

CuBr for KA² Reaction: En Route to Propargylic Amines Bearing a Quaternary Carbon Center

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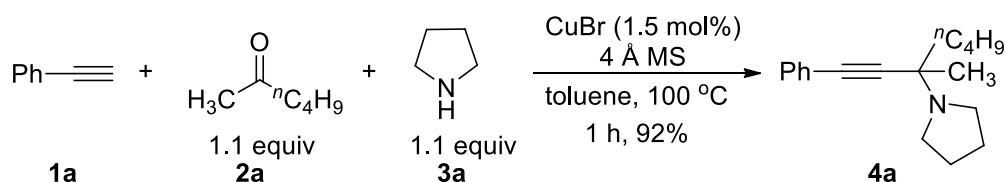
Supporting Information

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General Information. All reactions were carried out in oven dried Schlenk vessels. CuBr (99.0%) was purchased from Aladdin and kept in glove box. 4 Å molecular sieves was purchased from Alfa Aesar and kept in glove box after activation (heated at 450 °C for 10 h in Muffle furnace, taken out after cooling to 200 °C and then kept in a glove box to allow to cool to room temperature) under N₂. Toluene was dried over sodium wire with benzophenone as the indicator and distilled freshly before use. Anhydrous benzene was purchased from Aladdin and used without further treatment. Other reagents were used without further treatment. All the temperatures are referred to the oil baths used.

(1) 1-(3-Methyl-1-phenylhept-1-yn-3-yl)pyrrolidine **4a** (tangxj-4-141)

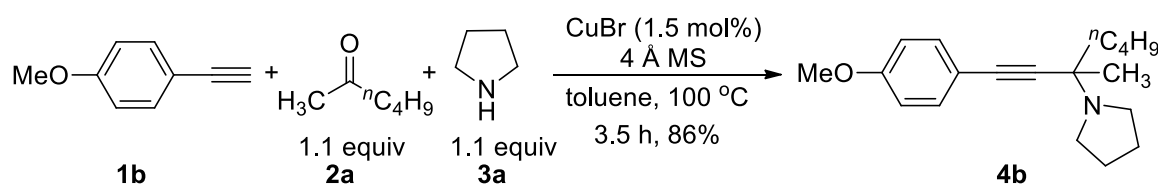


Typical Procedure 1: To a dried Schlenk tube was added 4 Å MS (3.0012 g) inside a glove box. The Schlenk tube was then dried under vacuum with a heating gun. CuBr (0.0218 g, 0.15 mmol), **1a** (1.0211 g, 10 mmol)/toluene (3 mL), **2a** (1.1025 g, 11 mmol)/toluene (3 mL), and **3a** (0.7824 g, 11 mmol)/toluene (4 mL) were then added sequentially under Ar atmosphere. The Schlenk tube was then placed in a pre-heated oil bath at 100 °C with stirring for 1 h as monitored by TLC. After cooling to room temperature, the crude reaction mixture was filtrated through a short pad of silica gel eluted with acetone (50 mL). After evaporation, the residue was analyzed by ¹H NMR measurement with 70 µL of mesitylene added as the reference and then purified via chromatography on silica gel to afford **4a** (2.3577 g, 92%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL/180 mL/1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.38 (m, 2 H, Ar-H), 7.29-7.19 (m, 3 H, Ar-H), 2.84-2.72 (m, 4 H, CH₂NCH₂), 1.85-1.72 (m, 5 H, 2 × CH₂ + one proton of

CH₂), 1.72-1.62 (m, 1 H, one proton of CH₂), 1.56-1.27 (m, 7 H, 2 × CH₂ + CH₃), 0.94 (t, *J* = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.5, 127.9, 127.4, 123.5, 91.2, 84.2, 57.6, 47.6, 41.1, 26.3, 25.7, 23.5, 23.0, 14.0; MS (ESI) *m/z* 256 (M+H⁺), 185 (M+H⁺-pyrrolidine); IR (neat): ν = 2956, 2870, 2807, 1598, 1489, 1463, 1444, 1370, 1334, 1302, 1263, 1190, 1144, 1091, 1069, 1000 cm⁻¹; HRMS calcd for C₁₈H₂₅N [M⁺]: 255.1987. Found: 255.1989.

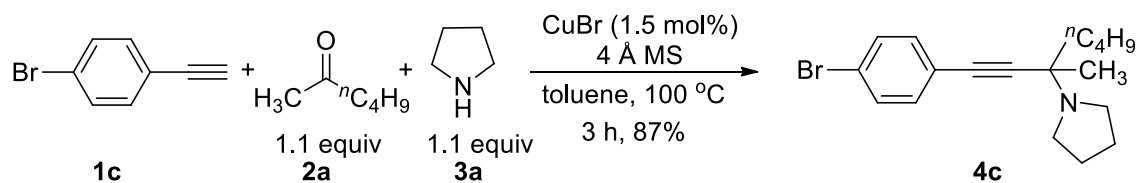
The following compounds were prepared according to this Typical Procedure.

(2) 1-(1-(4-Methoxyphenyl)-3-methylhept-1-yn-3-yl)pyrrolidine **4b** (tangxj-4-151)



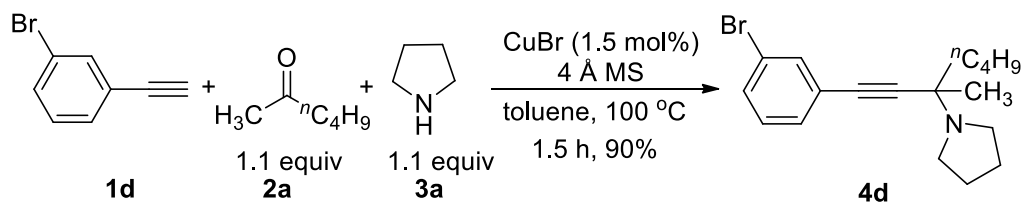
The reaction of 4 Å MS (2.9979 g), CuBr (0.0212 g, 0.15 mmol), **1b** (1.3452 g, 10 mmol), **2a** (1.1018 g, 11 mmol)/toluene (5 mL), and **3a** (0.7825 g, 11 mmol)/toluene (5 mL) afforded **4b** (2.5084 g, 86%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.35 (d, *J* = 8.8 Hz, 2 H, Ar-H), 6.81 (d, *J* = 8.8 Hz, 2 H, Ar-H), 3.78 (s, 3 H, OCH₃), 2.84-2.72 (m, 4 H, CH₂NCH₂), 1.84-1.61 (m, 6 H, 3 × CH₂), 1.55-1.28 (m, 7 H, 2 × CH₂ + CH₃), 0.93 (t, *J* = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 159.0, 133.0, 115.7, 113.6, 89.7, 83.9, 57.7, 55.1, 47.6, 41.3, 26.5, 25.9, 23.5, 23.1, 14.0; MS (ESI) *m/z* 286 (M+H⁺), 215 (M+H⁺-pyrrolidine); IR (neat): ν = 2955, 1606, 1508, 1463, 1370, 1335, 1288, 1244, 1169, 1143, 1103, 1001 cm⁻¹; HRMS calcd for C₁₉H₂₇NO [M⁺]: 285.2093. Found: 285.2088.

(3) 1-(1-(4-Bromophenyl)-3-methylhept-1-yn-3-yl)pyrrolidine **4c** (tangxj-4-144)



The reaction of 4 Å MS (3.0015 g), CuBr (0.0218 g, 0.15 mmol), **1c** (1.8014 g, 10 mmol)/toluene (3 mL), **2a** (1.1018 g, 11 mmol)/toluene (3 mL), and **3a** (0.7831 g, 11 mmol)/toluene (4 mL) afforded **4c** (2.9007 g, 87%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.40 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.26 (d, *J* = 8.0 Hz, 2 H, Ar-H), 2.82-2.70 (m, 4 H, CH₂NCH₂), 1.82-1.62 (m, 6 H, 3 × CH₂), 1.52-1.28 (m, 7 H, 2 × CH₂ + CH₃), 0.93 (t, *J* = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 133.1, 131.3, 122.4, 121.6, 92.7, 83.2, 57.8, 47.7, 41.1, 26.4, 25.7, 23.5, 23.1, 14.0; MS (ESI) *m/z* 336 (M(⁸¹Br)+H⁺), 334 (M(⁷⁹Br)+H⁺), 265 (M(⁸¹Br)+H⁺-pyrrolidine), 263 (M(⁷⁹Br)+H⁺-pyrrolidine); IR (neat): ν = 2956, 2869, 2807, 1484, 1462, 1392, 1370, 1262, 1145, 1093, 1069, 1010 cm⁻¹; HRMS calcd for C₁₈H₂₄⁷⁹BrN [M⁺]: 333.1092. Found: 333.1102.

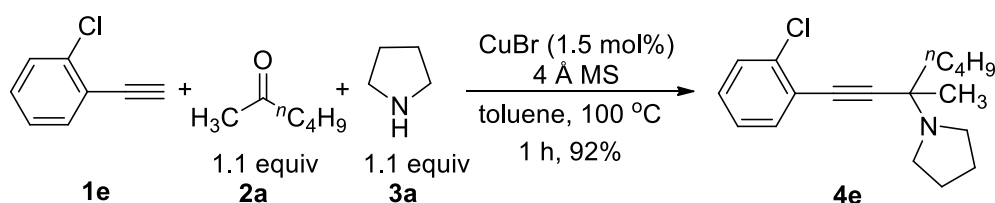
(4) 1-(1-(3-Bromophenyl)-3-methylhept-1-yn-3-yl)pyrrolidine **4d** (tangxj-4-154)



The reaction of 4 Å MS (3.0025 g), CuBr (0.0214 g, 0.15 mmol), **1d** (1.8002 g, 10 mmol)/toluene (3 mL), **2a** (1.1010 g, 11 mmol)/toluene (3 mL), and **3a** (0.7831 g, 11 mmol)/toluene (4 mL) afforded **4d** (2.9954 g, 90%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.56 (s, 1 H, Ar-H), 7.39 (d, *J* = 7.2 Hz, 1 H,

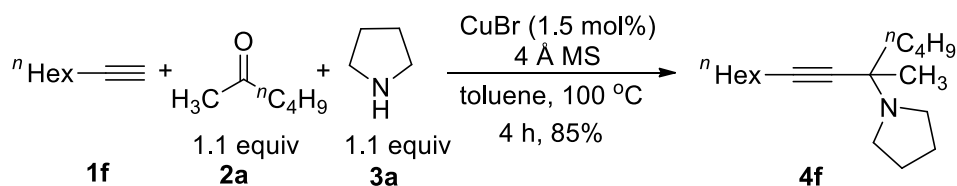
Ar-H), 7.33 (d, $J = 7.6$ Hz, 1 H, Ar-H), 7.15 (t, $J = 7.8$ Hz, 1 H, Ar-H), 2.82-2.72 (m, 4 H, CH₂NCH₂), 1.86-1.61 (m, 6 H, 3 × CH₂), 1.52-1.30 (m, 7 H, 2 × CH₂ + CH₃), 0.94 (t, $J = 7.2$ Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 134.2, 130.5, 130.0, 129.3, 125.4, 121.8, 92.9, 82.7, 57.6, 47.5, 40.9, 26.2, 25.6, 23.4, 23.0, 13.9; MS (ESI) m/z 336 (M(⁸¹Br)+H⁺), 334 (M(⁷⁹Br)+H⁺); IR (neat): $\nu = 2956, 2870, 2807, 1589, 1555, 1470, 1404, 1370, 1119, 1069, 1039$ cm⁻¹; HRMS calcd for C₁₈H₂₄⁷⁹BrN [M⁺]: 333.1092. Found: 333.1085.

(5) 1-(1-(2-Chlorophenyl)-3-methylhept-1-yn-3-yl)pyrrolidine **4e** (tangxj-4-155)



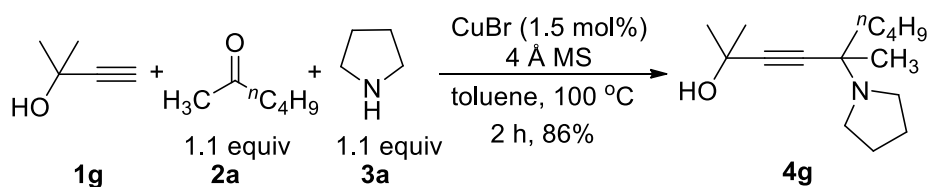
The reaction of 4 Å MS (3.0011 g), CuBr (0.0211 g, 0.15 mmol), **1e** (1.3602 g, 10 mmol)/toluene (3 mL), **2a** (1.1015 g, 11 mmol)/toluene (3 mL), and **3a** (0.7821 g, 11 mmol)/toluene (4 mL) afforded **4e** (2.6450 g, 92%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 180/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.47-7.41 (m, 1 H, Ar-H), 7.39-7.32 (m, 1 H, Ar-H), 7.21-7.11 (m, 2 H, Ar-H), 2.88-2.75 (m, 4 H, CH₂NCH₂), 1.86-1.65 (m, 6 H, 3 × CH₂), 1.60-1.29 (m, 7 H, 2 × CH₂ + CH₃), 0.94 (t, $J = 7.2$ Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 135.6, 133.1, 128.9, 128.4, 126.1, 123.3, 97.2, 80.9, 58.1, 47.6, 41.0, 26.4, 25.7, 23.6, 23.0, 14.0; MS (ESI) m/z 292 (M(³⁷Cl)+H⁺), 290 (M(³⁵Cl)+H⁺), 219 (M(³⁵Cl)+H⁺-pyrrolidine); IR (neat): $\nu = 2956, 2870, 2810, 2221, 1470, 1437, 1370, 1146, 1057, 1033, 1000$ cm⁻¹; HRMS calcd for C₁₈H₂₄³⁵ClN [M⁺]: 289.1597. Found: 289.1594.

(6) 1-(5-Methyltridec-6-yn-5-yl)pyrrolidine **4f** (tangxj-4-147)



The reaction of 4 Å MS (3.0021 g), CuBr (0.0219 g, 0.15 mmol), **1f** (1.1038 g, 10 mmol)/toluene (3 mL), **2a** (1.1021 g, 11 mmol)/toluene (3 mL), and **3a** (0.7823 g, 11 mmol)/toluene (4 mL) afforded **4f** (2.2463 g, 85%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 2.76-2.62 (m, 4 H, CH₂NCH₂), 2.19 (t, *J* = 6.6 Hz, 2 H, CH₂C≡C), 1.82-1.72 (m, 4 H, 2 × CH₂), 1.69-1.22 (m, 17 H, 7 × CH₂ + CH₃), 0.95-0.85 (m, 6 H, 2 × CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 83.9, 81.2, 57.3, 47.4, 41.5, 31.2, 29.1, 28.3, 26.5, 26.0, 23.5, 23.1, 22.5, 18.5, 14.0, 13.9; MS (ESI) *m/z* 264 (M+H⁺); IR (neat): ν = 2956, 2930, 2859, 2809, 1463, 1370, 1330, 1303, 1260, 1237, 1175 cm⁻¹; HRMS calcd for C₁₈H₃₃N [M⁺]: 263.2613. Found: 263.2603.

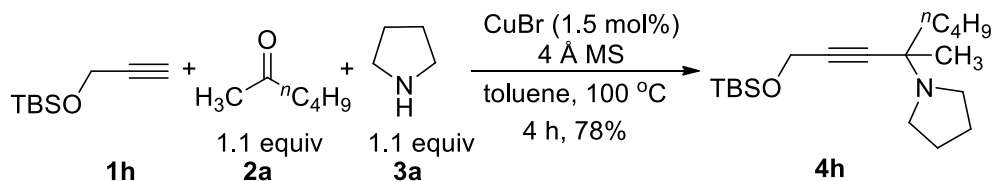
(7) 2,5-Dimethyl-5-(pyrrolidin-1-yl)non-3-yn-2-ol **4g** (tangxj-4-164)



The reaction of 4 Å MS (2.9979 g), CuBr (0.0214 g, 0.15 mmol), **1g** (0.8409 g, 10 mmol)/toluene (3 mL), **2a** (1.1033 g, 11 mmol)/toluene (3 mL), and **3a** (0.7821 g, 11 mmol)/toluene (4 mL) afforded **4g** (2.0509 g, 86%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 50/1 (200 mL) → 1/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 180 mL /900 mL /1 mL was applied to get the pure product.): solid; m.p. 53-55 °C (ethyl ether/petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 2.73-2.62 (m, 4 H, CH₂NCH₂), 2.23 (br s, 1 H, OH), 1.81-1.72 (m, 4 H, 2 × CH₂), 1.69-1.53 (m, 2 H, CH₂), 1.52 (s, 6 H, 2 × CH₃), 1.43-1.25 (m, 7 H, 2 × CH₂ + CH₃), 0.91 (t, *J* = 7.0 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 89.1, 83.3, 65.1, 57.1, 47.5, 41.0, 32.03, 32.00, 26.5, 25.7, 23.6, 23.1, 14.1; MS (ESI) *m/z* 238 (M+H⁺);

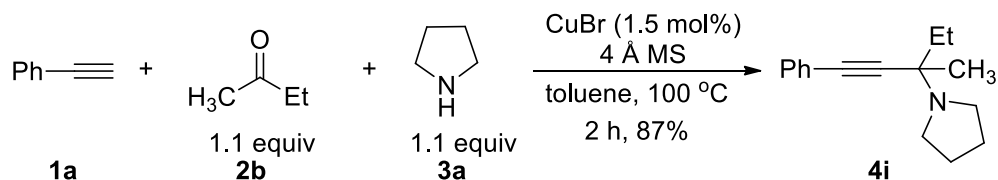
IR (neat): $\nu = 3132, 2987, 2951, 2926, 2871, 2833, 1470, 1455, 1372, 1246, 1219, 1173, 1145, 1090 \text{ cm}^{-1}$; Anal. Calcd for $\text{C}_{15}\text{H}_{27}\text{NO}$: C 75.90, H 11.46, N 5.90. Found: C 75.86, H 11.30, N 5.88.

(8) 1-(1-((tert-Butyldimethylsilyl)oxy)-4-methyloct-2-yn-4-yl)pyrrolidine **4h**
(tangxj-4-150, tangxj-5-154)



The reaction of 4 Å MS (3.0008 g), CuBr (0.0218 g, 0.15 mmol), **1h** (1.7032 g, 10 mmol)/toluene (3 mL), **2a** (1.1021 g, 11 mmol)/toluene (3 mL), and **3a** (0.7829 g, 11 mmol)/toluene (4 mL) afforded **4h** (2.5337 g, 78%) (eluent: petroleum ether/ethyl acetate = 150/1 (200 mL) → 50/1 (200 mL); finally petroleum ether/ethyl acetate/ Et_3N = 900 mL / 180 mL / 1 mL was applied to get the pure product.) as a liquid: ^1H NMR (400 MHz, CDCl_3) δ 4.36 (s, 2 H, OCH_2), 2.76-2.65 (m, 4 H, CH_2NCH_2), 1.81-1.73 (m, 4 H, $2 \times \text{CH}_2$), 1.71-1.52 (m, 2 H, CH_2), 1.48-1.24 (m, 7 H, $2 \times \text{CH}_2 + \text{CH}_3$), 0.94-0.88 (m, 12 H, $4 \times \text{CH}_3$), 0.13 (s, 6 H, CH_3SiCH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 86.2, 82.7, 57.3, 51.7, 47.5, 41.1, 26.4, 25.72, 25.70, 23.5, 23.1, 18.2, 14.0, -5.1; MS (ESI) m/z 324 ($\text{M}+\text{H}^+$); IR (neat): $\nu = 2956, 2931, 2859, 1464, 1368, 1253, 1092, 1001 \text{ cm}^{-1}$; HRMS calcd for $\text{C}_{19}\text{H}_{37}\text{NOSi}$ [M^+]: 323.2644. Found: 323.2638.

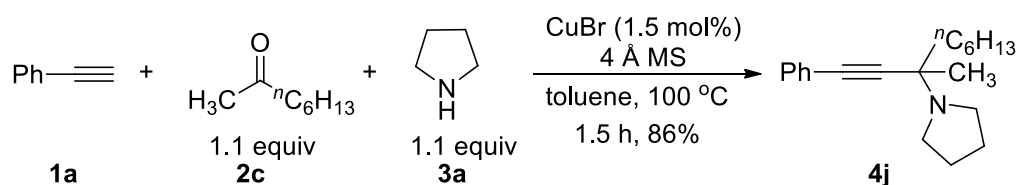
(9) 1-(3-Methyl-1-phenylpent-1-yn-3-yl)pyrrolidine **4i** (tangxj-4-156)



The reaction of 4 Å MS (3.0024 g), CuBr (0.0213 g, 0.15 mmol), **1a** (1.0205 g, 10 mmol)/toluene (3 mL), **2b** (0.7974 g, 11 mmol)/toluene (3 mL), and **3a** (0.7818 g, 11 mmol)/toluene (4 mL) afforded **4i** (1.9747 g, 87%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl

acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.46-7.35 (m, 2 H, Ar-H), 7.28-7.18 (m, 3 H, Ar-H), 2.84-2.70 (m, 4 H, CH₂NCH₂), 1.90-1.74 (m, 5 H, 2×CH₂ + one proton of CH₂), 1.74-1.62 (m, 1 H, one proton of CH₂), 1.41 (s, 3 H, CH₃), 1.04 (t, *J* = 7.4 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.4, 127.9, 127.3, 123.4, 90.9, 84.3, 58.1, 47.5, 33.8, 25.0, 23.4, 8.7; MS (ESI) *m/z* 228 (M+H⁺), 157 (M+H⁺-pyrrolidine); IR (neat): ν = 2967, 2936, 2874, 2807, 1598, 1488, 1460, 1444, 1369, 1292, 1174, 1145 cm⁻¹; HRMS calcd for C₁₆H₂₁N [M⁺]: 227.1674. Found: 227.1674.

(10) 1-(3-Methyl-1-phenylnon-1-yn-3-yl)pyrrolidine **4j** (tangxj-4-142)

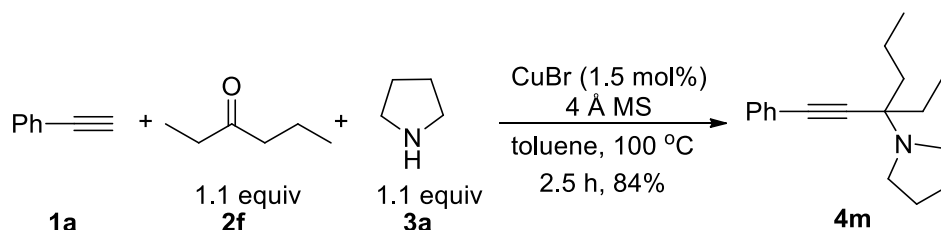


The reaction of 4 Å MS (3.0021 g), CuBr (0.0210 g, 0.15 mmol), **1a** (1.0221 g, 10 mmol)/toluene (3 mL), **2c** (1.4098 g, 11 mmol)/toluene (3 mL), and **3a** (0.7825 g, 11 mmol)/toluene (4 mL) afforded **4j** (2.4298 g, 86%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.37 (m, 2 H, Ar-H), 7.30-7.21 (m, 3 H, Ar-H), 2.85-2.71 (m, 4 H, CH₂NCH₂), 1.84-1.61 (m, 6 H, 3×CH₂), 1.55-1.41 (m, 5 H, CH₂ + CH₃), 1.36-1.27 (m, 6 H, 3×CH₂), 0.89 (t, *J* = 6.6 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.6, 128.0, 127.5, 123.5, 91.3, 84.2, 57.7, 47.6, 41.4, 31.7, 29.7, 25.8, 24.2, 23.5, 22.6, 14.0; MS (ESI) *m/z* 284 (M+H⁺), 256 (M+H⁺-CH₂=CH₂), 213 (M+H⁺-pyrrolidine); IR (neat): ν = 2928, 2869, 2808, 1573, 1489, 1463, 1370, 1102, 1070, 1026 cm⁻¹; HRMS calcd for C₂₀H₂₉N [M⁺]: 283.2300. Found: 283.2303.

