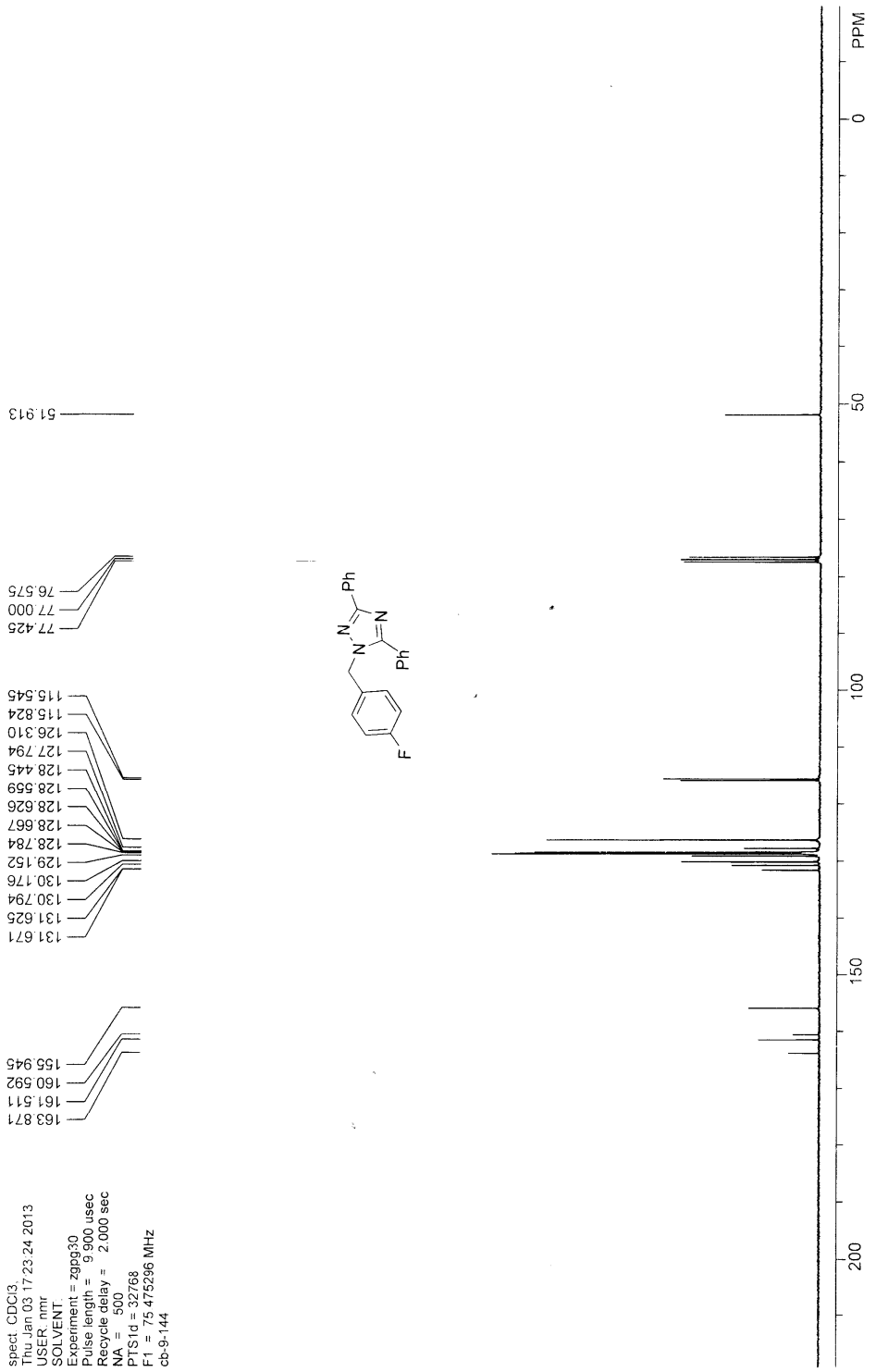

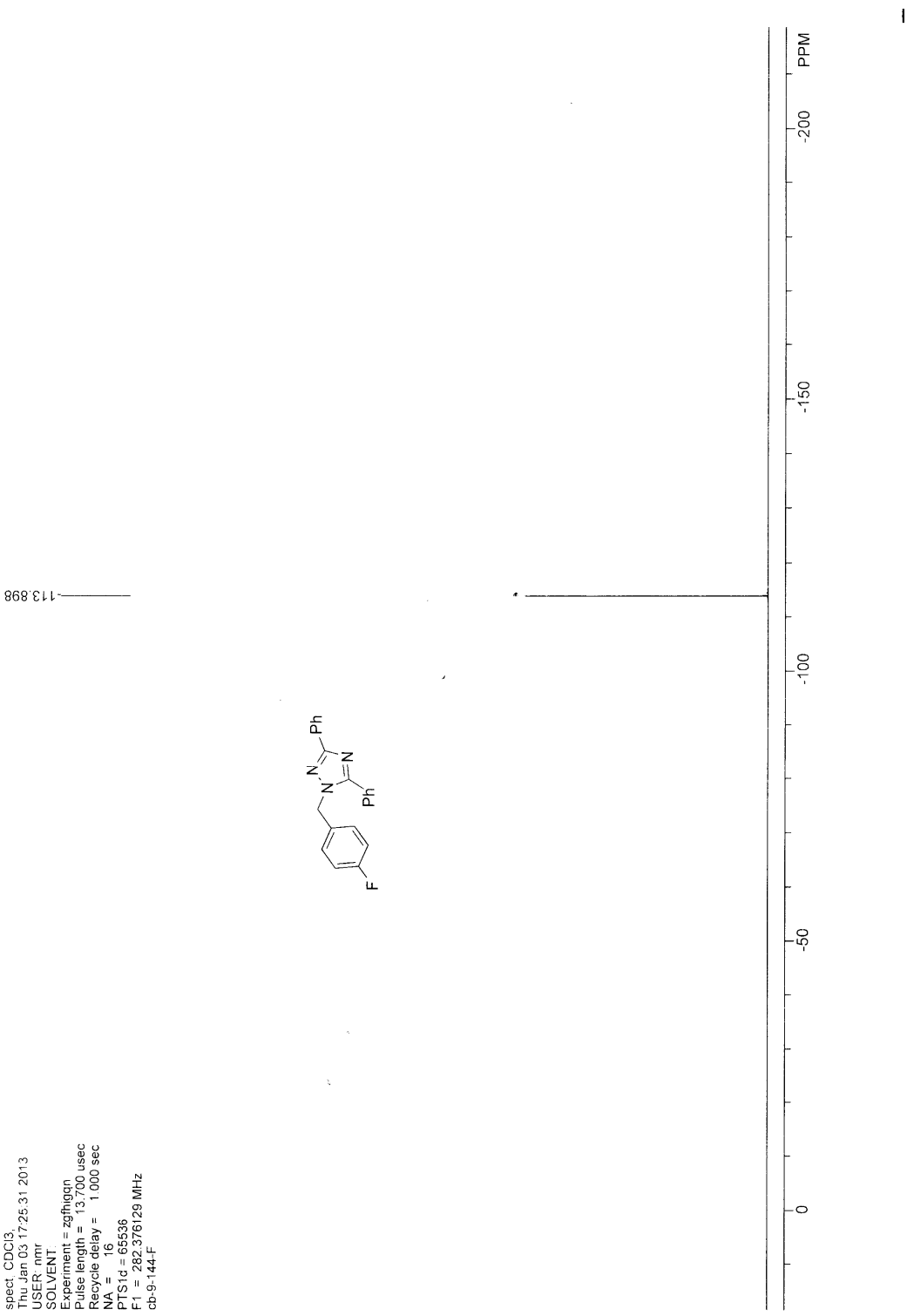

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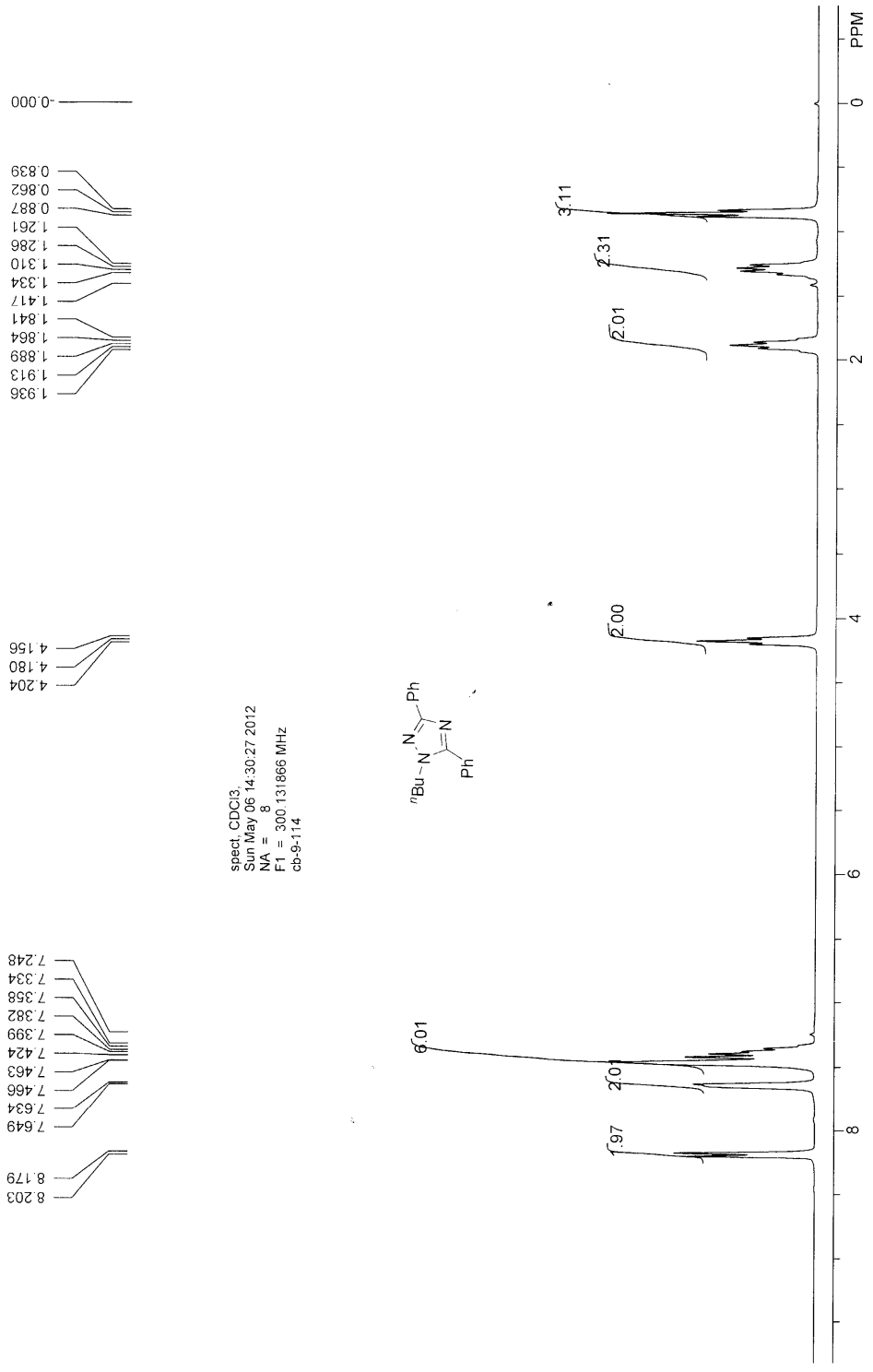

