SUPPORTING INFORMATION

Controlling Chemoselectivity in Copper-Catalyzed Decarboxylative A^3/A^3 Cross-Couplings: Direct Formation of Unsymmetrical 1,4-Diamino-2-Butynes

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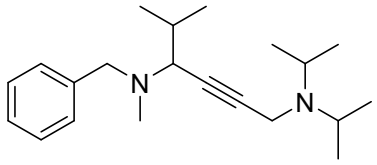
General Methods

All commercially available reagents were used without purification. Column chromatography was performed using silica gel (100–200 mesh). Visualization of the compounds was accomplished with UV light (254 nm) and iodine. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ operating at 400 MHz and 100 MHz, respectively. Proton chemical shifts are reported relative to the residual proton signals of the deuterated solvent $CDCl_3$ (7.28 ppm) or TMS. Carbon chemical shifts were internally referenced to the deuterated solvent signals in $CDCl_3$ (77.10 ppm). Chemical shifts are reported in δ (parts per million) values. Coupling constants *J* are reported in Hz. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), and multiple (m). High-resolution mass spectra were recorded on a Liquid Chromatograph Mass Spectrometer (LCMS-IT-TOF).

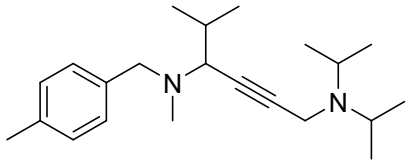
General procedure for the synthesis of unsymmetric 1,4-diamino-2-butynes

A mixture of amine **1** (0.6 mmol), aldehyde **2** (0.65 mmol), propiolic acid **3** (0.8 mmol) was added into a microwave vial along with a magnetic stir bar, and then CuI (0.05 mmol) and $CuCl_2$ (0.05 mmol) was added. The reaction vessel was sealed and irradiated in the cavity of Biotage microwave reactor at a ceiling temperature of 90 °C and a maximum power of 100 W for 15 min. and then 37% formaldehyde solution **4** (0.6 mmol), amine **5** (0.5 mmol) was added. The reaction vessel was sealed and irradiated in the cavity of Biotage microwave reactor at a ceiling temperature of 90 °C and a maximum power of 100 W for 5 min. The resulting reaction mixture was loaded on a silica gel column and flashed with 4−10% ethyl acetate in petroleum ether to afford the desired product **6** and **7** as a light yellow oil.

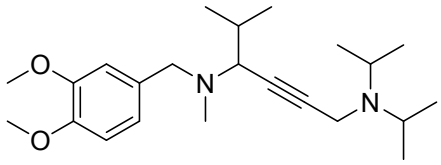
Spectroscopic data



***N*⁴-benzyl-*N*¹,*N*¹-diisopropyl-*N*⁴,5-dimethylhex-2-yne-1,4-diamine (6a).** Light yellow oil (143mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.26 (m, 4H), 7.24–7.19 (m, 1H), 3.64 (d, *J* = 16 Hz, 1H), 3.56 (d, *J* = 4 Hz, 2H), 3.45 (d, *J* = 16 Hz, 1H), 3.28–3.22 (m, 2H), 2.87 (d, *J* = 12 Hz, 1H), 2.16 (s, 3H), 1.84–1.75 (m, 1H), 1.15 (d, *J* = 4 Hz, 12H), 1.00 (t, *J* = 6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.9, 128.8, 128.1, 126.8, 84.5, 80.6, 63.1, 59.4, 48.2, 37.8, 34.0, 31.1, 20.8, 20.8, 19.8; HRMS (ESI) m/z calcd for $C_{21}H_{34}N_2$ $[M + H]^+$ 315.2795, found 315.2793.