(11) 1-(3-Methyl-1,5-diphenylpent-1-yn-3-yl)pyrrolidine **4k** (tangxj-4-157)

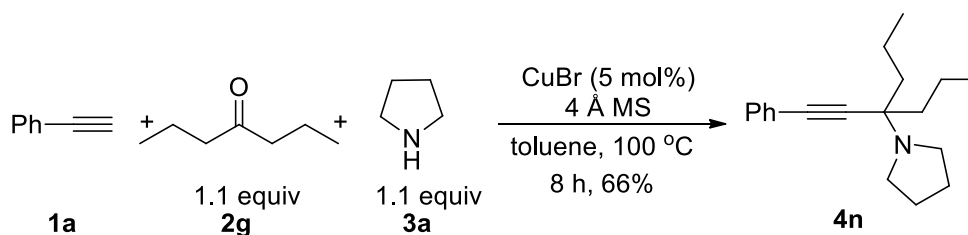
CH₃), 0.94 (d, $J = 7.2$ Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.6, 128.1, 127.5, 123.7, 91.9, 84.4, 61.5, 47.3, 35.1, 23.6, 19.4, 19.1, 15.5; MS (ESI) m/z 242 (M+H⁺), 171 (M+H⁺-pyrrolidine); IR (neat): $\nu = 2963, 2873, 2807, 1598, 1490, 1463, 1444, 1384, 1367, 1254, 1194, 1160, 1140$ cm⁻¹; HRMS calcd for C₁₇H₂₃N [M⁺]: 241.1830. Found: 241.1833.

(13) 1-(3-Ethyl-1-phenylhex-1-yn-3-yl)pyrrolidine **4m** (tangxj-4-173)



The reaction of 4 Å MS (3.0018 g), CuBr (0.0218 g, 0.15 mmol), **1a** (1.0205 g, 10 mmol) /toluene (3 mL), **2f** (1.1009 g, 11 mmol)/toluene (3 mL), and **3a** (0.7824 g, 11 mmol)/toluene (4 mL) afforded **4m** (2.1310 g, 84%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 100/1 (200 mL)→50/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.38 (m, 2 H, Ar-H), 7.30-7.22 (m, 3 H, Ar-H), 2.80-2.70 (m, 4 H, CH₂NCH₂), 1.85-1.62 (m, 8 H, 4×CH₂), 1.49-1.37 (m, 2 H, CH₂), 0.99-0.92 (m, 6 H, 2×CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.7, 128.1, 127.5, 123.7, 91.5, 84.6, 61.5, 47.3, 38.6, 29.6, 23.6, 16.9, 14.5, 8.2; MS (ESI) m/z 256 (M+H⁺), 185 (M+H⁺-pyrrolidine); IR (neat): $\nu = 2959, 2873, 2807, 1598, 1489, 1459, 1294, 1259, 1145, 1120, 1069, 1026$ cm⁻¹; HRMS calcd for C₁₈H₂₅N [M⁺]: 255.1987. Found: 255.1990.

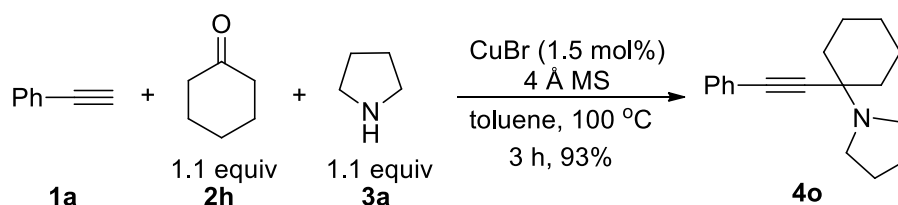
(14) 1-(4-(Phenylethynyl)heptan-4-yl)pyrrolidine **4n** (tangxj-5-22)



The reaction of 4 Å MS (3.0012 g), CuBr (0.0709 g, 0.5 mmol), **1a** (1.0201 g, 10

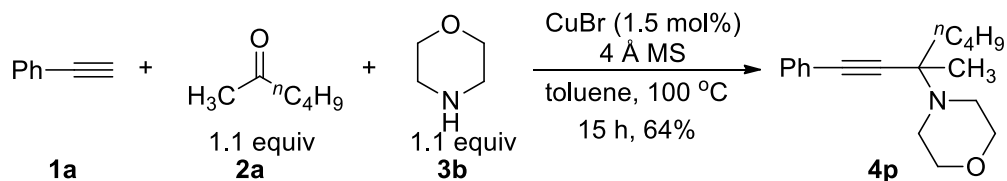
mmol) /toluene (3 mL), **2g** (1.2547 g, 11 mmol)/toluene (3 mL), and **3a** (0.7821 g, 11 mmol)/toluene (4 mL) afforded **4n** (1.7765 g, 66%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 200/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL/90 mL/1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.36 (m, 2 H, Ar-H), 7.30-7.19 (m, 3 H, Ar-H), 2.79-2.69 (m, 4 H, CH₂NCH₂), 1.82-1.62 (m, 8 H, 4×CH₂), 1.51-1.37 (m, 4 H, 2×CH₂), 0.94 (t, *J* = 7.4 Hz, 6 H, 2×CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.6, 128.1, 127.5, 123.7, 91.6, 84.5, 61.1, 47.3, 39.3, 23.5, 17.0, 14.5; MS (ESI) *m/z* 270 (M+H⁺), 199 (M+H⁺-pyrrolidine); IR (neat): ν = 2957, 2872, 2807, 1598, 1489, 1457, 1254, 1121 cm⁻¹; HRMS calcd for C₁₉H₂₇N [M⁺]: 269.2143. Found: 269.2138.

(15) 1-(1-(Phenylethynyl)cyclohexyl)pyrrolidine **4o** (tangxj-4-165)



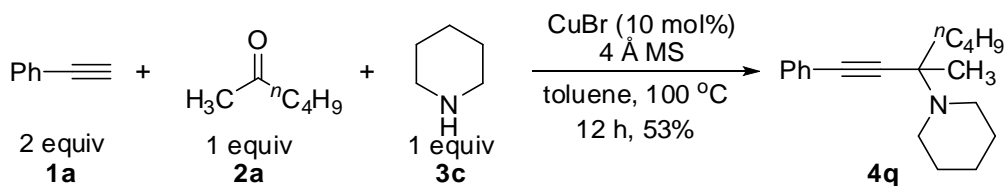
The reaction of 4 Å MS (3.0025 g), CuBr (0.0215 g, 0.15 mmol), **1a** (1.0217 g, 10 mmol) /toluene (3 mL), **2h** (1.0795 g, 11 mmol)/toluene (3 mL), and **3a** (0.7821 g, 11 mmol)/toluene (4 mL) afforded **4o**^[1] (2.3526 g, 93%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 100/1 (200 mL)→50/1 (200 mL)→5/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 700 mL/350 mL/1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.45-7.38 (m, 2 H, Ar-H), 7.30-7.21 (m, 3 H, Ar-H), 2.84-2.74 (m, 4 H, CH₂NCH₂), 2.07-1.98 (m, 2 H, 2×one proton of CH₂), 1.83-1.47 (m, 11 H, 5×CH₂ + one proton of CH₂), 1.30-1.17 (m, 1 H, one proton of CH₂); ¹³C NMR (100 MHz, CDCl₃) δ 131.5, 127.9, 127.4, 123.5, 90.2, 85.9, 59.0, 46.8, 37.7, 25.5, 23.3, 22.8; MS (ESI) *m/z* 254 (M+H⁺), 183 (M+H⁺-pyrrolidine); IR (neat): ν = 2929, 2854, 2806, 1598, 1488, 1444, 1289, 1265, 1158, 1124, 1068 cm⁻¹; HRMS calcd for C₁₈H₂₃N [M⁺]: 253.1830. Found: 253.1829.

(16) 4-(3-Methyl-1-phenylhept-1-yn-3-yl)morpholine **4p** (tangxj-4-162)



The reaction of 4 Å MS (2.9979 g), CuBr (0.0215 g, 0.15 mmol), **1a** (1.0217 g, 10 mmol) /toluene (3 mL), **2a** (1.1017 g, 11 mmol)/toluene (3 mL), and **3b** (0.9573 g, 11 mmol)/toluene (4 mL) afforded **4p** (1.7343 g, 64%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 200/1 (200 mL)→100/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /90 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.37 (m, 2 H, Ar-H), 7.30-7.22 (m, 3 H, Ar-H), 3.74 (t, *J* = 4.6 Hz, 4 H, CH₂OCH₂), 2.74-2.61 (m, 4 H, CH₂NCH₃), 1.74-1.65 (m, 2 H, CH₂), 1.51-1.40 (m, 2 H, CH₂), 1.40-1.28 (m, 5 H, CH₂ + CH₃), 0.94 (t, *J* = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.5, 128.0, 127.6, 123.2, 91.1, 84.5, 67.3, 57.6, 47.0, 38.7, 25.9, 23.6, 22.9, 14.0; MS (ESI) *m/z* 272 (M+H⁺), 185 (M+H⁺-morpholine), 129 (M+H⁺- morpholine - CH₃CH₂CH=CH₂); IR (neat): ν = 2956, 2817, 1598, 1489, 1453, 1270, 1118 cm⁻¹; HRMS calcd for C₁₈H₂₅NO [M⁺]: 271.1936. Found: 271.1928.

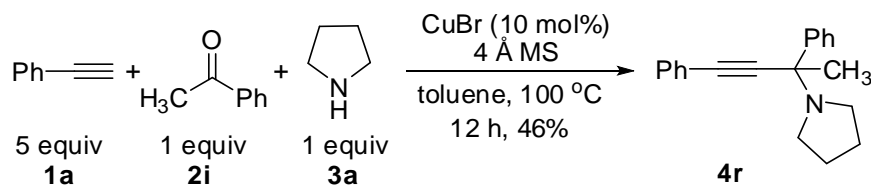
(17) 1-(3-Methyl-1-phenylhept-1-yn-3-yl)piperidine **4q** (tangxj-5-23)



The reaction of 4 Å MS (301.0 mg), CuBr (14.1 mg, 0.1 mmol), **1a** (204.2 mg, 2 mmol) /toluene (0.3 mL), **2a** (99.5 mg, 1 mmol)/toluene (0.3 mL), and **3c** (84.7 mg, 1 mmol)/toluene (0.4 mL) afforded **4q** (142.9 mg, 53%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 200/1 (200 mL)→150/1 (200 mL)→100/1 (200 mL)→50/1) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.46-7.39 (m, 2 H, Ar-H), 7.31-7.24 (m, 3 H, Ar-H), 2.72-2.55 (m, 4 H, CH₂NCH₂), 1.77-1.68 (m, 2 H, CH₂), 1.66-1.58 (m, 4 H, 2×CH₂), 1.52-1.29 (m, 9 H, 3×CH₂ + CH₃), 0.93 (t, *J* = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.6, 128.1, 127.5, 123.7, 92.5, 83.9, 58.1,

47.7, 39.2, 26.6, 26.4, 24.7, 23.9, 23.1, 14.1; MS (ESI) m/z 270 ($M+H^+$), 185 ($M+H^+$ -piperidine); IR (neat): ν = 2931, 2856, 2798, 1598, 1489, 1442, 1263, 1169, 1150, 1088, 1070, 1027 cm^{-1} ; HRMS calcd for $C_{19}H_{27}N$ [M^+]: 269.2143. Found: 269.2138.

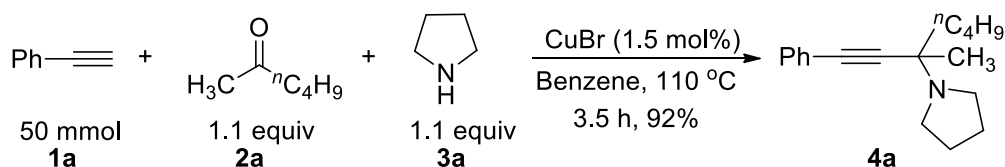
(18) 1-(2,4-Diphenylbut-3-yn-2-yl)pyrrolidine **4r** (tangxj-5-19)



The reaction of 4 Å MS (300.8 mg), CuBr (14.2 mg, 0.1 mmol), **1a** (509.7 mg, 5 mmol)/toluene (0.5 mL), **2i** (120.5 mg, 1 mmol)/toluene (0.5 mL), and **3a** (83.5 μ L, d = 0.852 g/mL, 71.1 mg, 1 mmol) afforded **4r** (126.6 mg, 46%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 200/1 (200 mL) \rightarrow 150/1 (200 mL) \rightarrow 100/1 (200 mL); finally petroleum ether/ethyl acetate/ Et_3N = 900 mL /18 mL /0.5 mL was applied to get the pure product.) as a liquid: 1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 7.2 Hz, 2 H, Ar-H), 7.56-7.47 (m, 2 H, Ar-H), 7.39-7.20 (m, 6 H, Ar-H), 2.82-2.71 (m, 2 H, CH_2N), 2.67-2.55 (m, 2 H, NCH_2), 1.84-1.69 (m, 7 H, $2 \times CH_2 + CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 131.8, 128.2, 128.0, 127.9, 127.0, 126.3, 123.4, 89.4, 87.2, 62.5, 48.4, 32.3, 23.8; MS (ESI) m/z 276 ($M+H^+$), 205 ($M+H^+$ -pyrrolidine); IR (neat): ν = 1598, 1489, 1445, 1365, 1222, 1105, 1027, 1000 cm^{-1} ; HRMS calcd for $C_{20}H_{21}N$ [M^+]: 275.1674. Found: 275.1670.

Reactions in benzene with a Dean-Stark trap in the absence of 4 Å molecular sieves.

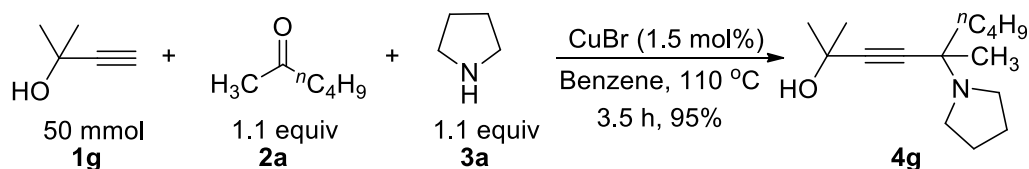
(1) 1-(3-Methyl-1-phenylhept-1-yn-3-yl)pyrrolidine **4a** (tangxj-5-128)



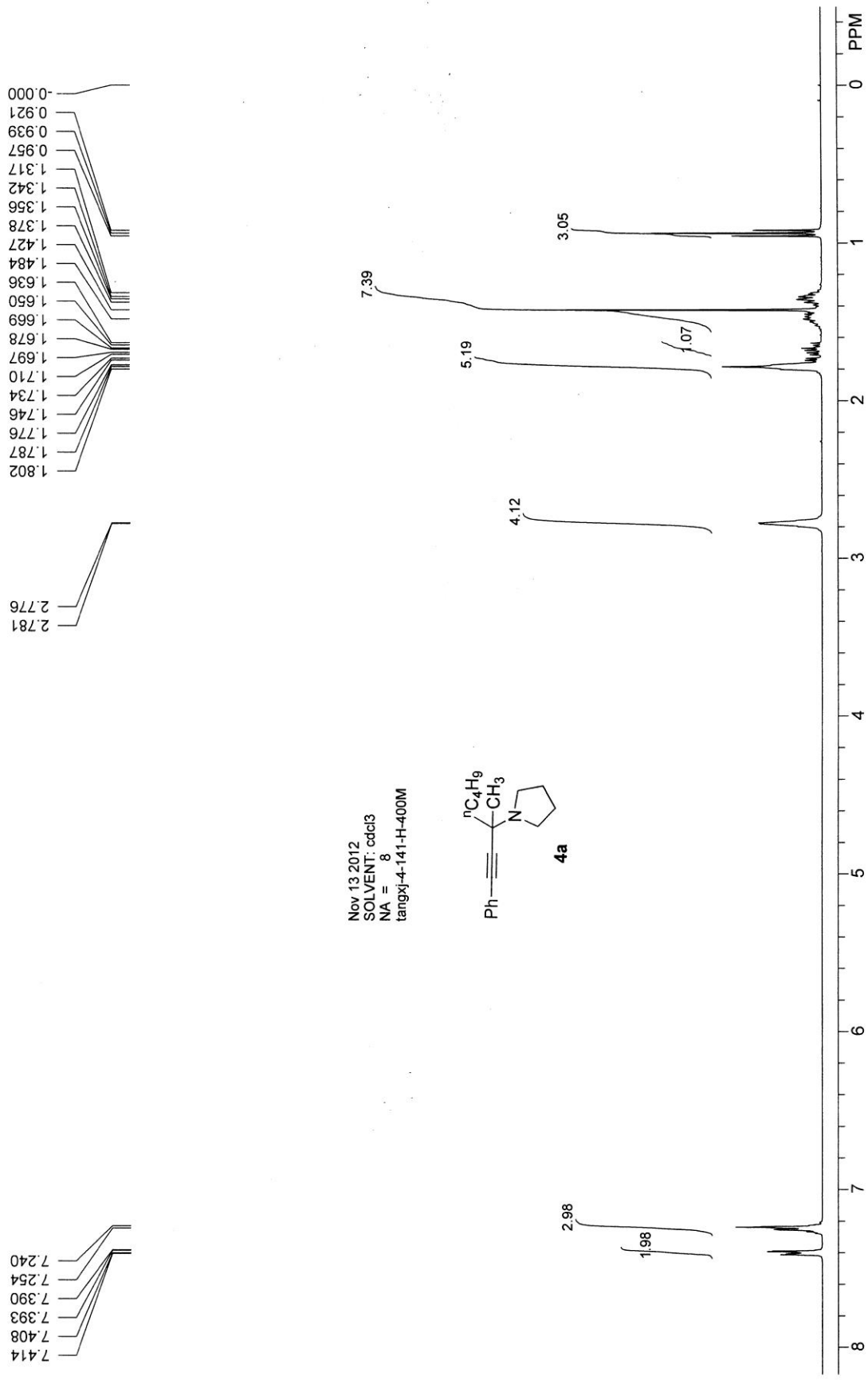
Typical Procedure 2: To a three-necked flask equipped with a Dean-Stark trap and a condenser dried under vacuum with a heating gun were added CuBr (0.1073 g, 0.75

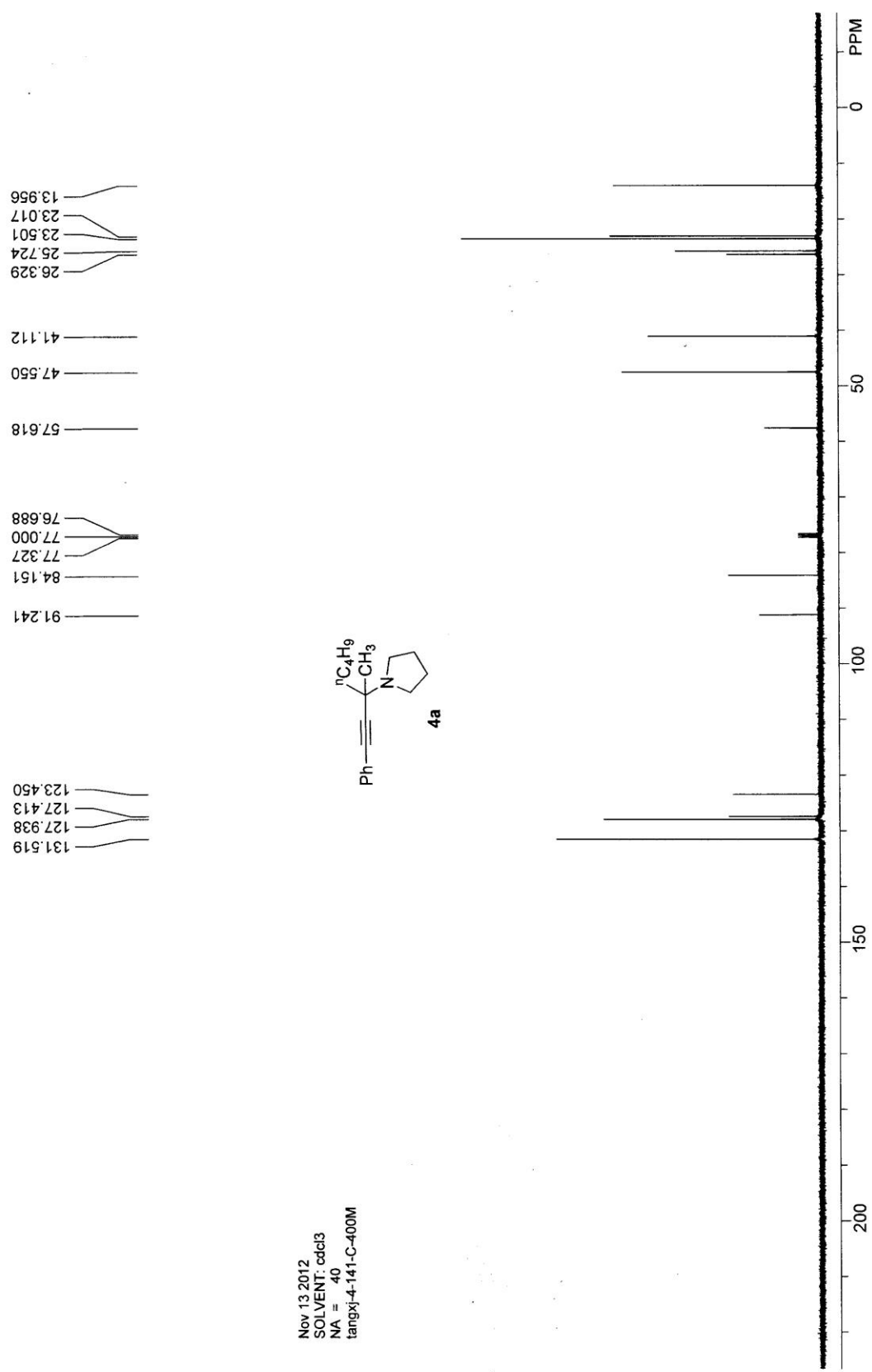
mmol), **1a** (5.1077 g, 50 mmol)/benzene (20 mL), **2a** (5.5095 g, 55 mmol)/benzene (20 mL), and **3a** (3.9121 g, 55 mmol)/benzene (10 mL) sequentially under Ar atmosphere. The flask was then placed in a pre-heated oil bath of 110 °C with stirring for 3.5 h as monitored by TLC. After cooling to room temperature, the crude reaction mixture was filtrated through a short pad of silica gel eluted with acetone (200 mL). After evaporation, the residue was purified by chromatography on silica gel to afford **4a** (11.7335 g, 92%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 150/1 (200 mL)→70/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 900 mL /180 mL /1 mL was applied to get the pure product.) as a liquid: ¹H NMR (400 MHz, CDCl₃) δ 7.44-7.38 (m, 2 H, Ar-H), 7.30-7.23 (m, 3 H, Ar-H), 2.84-2.73 (m, 4 H, CH₂NCH₂), 1.84-1.62 (m, 6 H, 3×CH₂), 1.57-1.29 (m, 7 H, 2×CH₂ + CH₃), 0.94 (t, *J* = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.5, 128.0, 127.4, 123.5, 91.3, 84.2, 57.7, 47.6, 41.1, 26.4, 25.7, 23.5, 23.0, 14.0.