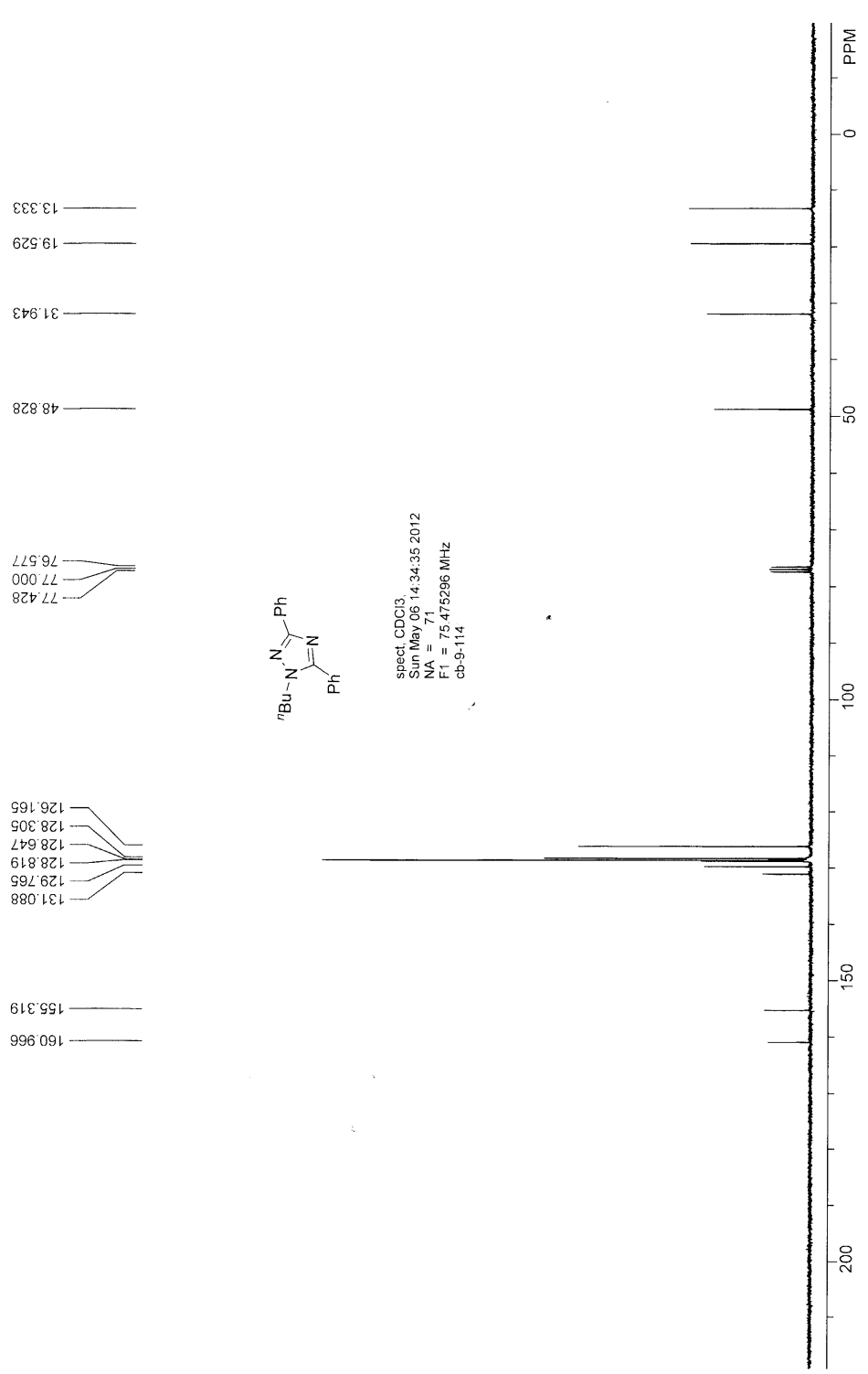

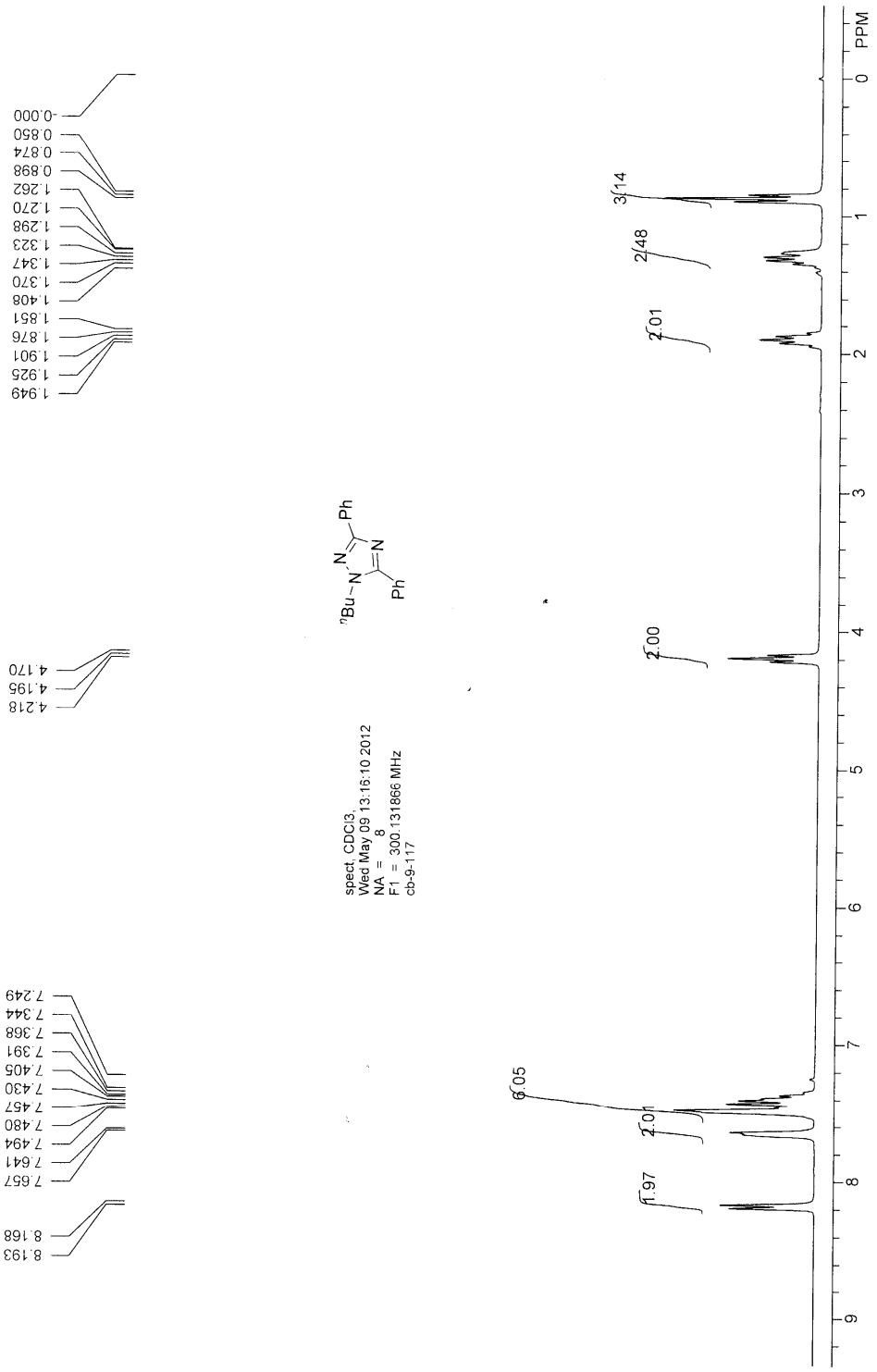

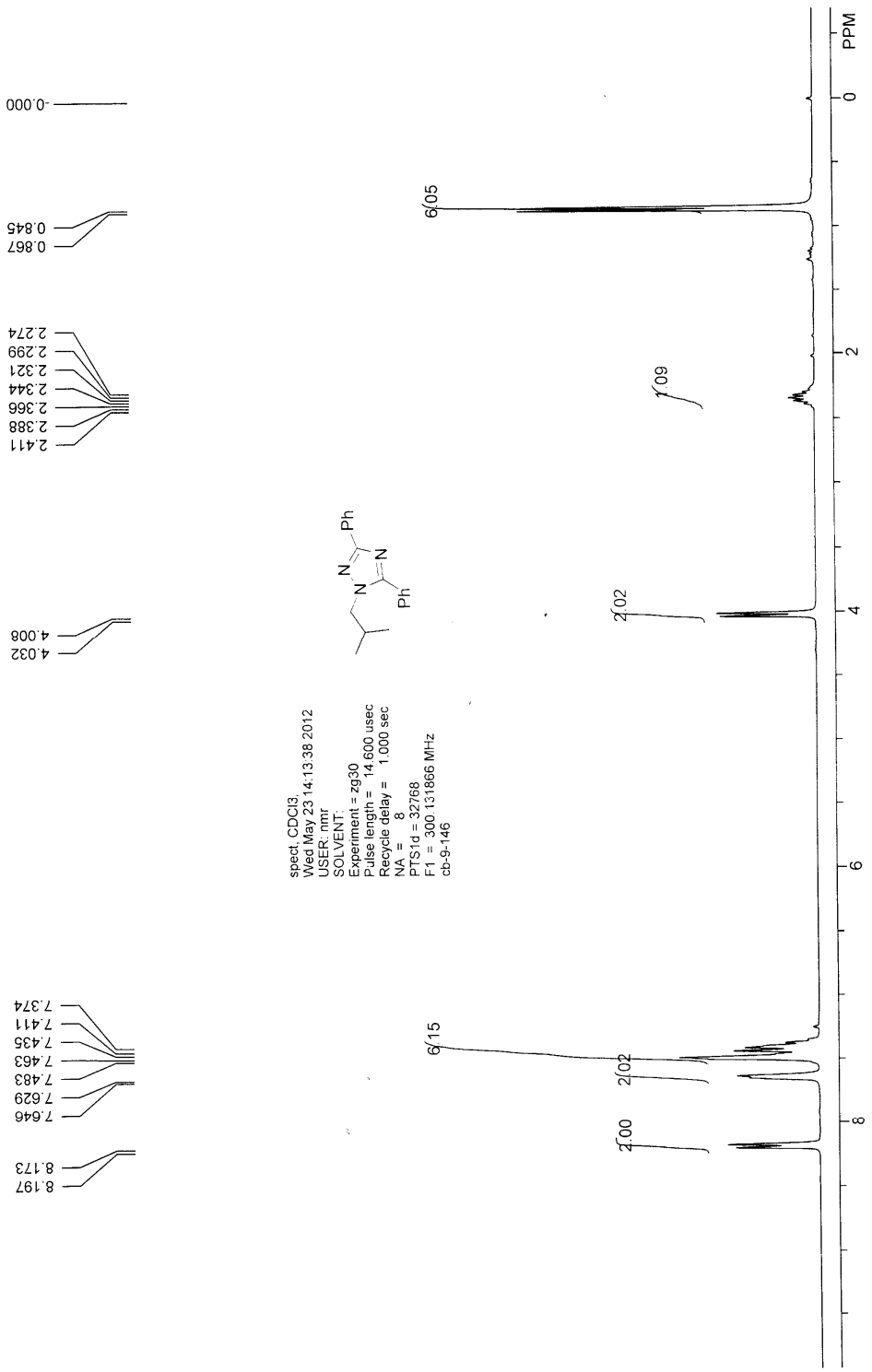

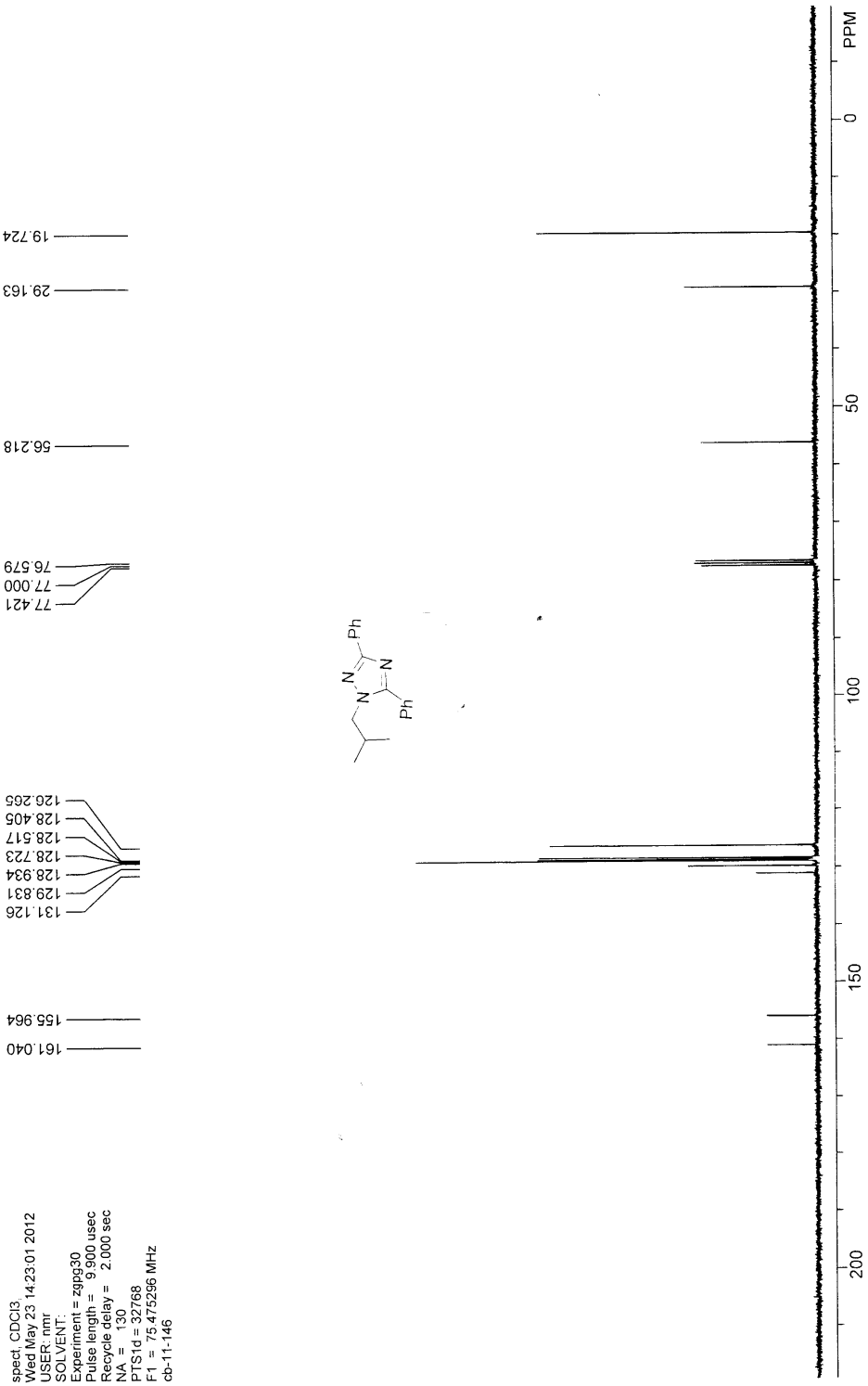

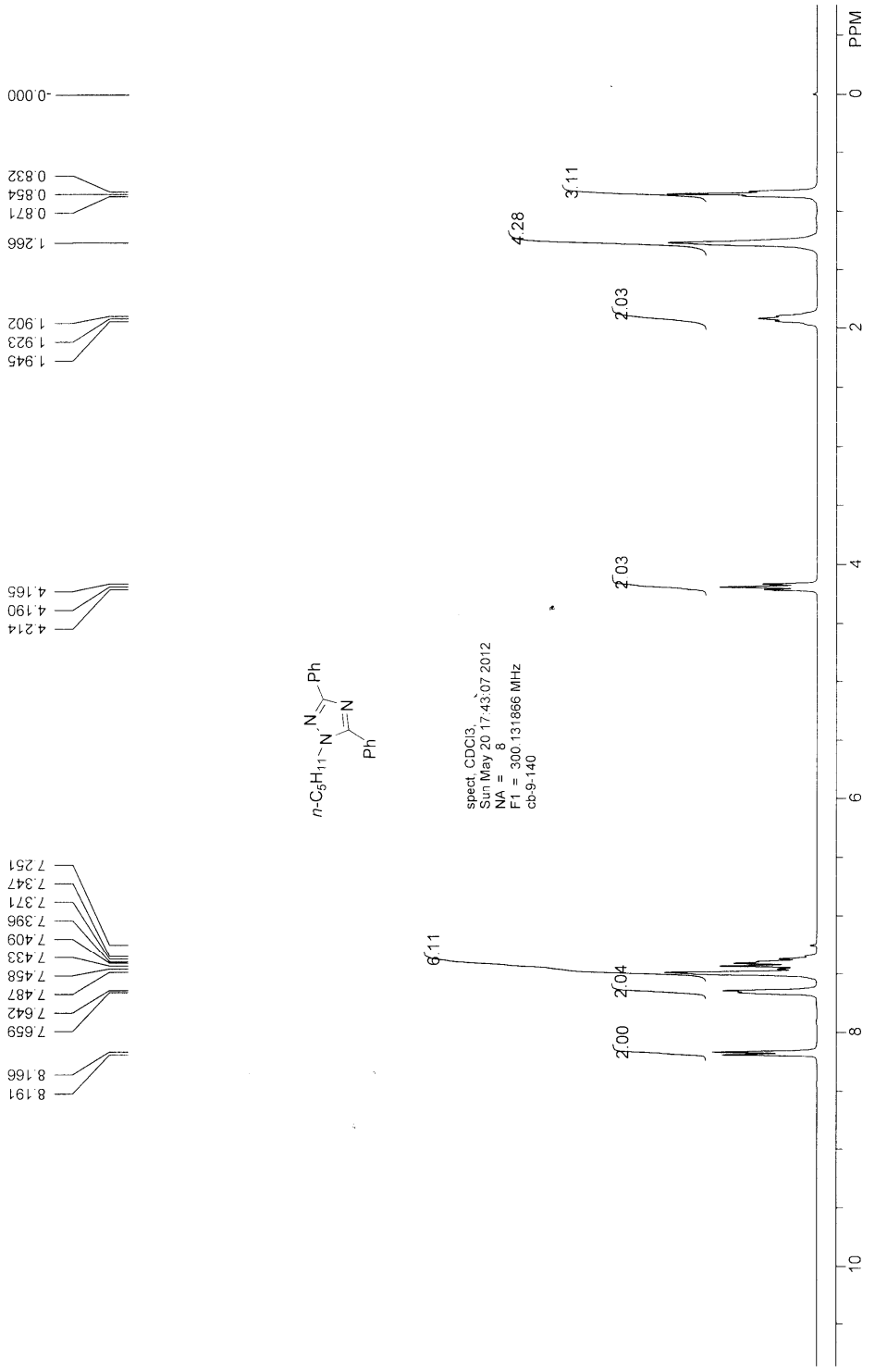

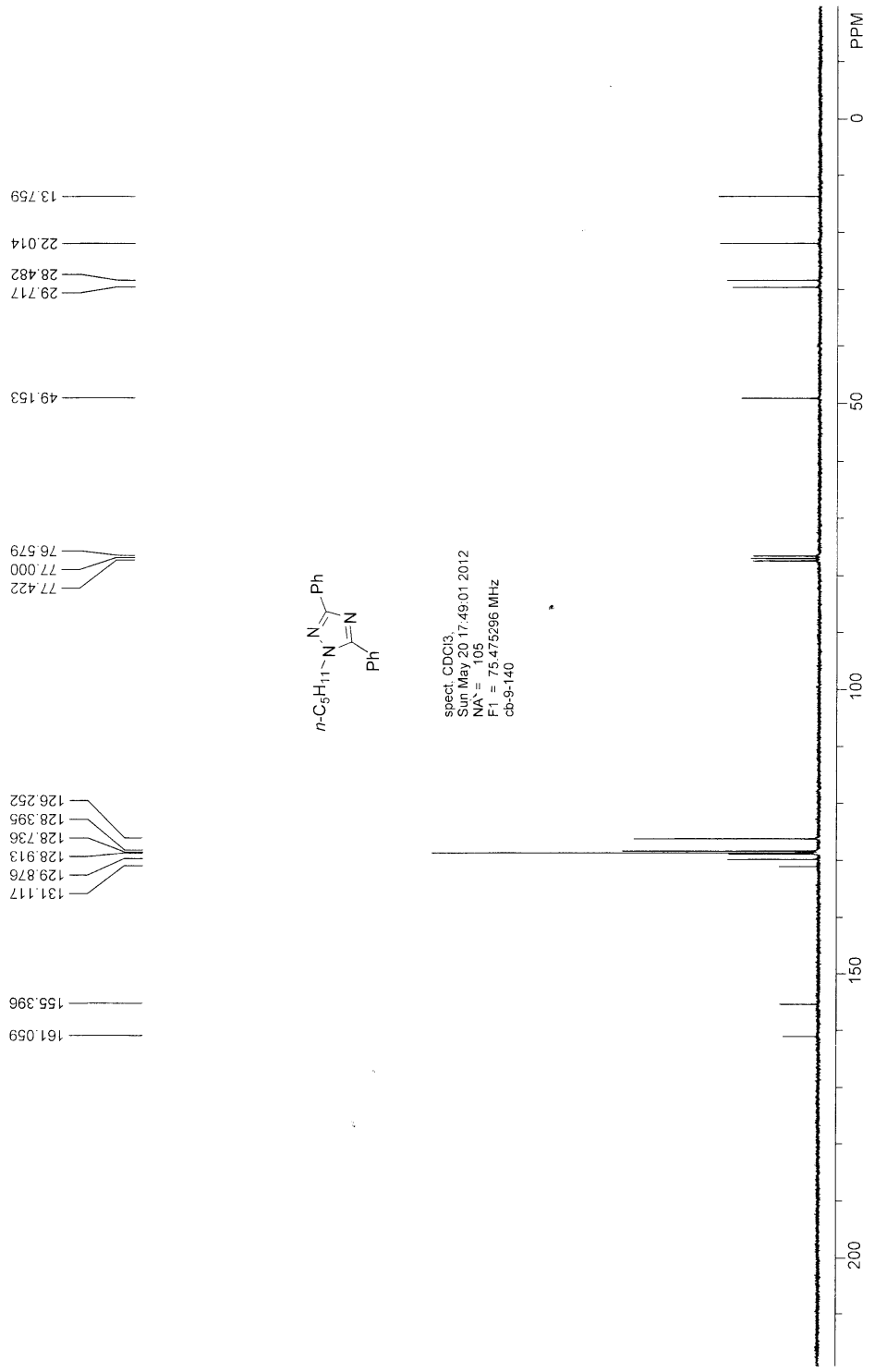

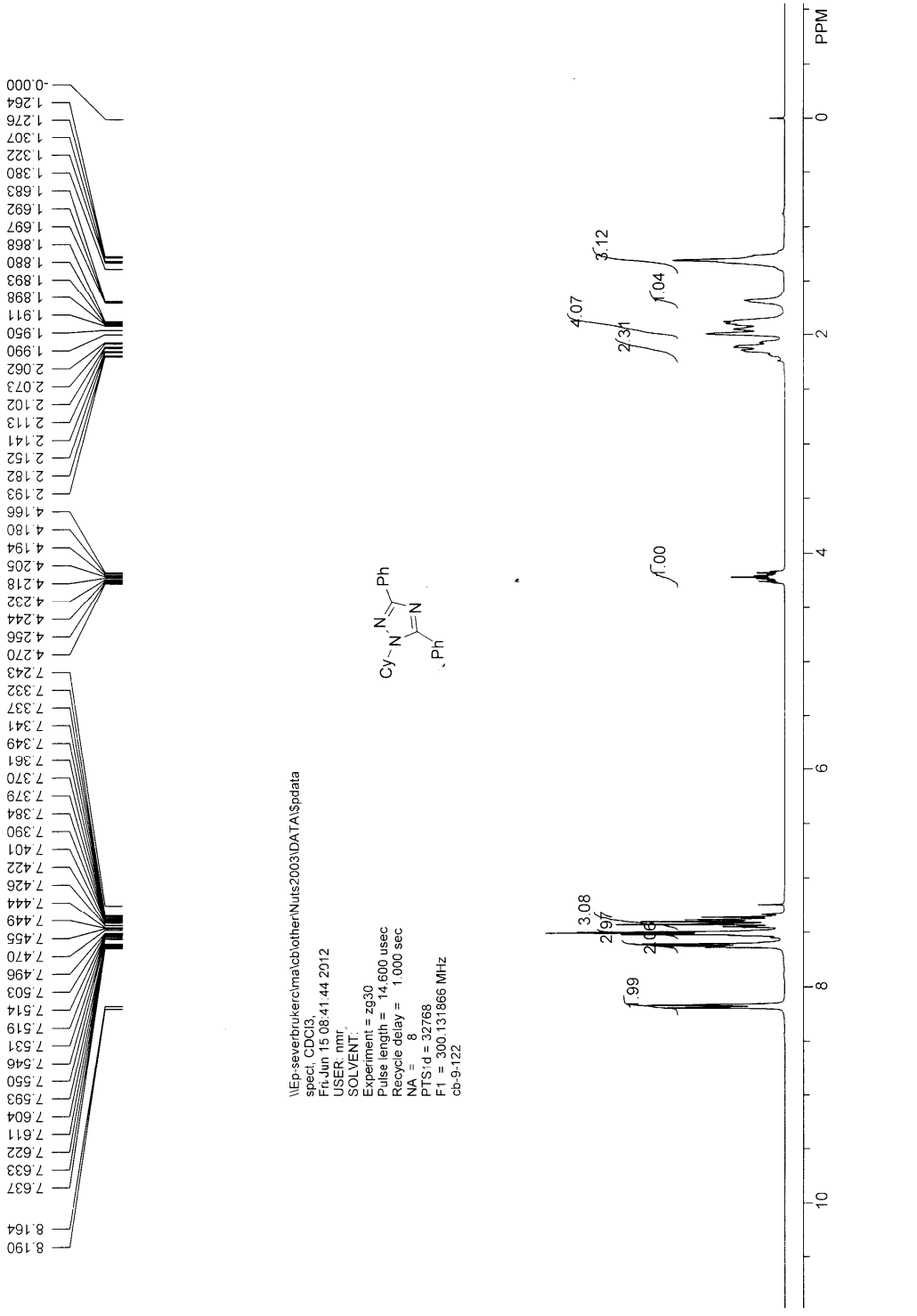