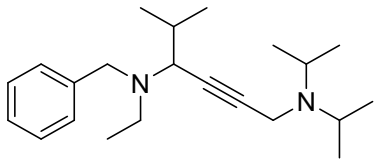


***N*¹,*N*¹-diisopropyl-*N*⁴,5-dimethyl-*N*⁴-(4-methylbenzyl)hex-2-yne-1,4-diamine (6b).** Light yellow oil (178mg, 92% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8 Hz, 2H), 7.07 (d, *J* = 8 Hz, 2H), 3.57 (d, *J* = 16 Hz, 1H), 3.53 (d, *J* = 2 Hz, 2H), 3.38 (d, *J* = 12 Hz, 1H), 3.25–3.19 (m, 2H), 2.83 (d, *J* = 8 Hz, 1H), 2.30 (s, 3H), 2.12 (s, 3H), 1.81–1.72 (m, 1H), 1.12 (d, *J* = 4 Hz, 12H), 0.98–0.95 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8, 136.3, 128.8, 128.8, 84.4, 80.7, 62.9, 59.1, 48.2, 37.7, 34.0, 31.0, 21.1, 20.8, 20.8, 19.8; HRMS (ESI) m/z calcd for $C_{22}H_{36}N_2$ $[M + H]^+$ 329.2951, found 329.2951.

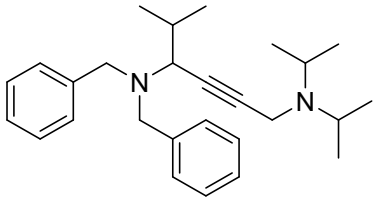


***N*⁴-(3,4-dimethoxybenzyl)-*N*¹,*N*¹-diisopropyl-*N*⁴,5-dimethylhex-2-yne-1,4-diamine (6c).** Light yellow oil (142mg, 76% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (d, *J* = 4 Hz, 1H), 6.85–6.78 (m, 2H), 3.87 (s, 6H), 3.60–3.56 (m, 3H), 3.40 (d, *J* = 12 Hz,

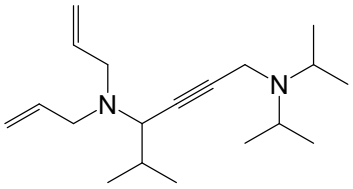
1H), 3.30–3.21 (m, 2H), 2.84 (d, *J* = 12 Hz, 1H), 2.17 (s, 3H), 1.84–1.75 (m, 1H), 1.15 (d, *J* = 4 Hz, 12H), 0.99 (t, *J* = 8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.8, 147.9, 132.4, 120.78, 111.8, 110.7, 84.4, 80.6, 62.3, 59.2, 55.9, 55.7, 48.2, 37.6, 34.0, 30.9, 20.8, 20.7, 19.8; HRMS (ESI) m/z calcd for $C_{23}H_{38}N_2O_2$ $[M + H]^+$ 375.3006, found 375.3005.



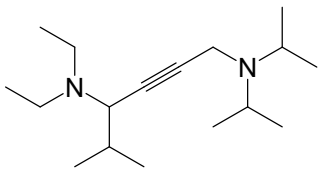
N*^{4}*-benzyl-N*^{4}*-ethyl-N*^{1}*,N*^{1}*-diisopropyl-5-methylhex-2-yne-1,4-diamine (6d). Light yellow oil (115mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8 Hz, 2H), 7.28 (t, *J* = 8 Hz, 2H), 7.24–7.19 (m, 1H), 3.81 (d, *J* = 16 Hz, 1H), 3.54 (d, *J* = 2 Hz, 2H), 3.37 (d, *J* = 12 Hz, 1H), 3.27–3.21 (m, 2H), 2.90 (d, *J* = 8 Hz, 1H), 2.59–2.50 (m, 1H), 2.41–2.33 (m, 1H), 1.83–1.74 (m, 2H), 1.14 (d, *J* = 8 Hz, 12H), 1.03 (t, *J* = 8 Hz, 3H), 1.00–0.95 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.7, 128.7, 128.0, 126.5, 83.6, 81.5, 59.9, 55.4, 48.2, 44.8, 34.0, 31.1, 29.7, 20.8, 20.7, 20.1, 13.6; HRMS (ESI) m/z calcd for $C_{22}H_{36}N_2$ $[M + H]^+$ 329.2951, found 329.2951.