(2) 2,5-Dimethyl-5-(pyrrolidin-1-yl)non-3-yn-2-ol **4g** (tangxj-5-138)

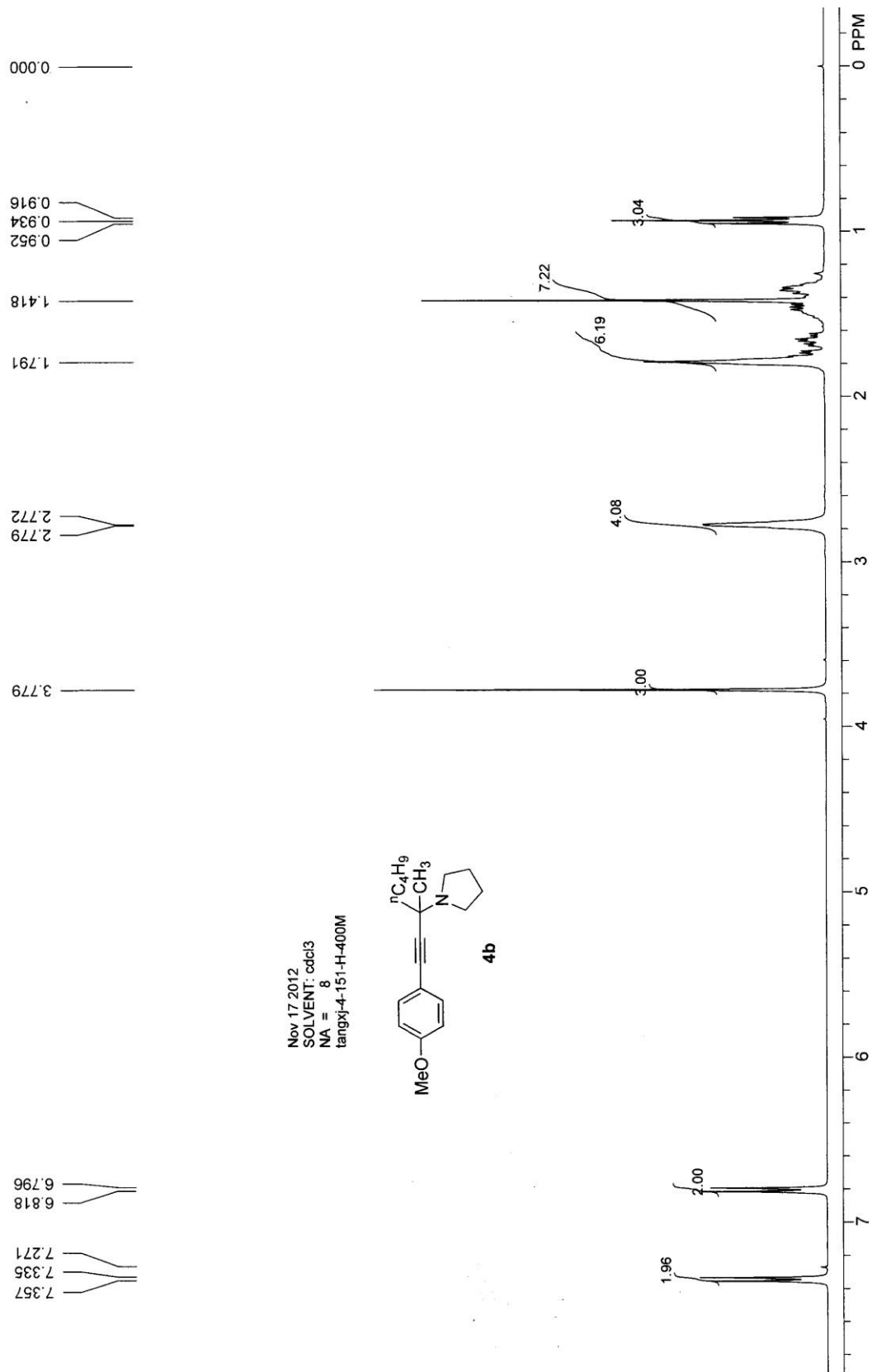


Following the above procedure, the reaction of CuBr (0.1079 g, 0.75 mmol), **1g** (4.2071 g, 50 mmol)/benzene (20 mL), **2a** (5.5095 g, 55 mmol)/benzene (20 mL), and **3a** (3.9122 g, 55 mmol)/benzene (10 mL) afforded **4g** (11.3311 g, 95%) (eluent: petroleum ether (200 mL); then petroleum ether/ethyl acetate = 50/1 (200 mL)→1/1 (200 mL); finally petroleum ether/ethyl acetate/Et₃N = 180 mL /900 mL/1 mL was applied to get the pure product.) as a solid: ¹H NMR (400 MHz, CDCl₃) δ 2.74-2.61 (m, 4 H, CH₂NCH₂), 2.52 (br s, 1 H, OH), 1.82-1.72 (m, 4 H, 2×CH₂), 1.70-1.49 (m, 8 H, CH₂ + 2×CH₃), 1.43-1.26 (m, 7 H, 2×CH₂ + CH₃), 0.91 (t, *J* = 7.2 Hz, 3 H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 89.1, 83.1, 64.9, 57.1, 47.5, 41.0, 32.02, 31.99, 26.4, 25.7, 23.5, 23.0, 14.0.

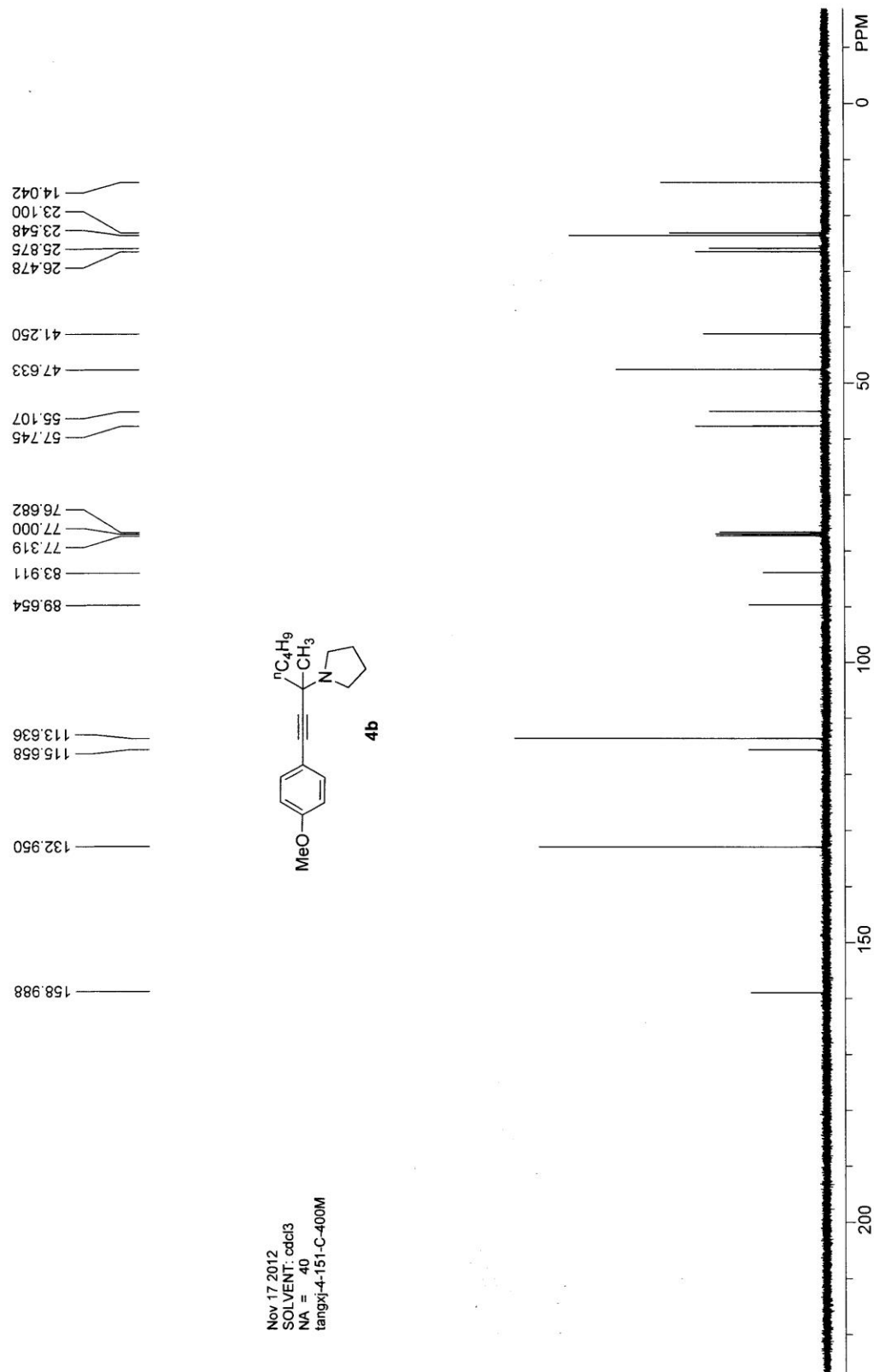




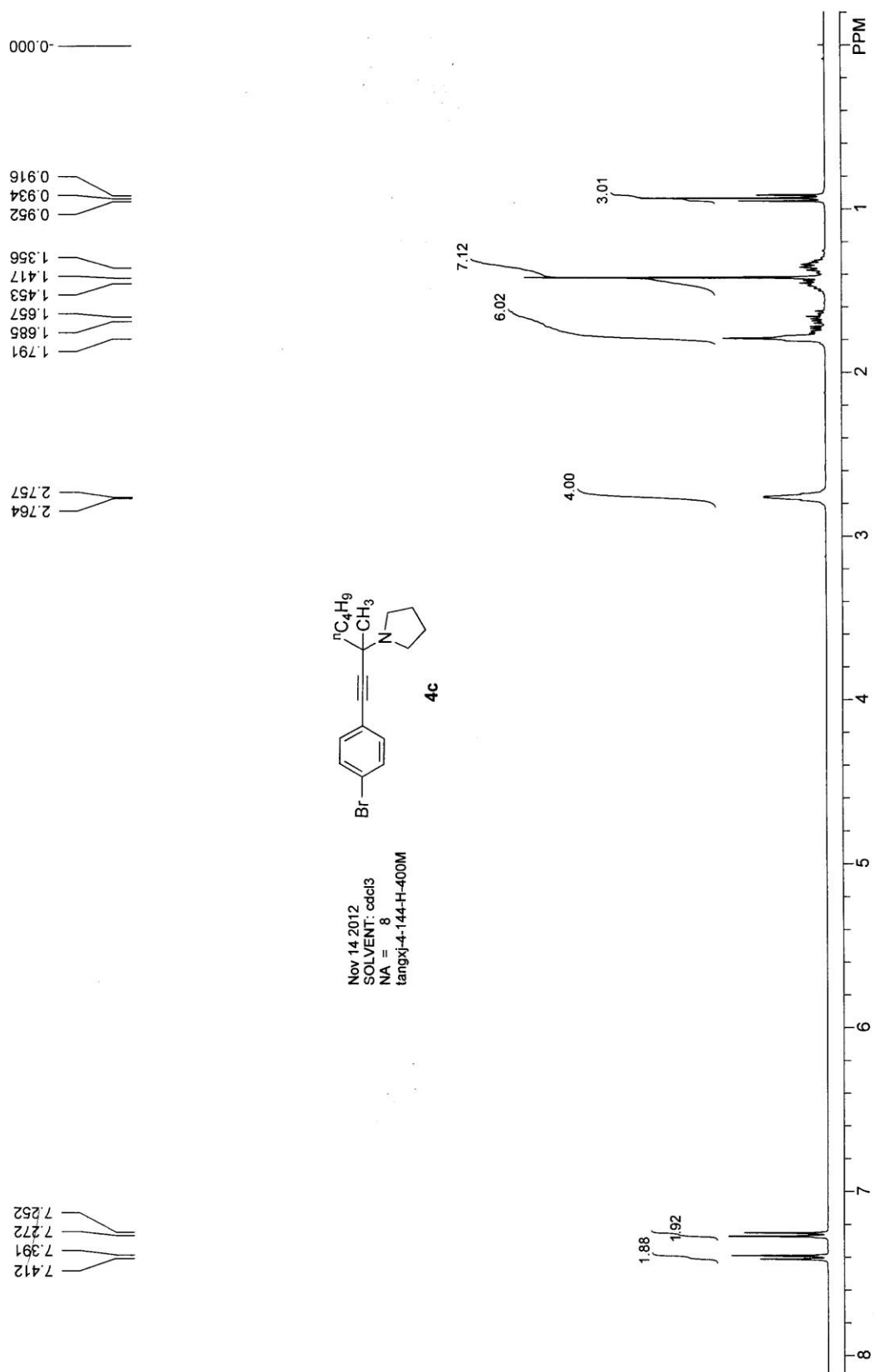
Nov 13 2012
SOLVENT: cdcl3
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tangxi-4-141-C-400M

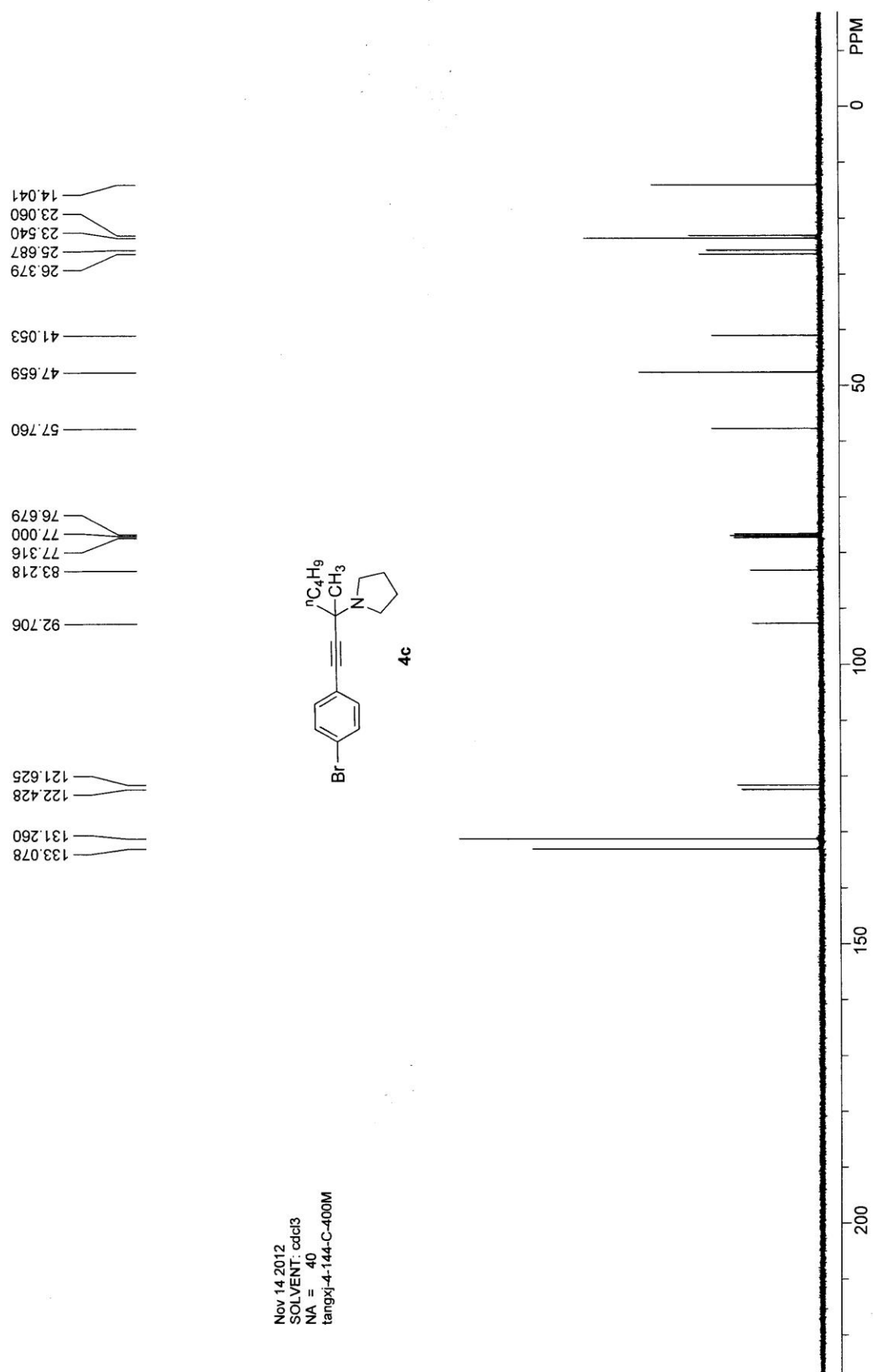


Nov 17 2012
SOLVENT: cdcl3
NA = 8
tangxi-4-151-H-400M

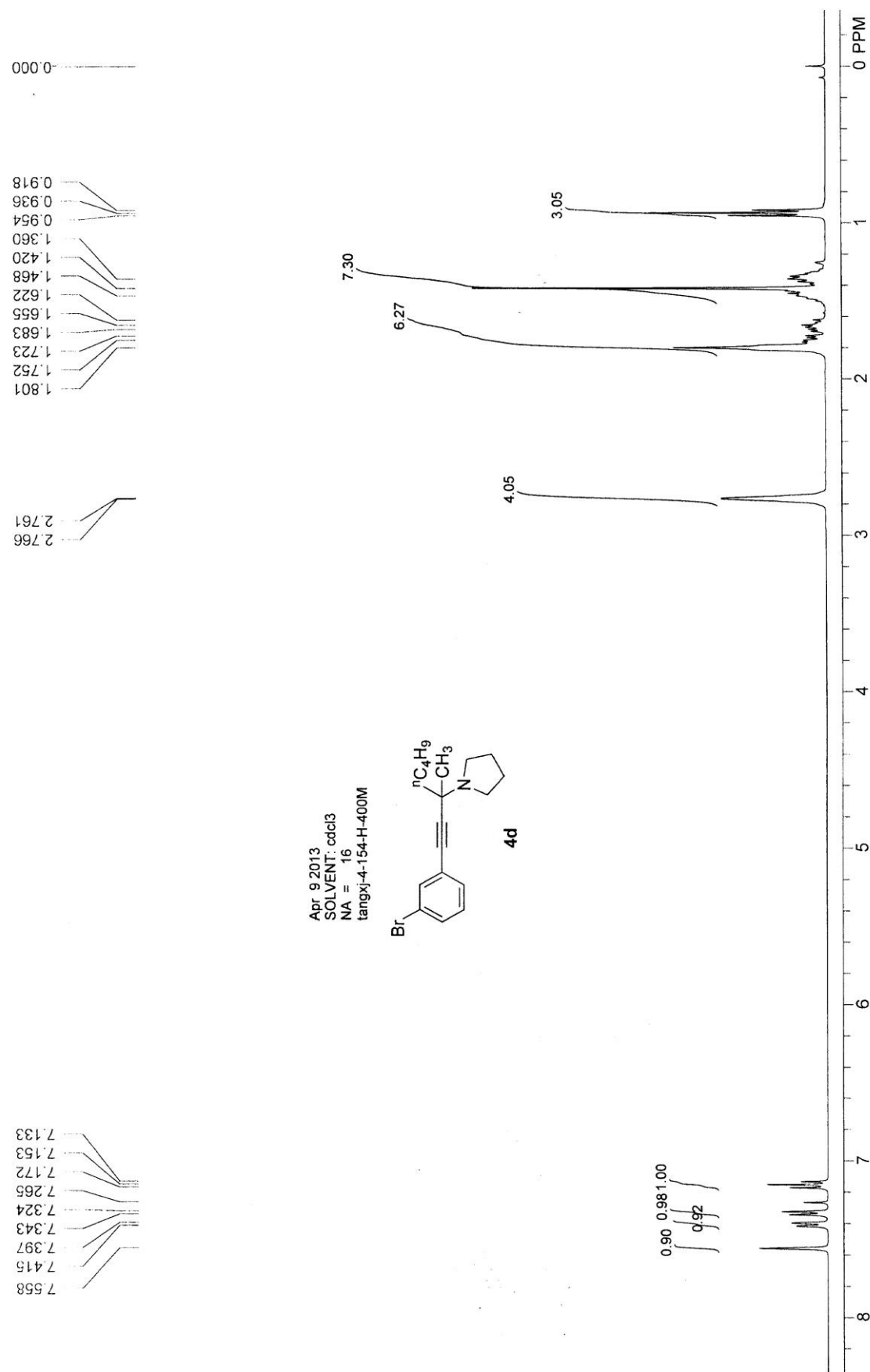


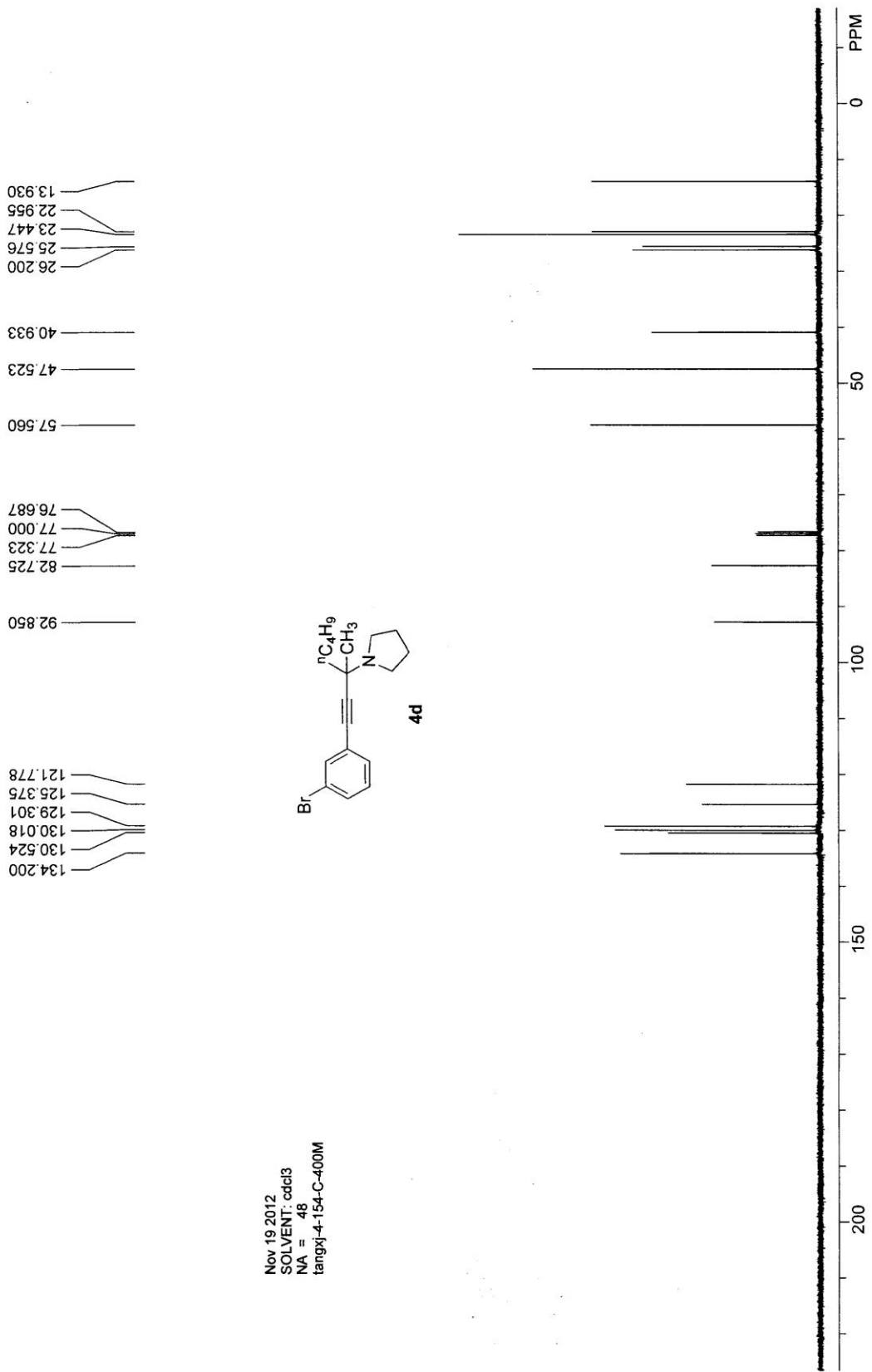
Nov 17 2012
SOLVENT: cdcl3
NA = 40
tangxi-4-151-C-400M