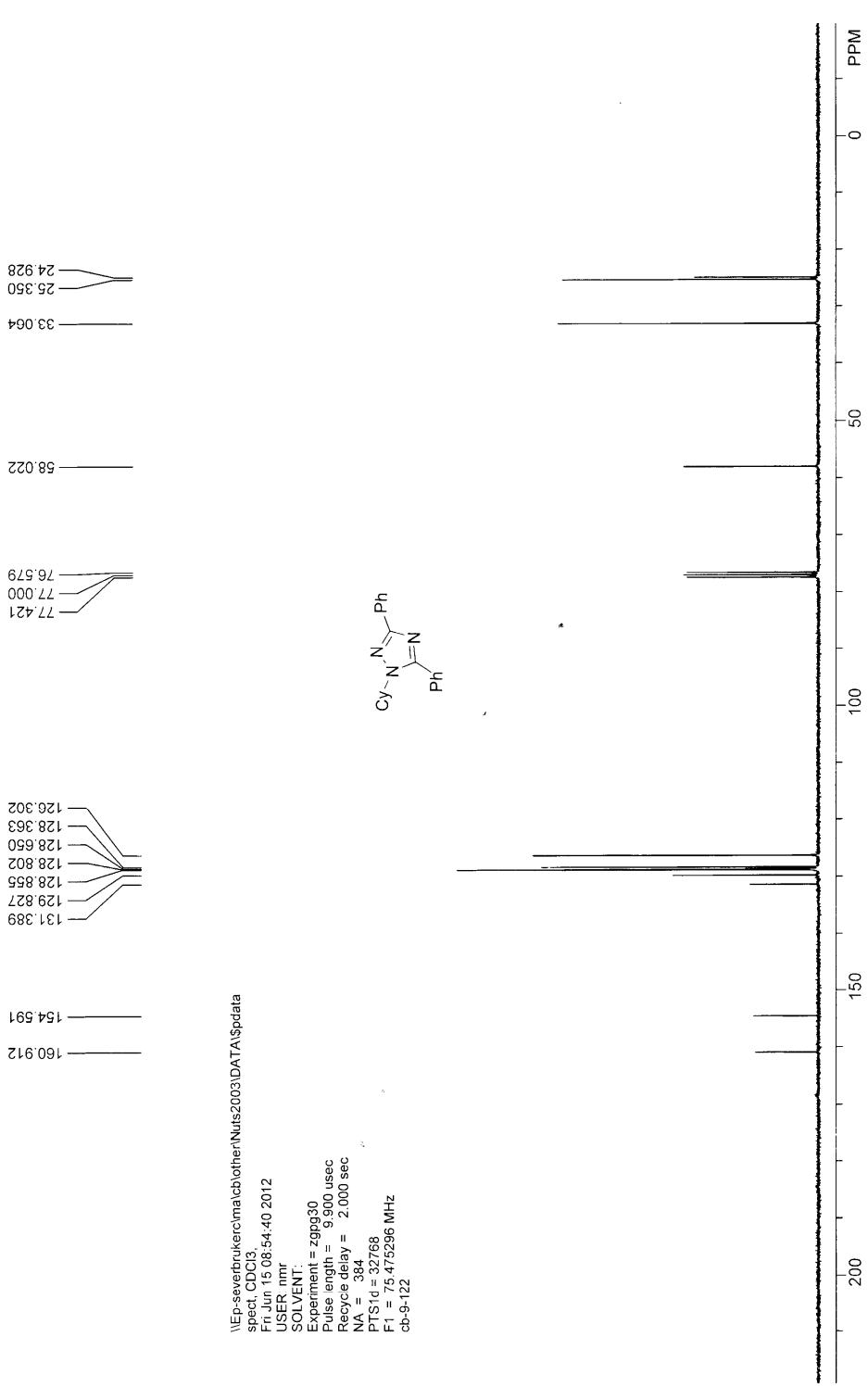

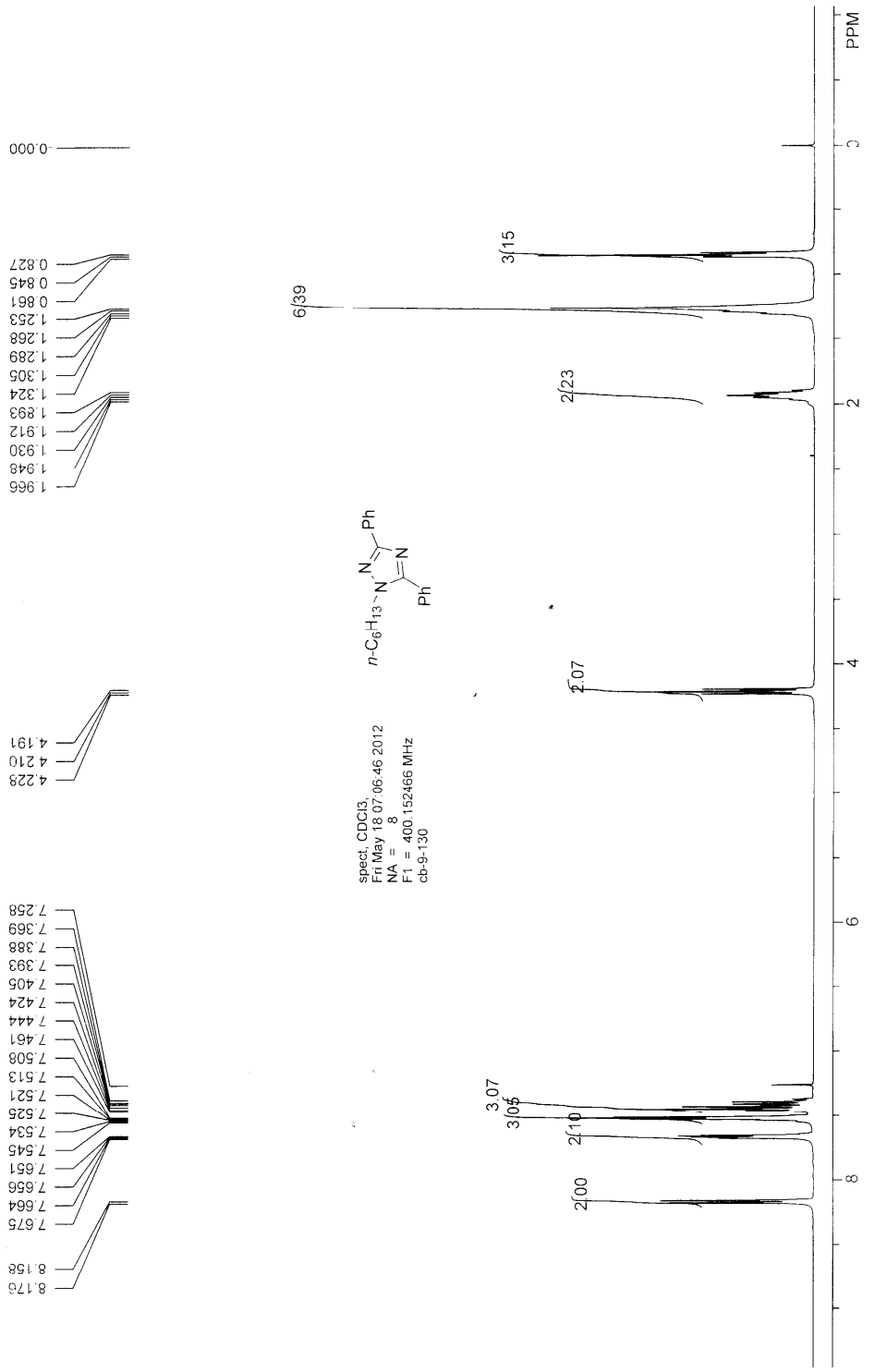

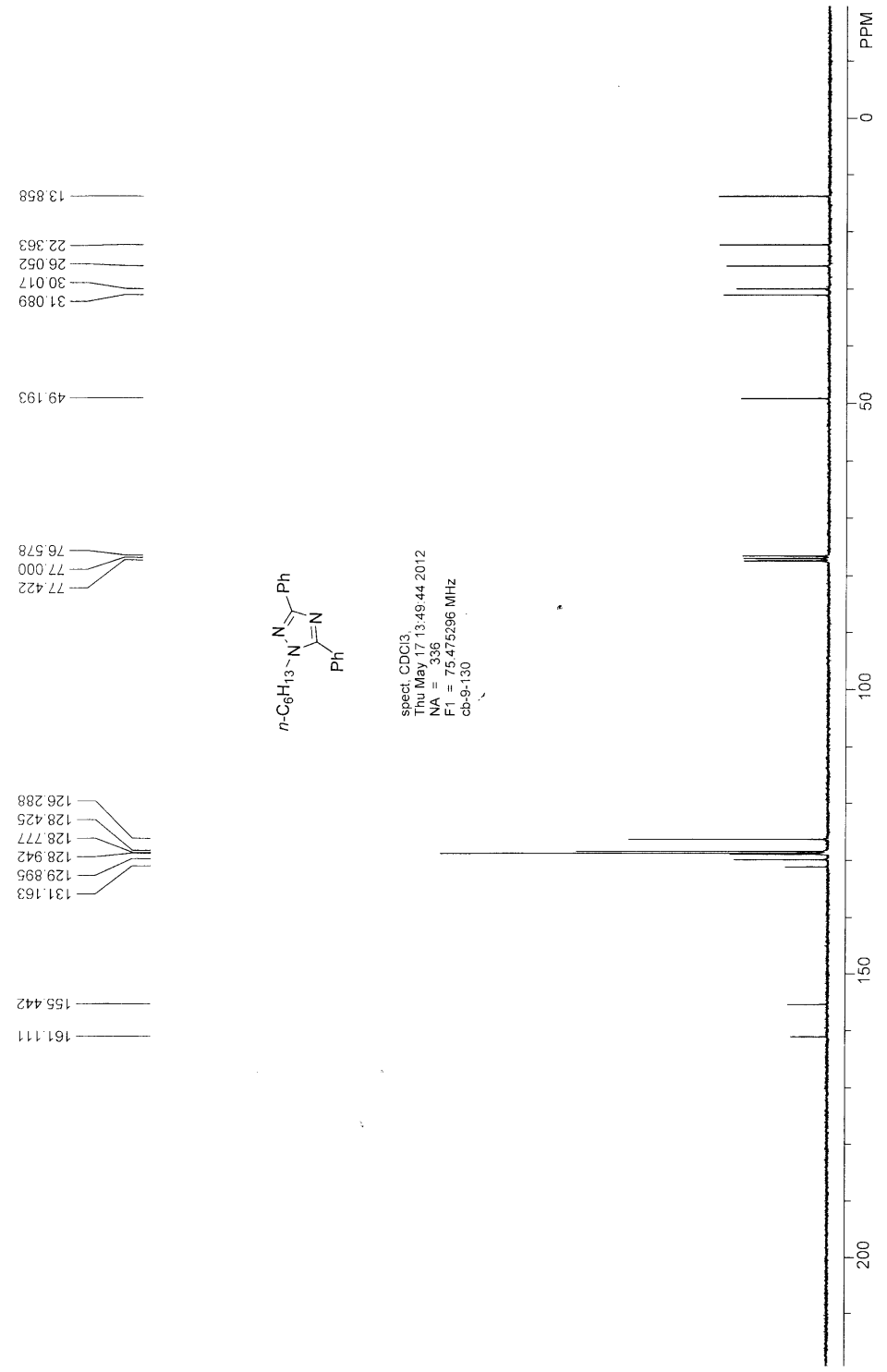

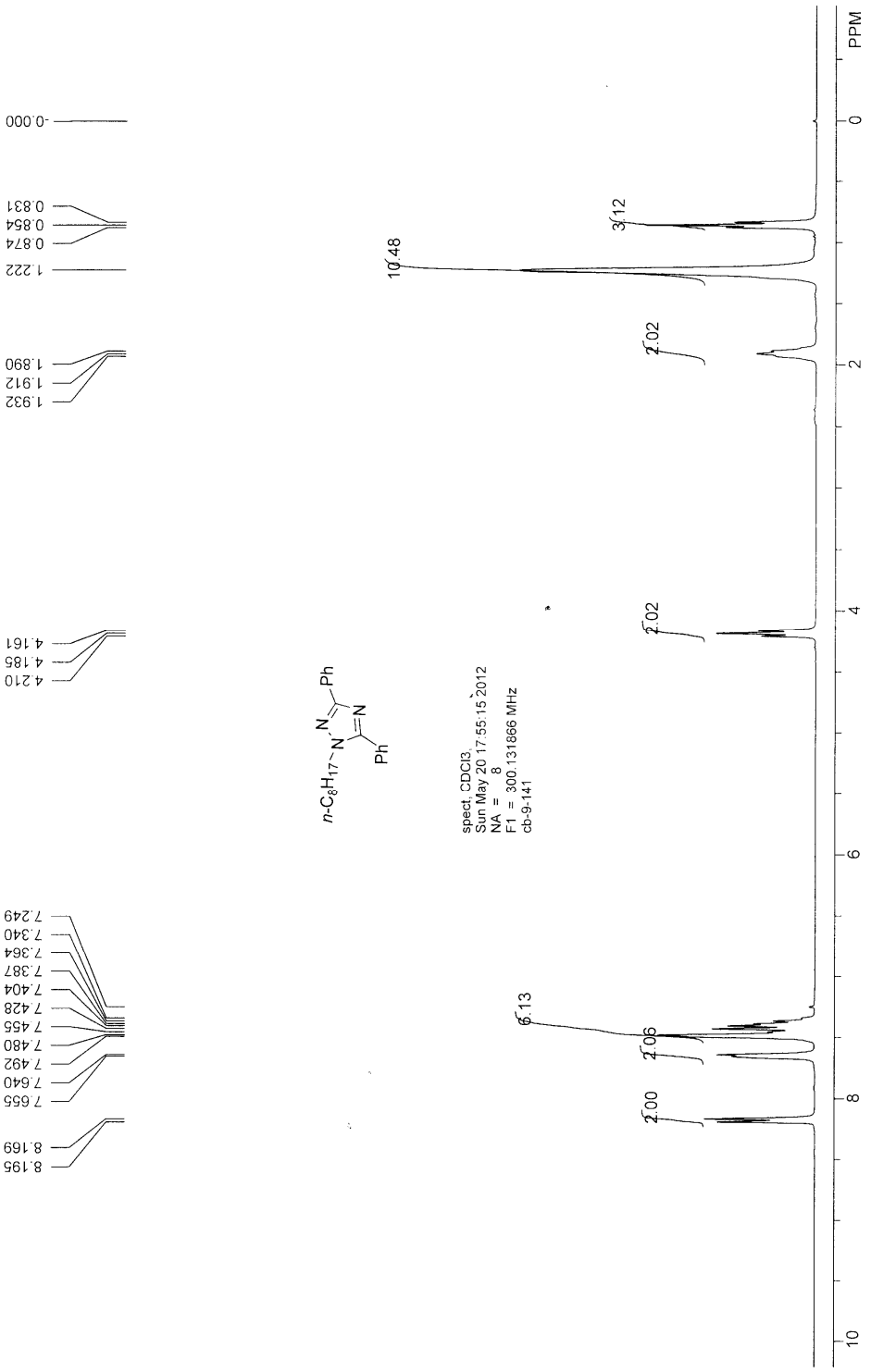

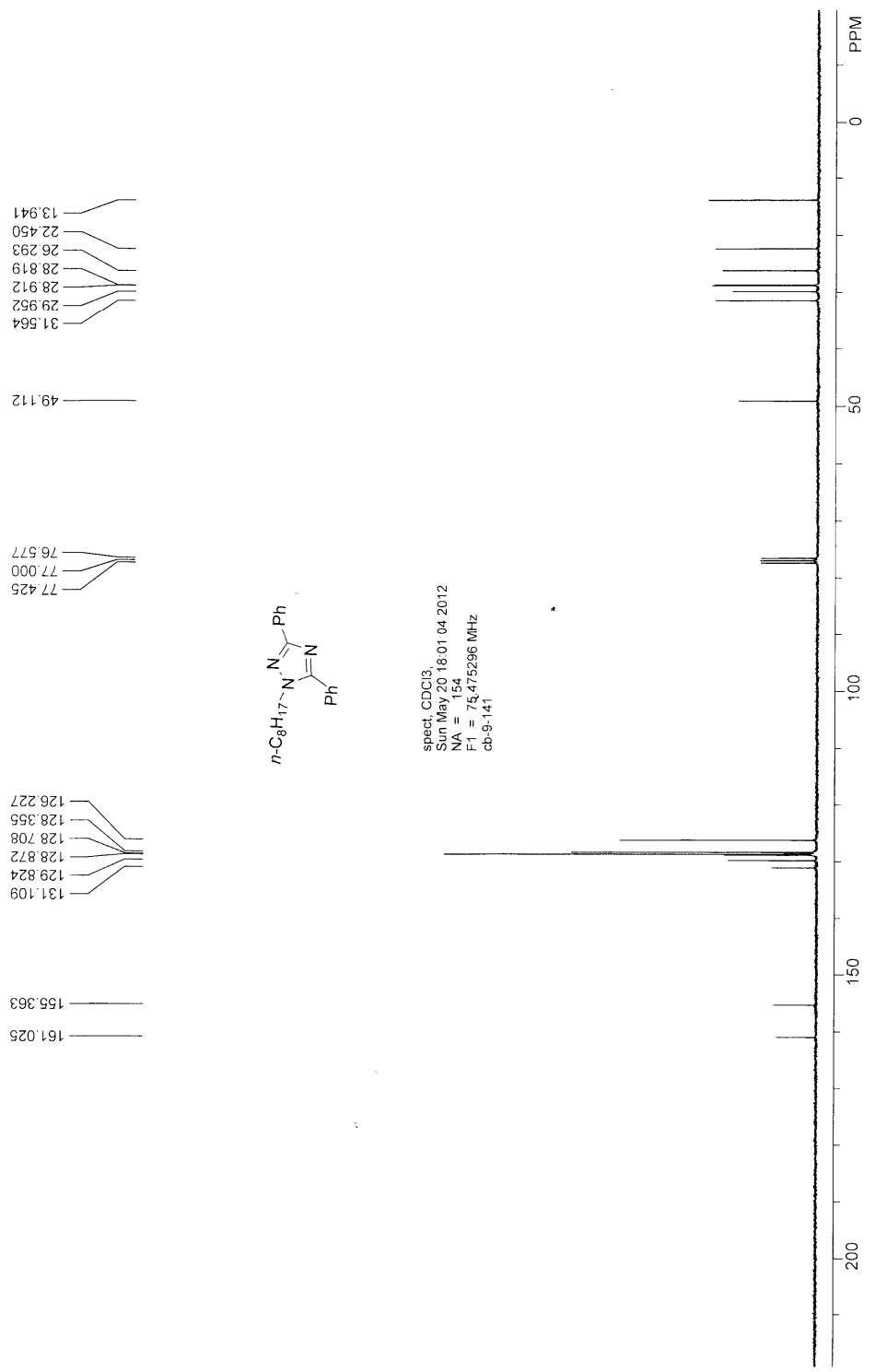

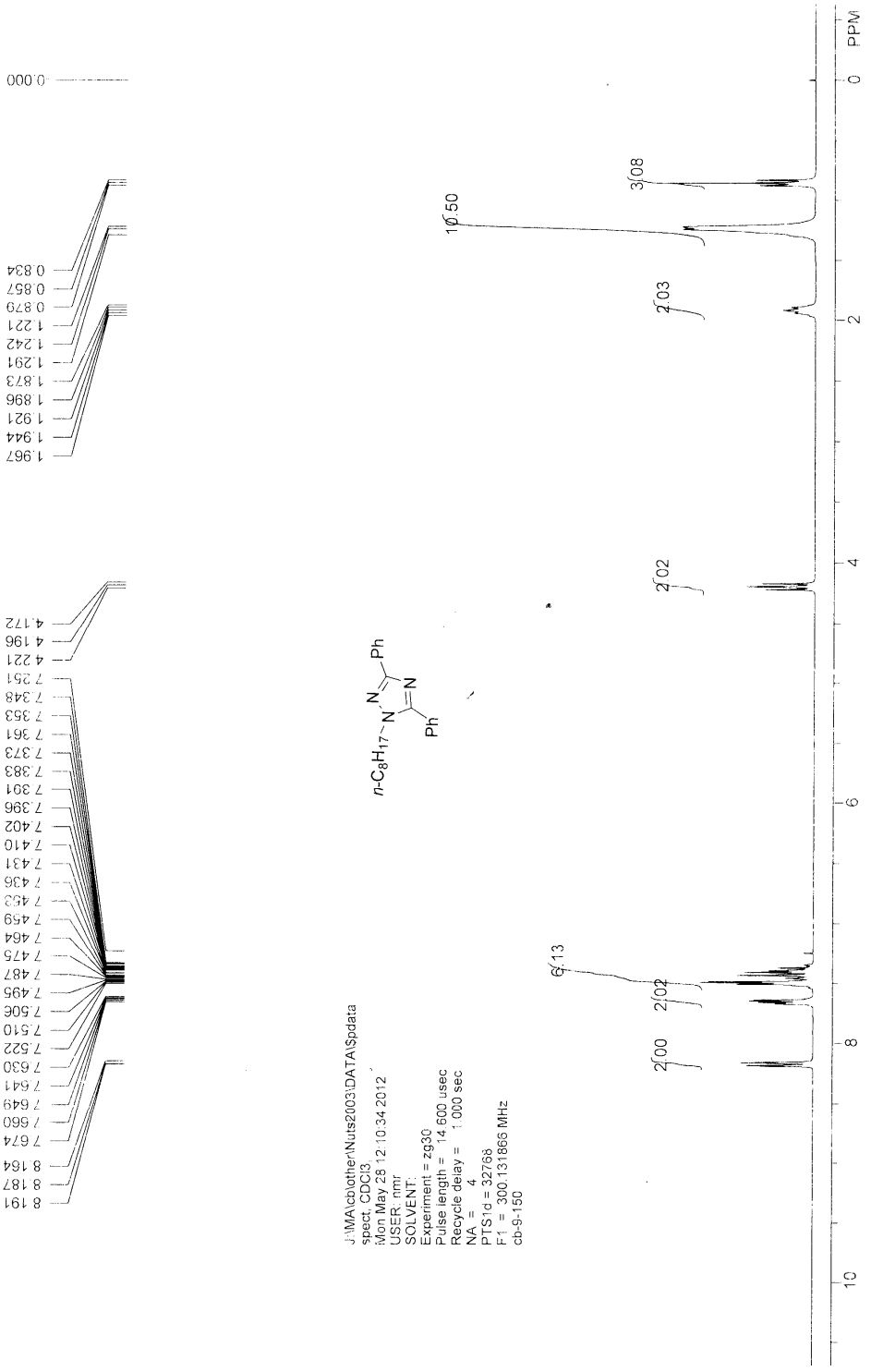

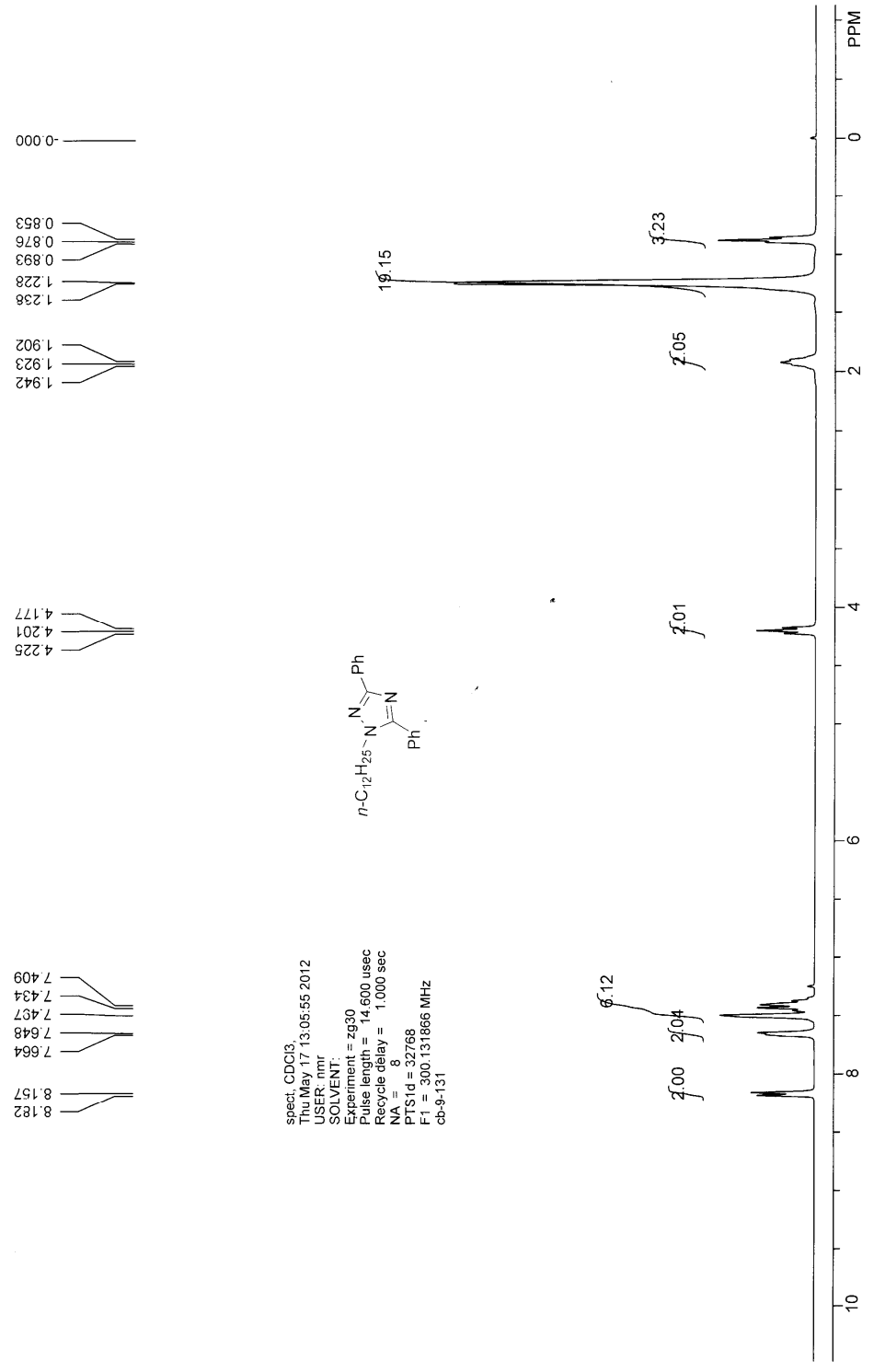

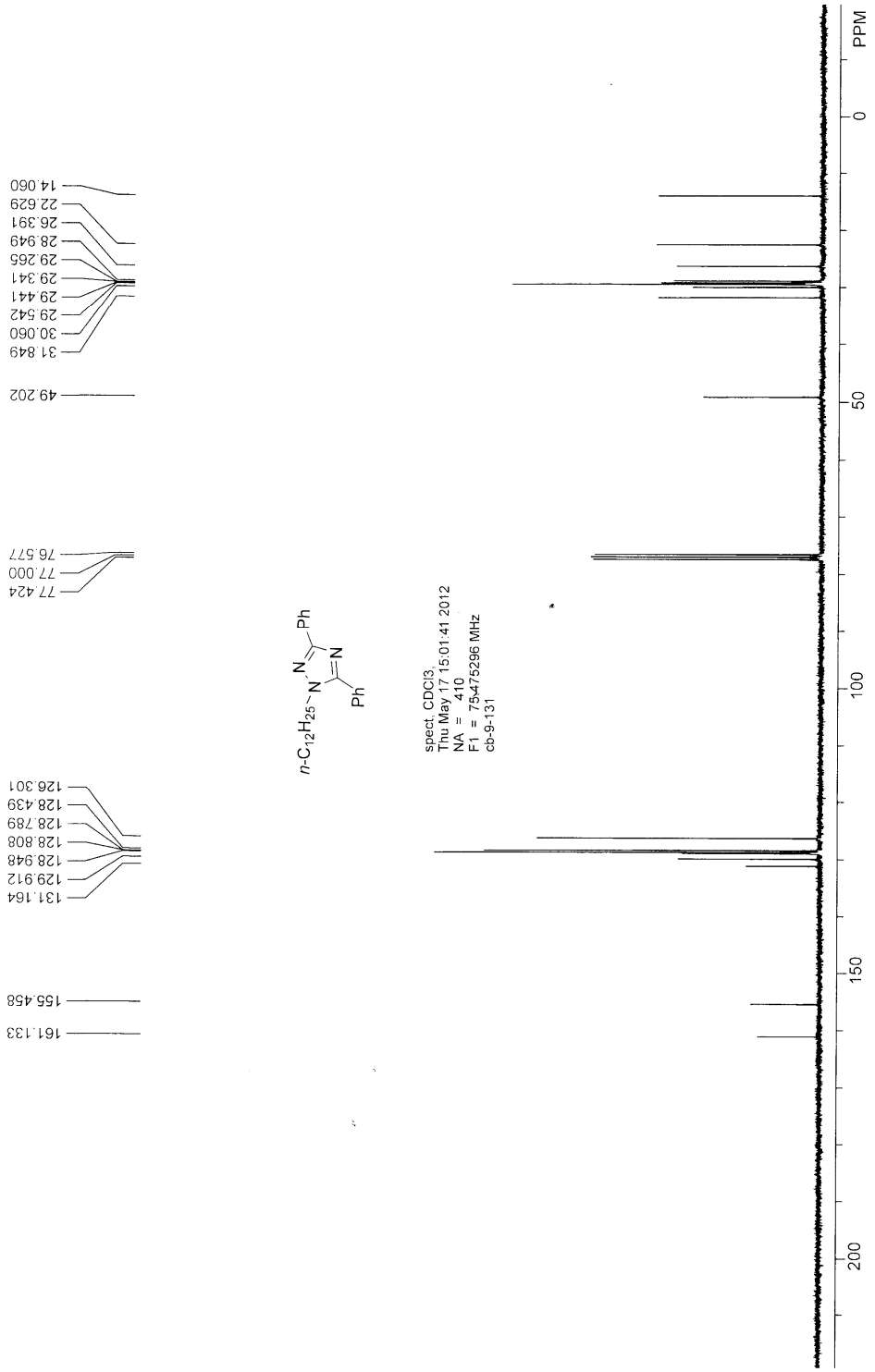