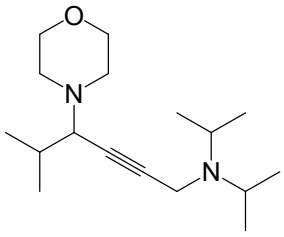
N*^{4}*,N*^{4}*-dibenzyl-N*^{1}*,N*^{1}*-diisopropyl-5-methylhex-2-yne-1,4-diamine (6e). Light yellow oil (123mg, 63% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 4 Hz, 4H), 7.28 (t, *J* = 8 Hz, 4H), 7.22–7.18 (m, 2H), 3.81 (d, *J* = 12 Hz, 2H), 3.59 (s, 2H), 3.39 (d, *J* = 12 Hz, 2H), 3.32–3.25 (m, 2H), 2.89 (d, *J* = 8 Hz, 1H), 1.93–1.84 (m, 1H), 1.18 (d, *J* = 4 Hz, 12H), 1.00–0.95 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 128.9, 128.2, 126.8, 84.4, 80.9, 59.4, 55.2, 48.3, 34.1, 30.9, 29.8, 21.0, 20.9, 20.0; HRMS (ESI) m/z calcd for $C_{27}H_{38}N_2$ $[M + H]^+$ 391.3108, found 391.3109.



***N*⁴,*N*⁴-diallyl-*N*¹,*N*¹-diisopropyl-5-methylhex-2-yne-1,4-diamine (6f).** Light yellow oil (75mg, 52% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84–5.74 (m, 2H), 5.18 (d, *J* = 16 Hz, 2H), 5.08 (d, *J* = 12 Hz, 2H), 3.52 (d, *J* = 4 Hz, 2H), 3.26–3.19 (m, 4H), 2.99 (d, *J* = 12 Hz, 1H), 2.87–2.81 (m, 2H), 1.80–1.71 (m, 1H), 1.12 (d, *J* = 8 Hz, 12H), 1.01 (d, *J* = 8 Hz, 3H), 0.94 (d, *J* = 8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.1, 116.4, 83.8, 81.1, 59.7, 54.0, 48.2, 33.9, 31.1, 29.7, 20.7, 20.0; HRMS (ESI) m/z calcd for $C_{19}H_{34}N_2$ $[M + H]^+$ 291.2795, found 291.2793.

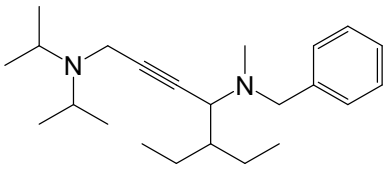


***N*⁴,*N*⁴-diethyl-*N*¹,*N*¹-diisopropyl-5-methylhex-2-yne-1,4-diamine (6g).** Light yellow oil (97mg, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.50 (d, *J* = 4 Hz, 2H), 3.24–3.17 (m, 2H), 2.93 (d, *J* = 8 Hz, 1H), 2.62–2.54 (m, 2H), 2.35–2.27 (m, 2H), 1.78–1.69 (m, 1H), 1.11 (d, *J* = 8 Hz, 12H), 1.03–0.99 (m, 9H), 0.94 (d, *J* = 4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 83.1, 81.8, 60.2, 48.1, 44.9, 33.9, 31.2, 29.7, 20.7, 20.6, 20.1, 13.8; HRMS (ESI) m/z calcd for $C_{17}H_{34}N_2$ $[M + H]^+$ 267.2795, found 267.2795.