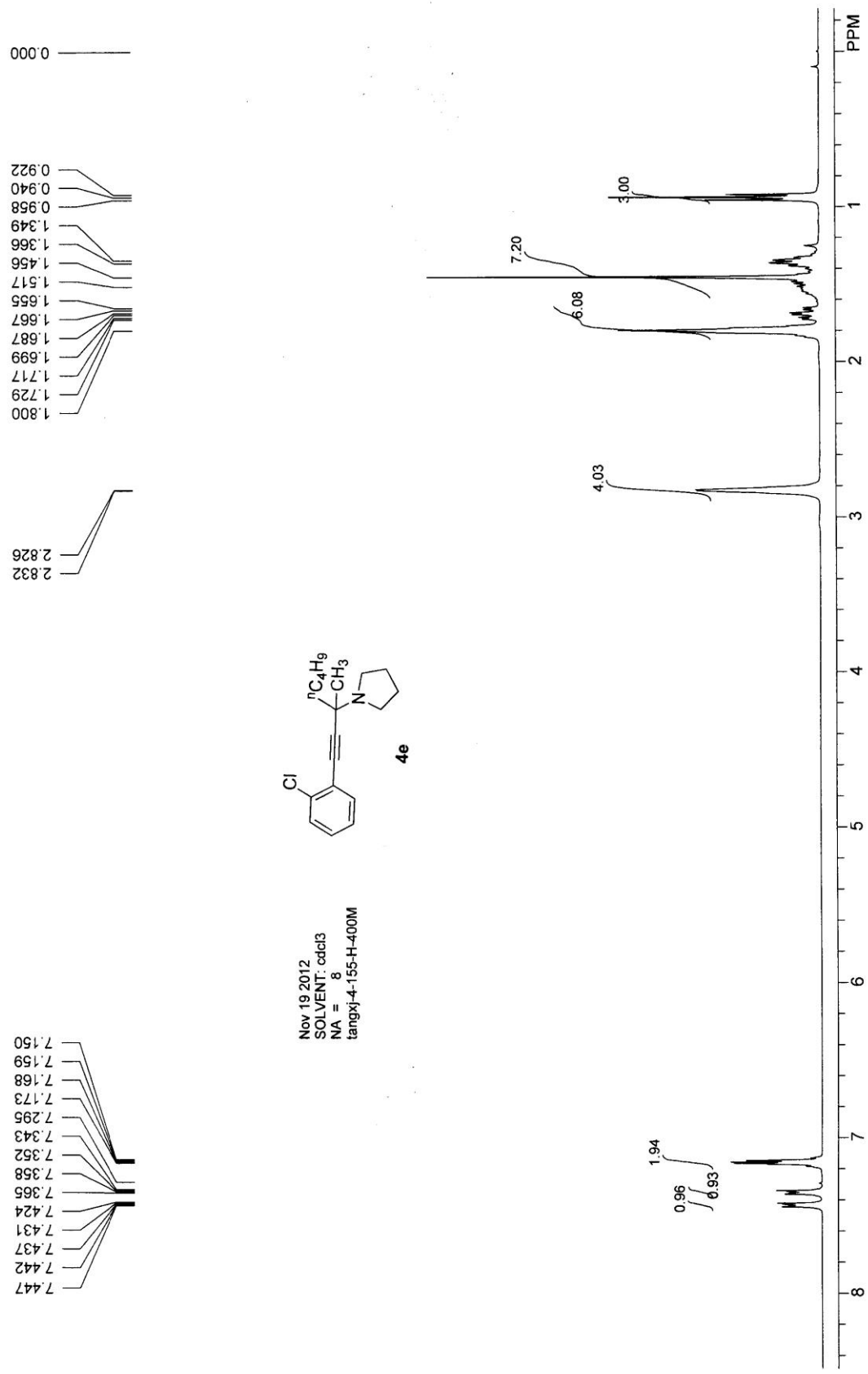


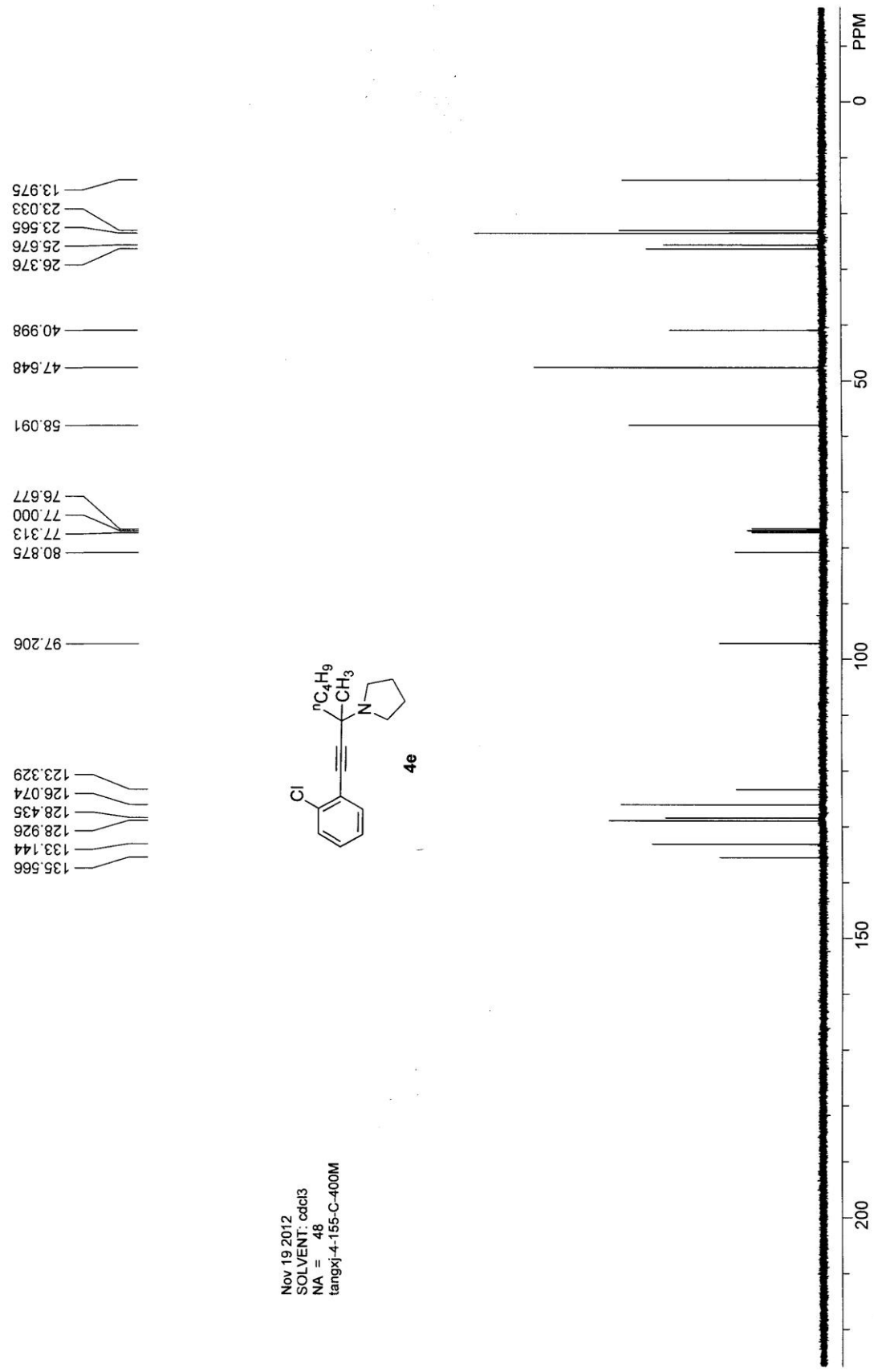
Nov 14 2012
SOLVENT: cdcl3
NA = 40
tangxi-4-144-C-400M



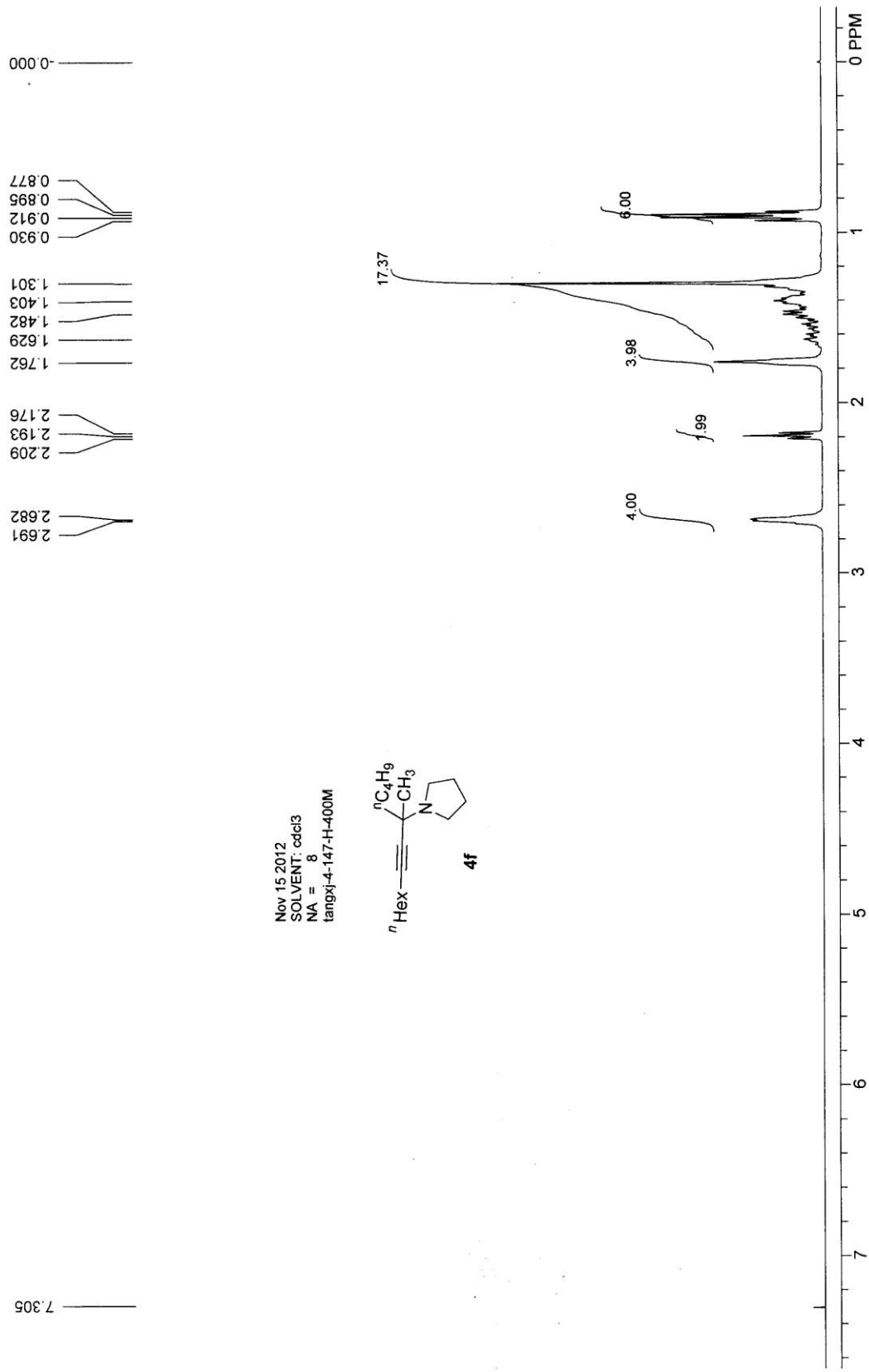


Nov 19 2012
SOLVENT: cdd3
NA = 48
tangxi-4-154-C-400M

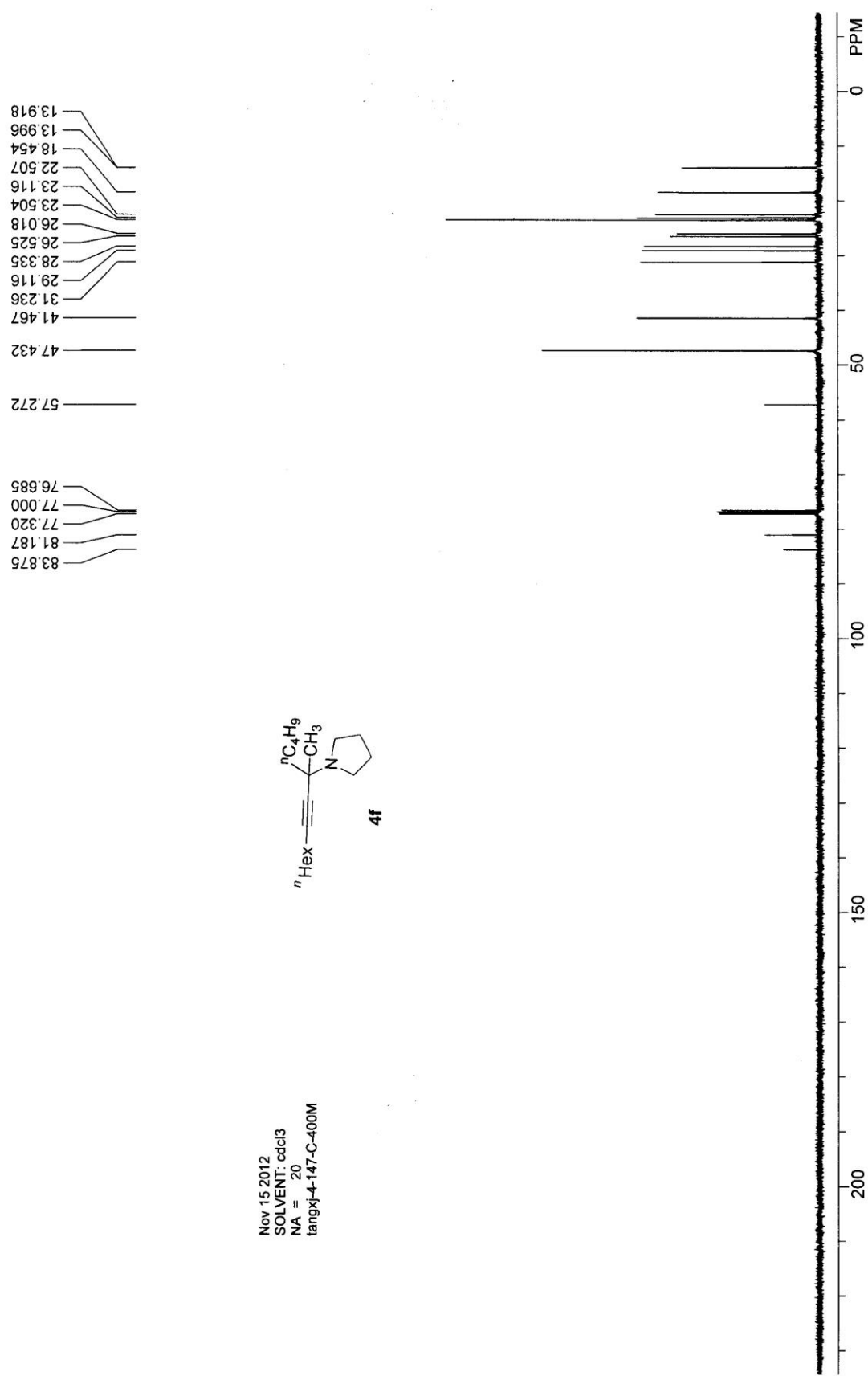


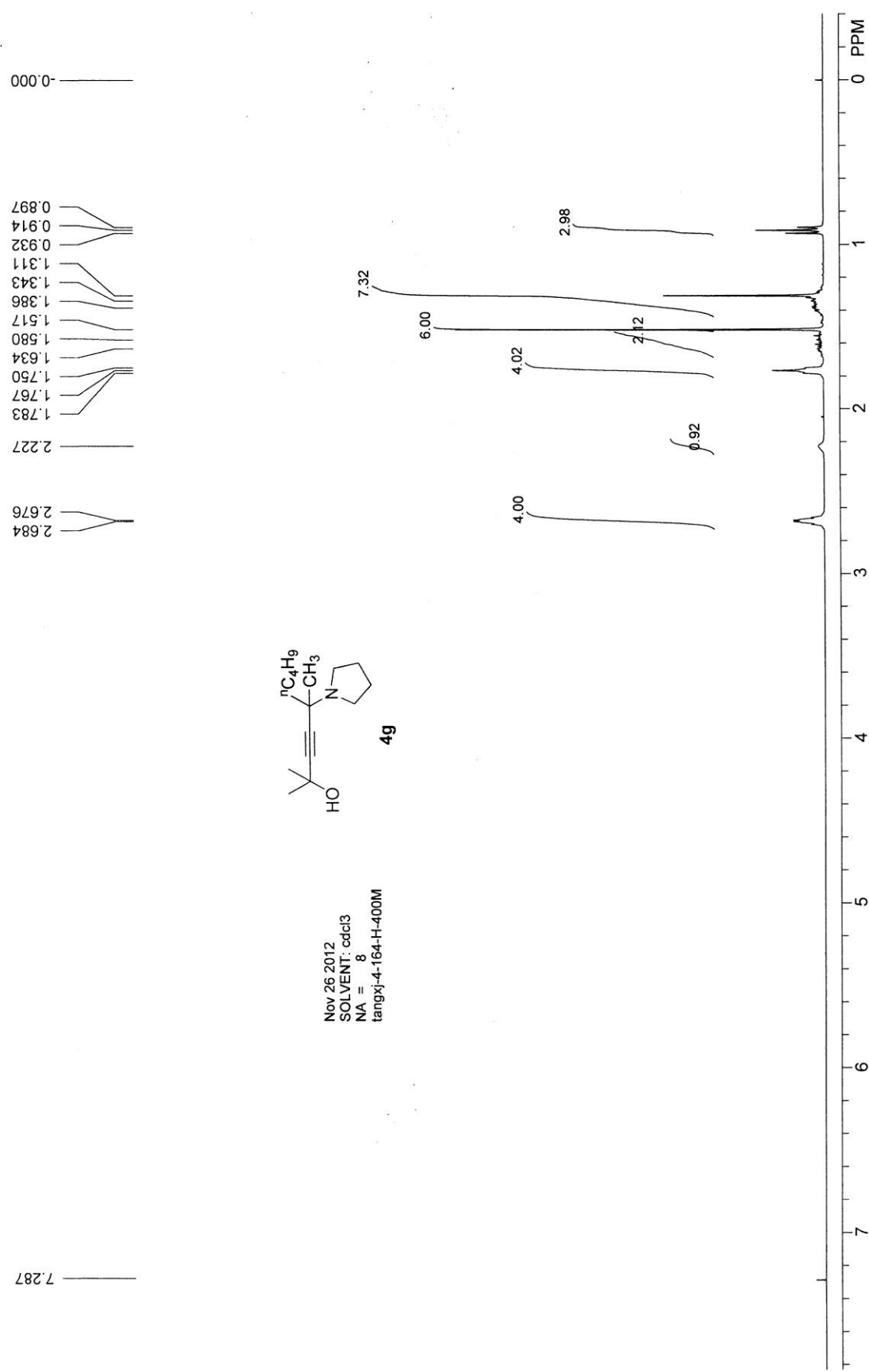


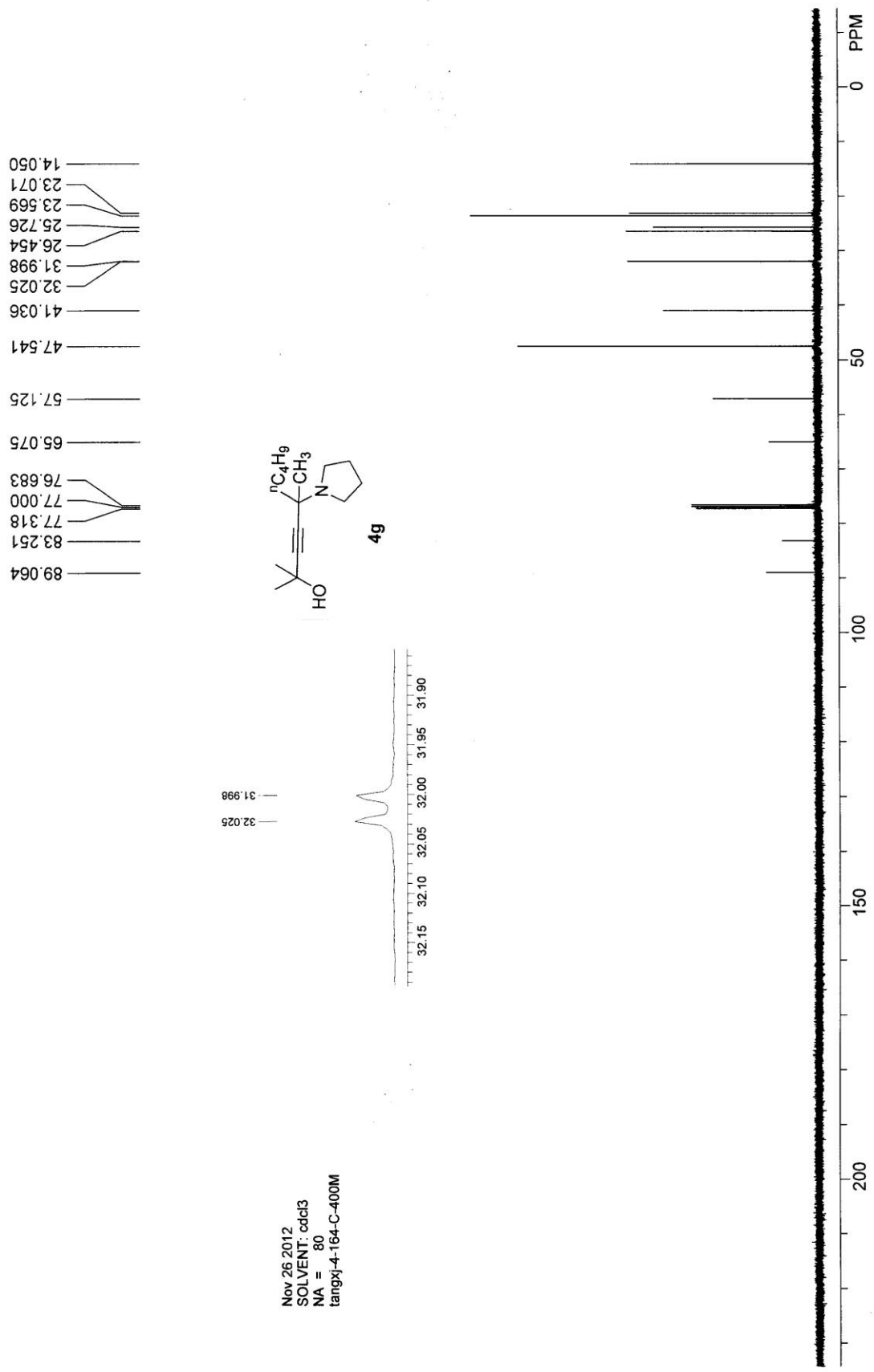
Nov 19 2012
SOLVENT: cdcl3
NA = 48
tangxi-4-155-C-400M