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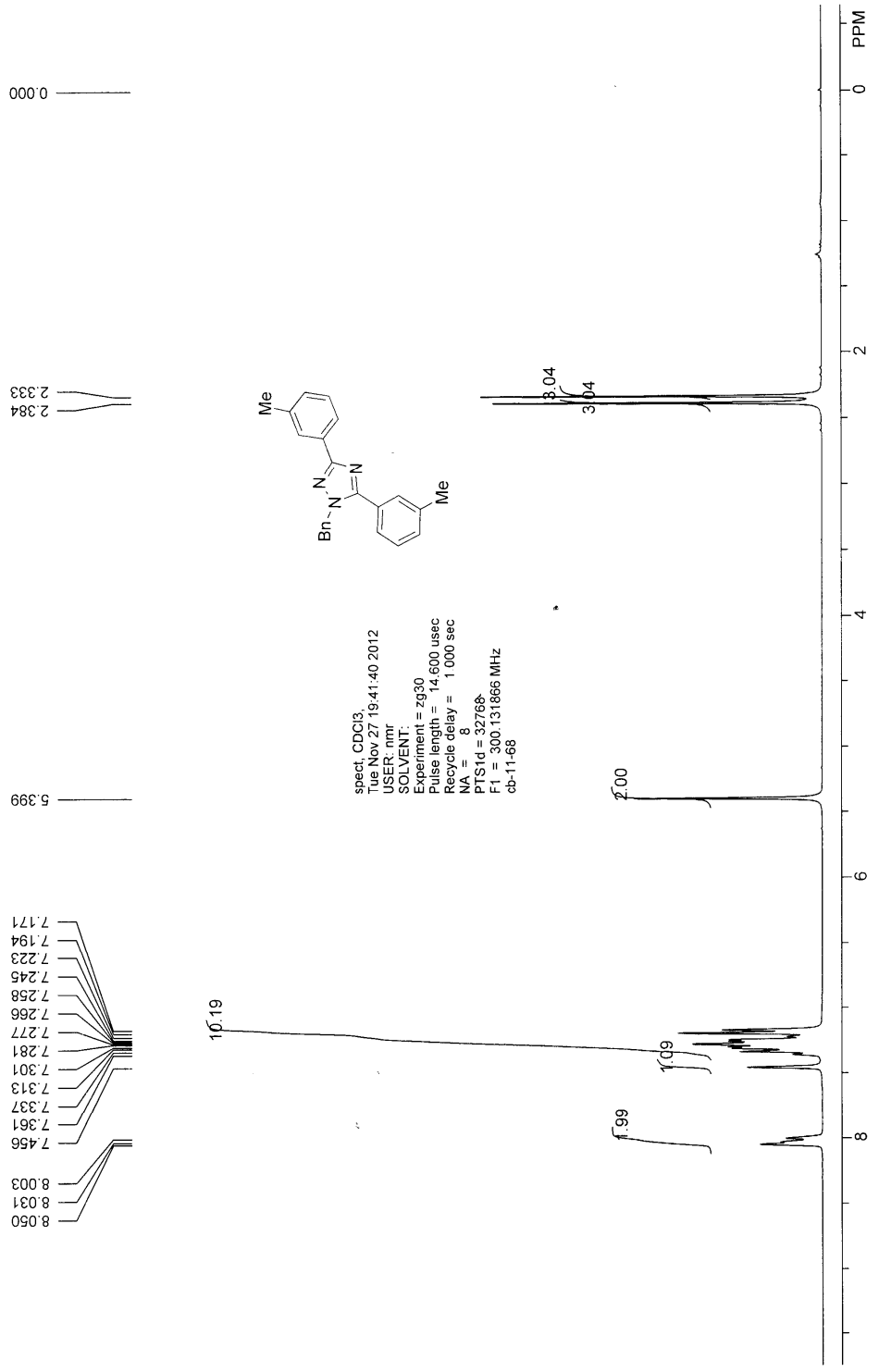
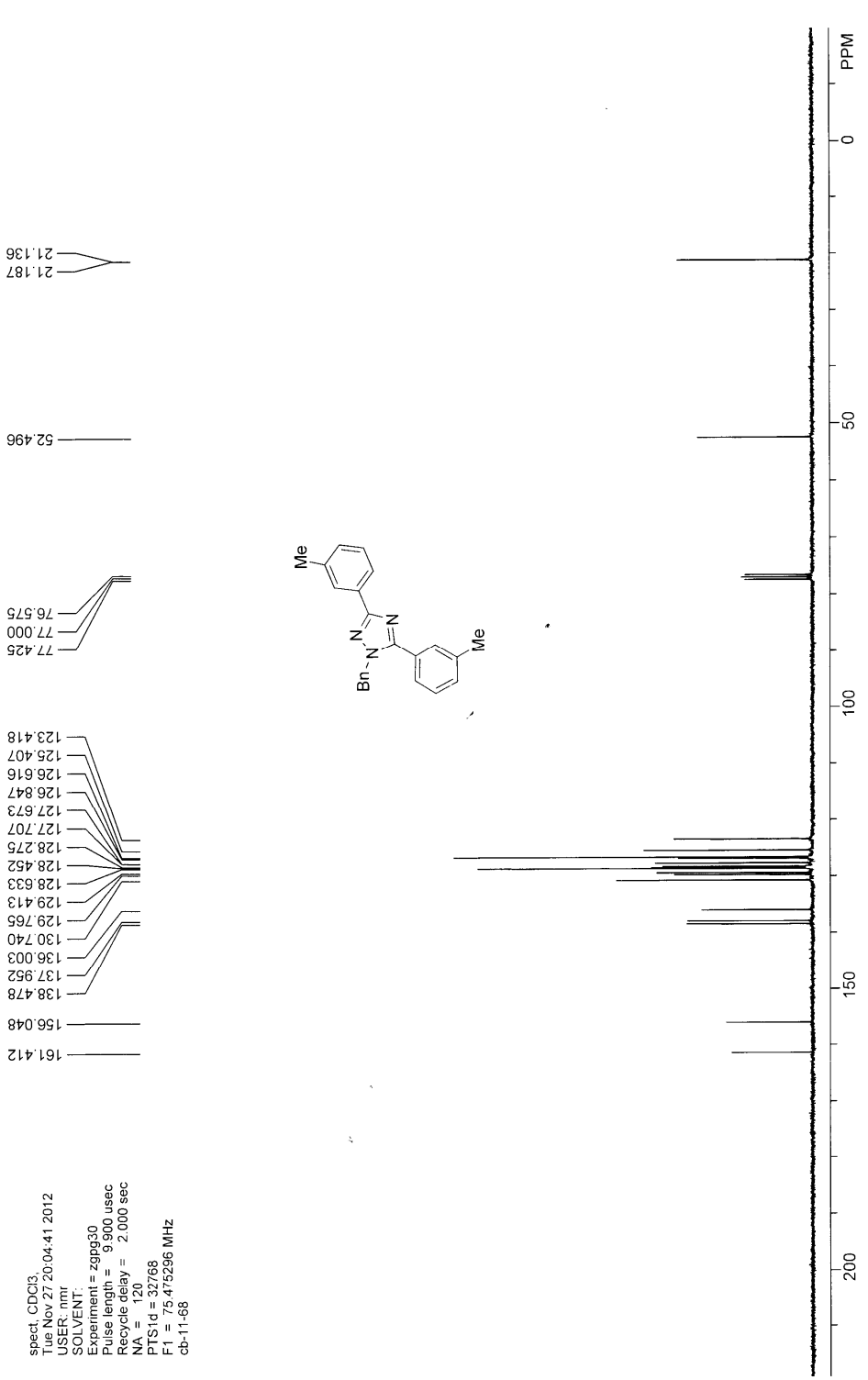
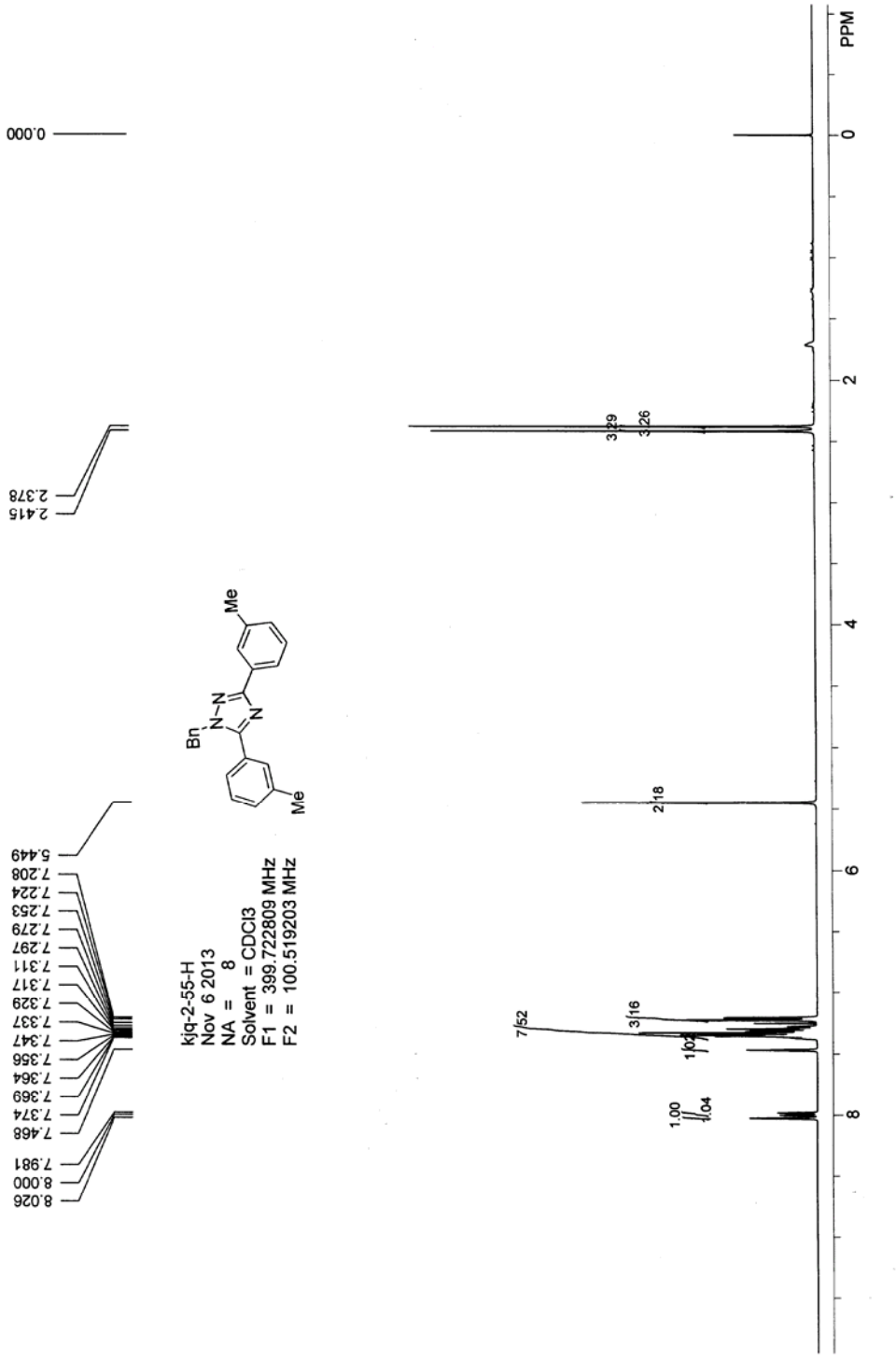
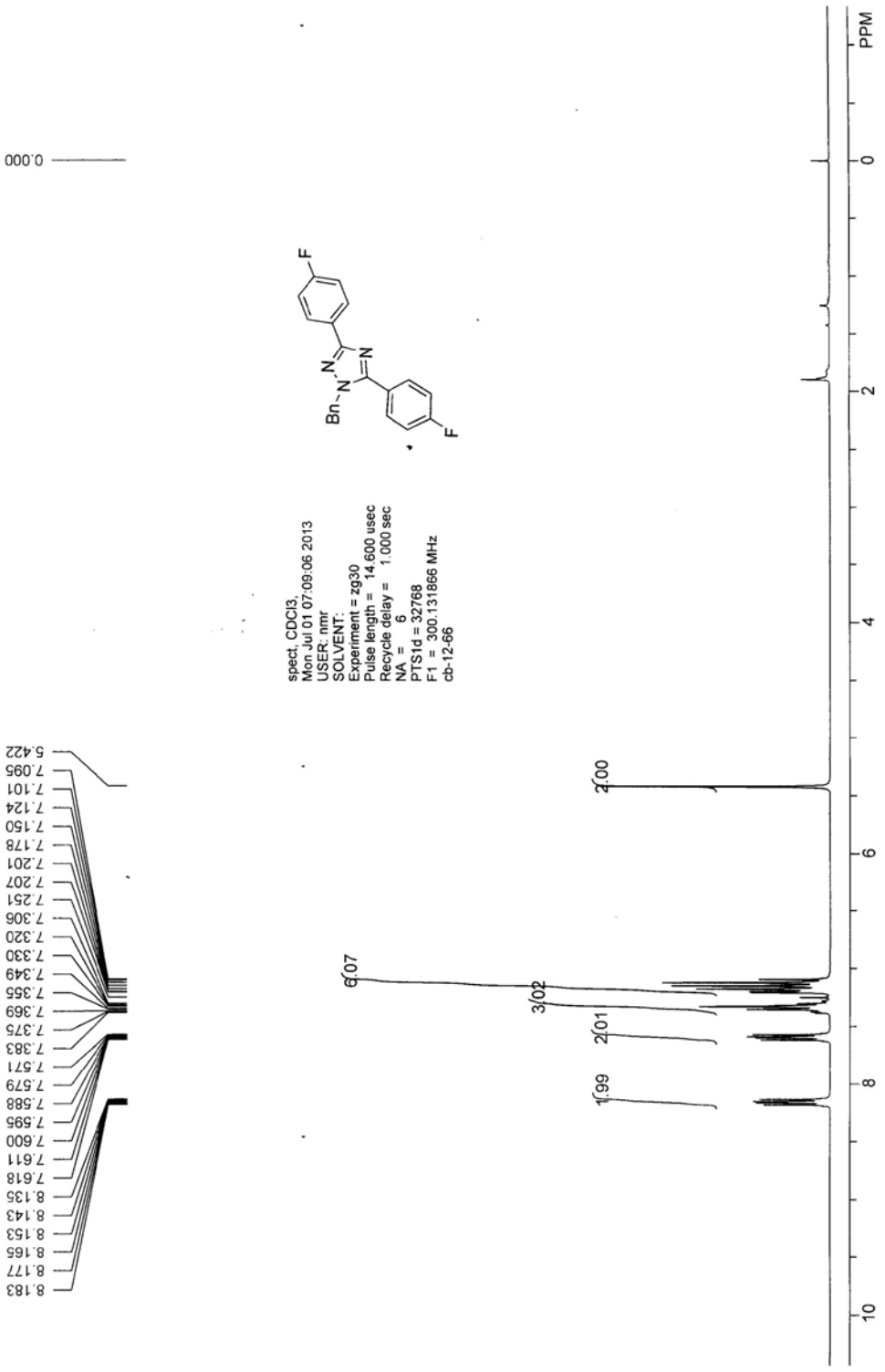
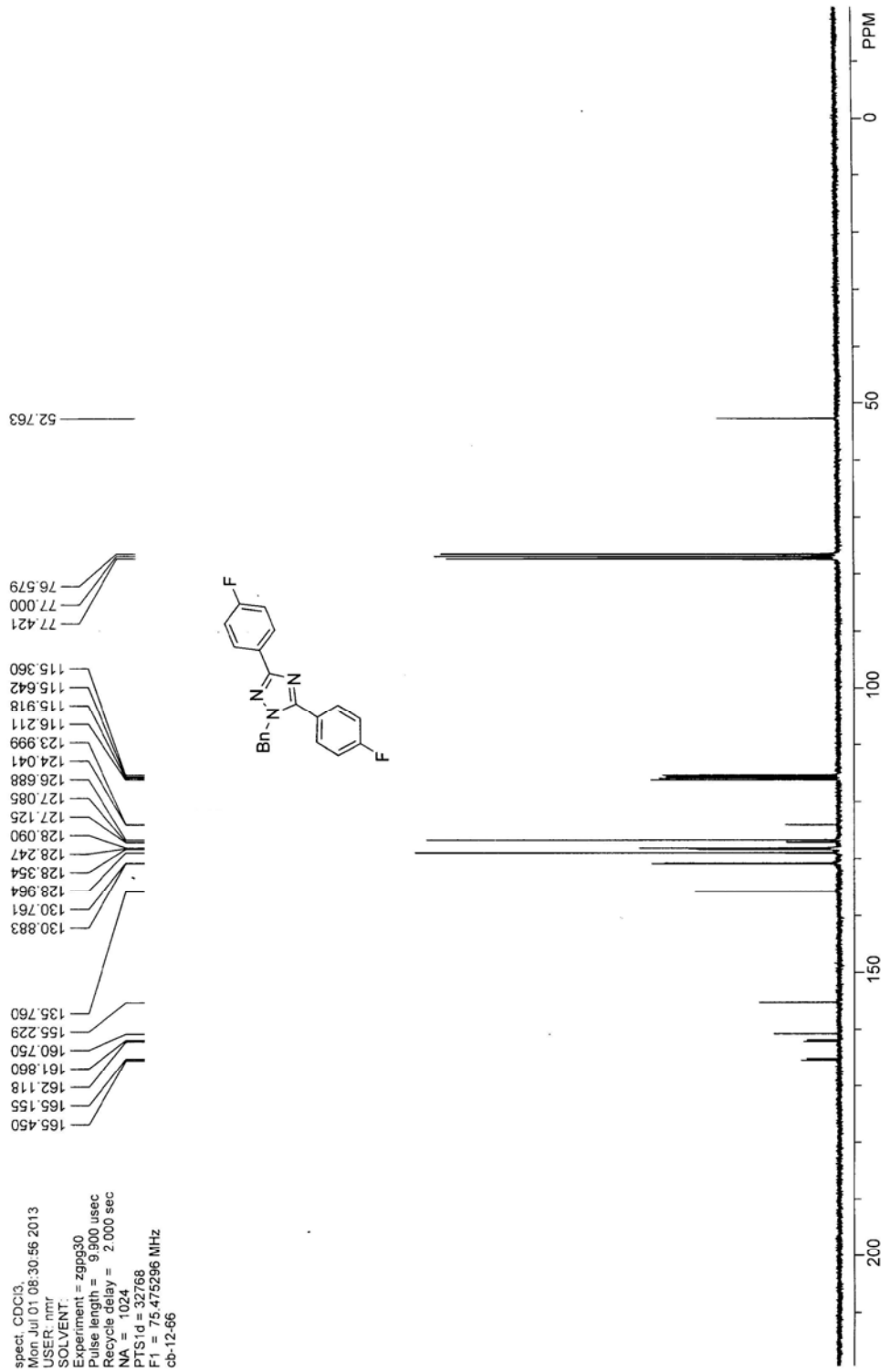
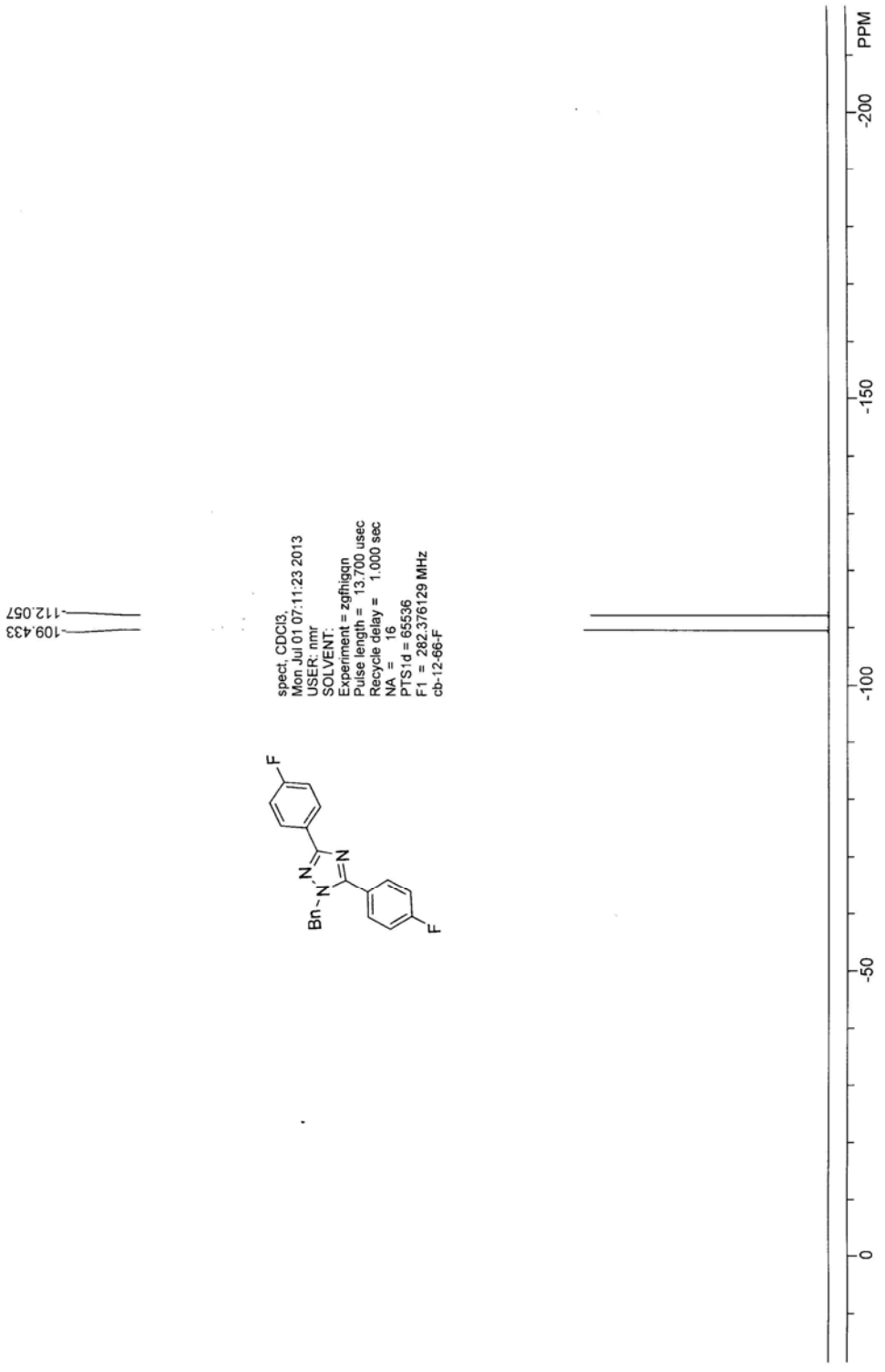