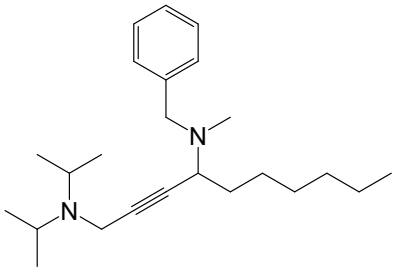


***N,N*-diisopropyl-5-methyl-4-morpholinohex-2-yn-1-amine (6h).** Light yellow oil (93mg, 66% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76–3.66 (m, 4H), 3.51 (d, *J* = 4 Hz, 2H), 3.26–3.16 (m, 2H), 2.78 (d, *J* = 8 Hz, 1H), 2.63–2.58 (m, 2H), 2.44–2.39 (m, 2H), 1.83–1.74 (m, 1H), 1.11 (d, *J* = 8 Hz, 12H), 1.03 (d, *J* = 4 Hz, 3H), 0.96 (d, *J* = 8 Hz, 3H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 85.1, 80.1, 67.2, 64.8, 50.0, 48.2, 33.9, 29.9,

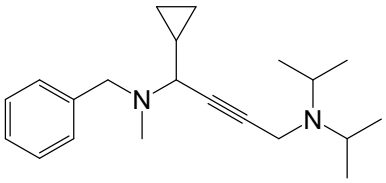
29.7, 20.7, 20.2, 19.8; HRMS (ESI) m/z calcd for $C_{17}H_{32}N_2O$ $[M + H]^+$ 281.2587, found 281.2585.



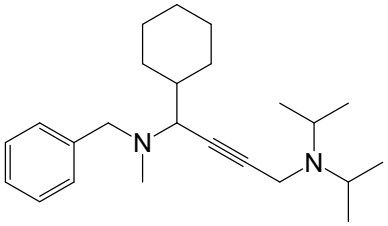
N^4-benzyl-5-ethyl-N^1,N^1-diisopropyl-N^4-methylhept-2-yne-1,4-diamine (6i). Light yellow oil (111mg, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 4H), 7.23–7.19 (m, 1H), 3.63 (d, *J* = 16 Hz, 1H), 3.56 (d, *J* = 4 Hz, 2H), 3.46 (d, *J* = 12 Hz, 1H), 3.28–3.22 (m, 2H), 3.14 (d, *J* = 12 Hz, 1H), 2.14 (s, 3H), 1.71–1.61 (m, 2H), 1.56–1.48 (m, 1H), 1.46–1.32 (m, 2H), 1.14 (d, *J* = 8 Hz, 12H), 0.84 (t, *J* = 8 Hz, 3H), 0.78 (t, *J* = 8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.9, 128.9, 128.1, 126.8, 84.6, 80.6, 59.6, 59.0, 48.2, 42.2, 37.7, 34.0, 29.7, 22.2, 20.8, 20.8, 20.4, 10.5, 9.6; HRMS (ESI) m/z calcd for $C_{23}H_{38}N_2$ $[M + H]^+$ 343.3108, found 343.3108.



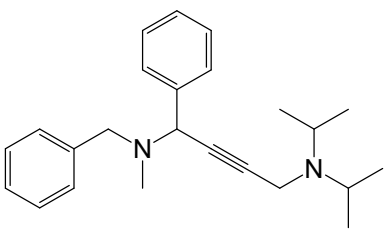
N^4-benzyl-N^1,N^1-diisopropyl-N^4-methyldec-2-yne-1,4-diamine (6j). Light yellow oil (159mg, 89% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 4H), 7.25–7.21 (m, 1H), 3.66 (d, *J* = 12 Hz, 1H), 3.55 (d, *J* = 4 Hz, 2H), 3.45 (d, *J* = 16 Hz, 1H), 3.37–3.33 (m, 1H), 3.30–3.21 (m, 2H), 2.20 (s, 3H), 1.66–1.59 (m, 2H), 1.48–1.38 (m, 2H), 1.27 (s, 6H), 1.15 (d, *J* = 8 Hz, 12H), 0.88 (t, *J* = 8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 129.0, 128.2, 126.9, 84.0, 81.3, 59.2, 55.7, 48.2, 37.9, 34.1, 34.0, 31.8, 29.0, 26.6, 22.6, 20.8, 20.7, 14.1; HRMS (ESI) m/z calcd for $C_{24}H_{40}N_2$ $[M + H]^+$ 357.3264, found 357.3266.