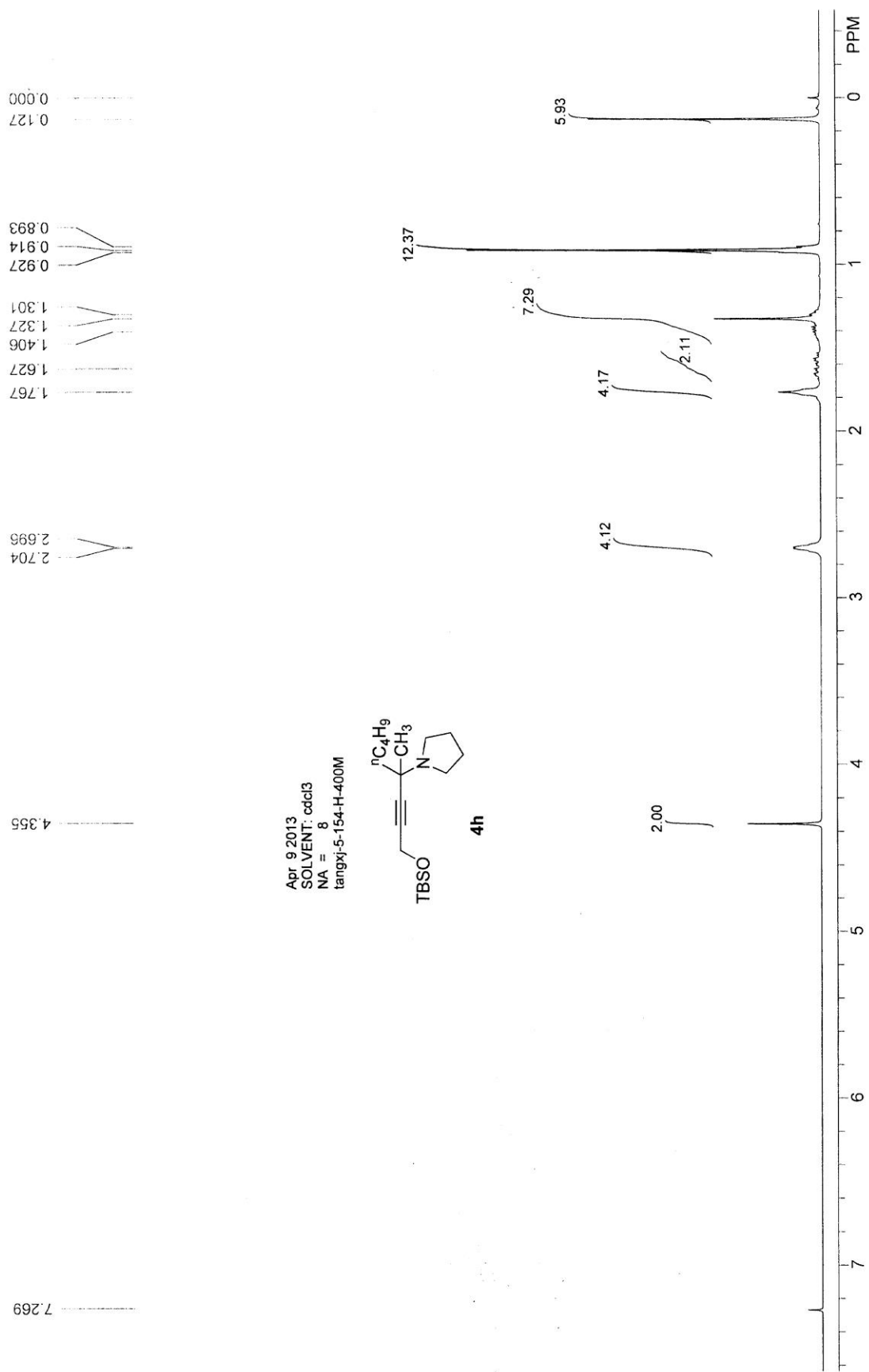


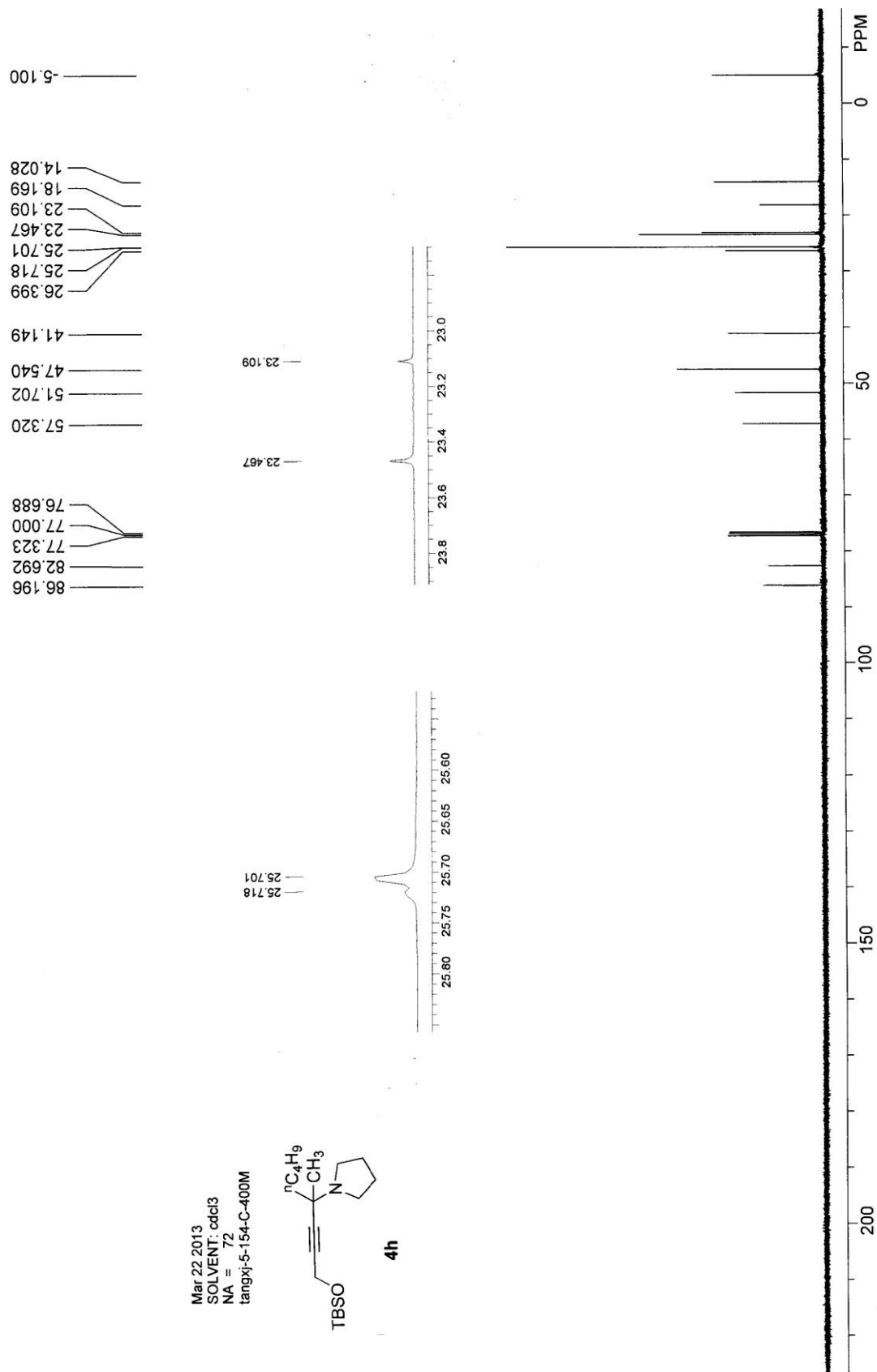
Nov 15 2012
SOLVENT: cdcl3
NA = 8
tavg[4-147-H-400M]