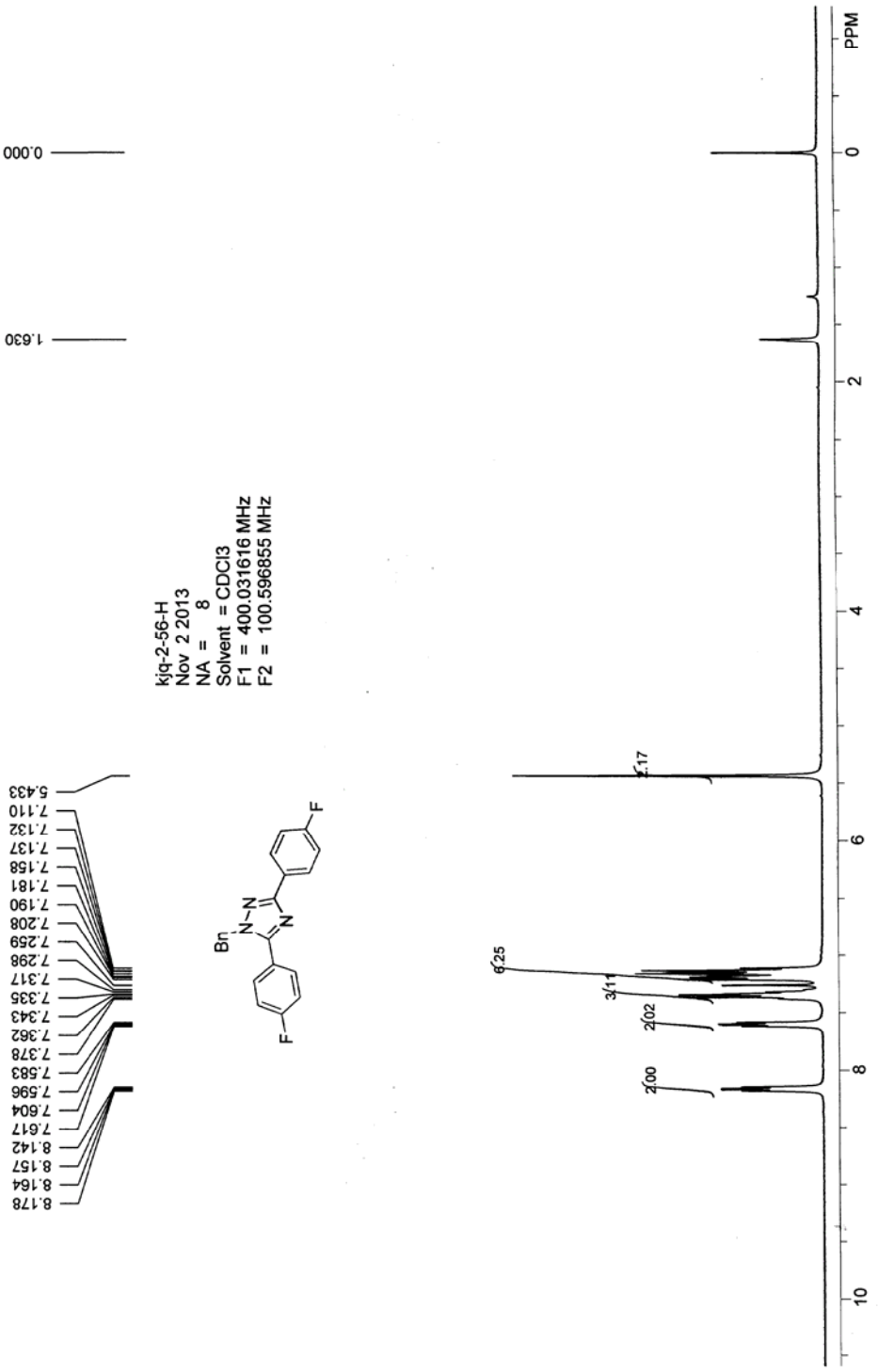


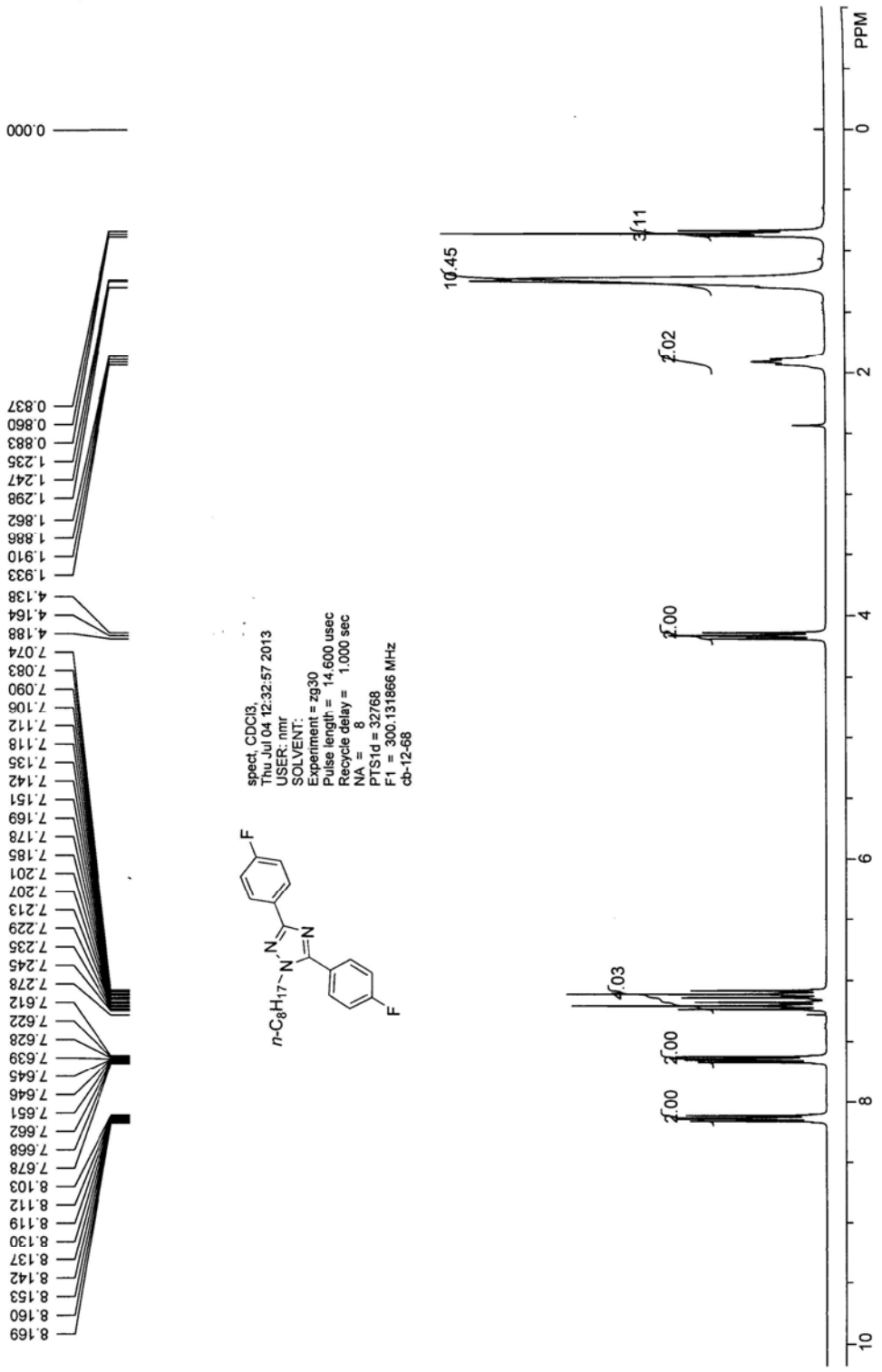


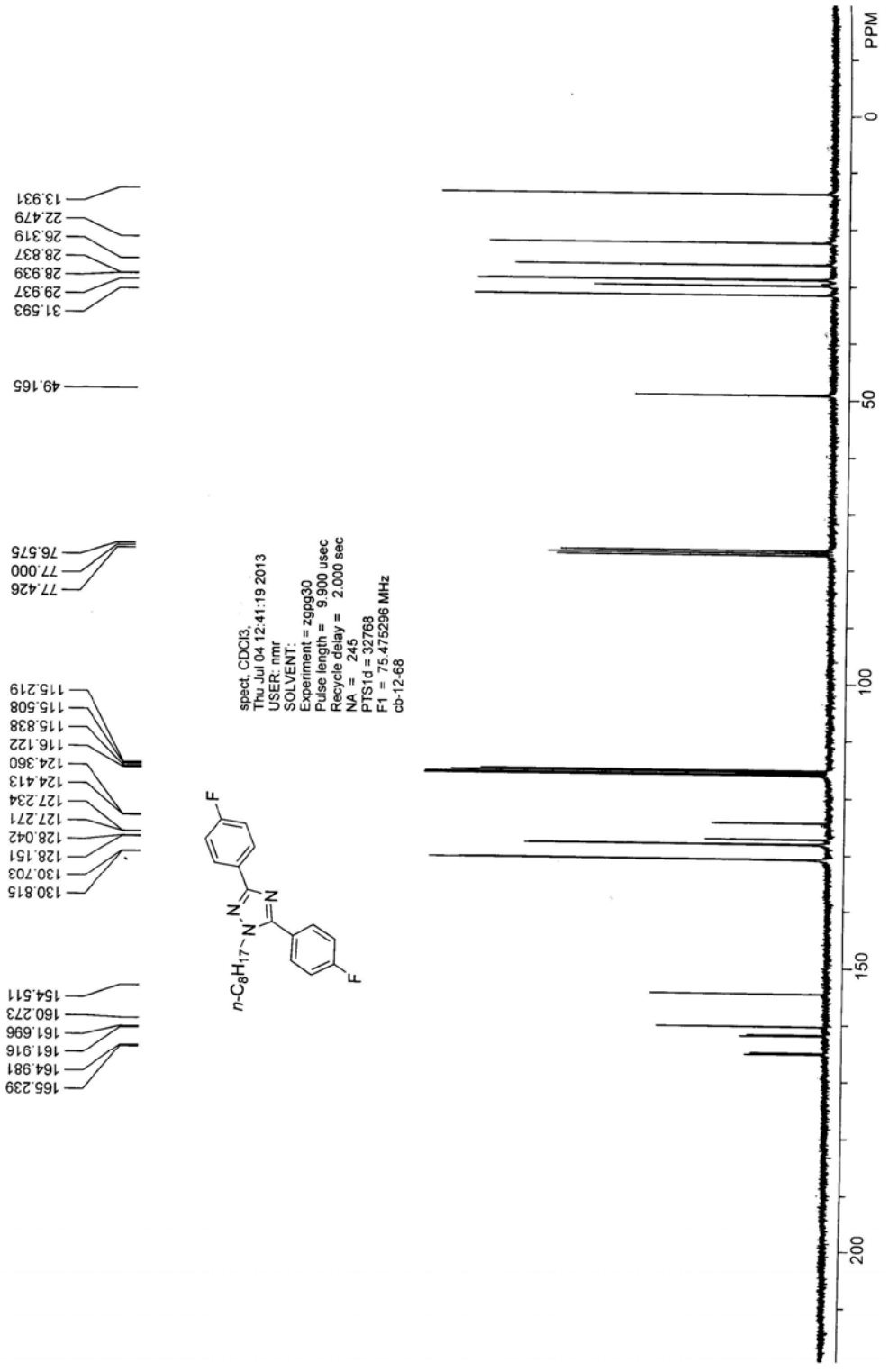


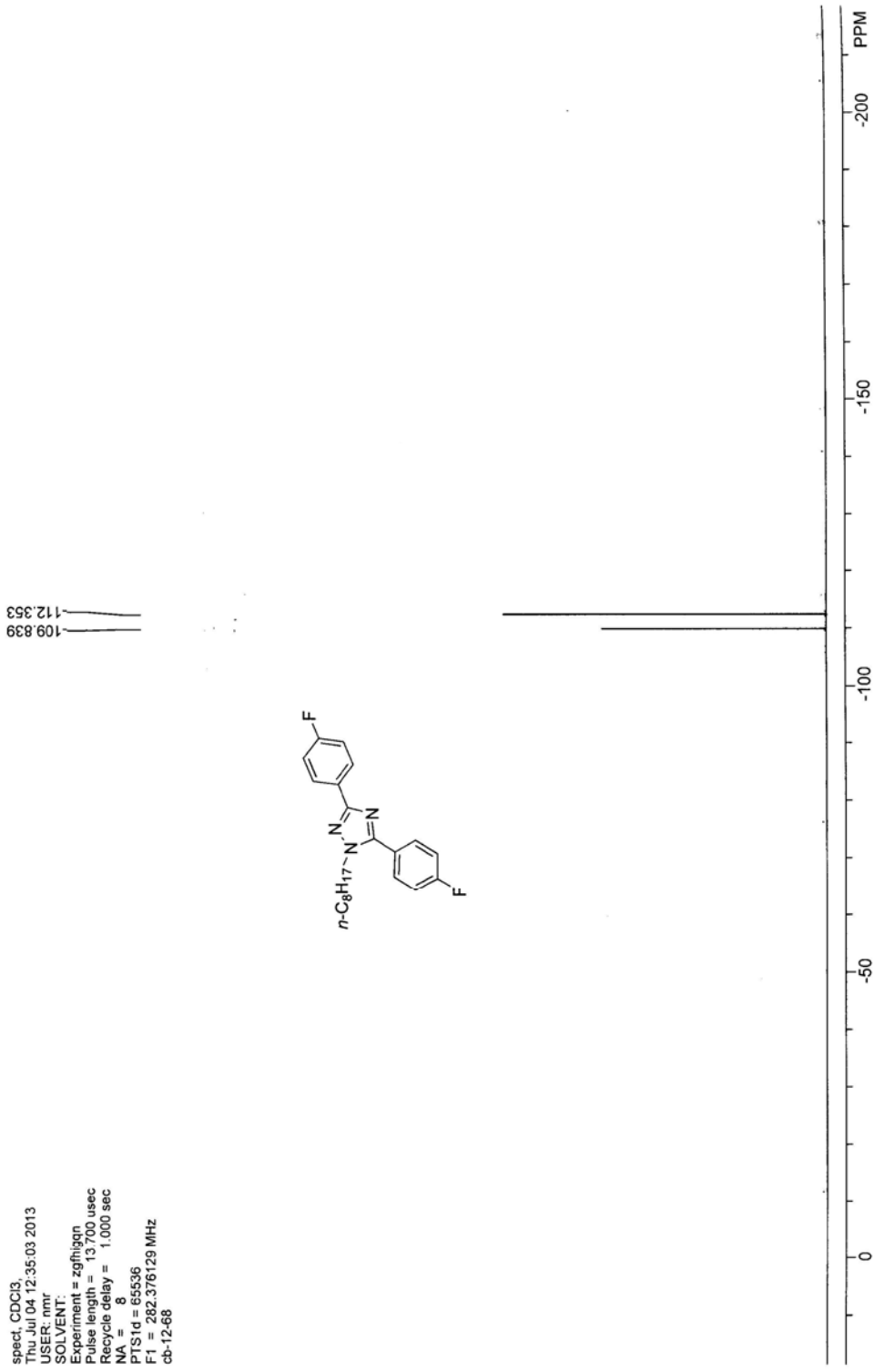


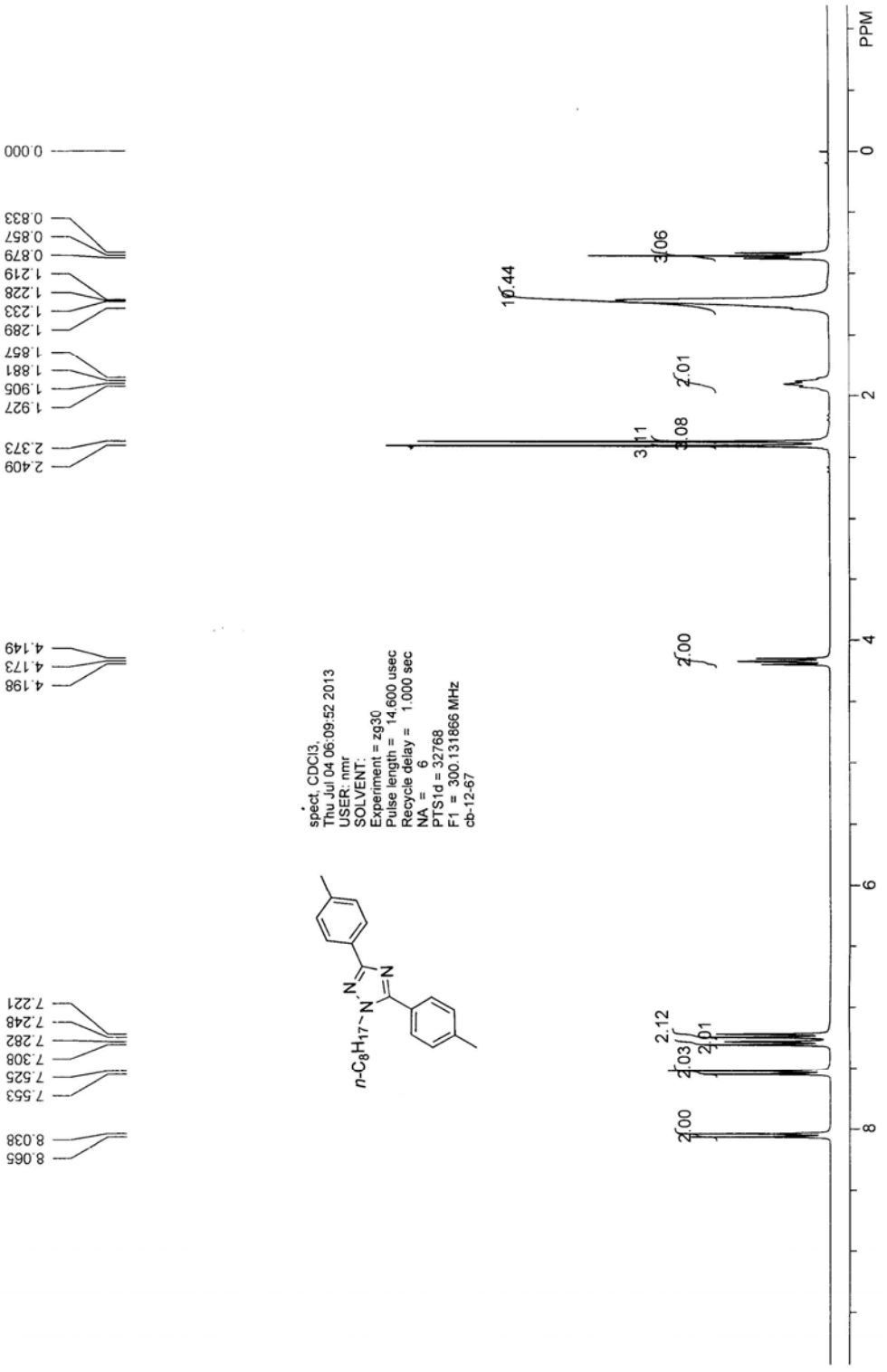


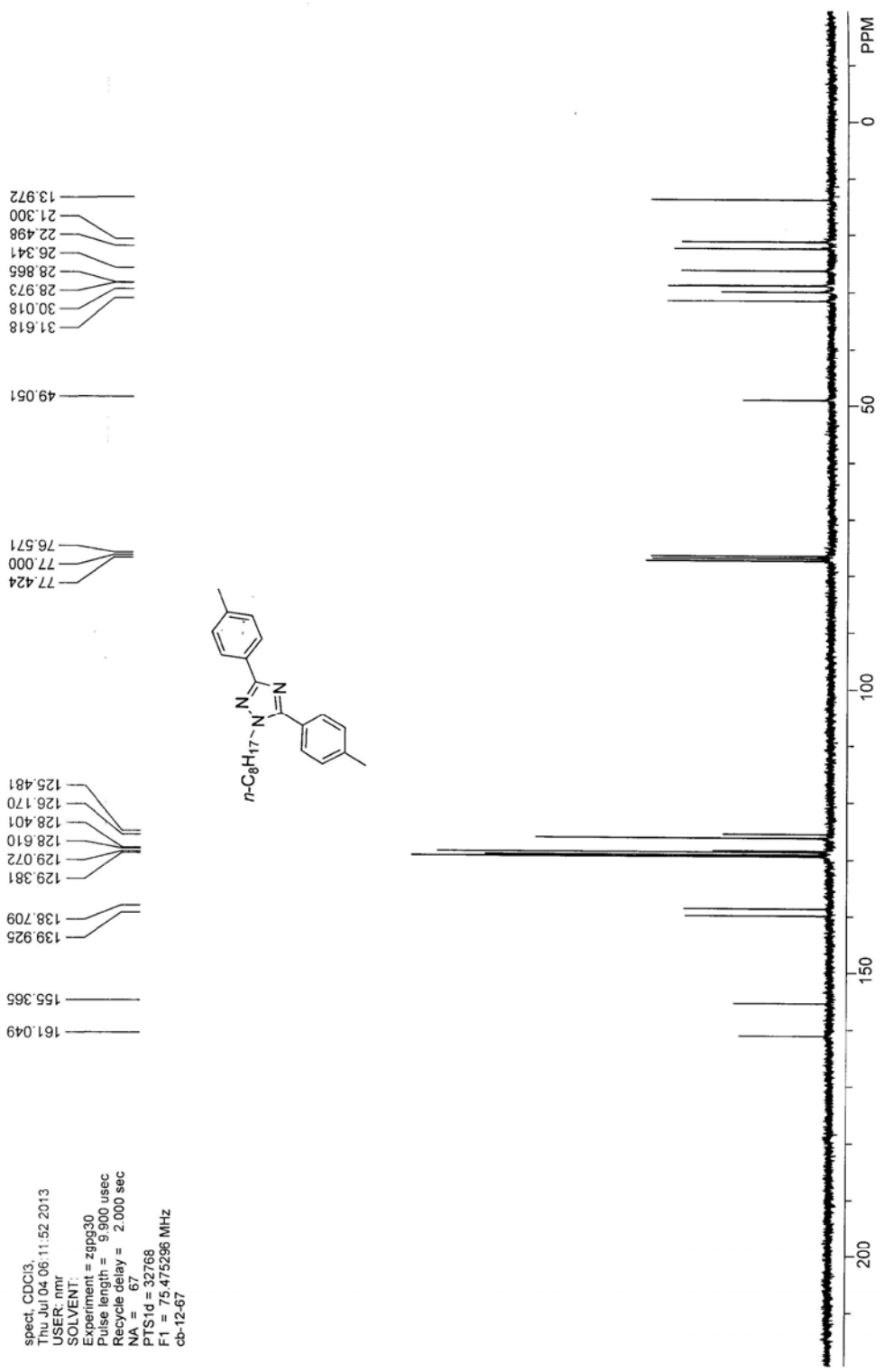


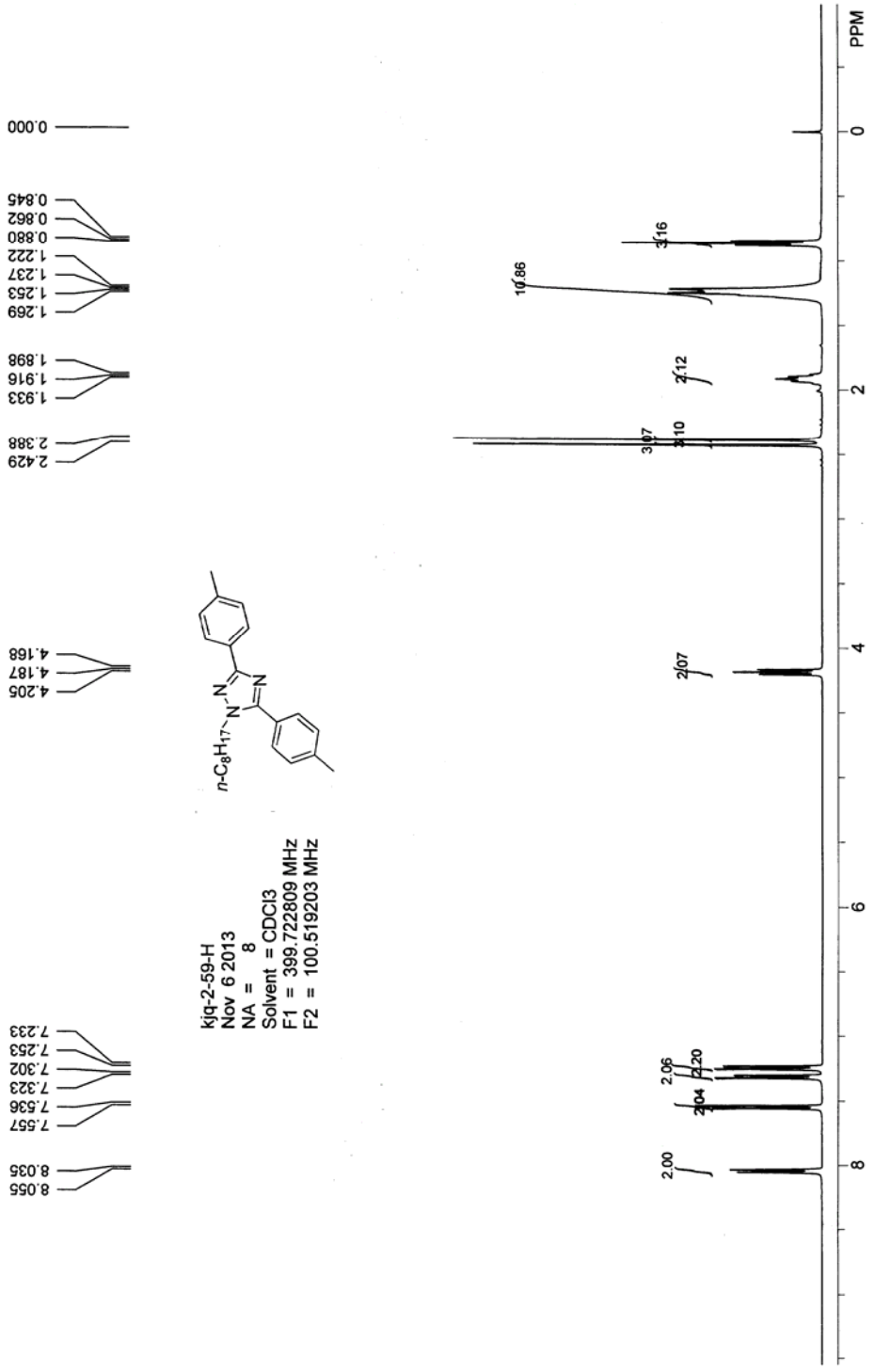


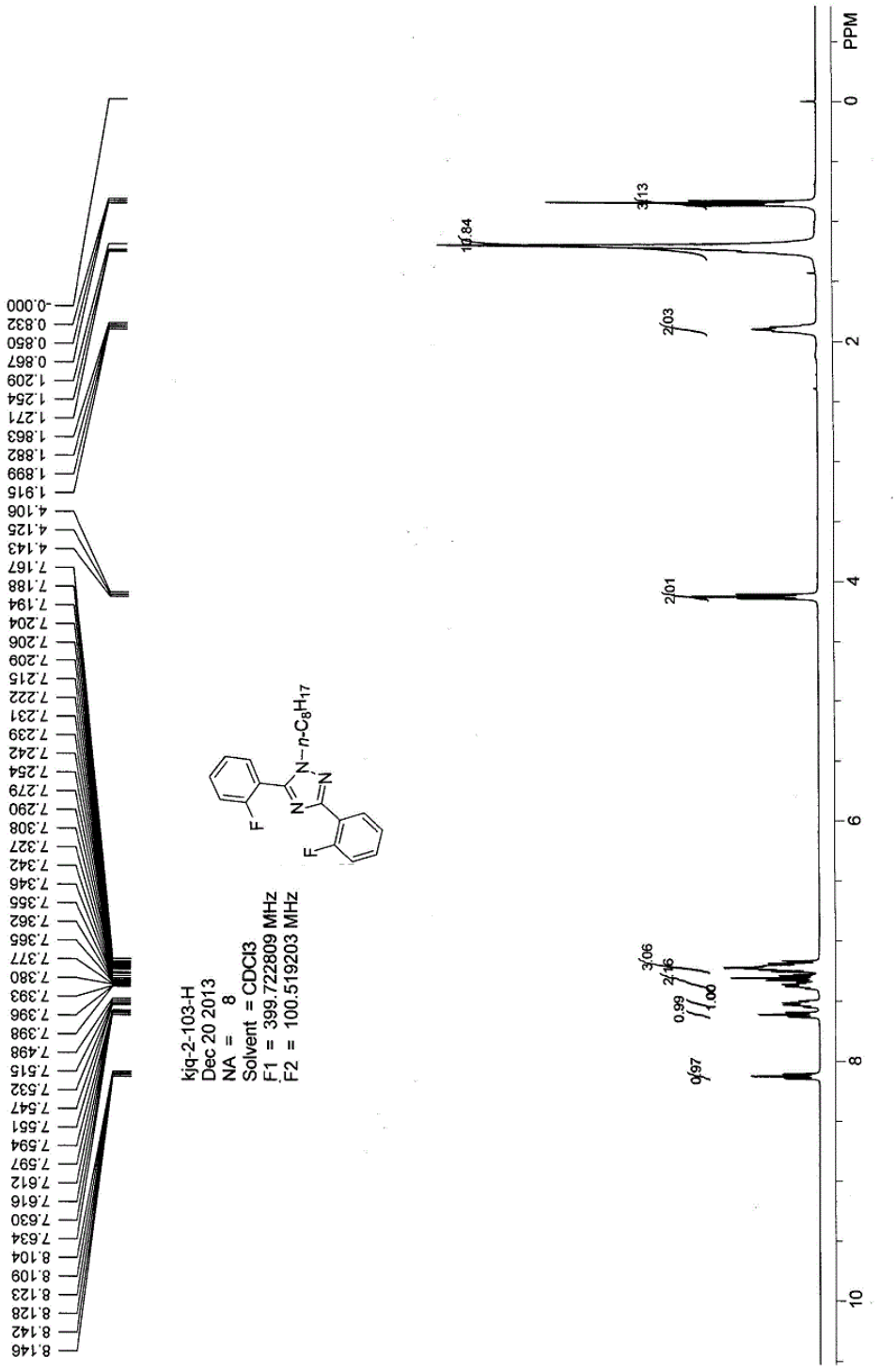




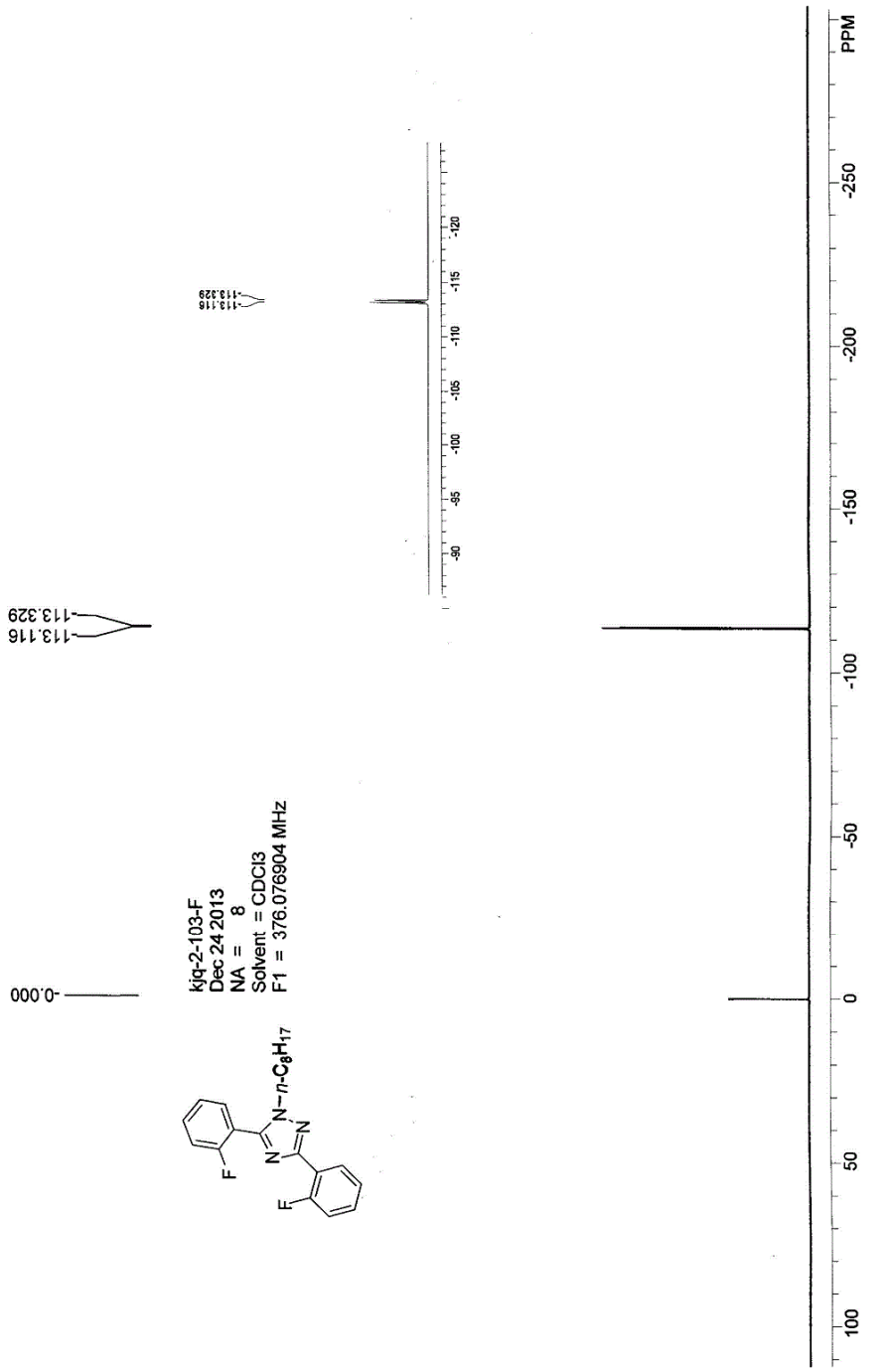


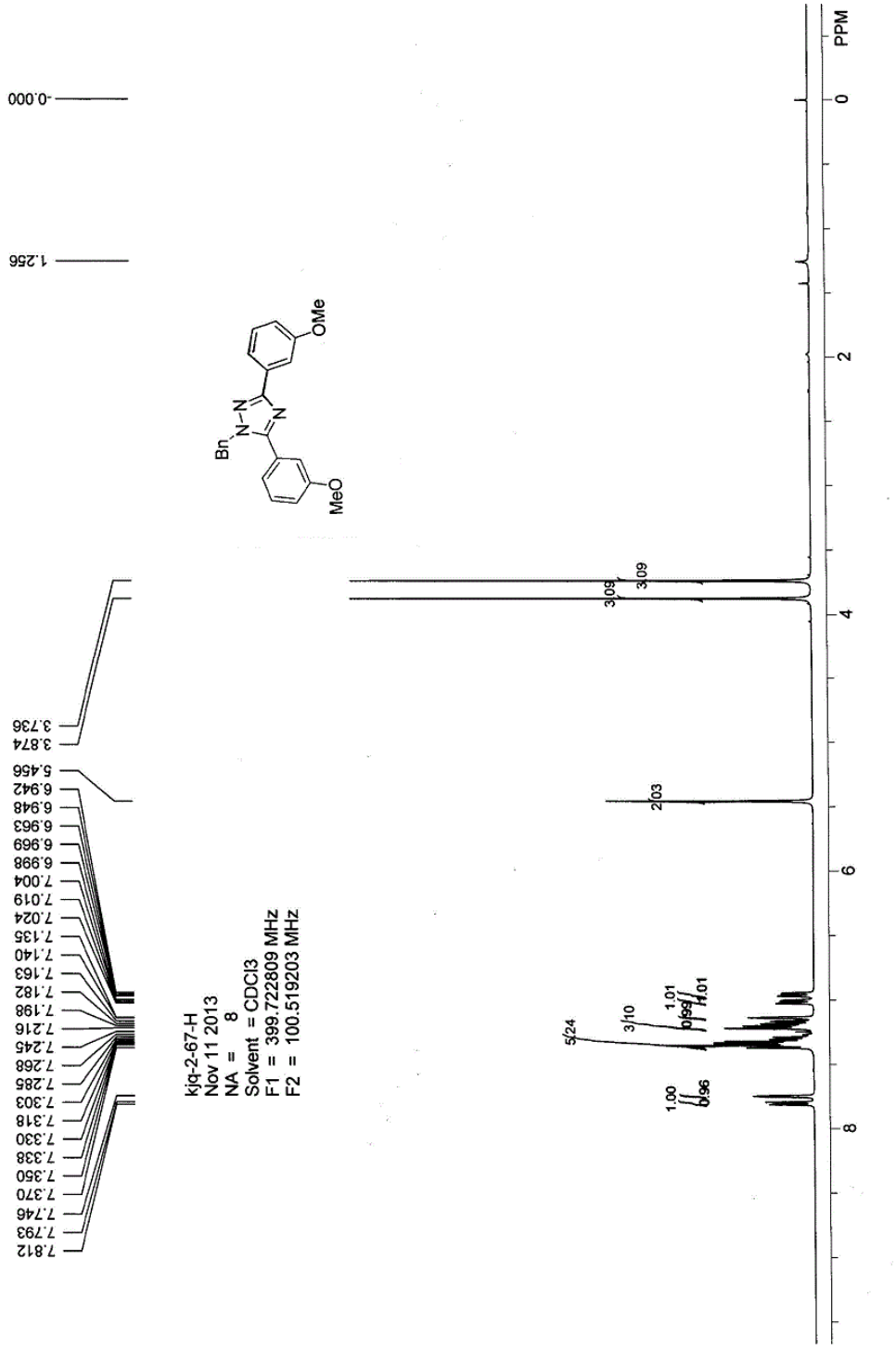


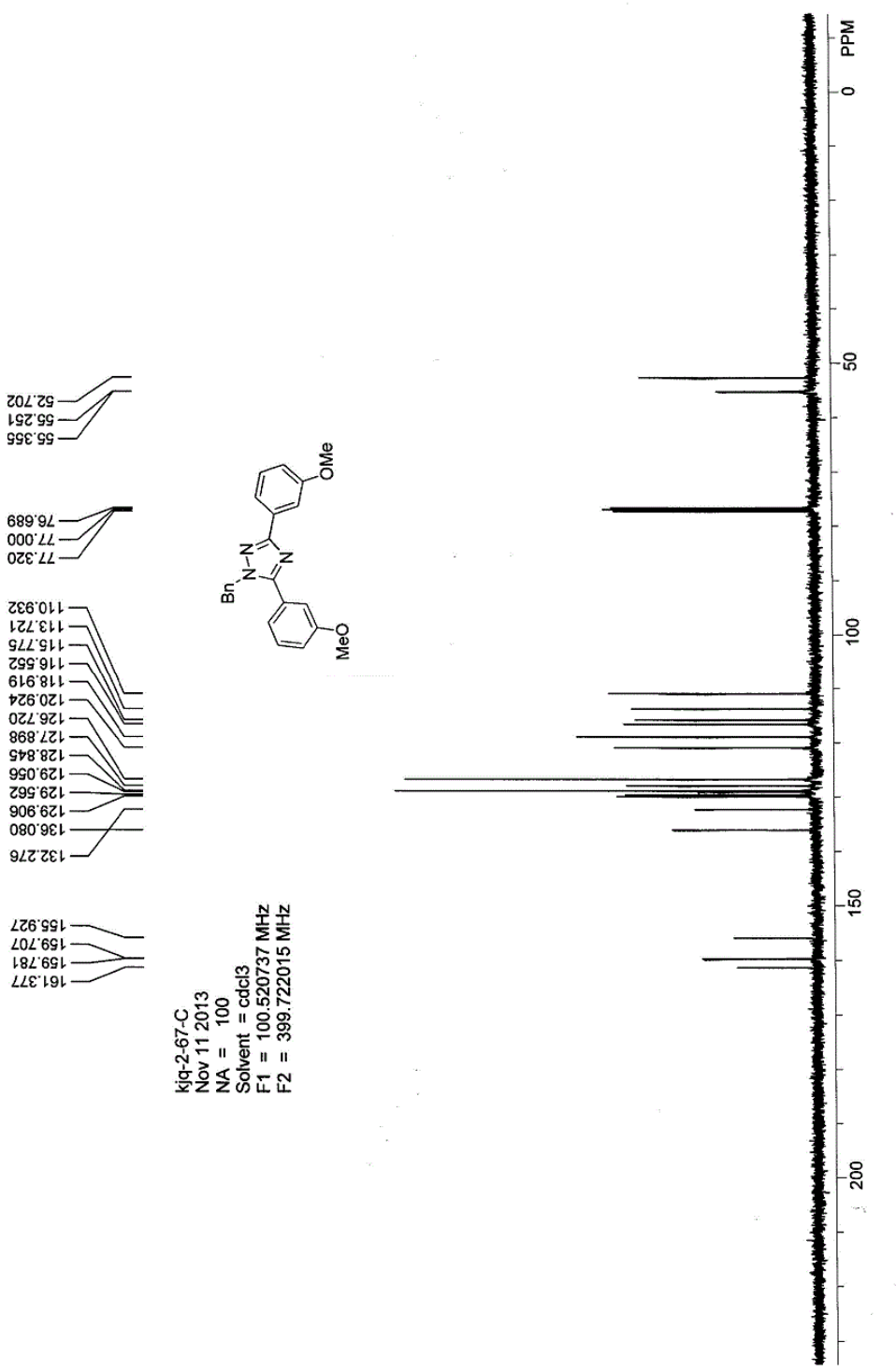


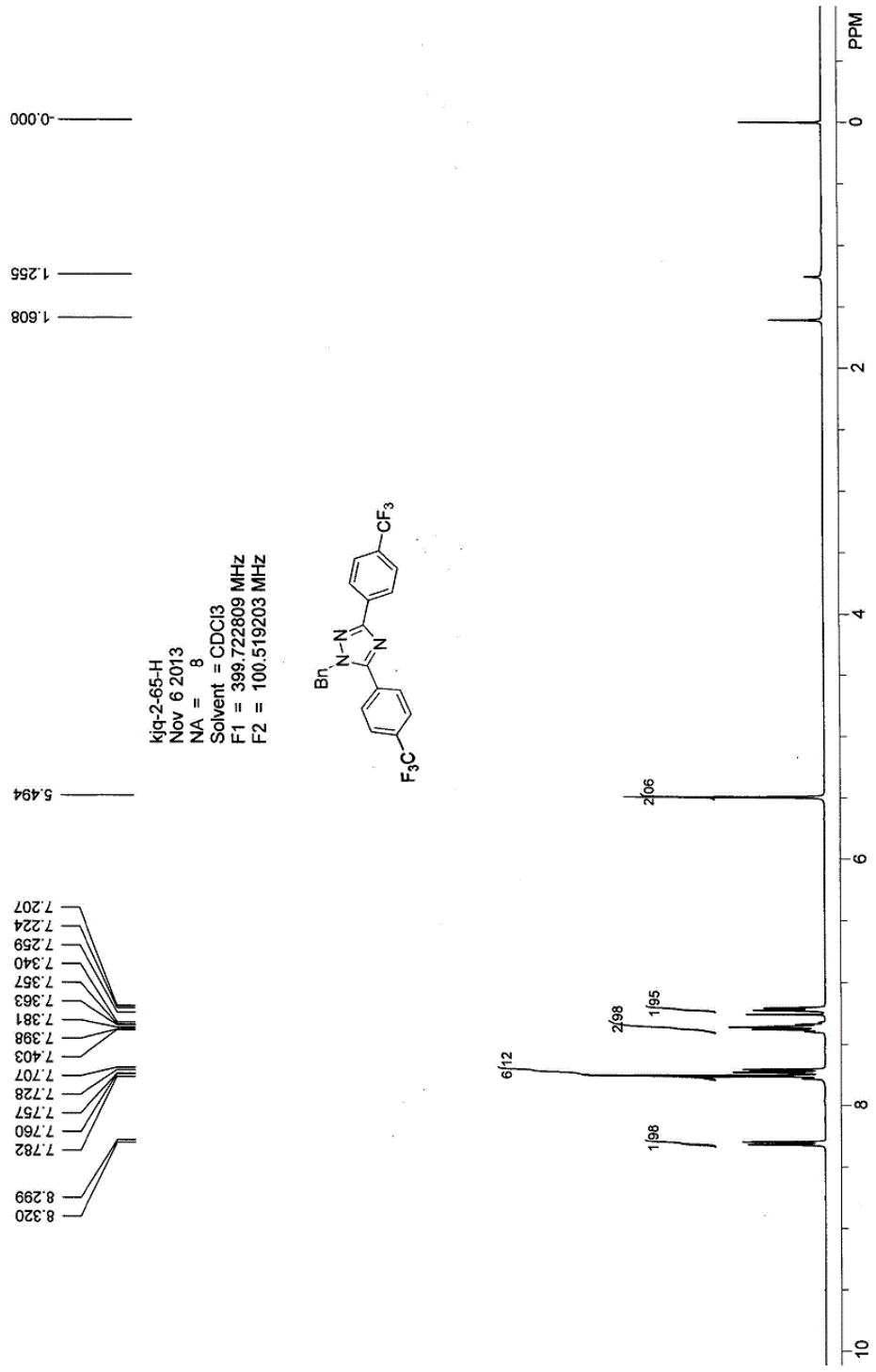


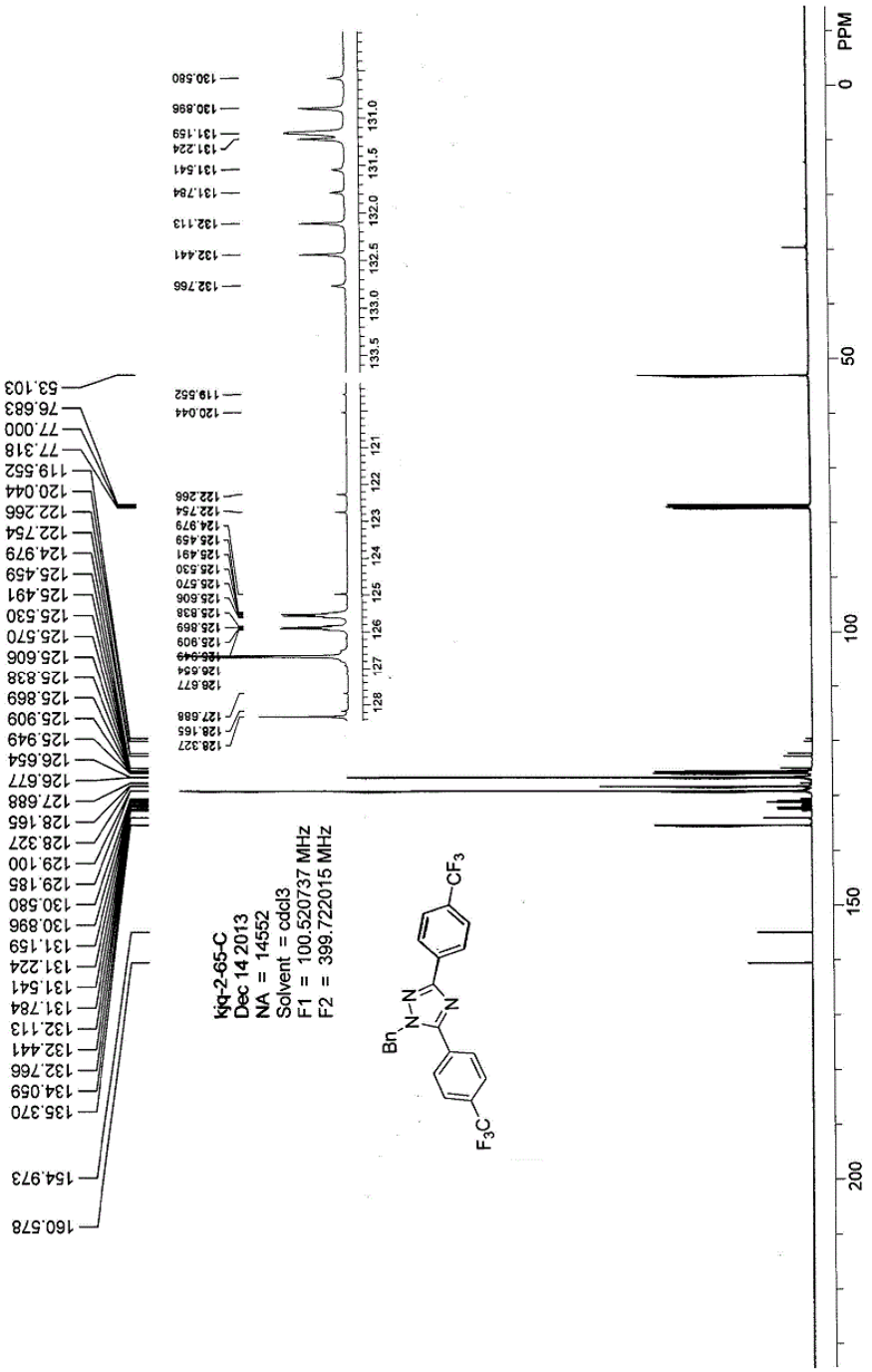

KJQ-2-103-C
Dec 26 2013
NA = 1120
Solvent = cdcl3
F1 = 150.830246 MHz
14.020
22.541
26.352
28.859
28.978
29.665
31.649
49.397
49.419
76.792
77.000
77.215
116.086
116.227
116.365
116.509
116.549
116.649
119.093
119.171
124.031
124.052
124.715
124.740
130.182
130.201
130.491
130.549
131.957
131.971
132.360
132.420
150.364
150.370
158.224
158.255
158.892
159.421
160.551
161.100
N
N
N
n-C8H17
F
F
impurity
PPM