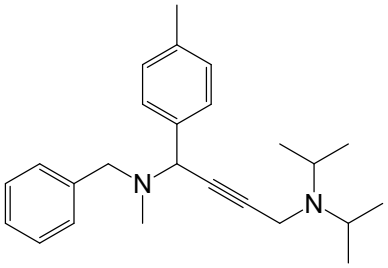
N*[1]*-benzyl-1-cyclopropyl-N*[4]*,N*[4]*-diisopropyl-N*[1]*-methylbut-2-yne-1,4-diamine (6k). Light yellow oil (137mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.30 (m, 4H), 7.26–7.22 (m, 1H), 3.76 (d, *J* = 12 Hz, 1H), 3.55 (d, *J* = 4 Hz, 2H), 3.46 (d, *J* = 12 Hz, 1H), 3.41 (d, *J* = 4 Hz, 1H), 3.28–3.22 (m, 1H), 2.30 (s, 3H), 1.15 (d, *J* = 8 Hz, 12H), 0.90–0.83 (m, 1H), 0.56–0.49 (m, 1H), 0.47–0.40 (m, 2H), 0.30–0.23 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.45, 129.0, 128.2, 126.9, 85.0, 78.1, 59.3, 58.8, 48.2, 38.5, 33.9, 29.7, 20.8, 20.7, 13.5, 3.3, 1.9; HRMS (ESI) m/z calcd for $C_{21}H_{32}N_2$ $[M + H]^+$ 313.2638, found 313.2638.



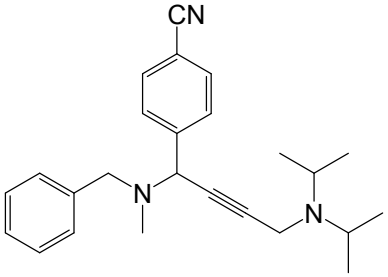
N*[1]*-benzyl-1-cyclohexyl-N*[4]*,N*[4]*-diisopropyl-N*[1]*-methylbut-2-yne-1,4-diamine (6l). Light yellow oil (159mg, 90% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.29 (m, 4H), 7.24–7.20 (m, 1H), 3.64 (d, *J* = 12 Hz, 1H), 3.55 (d, *J* = 2 Hz, 2H), 3.45 (d, *J* = 16 Hz, 1H), 3.28–3.22 (m, 2H), 2.99 (d, *J* = 8 Hz, 1H), 2.15 (s, 3H), 2.03 (d, *J* = 12 Hz, 1H), 1.71 (d, *J* = 16 Hz, 2H), 1.64 (d, *J* = 12 Hz, 1H), 1.53–1.45 (m, 1H), 1.30–1.20 (m, 4H), 1.14 (d, *J* = 8 Hz, 12H), 0.90–0.82 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.9, 128.8, 128.1, 126.7, 84.8, 80.3, 61.6, 59.4, 48.2, 40.2, 37.8, 34.0, 31.3, 30.2, 29.7, 26.8, 26.2, 26.0, 20.8; HRMS (ESI) m/z calcd for $C_{24}H_{38}N_2$ $[M + H]^+$ 355.3108, found 355.3108.