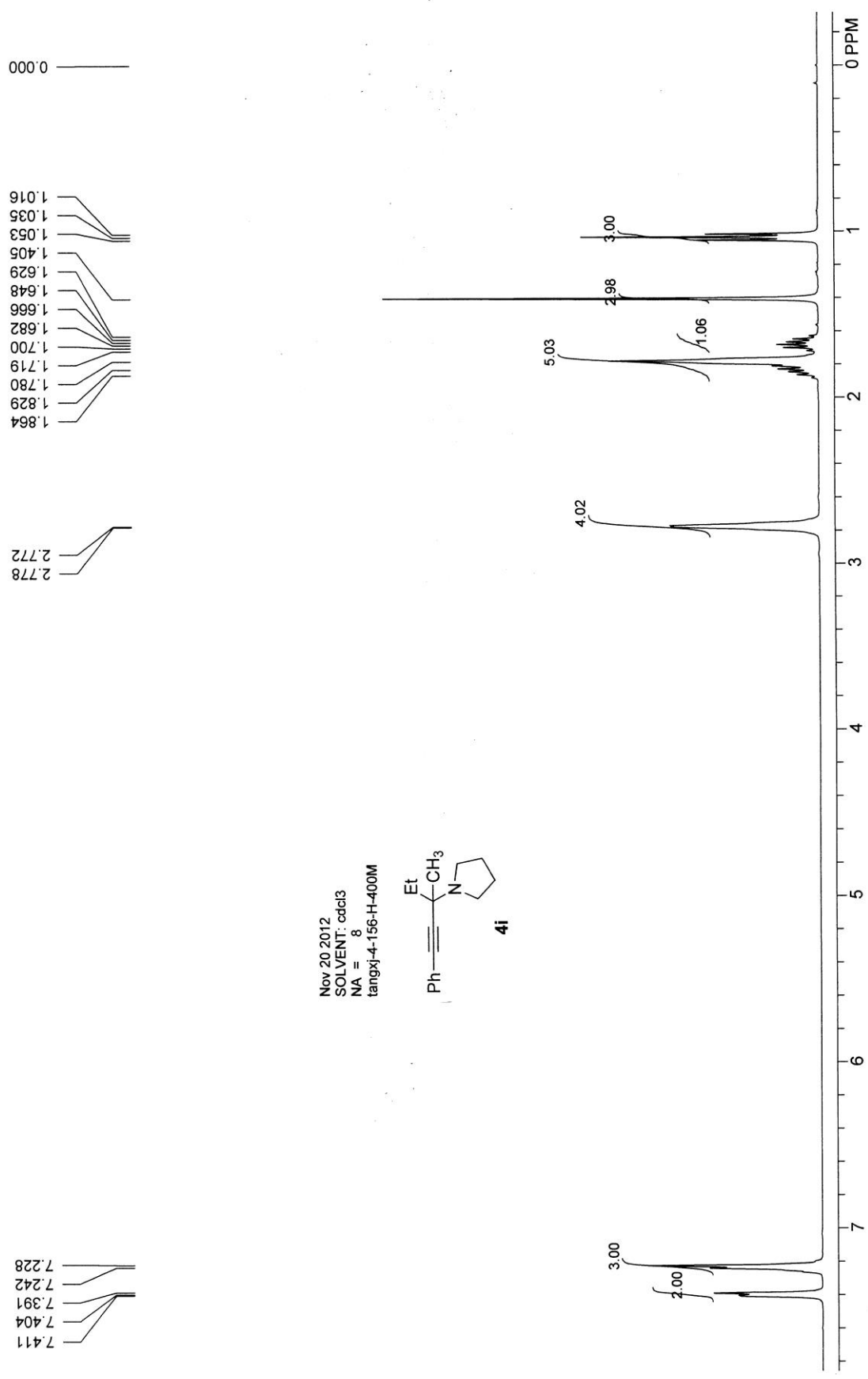


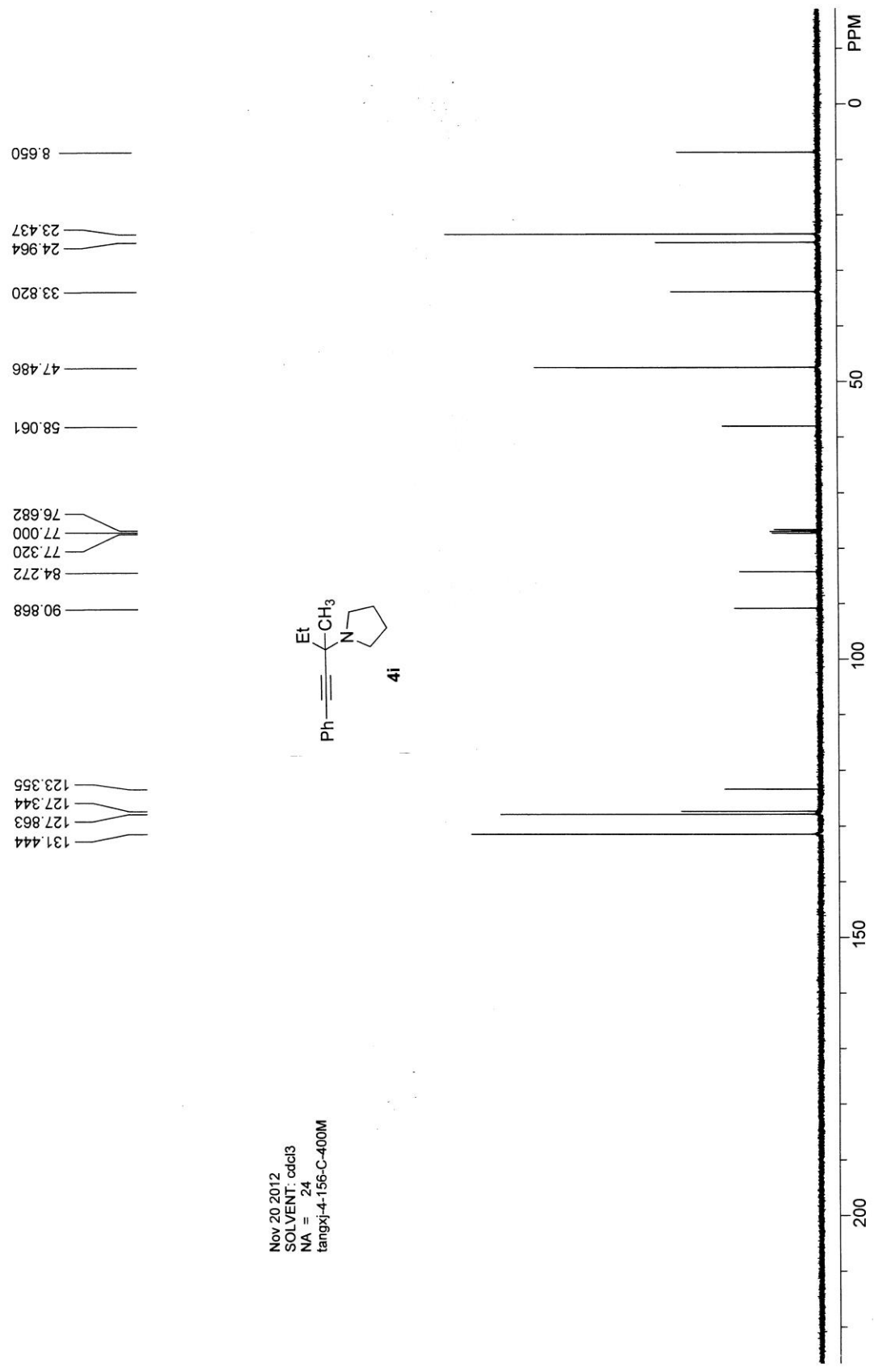




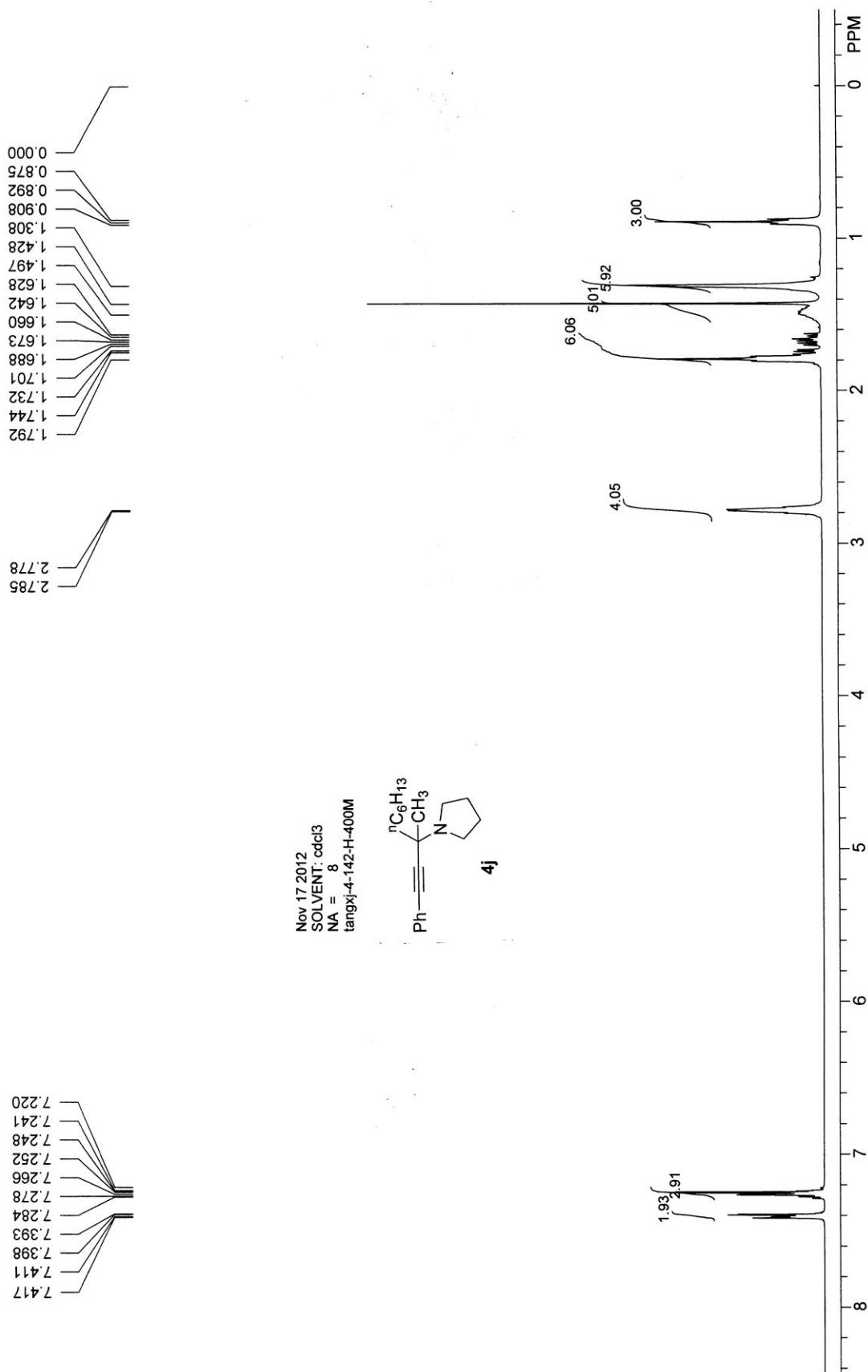


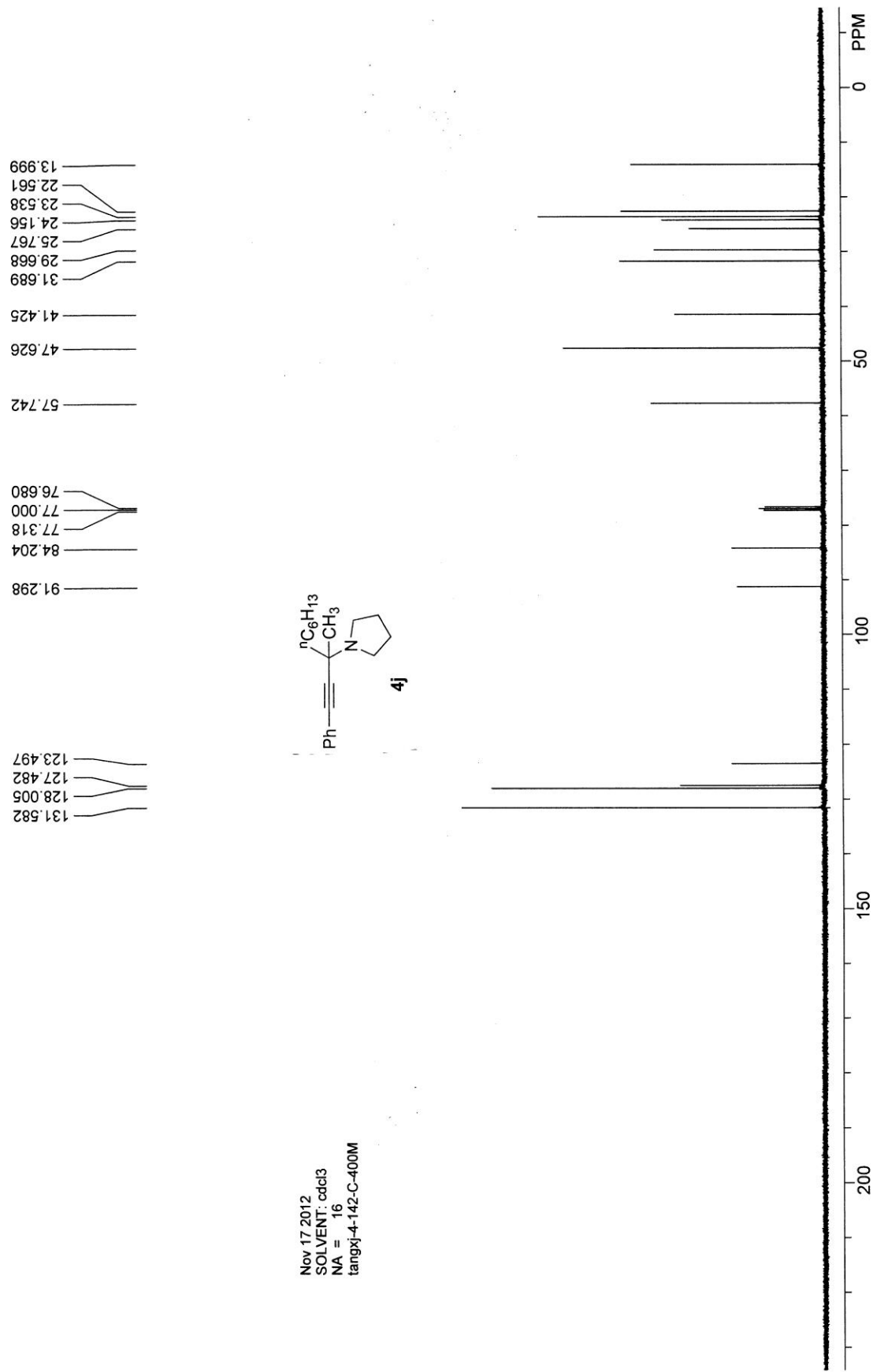




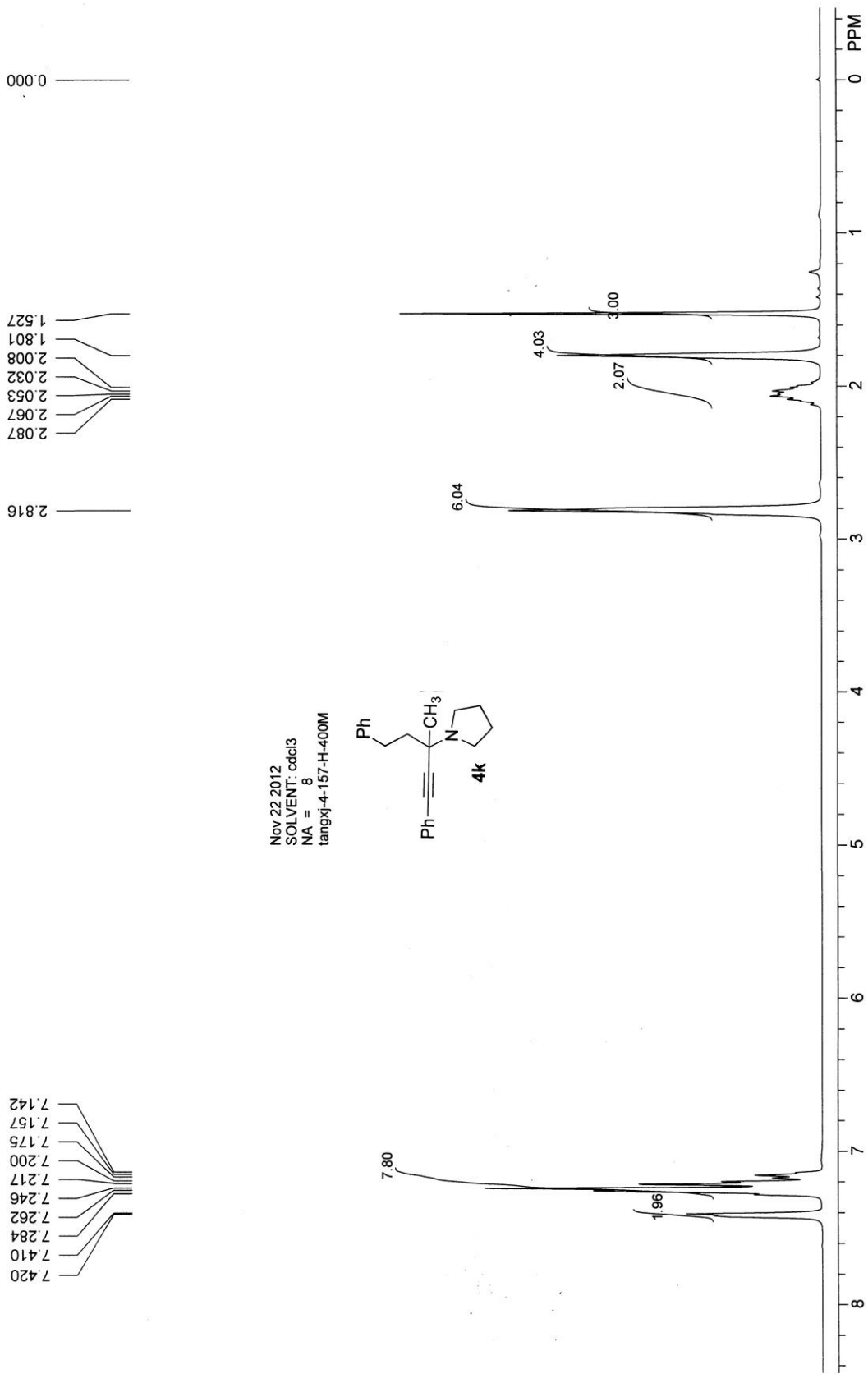


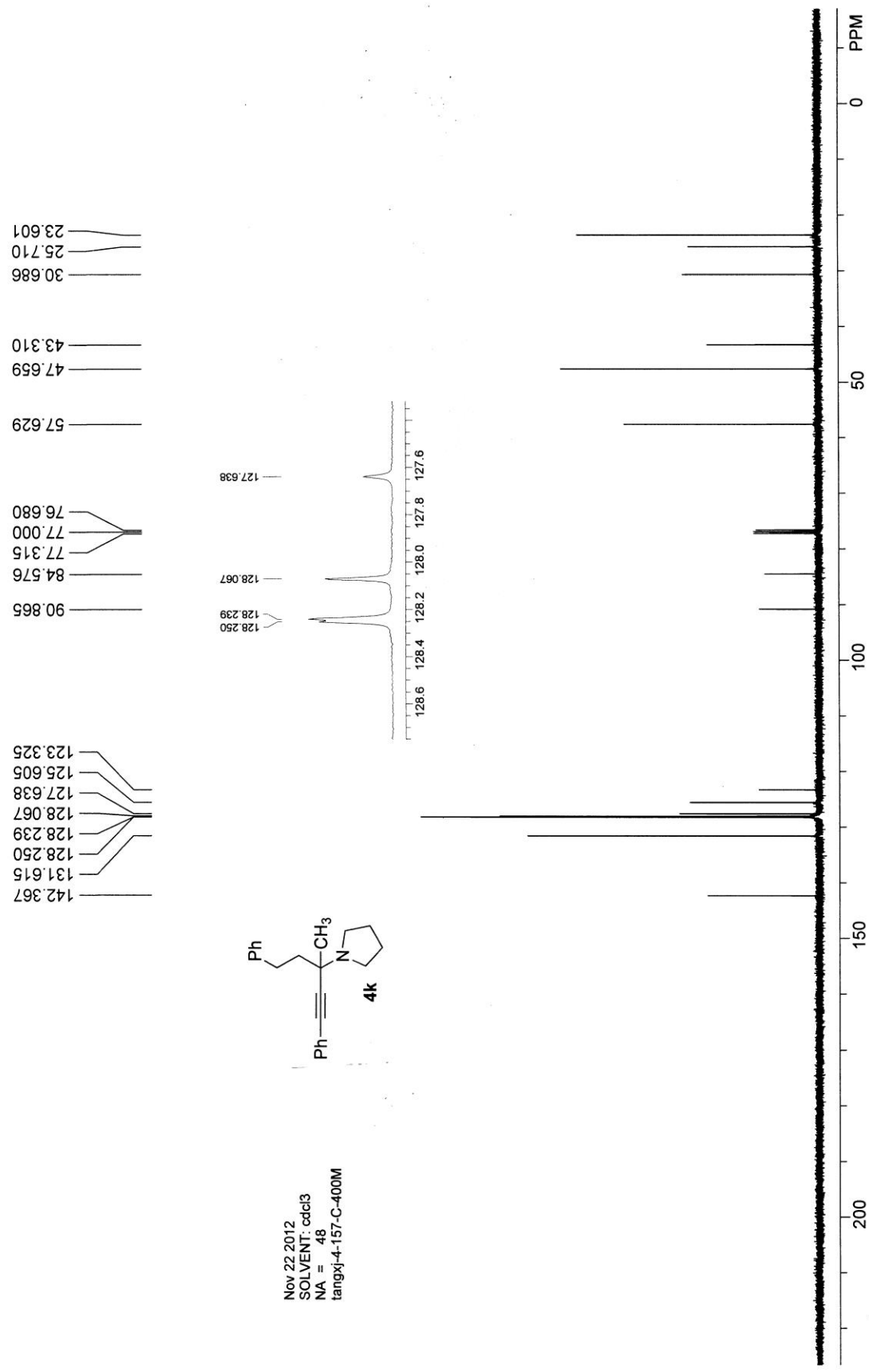
Nov 20 2012
SOLVENT: cdcl3
NA = 24
tangxi-4-156-C-400M



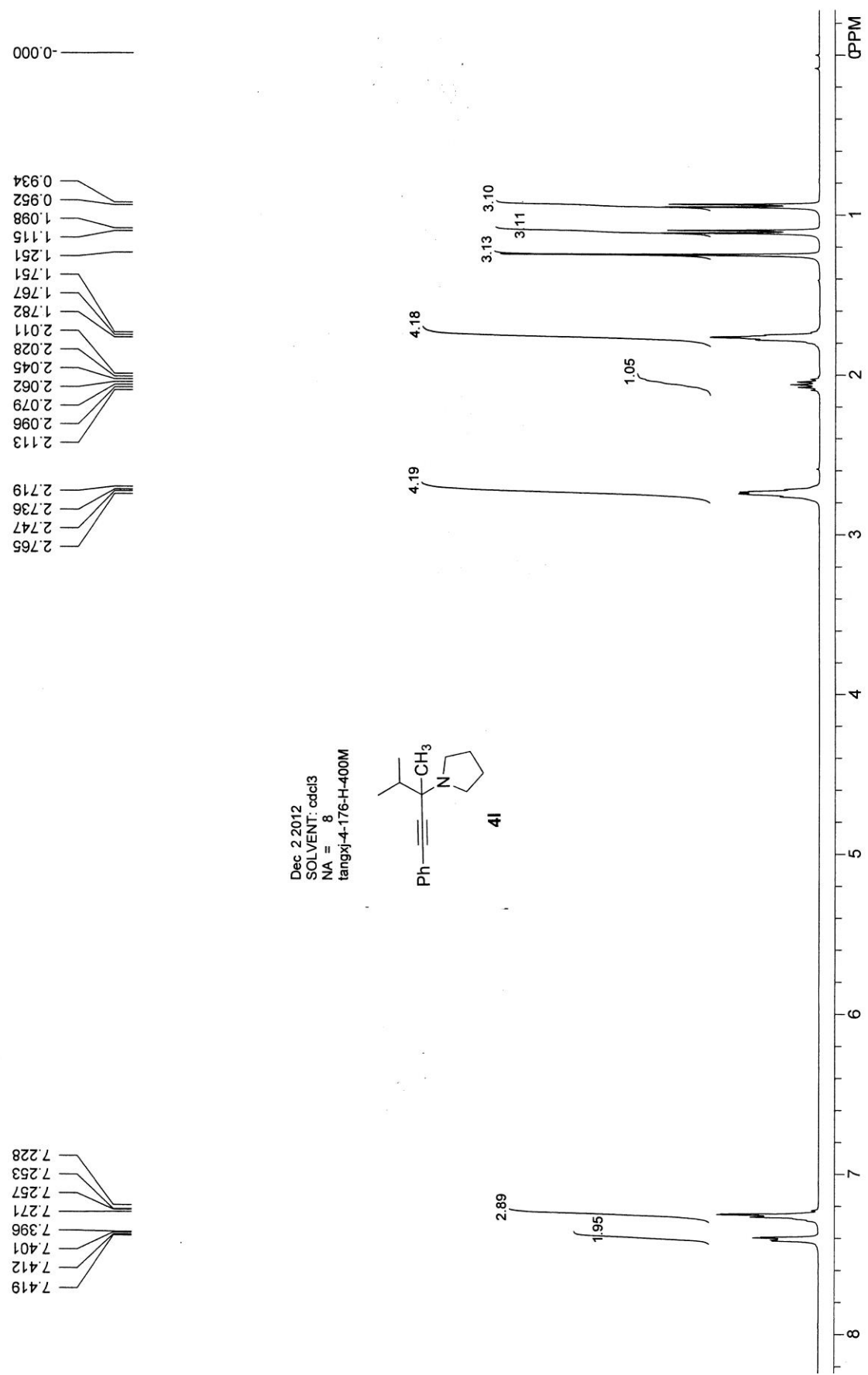


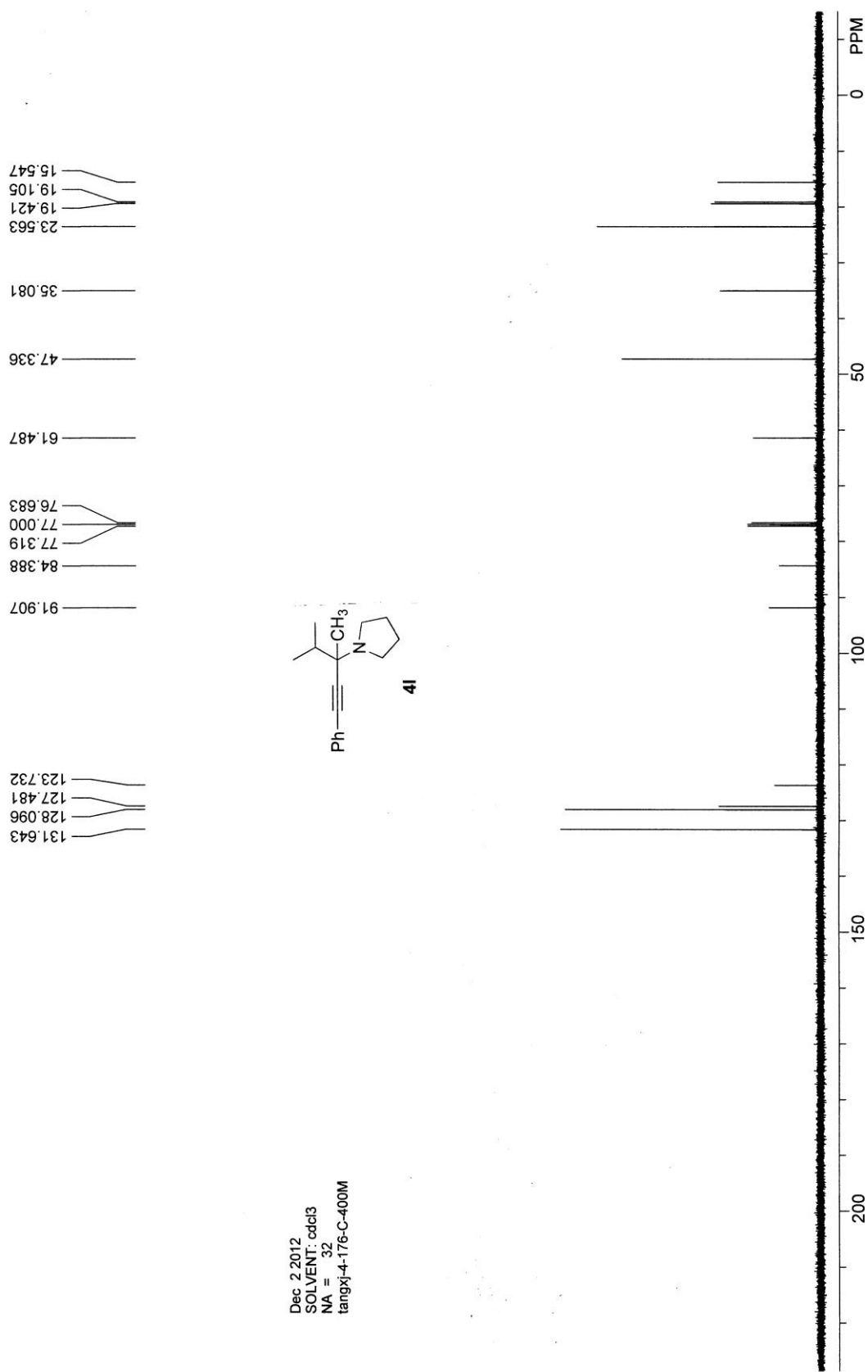
Nov 17 2012
SOLVENT: cdcl3
NA = 16
tangxi-4-142-C-400M

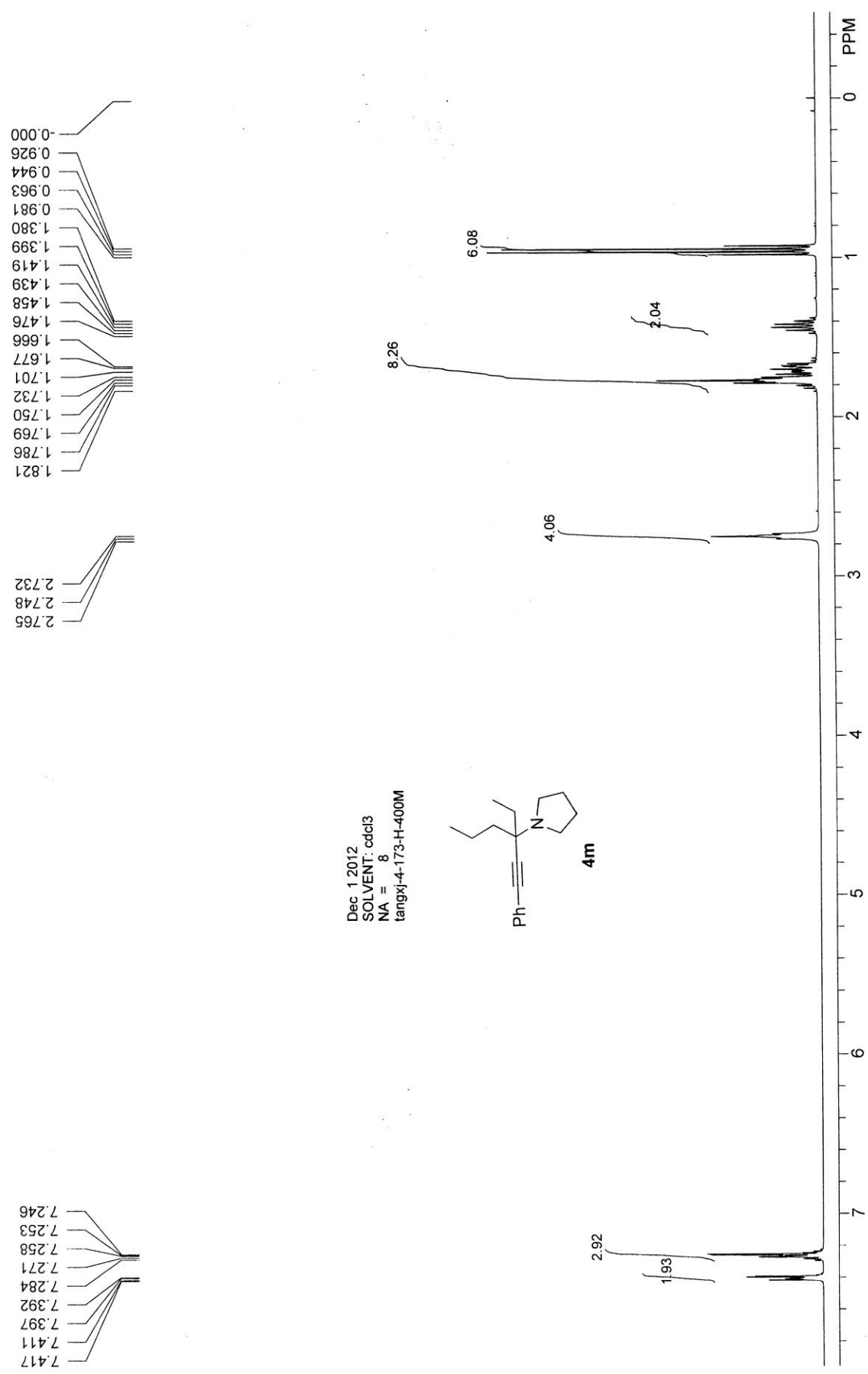




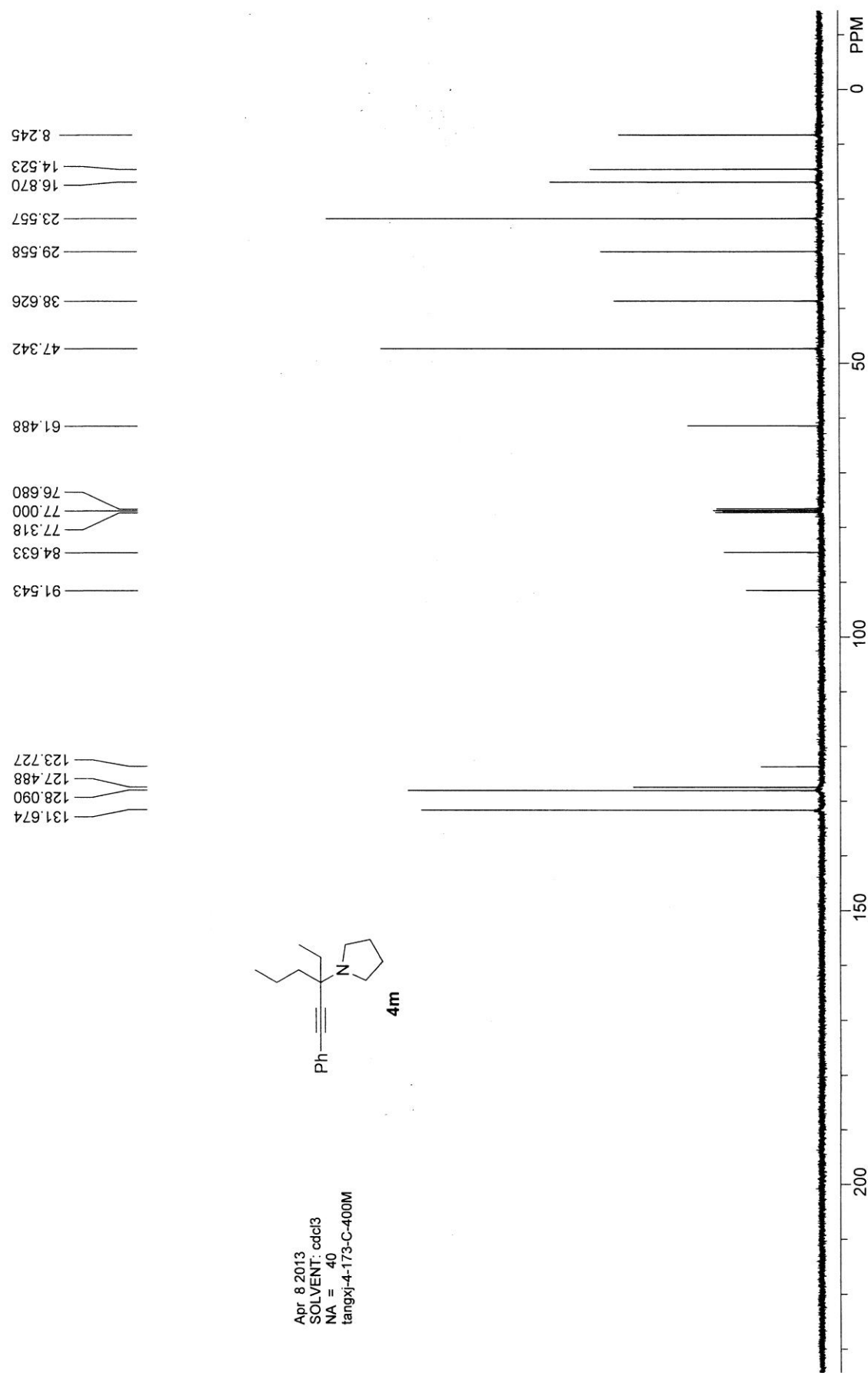
Nov 22 2012
SOLVENT: cdcl3
NA = 48
tangxi-4-157-C-400M



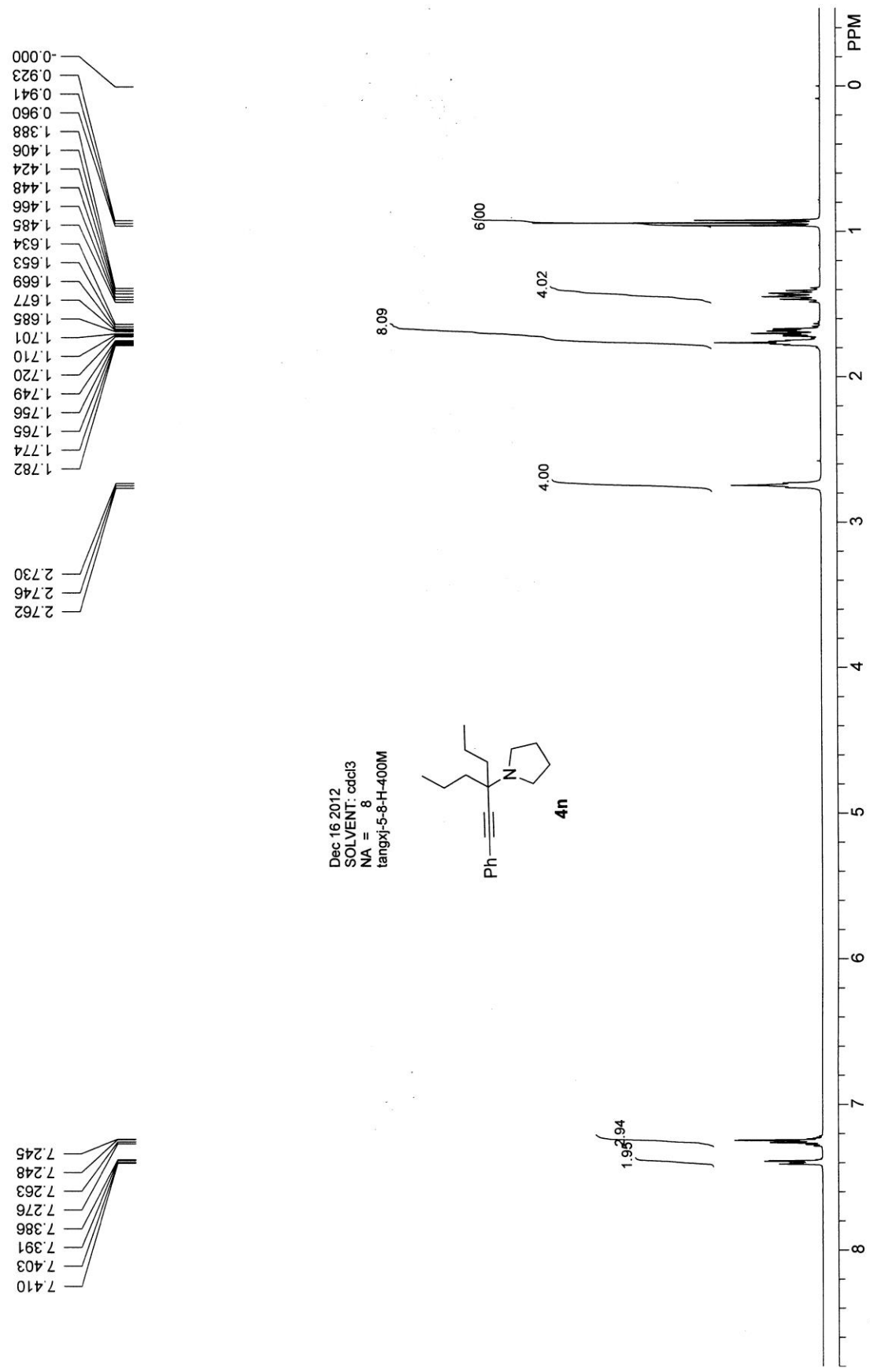


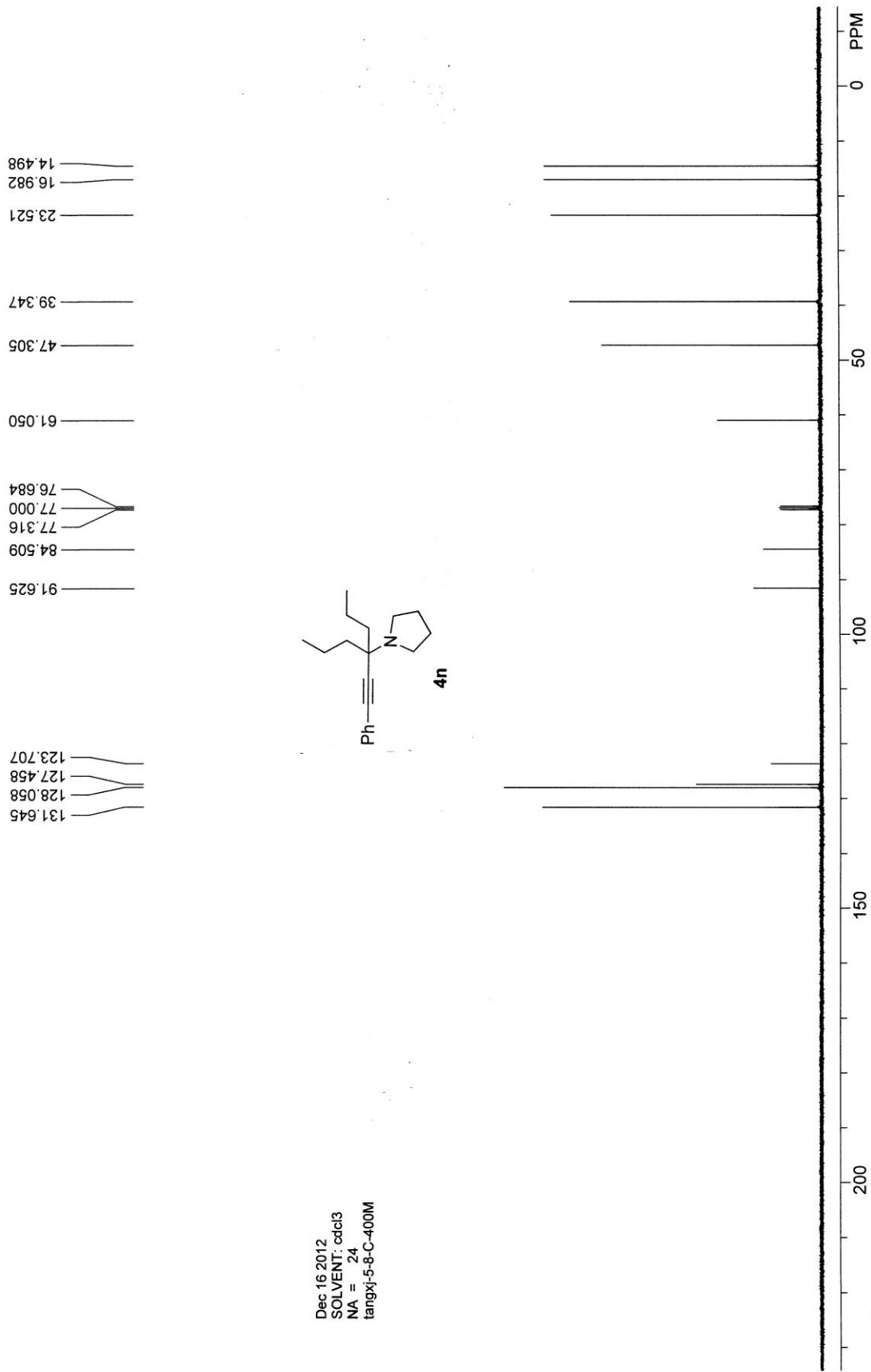


Dec 1 2012
SOLVENT: cdcl3
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tangxi-4-173-H-400M