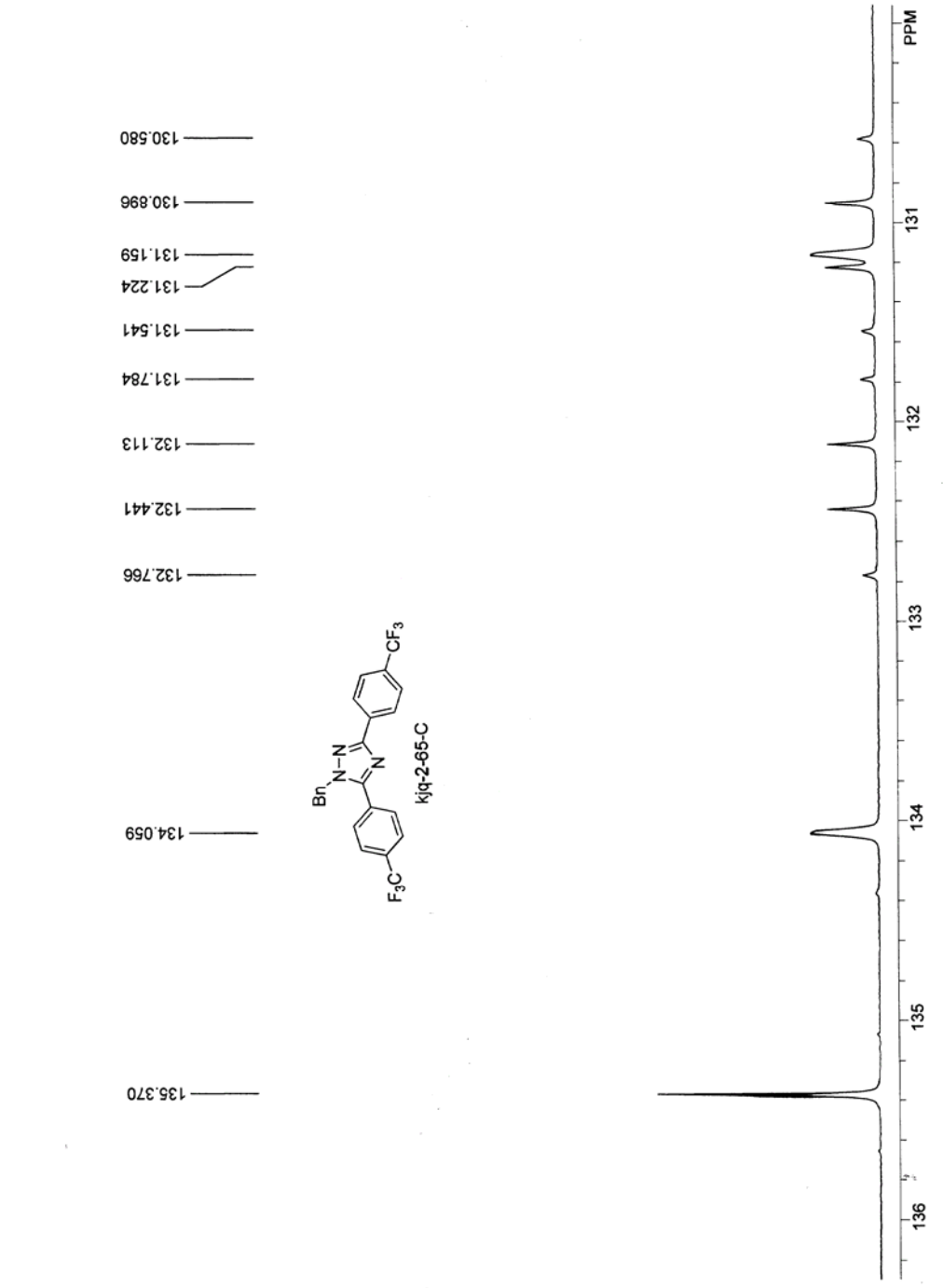

kjq-2-103-F
Dec 24 2013
NA = 8
Solvent = CDCl3
F1 = 376.076904 MHz
N–n-C8H17
F
F
-0.000
113.329
113.116
-113.118
-113.329
PPM
100
50
0
-50
-100
-150
-200
-250
-90
-95
-100
-105
-110
-115
-120

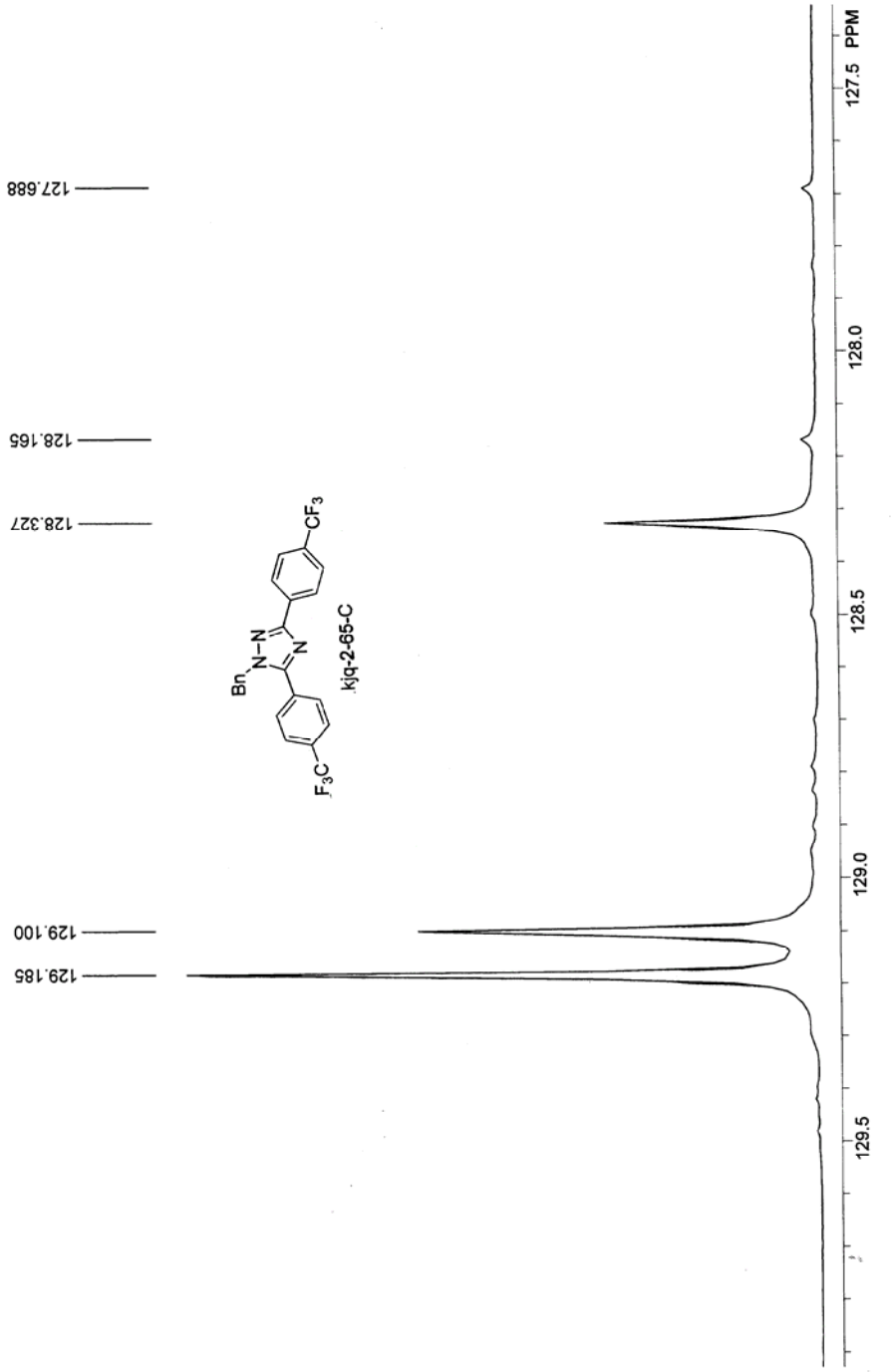

kjq-2-67-H
Nov 11 2013
NA = 8
Solvent = CDCl3
F1 = 399.722809 MHz
F2 = 100.519203 MHz
Bn
N
N
N
OMe
MeO
PPM
0
2
4
6
8
3.09
3.09
2.03
5.24
3.10
1.01
1.01
1.00
0.96
-0.000
1.256
3.736
3.874
5.456
6.942
6.948
6.963
6.969
6.998
7.004
7.019
7.024
7.135
7.140
7.163
7.182
7.198
7.216
7.245
7.268
7.285
7.303
7.318
7.330
7.338
7.350
7.370
7.746
7.793
7.812

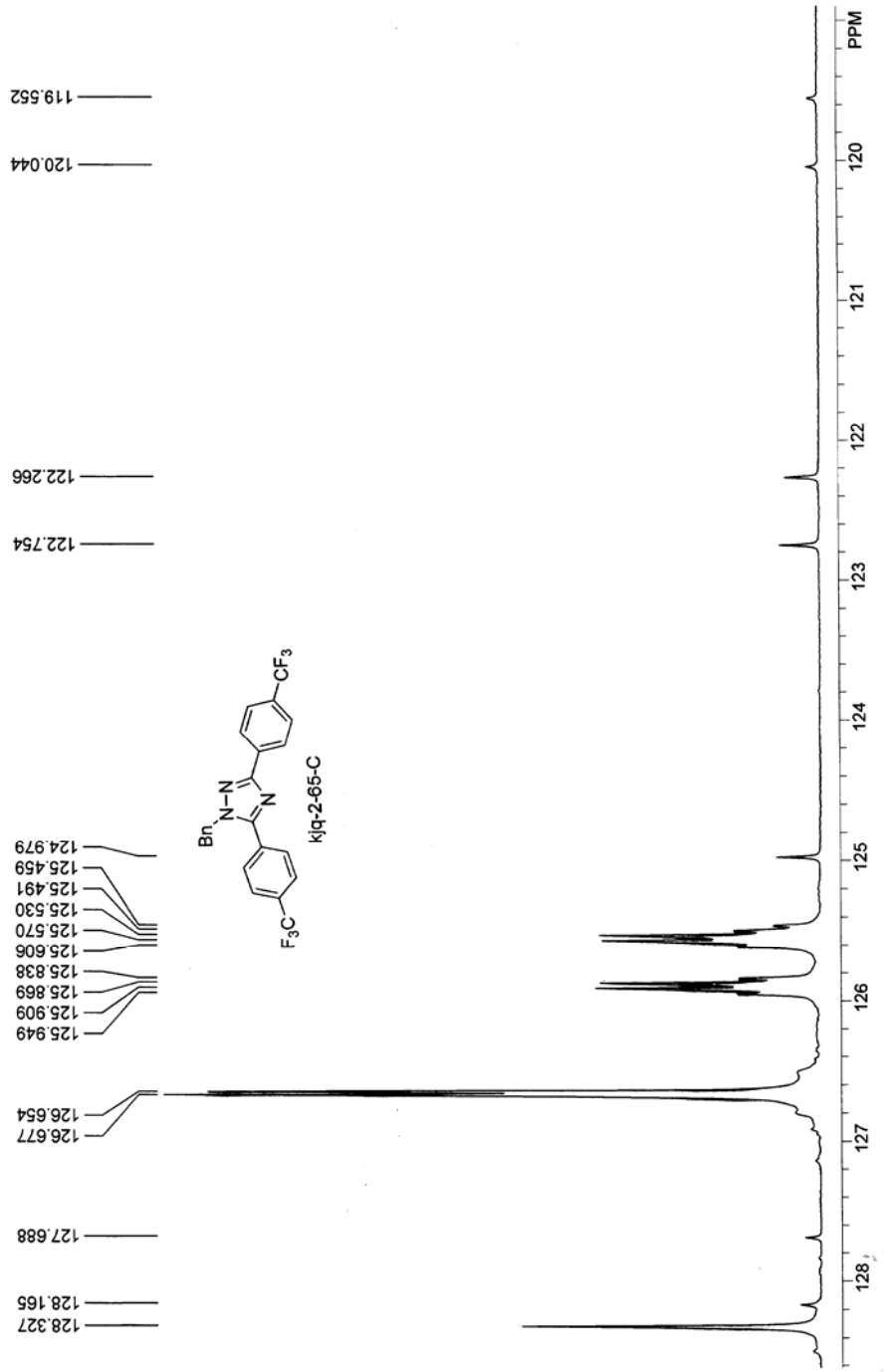


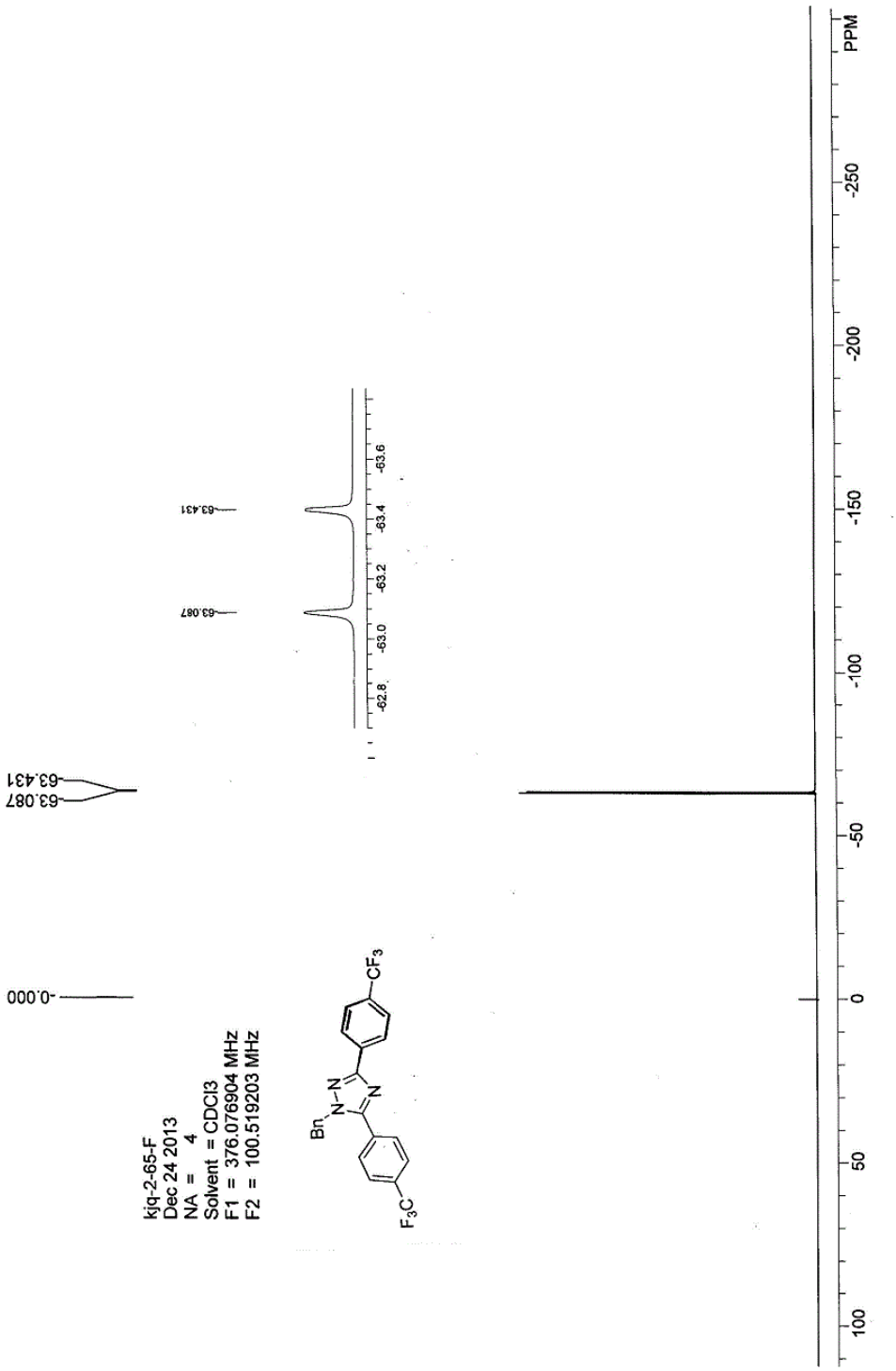


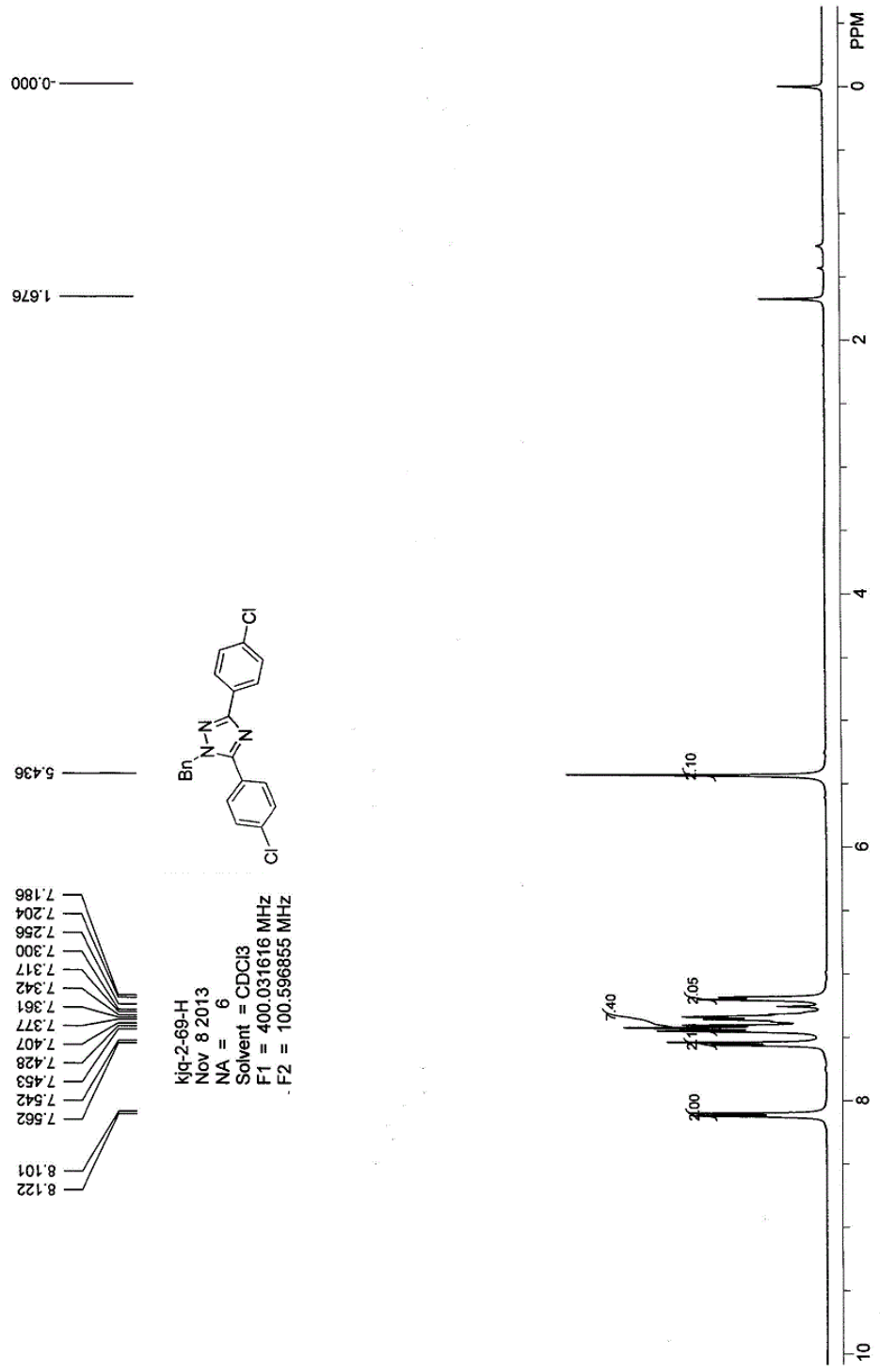


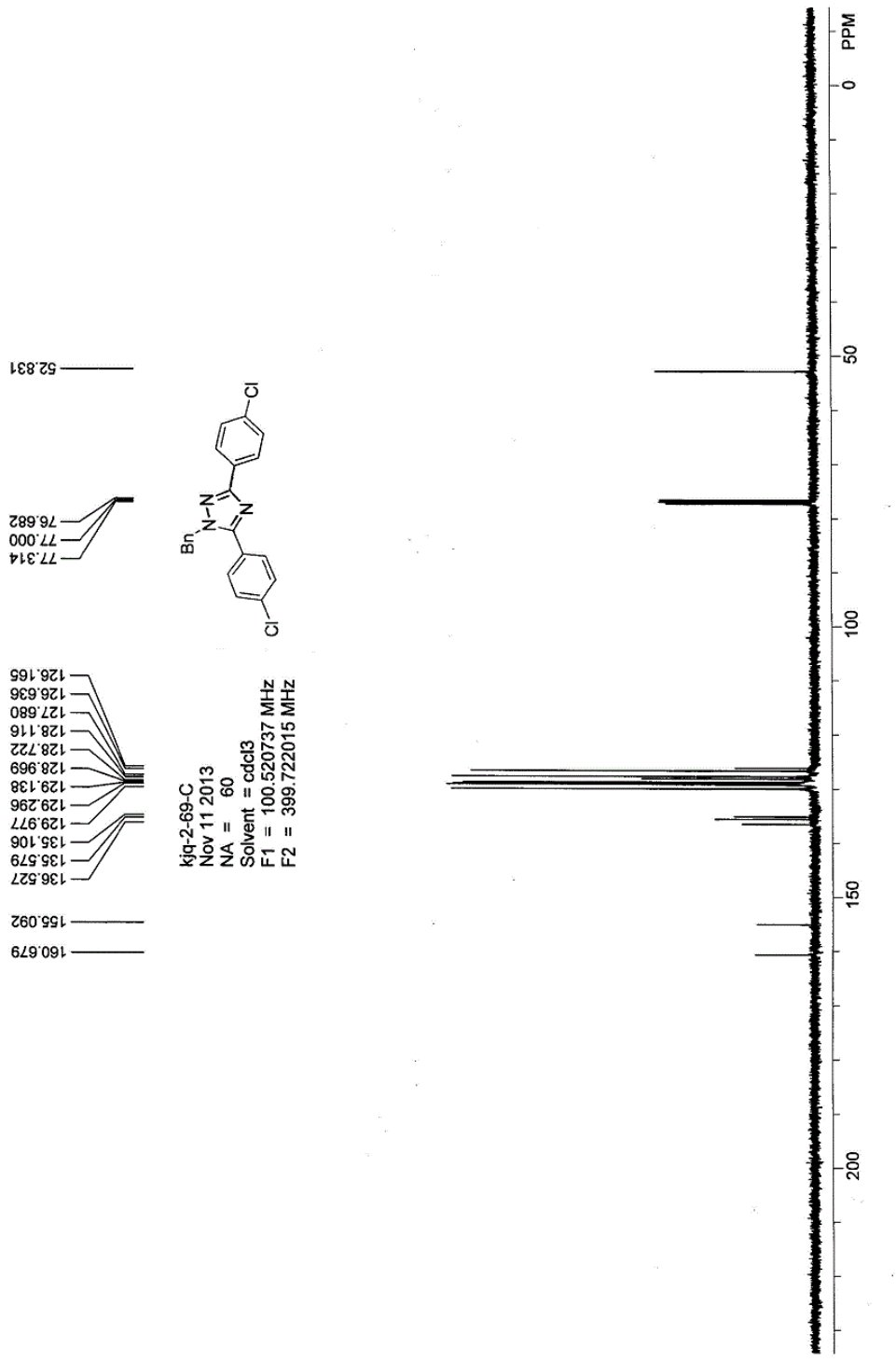


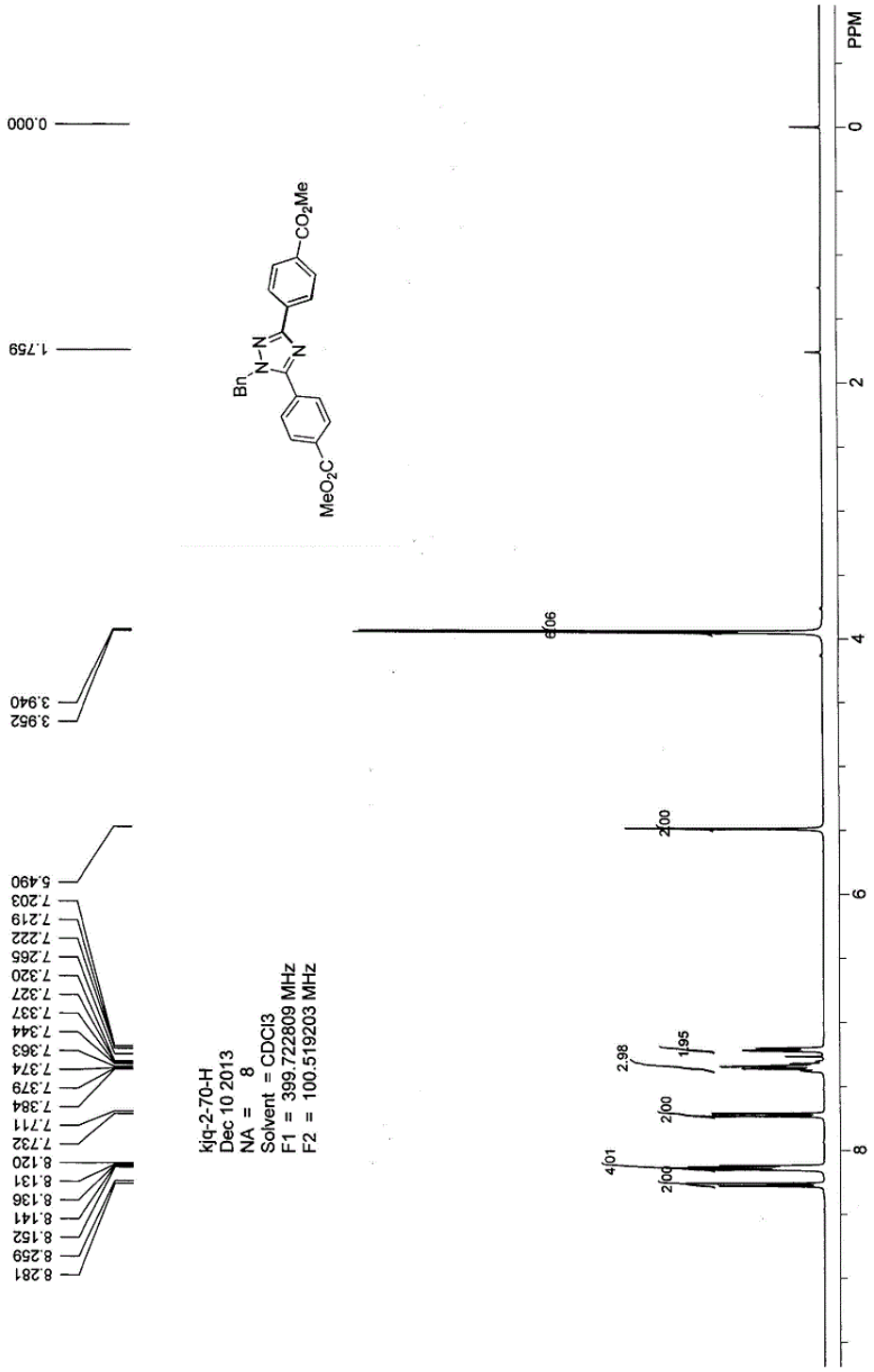

127.688
128.165
128.327
129.100
129.185
127.5
128.0
128.5
129.0
129.5
PPM
kjq-2-65-C
Bn
N
N
N
CF3
F3C

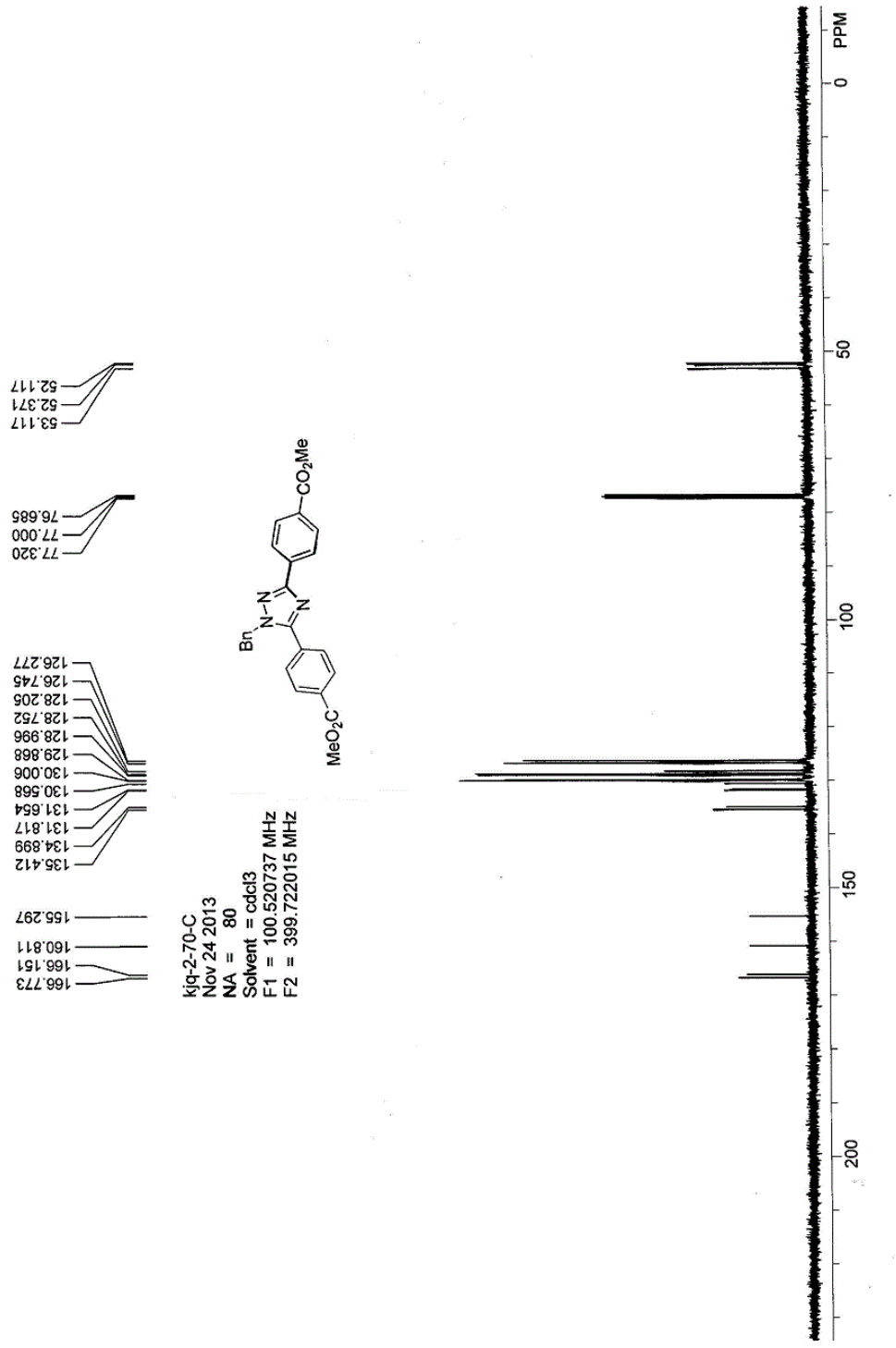

119.552
120.044
122.266
122.754
124.979
125.459
125.491
125.530
125.570
125.606
125.838
125.869
125.909
125.949
126.654
126.677
127.688
128.165
128.327
Bn
N
N
N
CF3
F3C
kjq-2-65-C
PPM
120
121
122
123
124
125
126
127
128

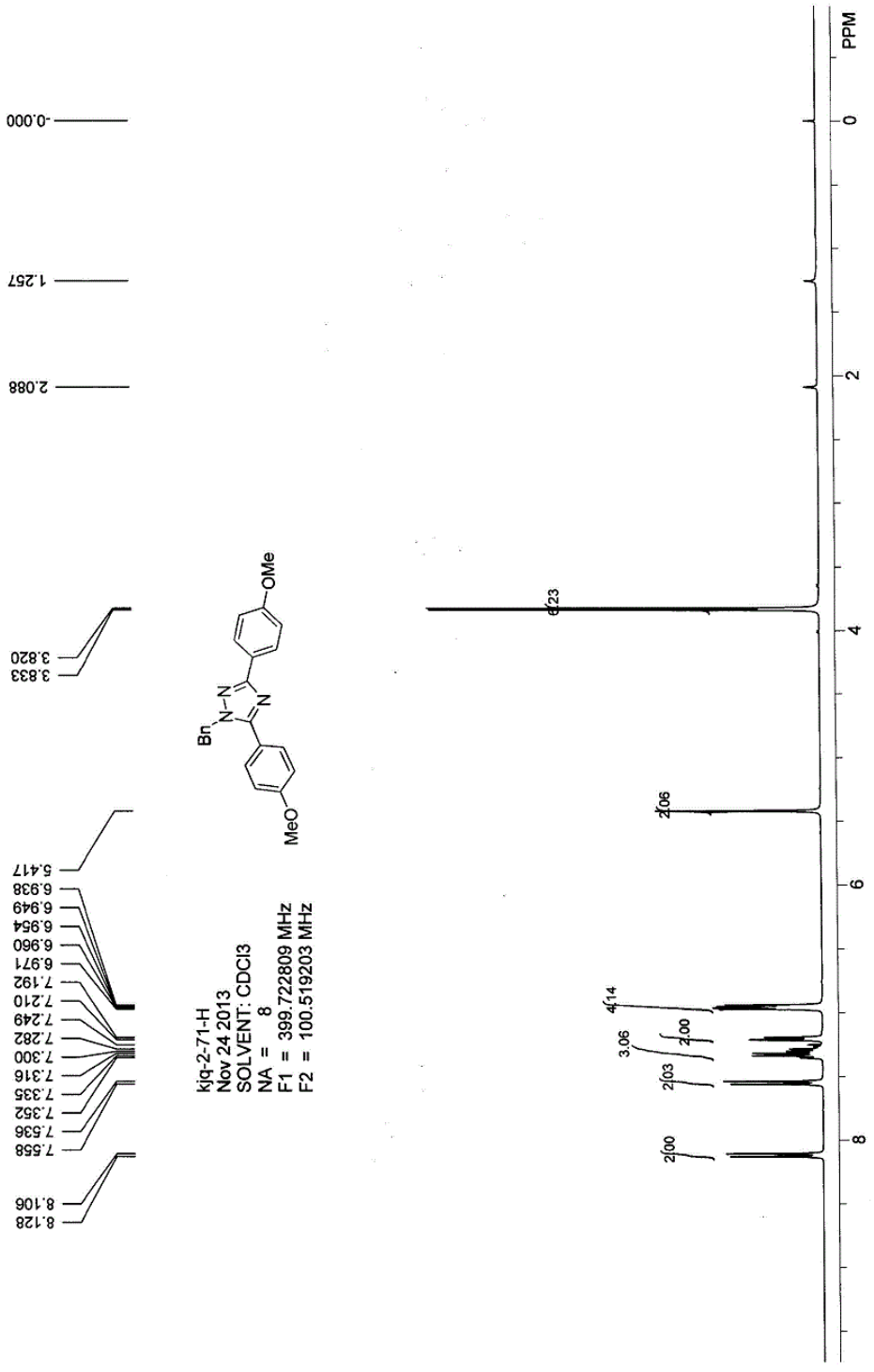

kjq-2-65-F
Dec 24 2013
NA = 4
Solvent = CDCl3
F1 = 376.076904 MHz
F2 = 100.519203 MHz
-0.000
-63.087
-63.431
-63.087
-63.431
-62.8
-63.0
-63.2
-63.4
-63.6
Bn
N
N
N
CF3
F3C
PPM
100
50
0
-50
-100
-150
-200
-250

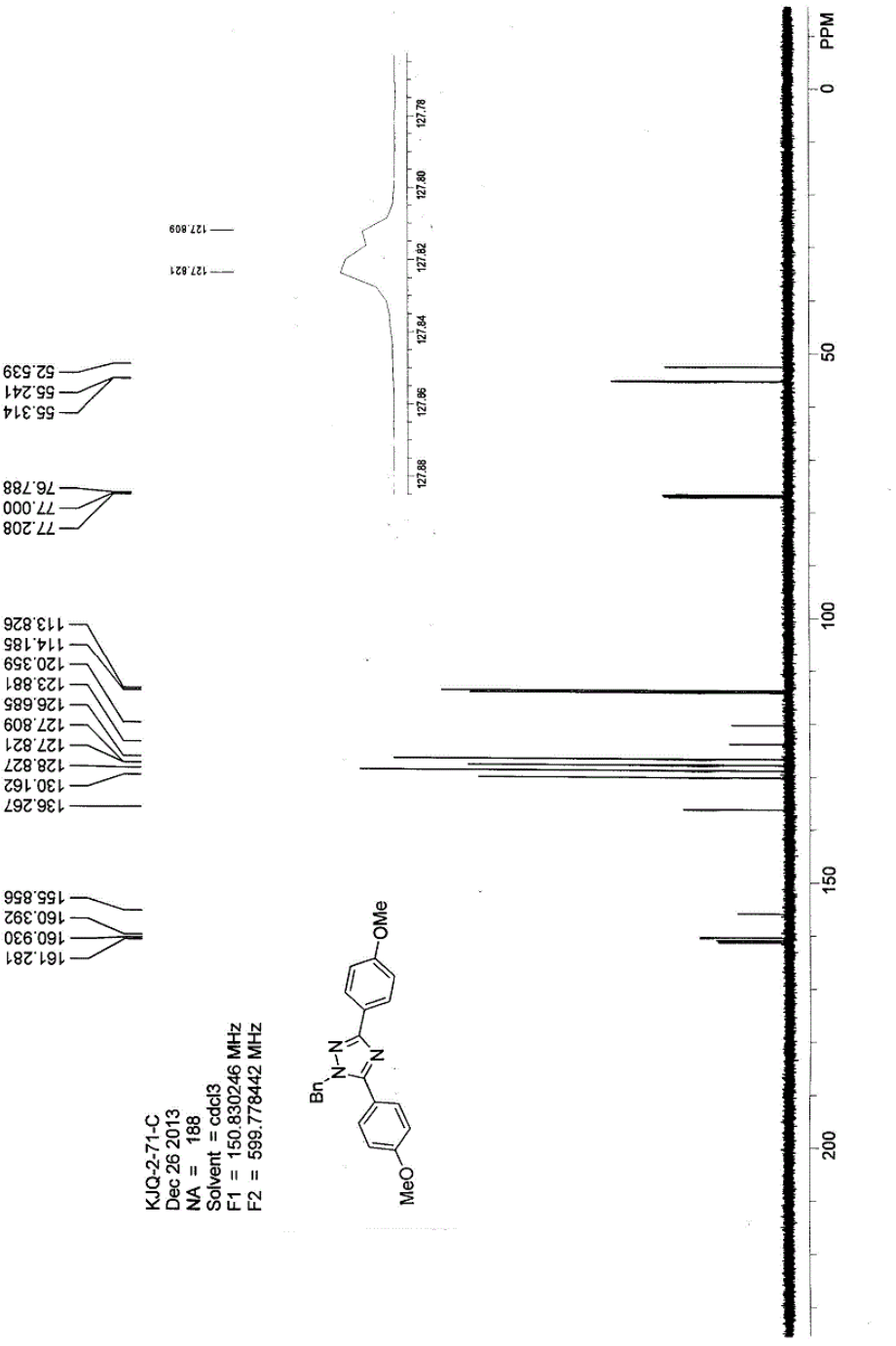

kjq-2-69-H
Nov 8 2013
NA = 6
Solvent = CDCl3
F1 = 400.031616 MHz
F2 = 100.596855 MHz
Bn
Cl
Cl
N
N
N
0.000
1.676
5.436
7.186
7.204
7.256
7.300
7.317
7.342
7.361
7.377
7.407
7.428
7.453
7.542
7.562
8.101
8.122
2.10
2.05
2.00
7.40
PPM
0
2
4
6
8
10

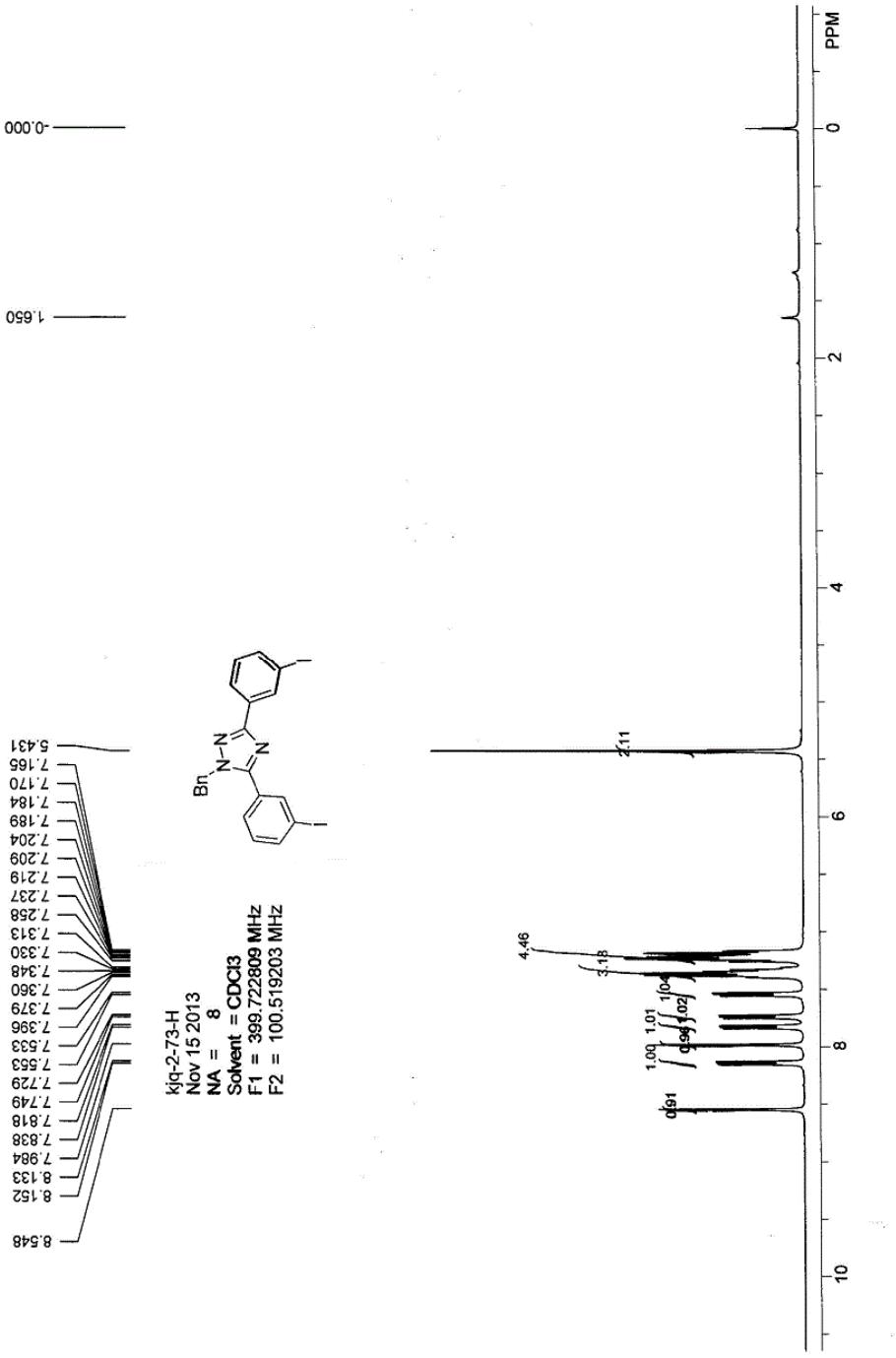


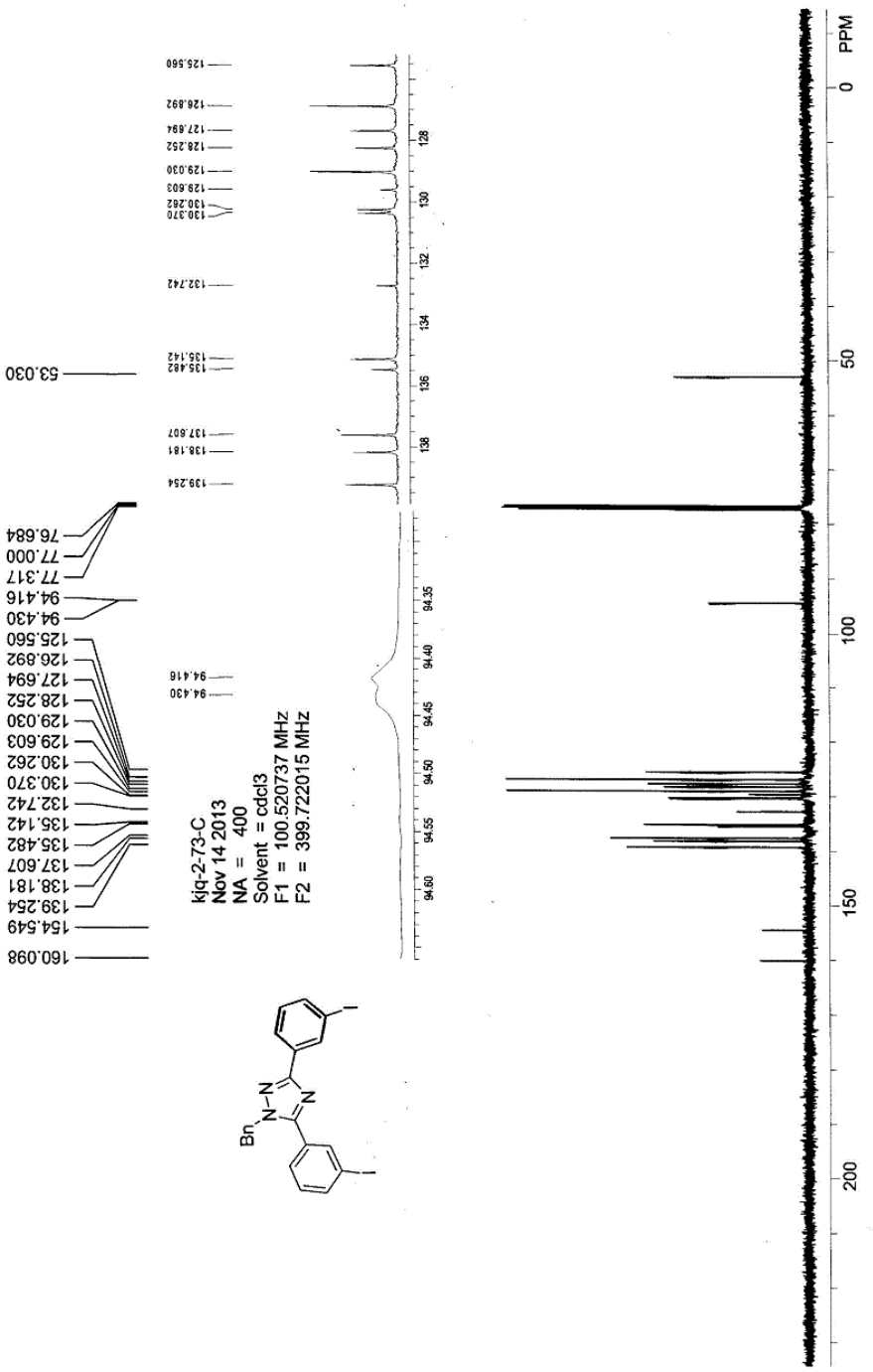


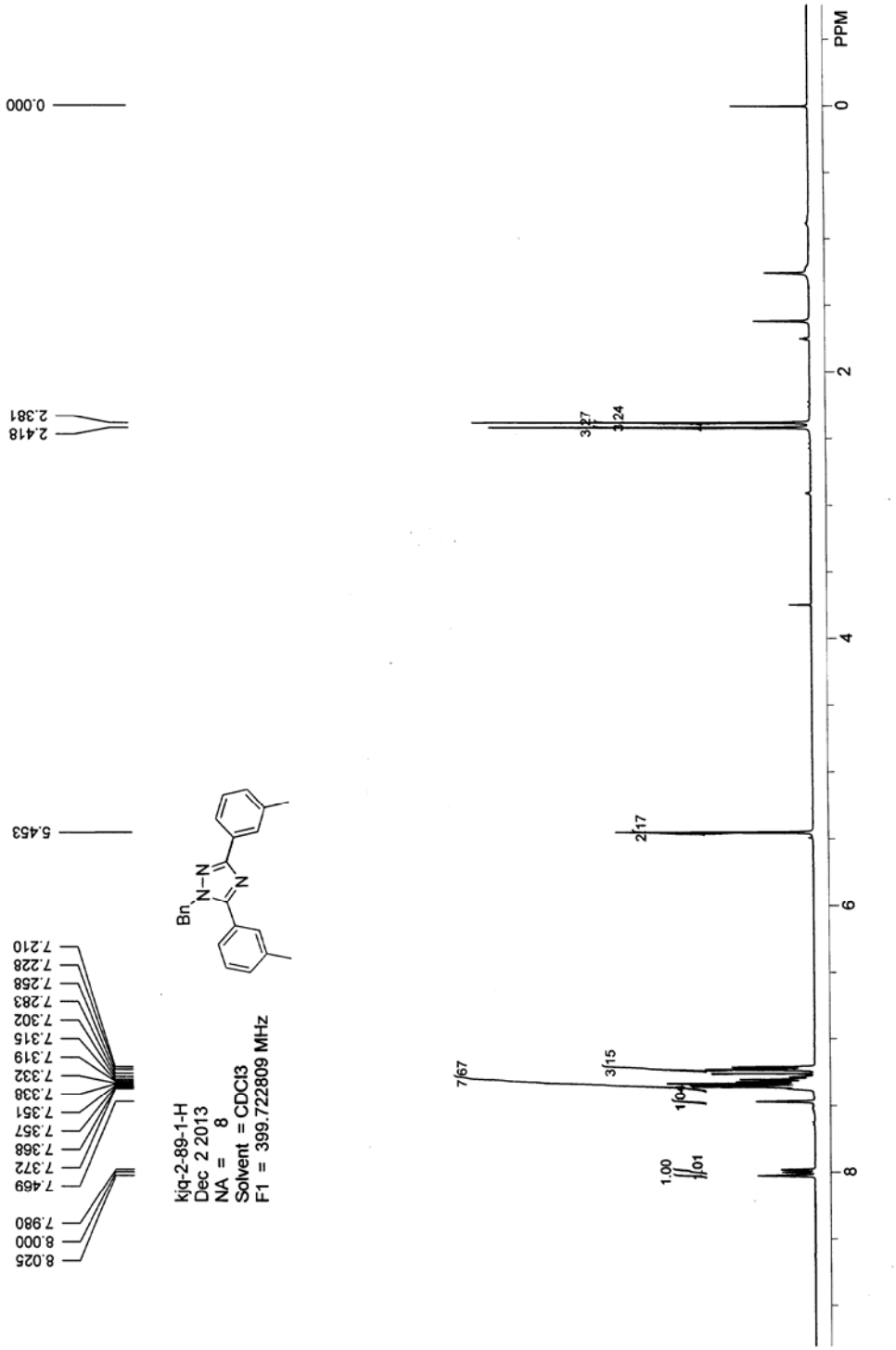

kjq-2-70-C
Nov 24 2013
NA = 80
Solvent = cdcl3
F1 = 100.520737 MHz
F2 = 399.722015 MHz
Bn
N
N
N
CO2Me
MeO2C
52.117
52.371
53.117
76.685
77.000
77.320
126.277
126.745
128.205
128.752
128.996
129.868
130.006
130.568
131.654
131.817
134.899
135.412
155.297
160.811
166.151
166.773
PPM
0
50
100
150
200