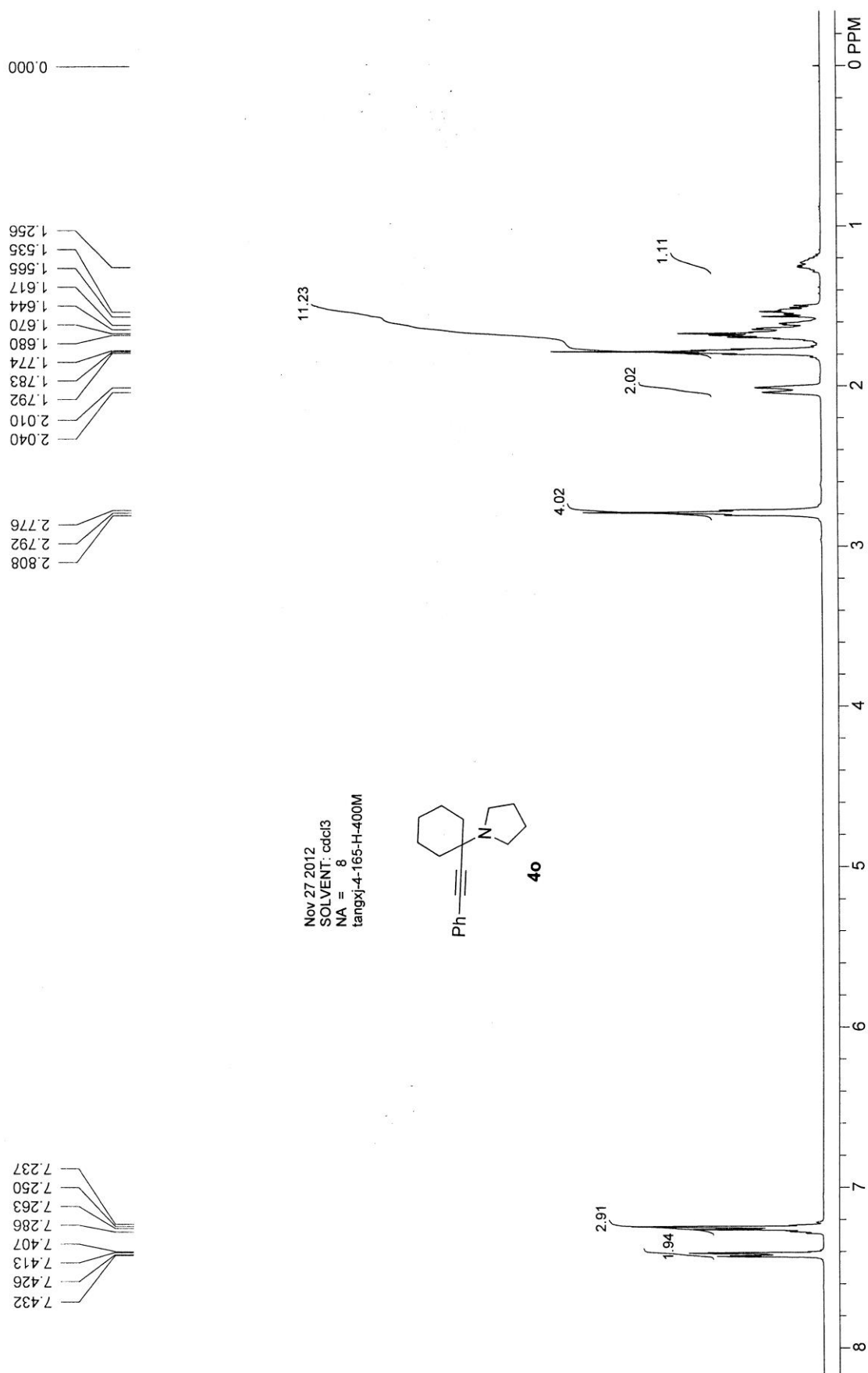


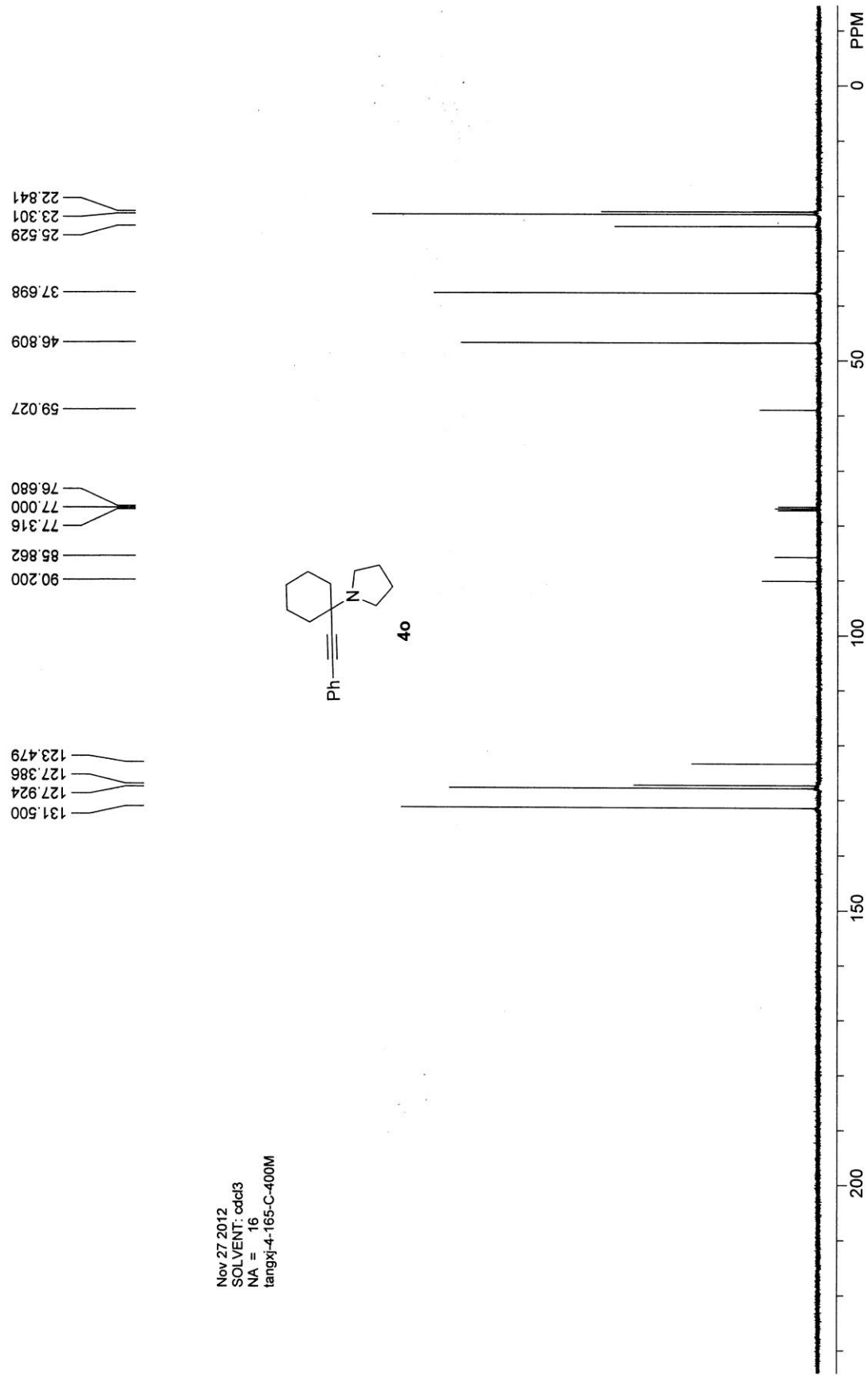
Apr 8 2013
SOLVENT: cdcl3
NA = 40
tangxi-4-173-C-400M



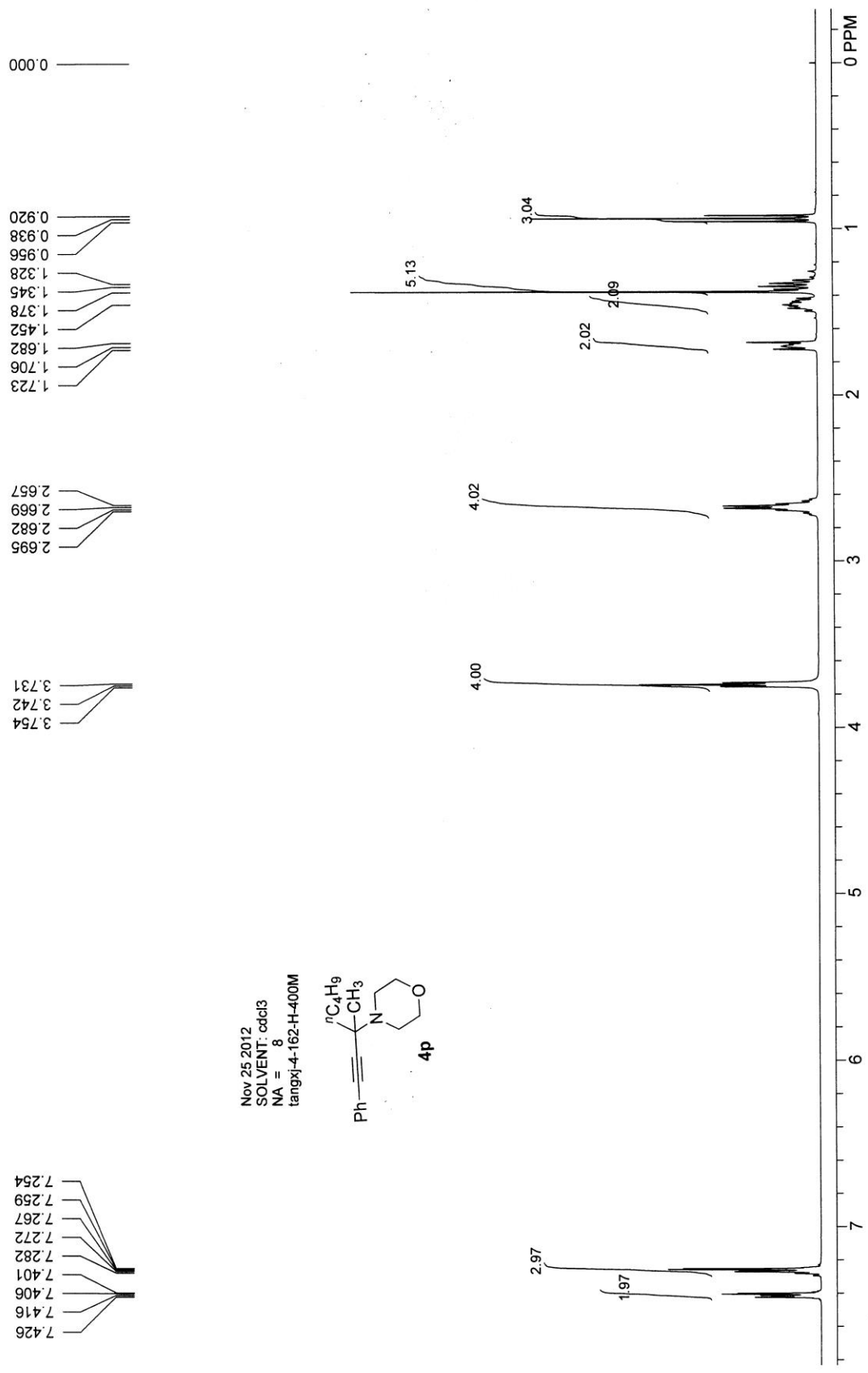


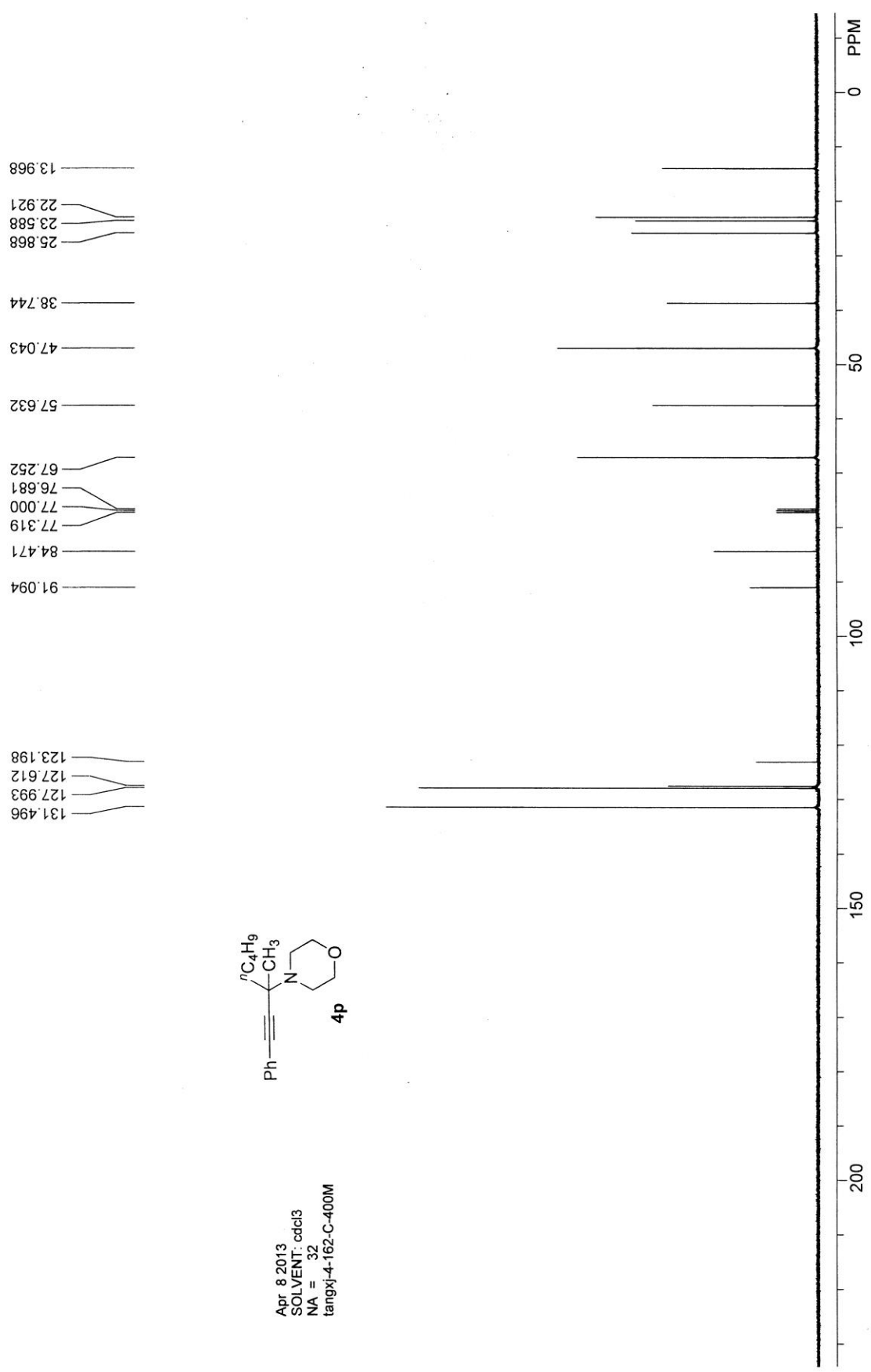
Dec 16 2012
SOLVENT: cdcl3
NA = 24
tangxi-5-8-C-400M

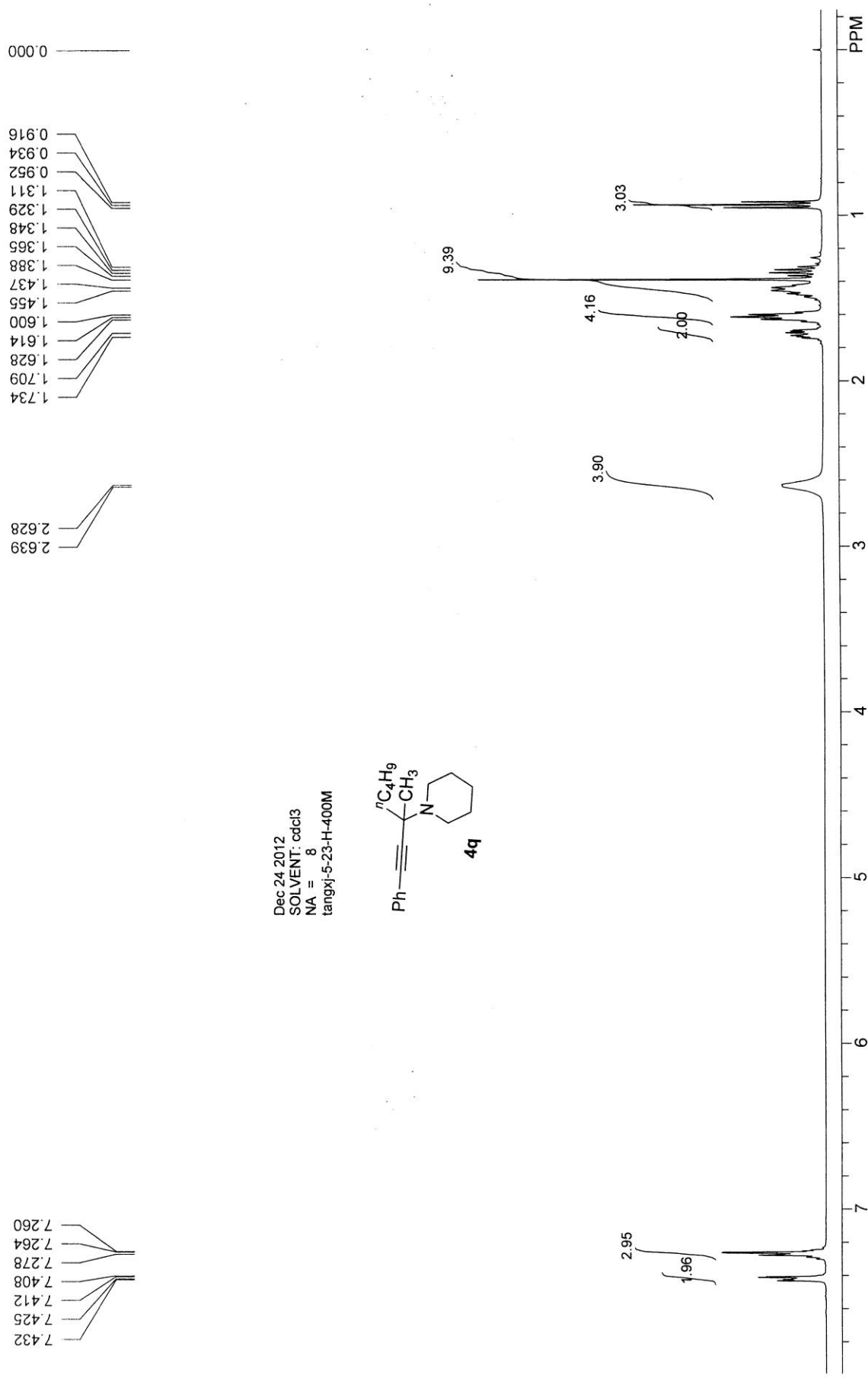


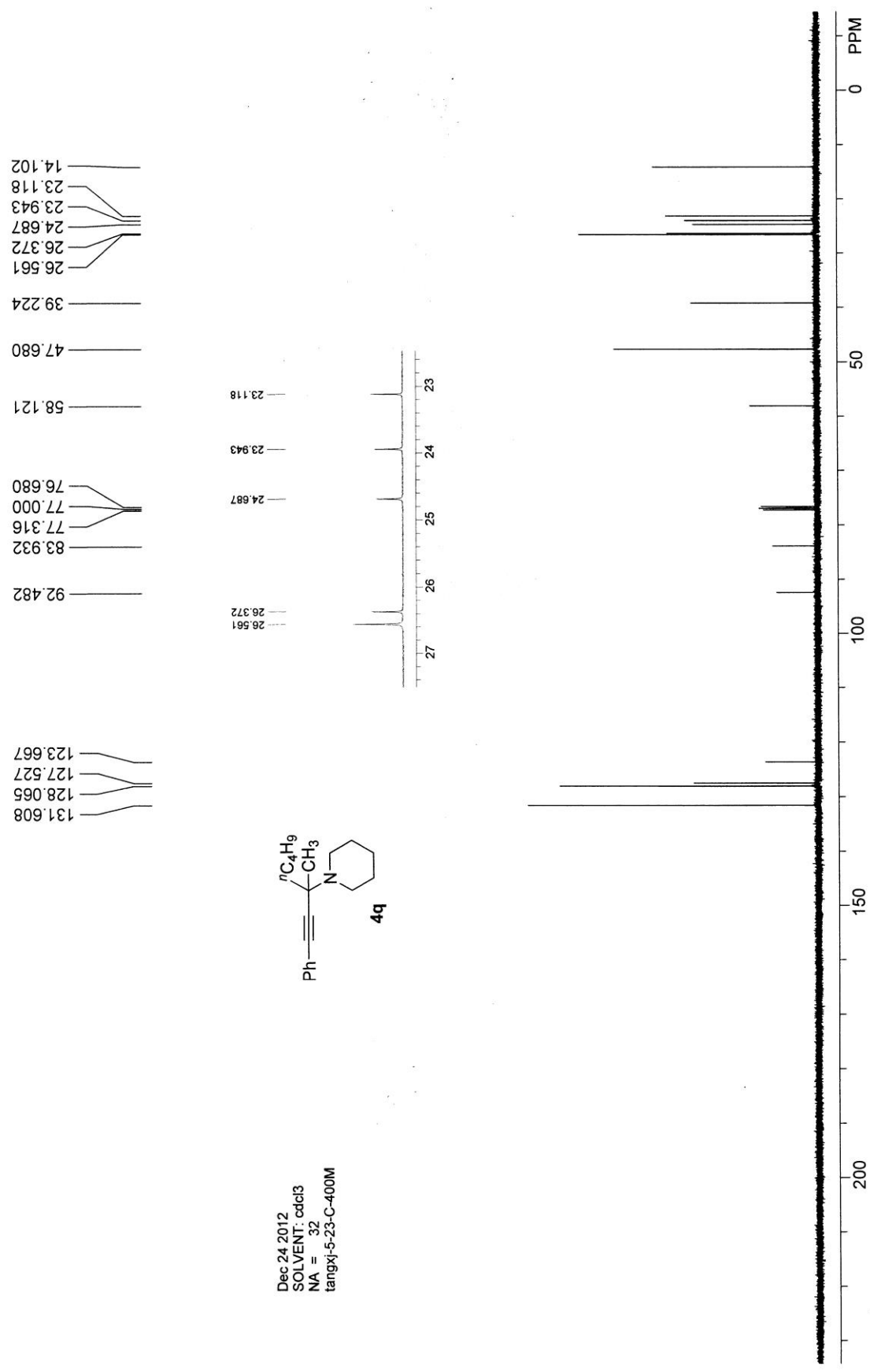


Nov 27 2012
SOLVENT: odd3
NA = 16
tangxi-4-165-C-400M

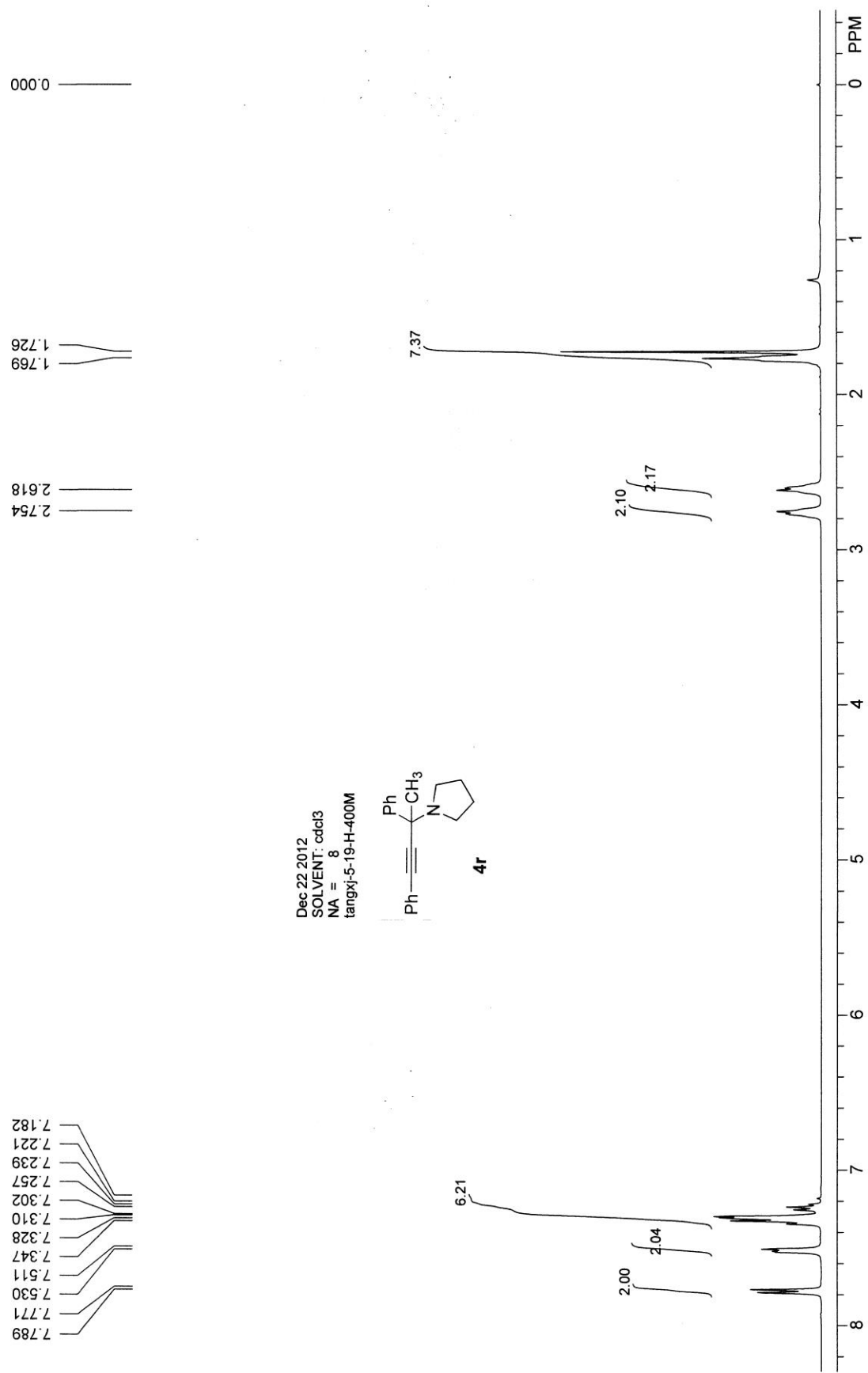


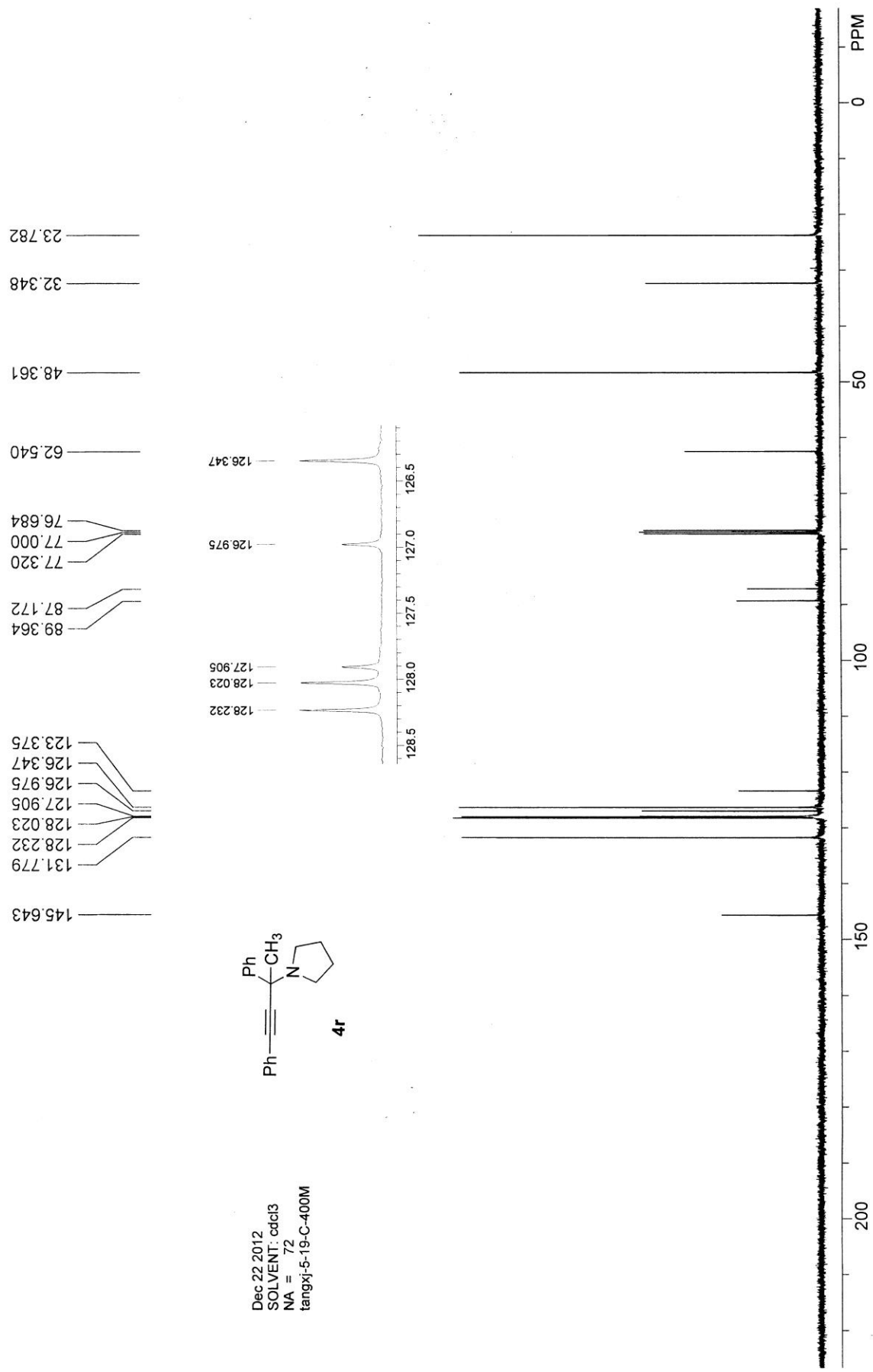




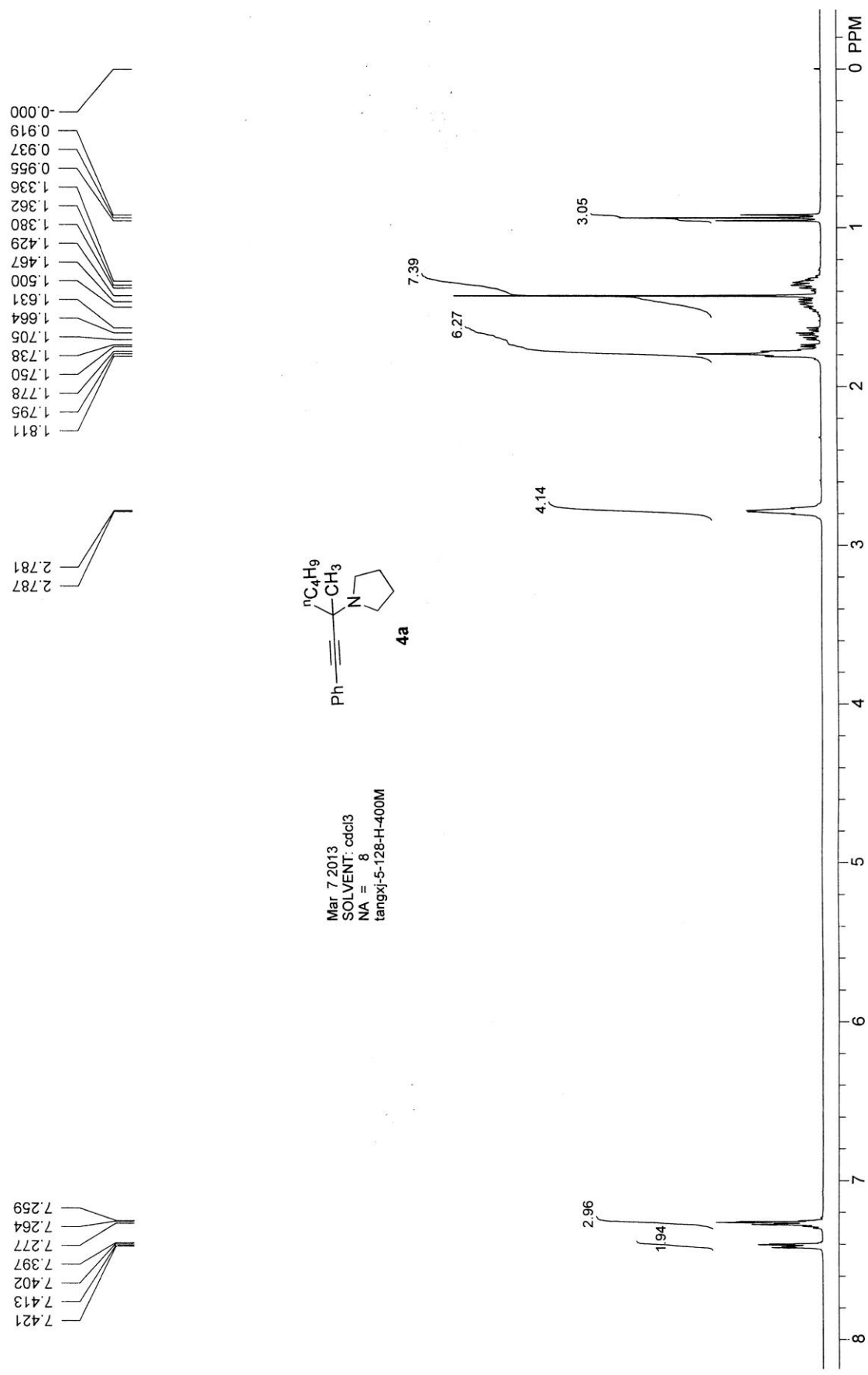


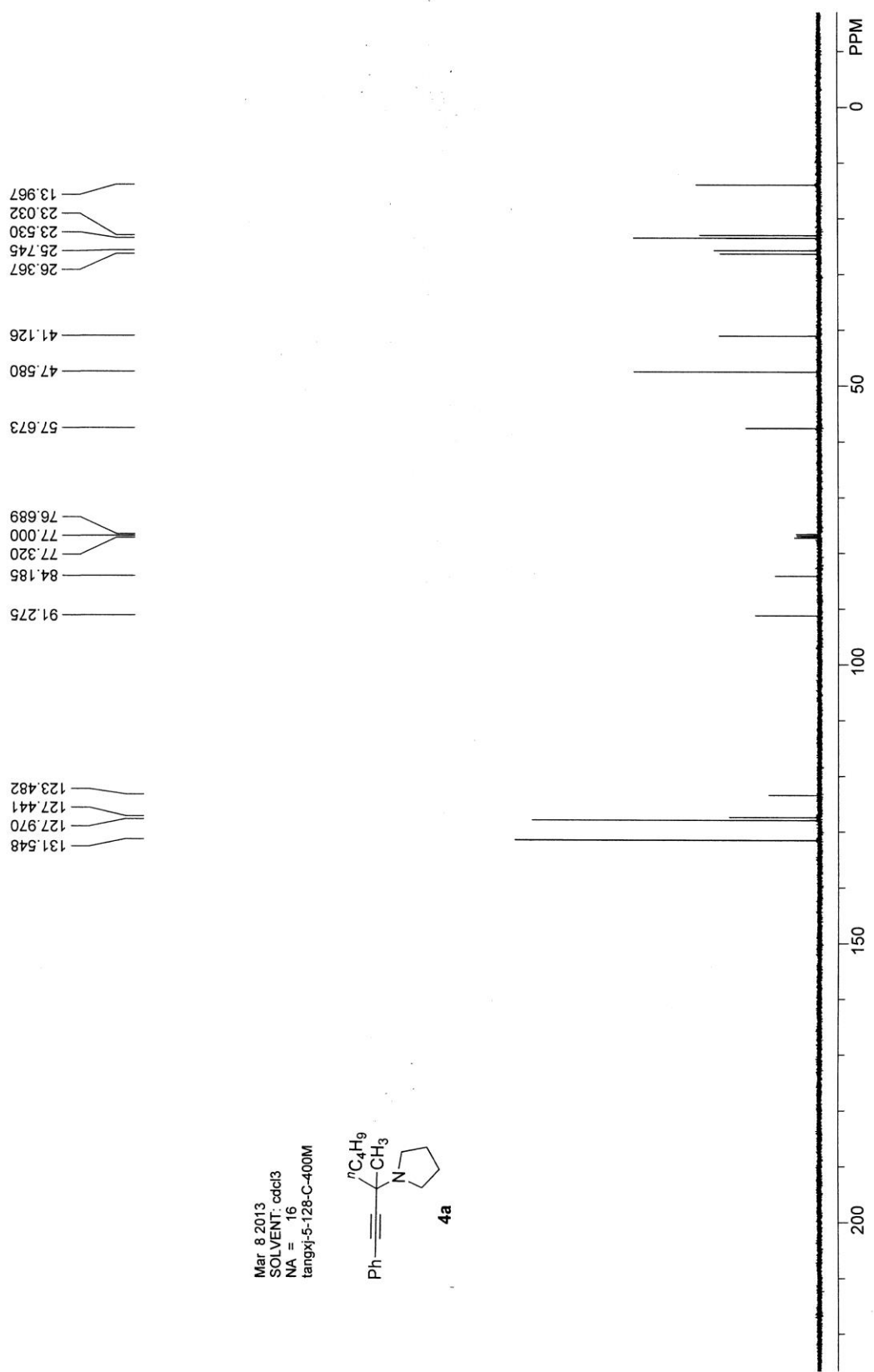
Dec 24 2012
SOLVENT: cdcl3
NA = 32
tangxi-5-23-C-400M



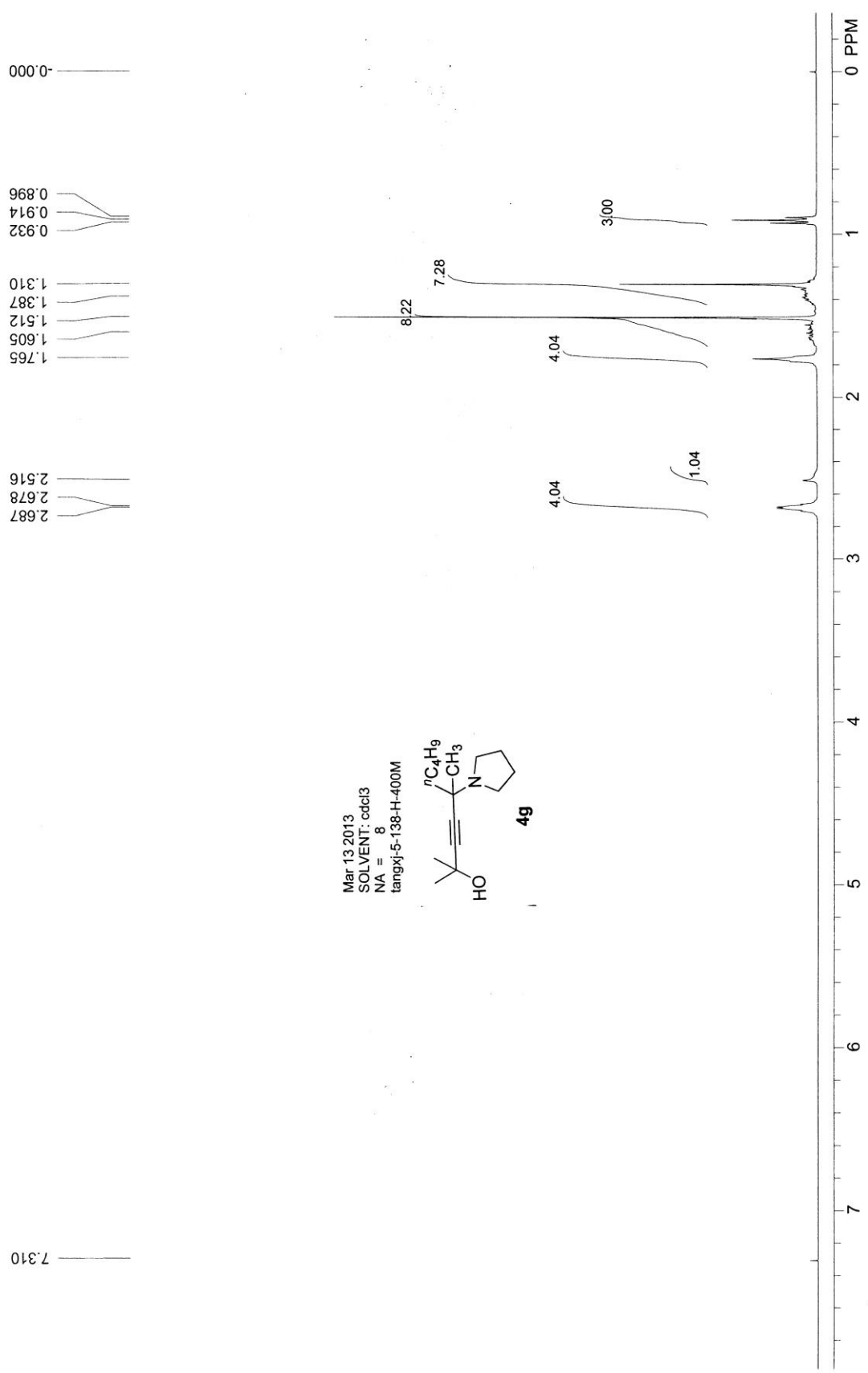


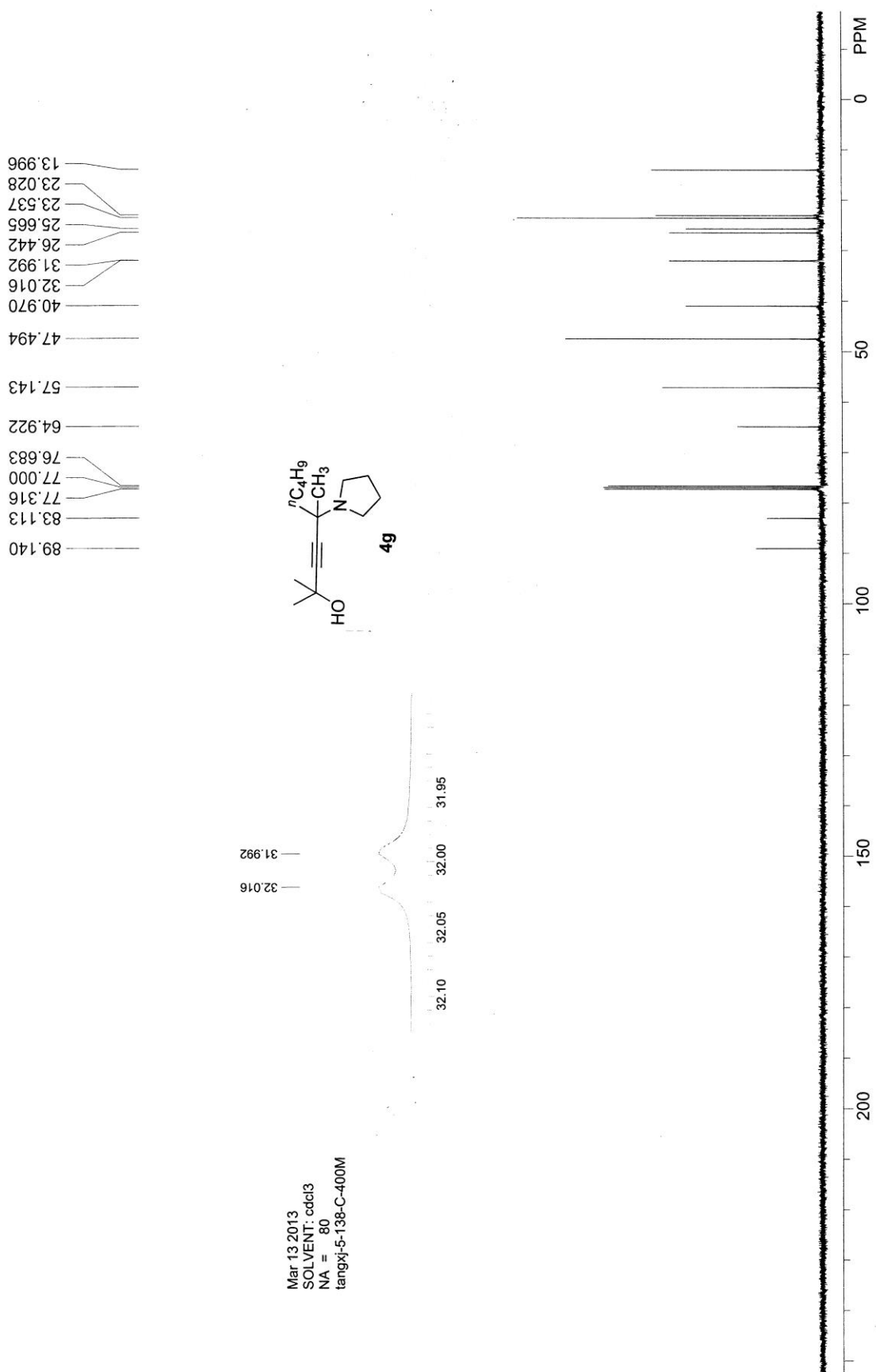
Dec 22 2012
SOLVENT: cdcl3
NA = 72
tangxi-5-19-C-400M





Mar 8 2013
SOLVENT: cdcl3
NA = 16
tangxi-5-128-C-400M





Reference:

1. A. R. Katritzky, H. Yang, S. K. Singh, *J. Org. Chem.* **2005**, 70, 286.