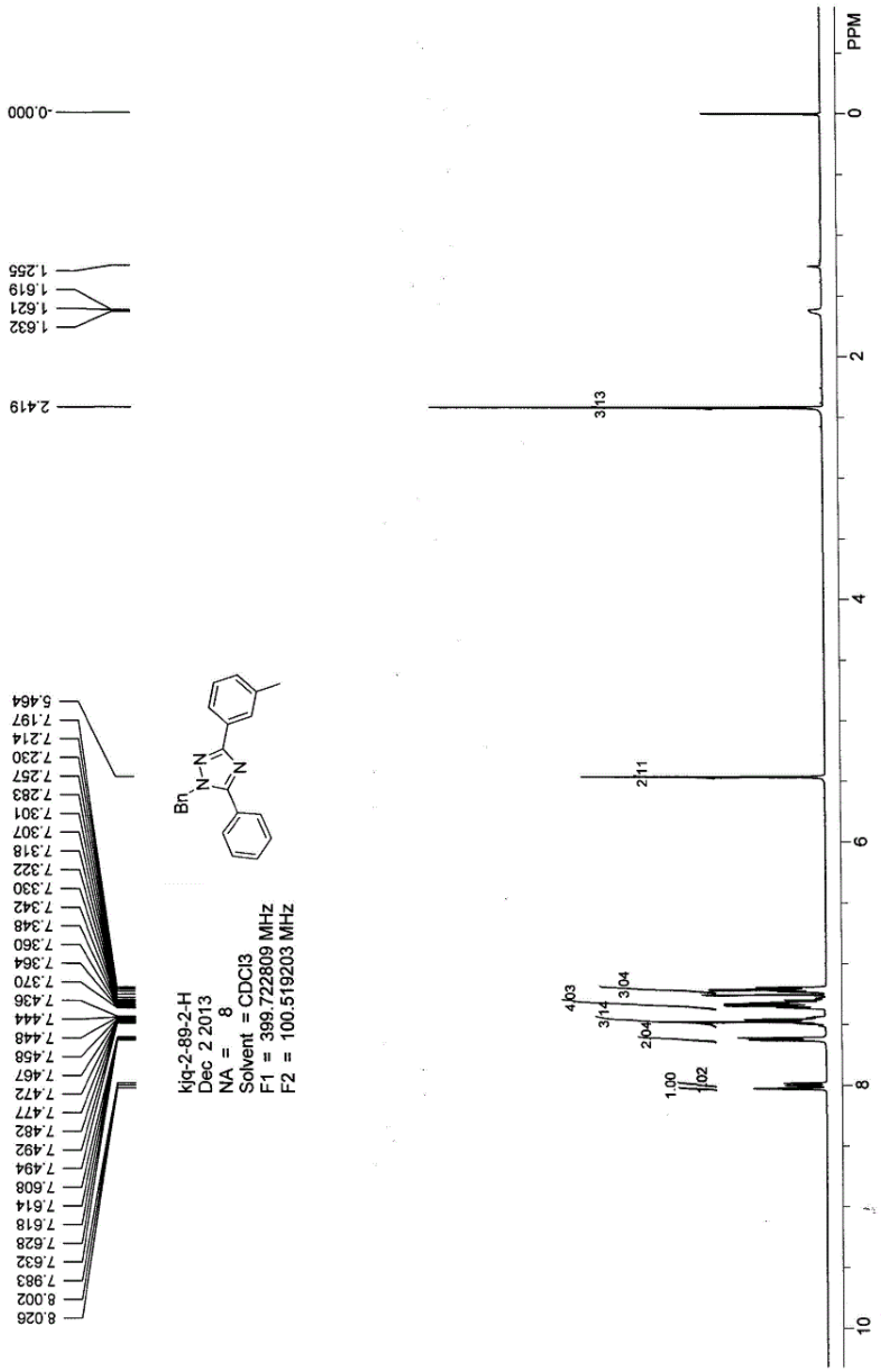


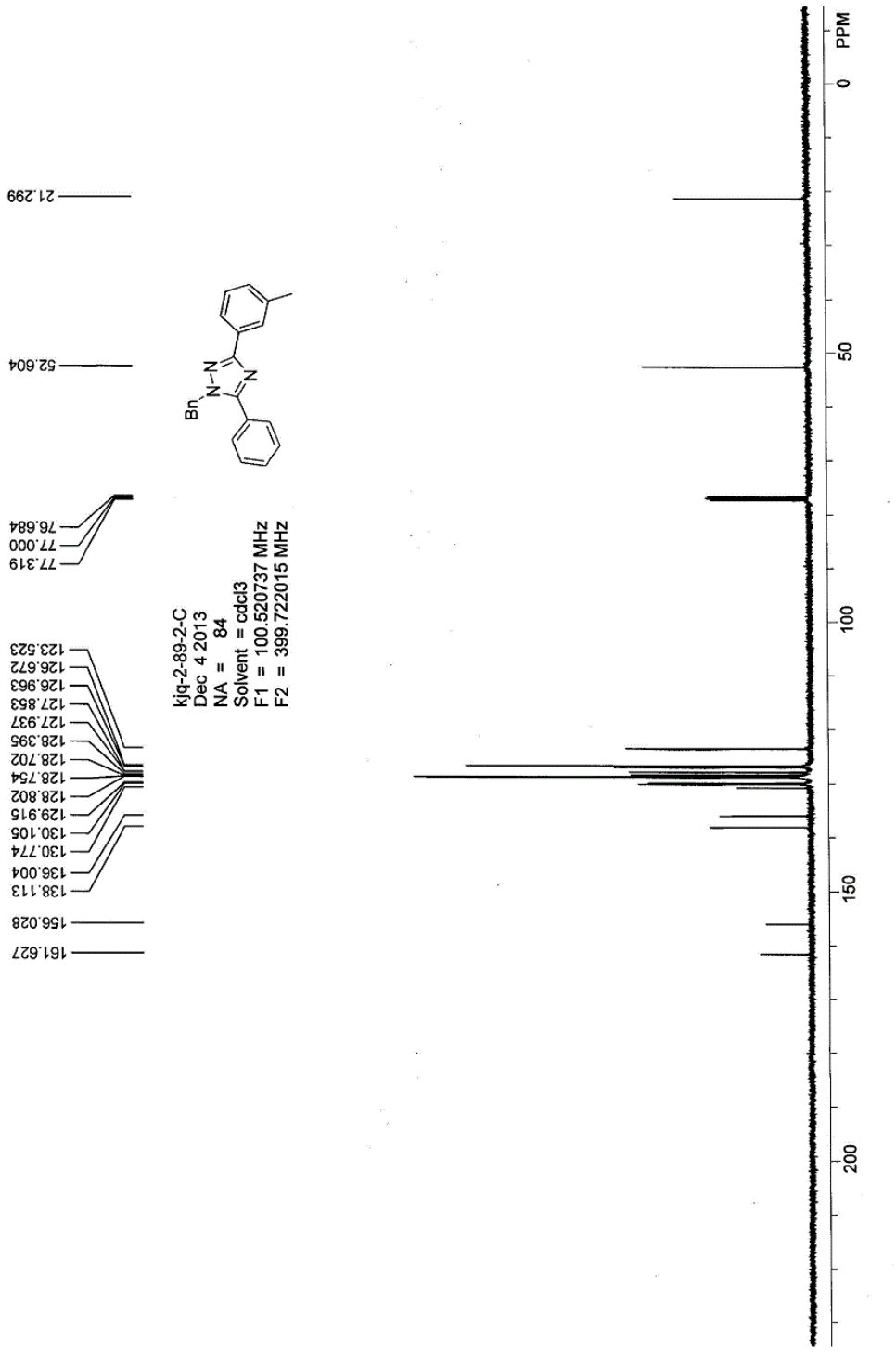


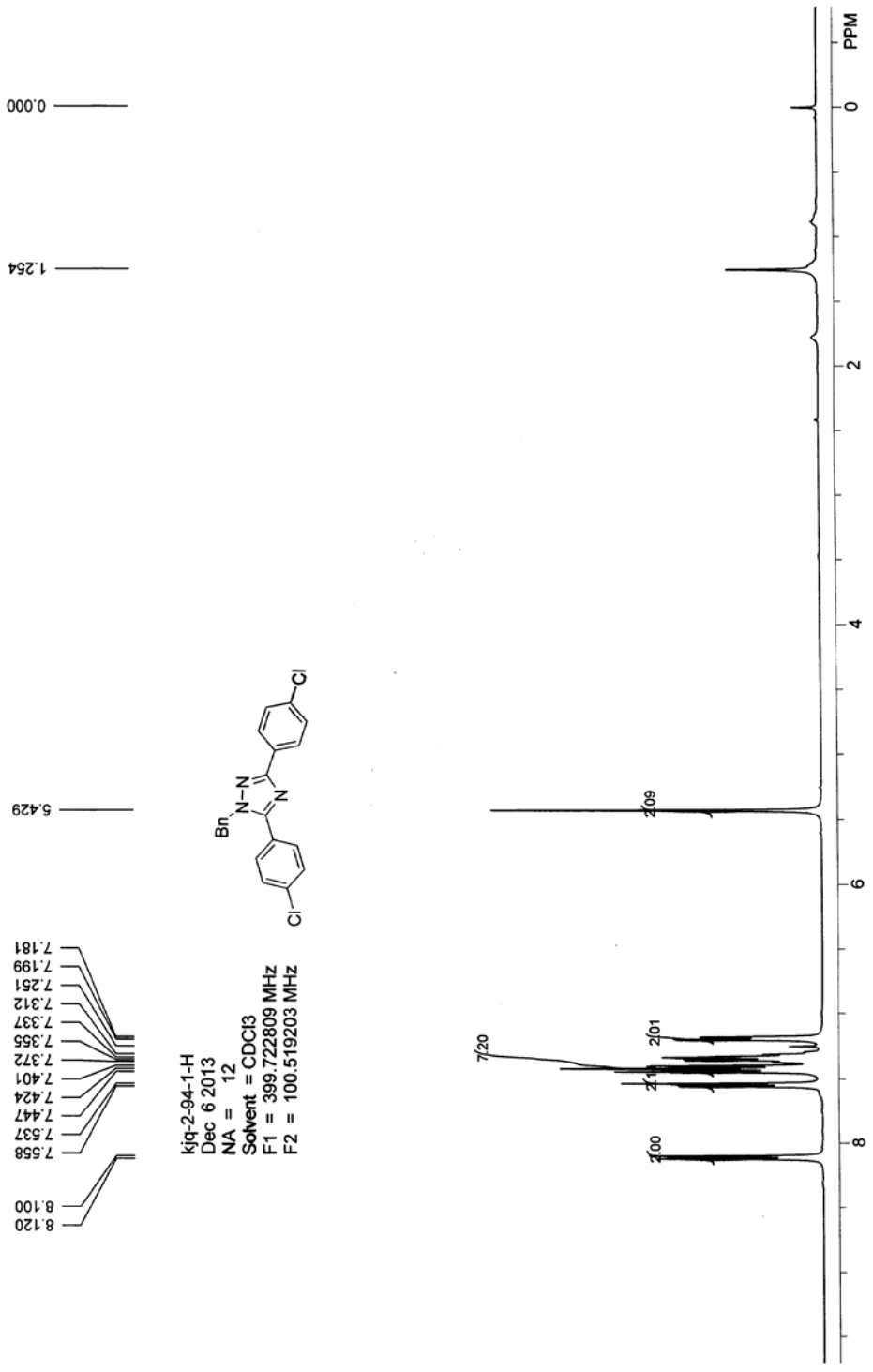


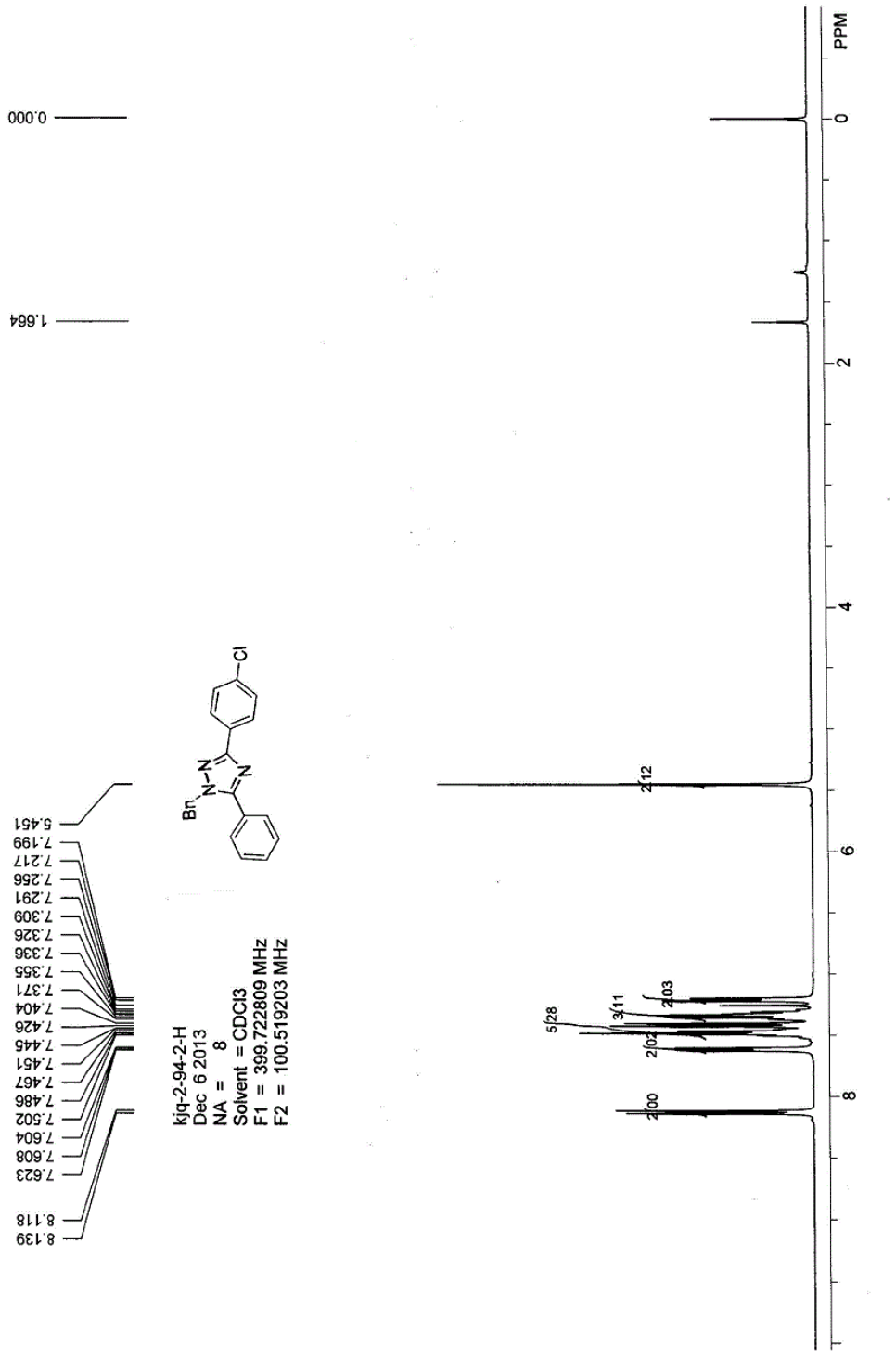


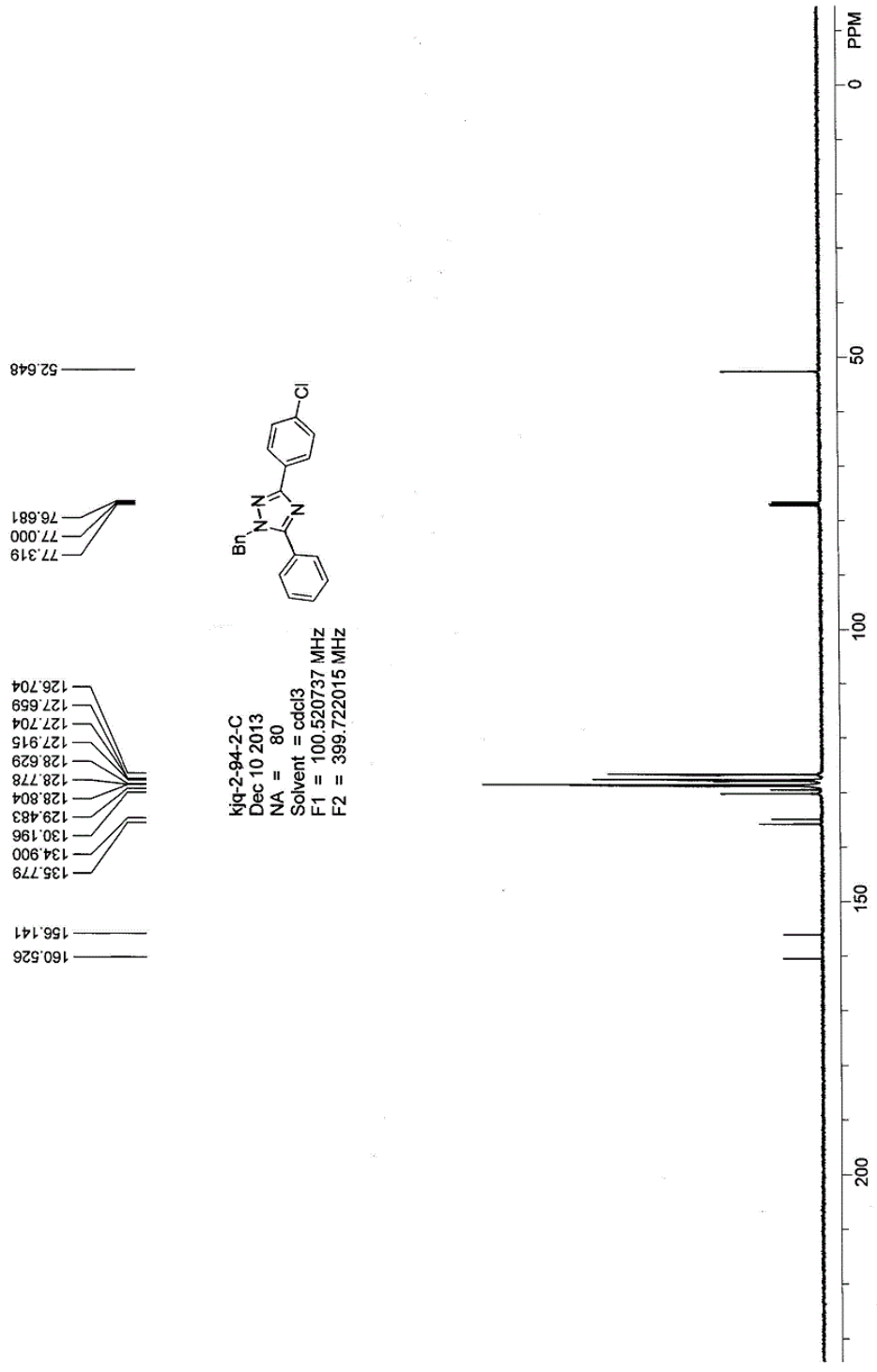


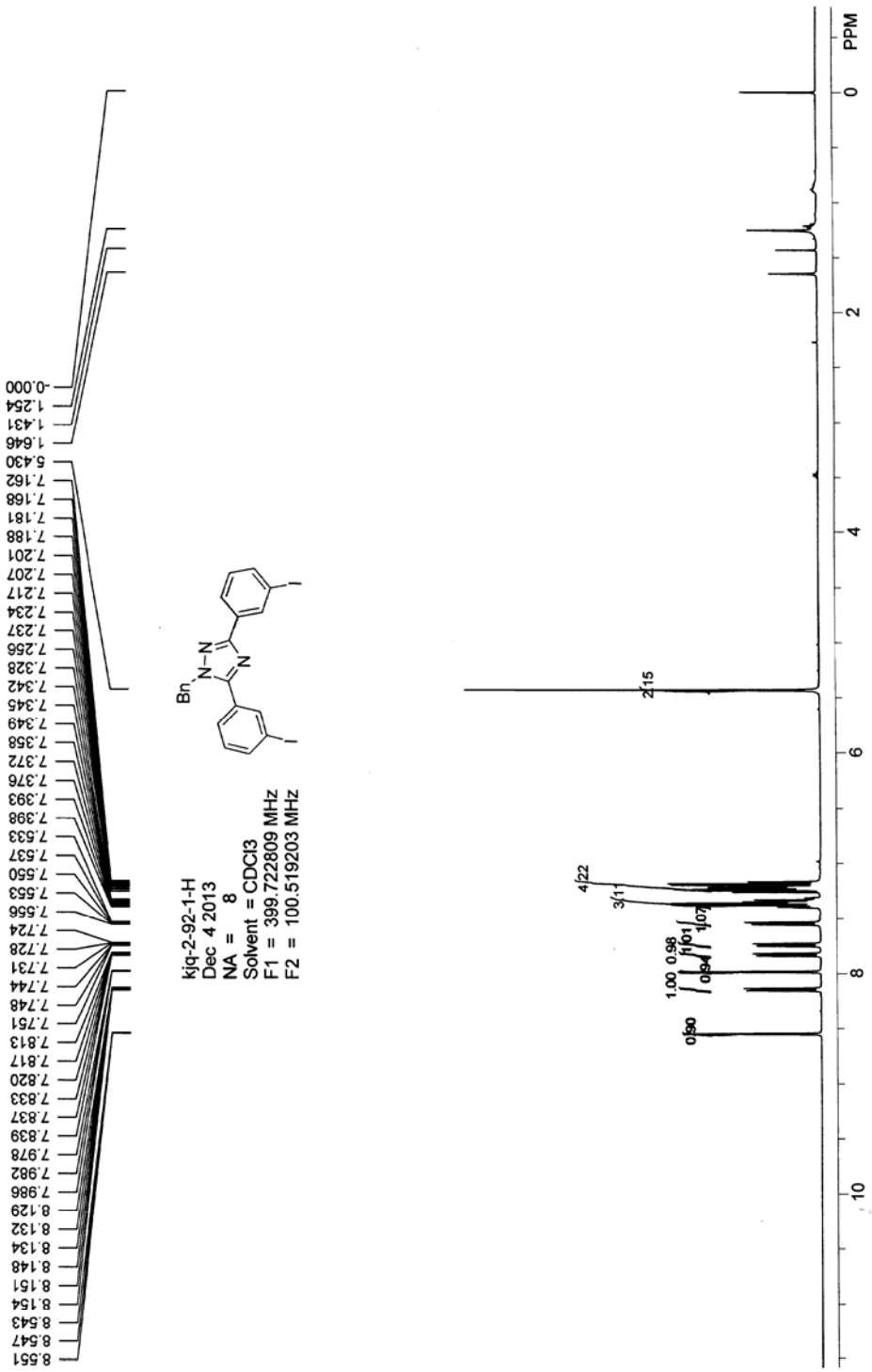


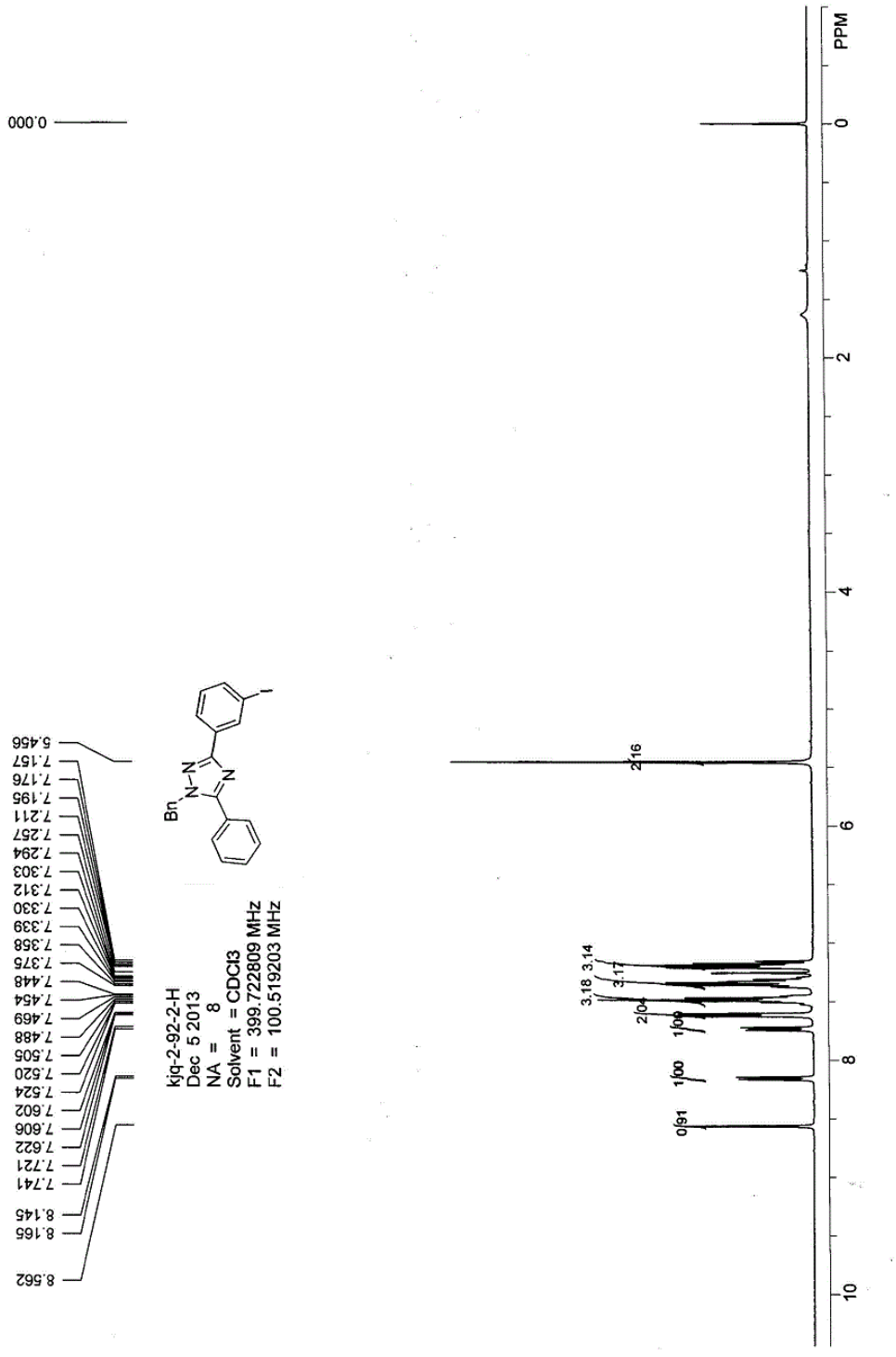

21.299
52.604
76.684
77.000
77.319
123.523
126.672
126.963
127.853
127.937
128.395
128.702
128.754
128.802
129.915
130.105
130.774
136.004
138.113
156.028
161.627
Bn
kjq-2-89-2-C
Dec 4 2013
NA = 84
Solvent = cdcl3
F1 = 100.520737 MHz
F2 = 399.722015 MHz
PPM
0
50
100
150
200






52.648
76.681
77.000
77.319
126.704
127.659
127.704
127.915
128.629
128.778
128.804
129.483
130.196
134.900
135.779
156.141
160.526
Bn
N
N
N
Cl
kjq-2-94-2-C
Dec 10 2013
NA = 80
Solvent = cdcl3
F1 = 100.520737 MHz
F2 = 399.722015 MHz
PPM
0
50
100
150
200




0.000
5.456
7.157
7.176
7.195
7.211
7.257
7.294
7.303
7.312
7.330
7.339
7.358
7.375
7.448
7.454
7.469
7.488
7.505
7.520
7.524
7.602
7.606
7.622
7.721
7.741
8.145
8.165
8.562
Bn
N
N
N
kjq-2-92-2-H
Dec 5 2013
NA = 8
Solvent = CDCl3
F1 = 399.722809 MHz
F2 = 100.519203 MHz
2.16
3.18
3.14
3.17
2.04
1.00
1.00
0.91
PPM
0
2
4
6
8
10