N^1-benzyl-N^4,N^4-diisopropyl-N^1-methyl-1-phenylbut-2-yne-1,4-diamine (6m). Light yellow oil (99mg, 57% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8 Hz, 2H), 7.37 (d, *J* = 8 Hz, 2H), 7.34–7.30 (m, 4H), 7.26–7.21 (m, 2H), 4.69 (s, 1H), 3.65 (d, *J* = 8 Hz, 3H), 3.56 (d, *J* = 12 Hz, 1H), 3.34–3.27 (m, 2H), 2.16 (s, 3H), 1.18 (d, *J* = 8 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 139.5, 129.0, 128.4, 128.3, 128.0, 127.3, 127.0, 87.4, 78.4, 59.3, 58.9, 48.4, 38.0, 34.2, 29.8, 20.9, 20.9; HRMS (ESI) m/z calcd for $C_{24}H_{32}N_2$ $[M + H]^+$ 349.2638, found 349.2639.

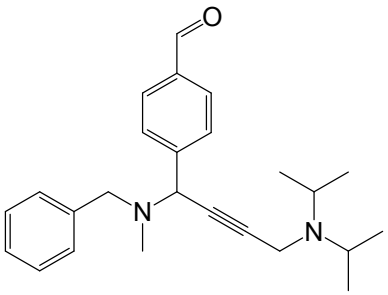


N^1-benzyl-N^4,N^4-diisopropyl-N^1-methyl-1-(p-tolyl)but-2-yne-1,4-diamine (6n). Light yellow oil (112mg, 62% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8 Hz, 2H), 7.37 (d, *J* = 4 Hz, 2H), 7.31 (t, *J* = 6 Hz, 2H), 7.24 (d, *J* = 8 Hz, 1H), 7.14 (d, *J* = 8 Hz, 2H), 4.66 (s, 1H), 3.67–3.62 (m, 3H), 3.54 (d, *J* = 12 Hz, 1H), 3.34–3.28 (m, 2H), 2.33 (s, 3H), 2.15 (s, 3H), 1.18 (d, *J* = 8 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 136.9, 136.6, 129.0, 128.7, 128.3, 127.0, 87.1, 78.1, 59.1, 58.8, 48.4, 38.0, 34.2, 29.7, 21.1, 20.9, 20.8; HRMS (ESI) m/z calcd for $C_{25}H_{34}N_2$ $[M + H]^+$ 363.2795, found 363.2794.

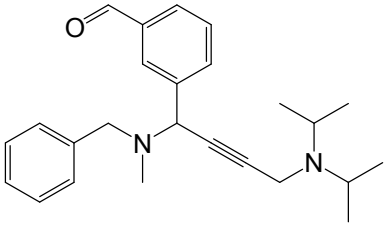


4-(1-(benzyl(methyl)amino)-4-(diisopropylamino)but-2-yn-1-yl)benzonitrile (6o). Light yellow oil (153mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8 Hz, 2H), 7.62 (d, *J* = 12 Hz, 2H), 7.38–7.31 (m, 4H), 7.25 (d, *J* = 4 Hz, 1H), 4.68 (s, 1H), 3.67–3.64 (m, 3H), 3.58 (d, *J* = 12 Hz, 1H), 3.33–3.26 (m, 2H), 2.14 (s, 3H), 1.18 (d,

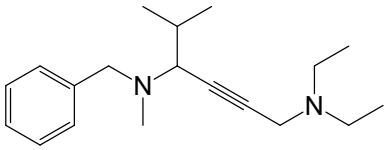
J = 8 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 138.8, 131.9, 129.0, 128.9, 128.4, 127.3, 118.9, 111.2, 88.6, 76.9, 59.1, 58.7, 48.4, 38.0, 34.2, 29.7, 20.8, 20.8; HRMS (ESI) m/z calcd for $C_{27}H_{27}N_3$ $[M + H]^+$ 394.2278, found 394.2276.



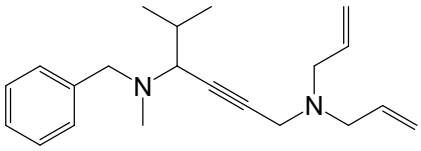
4-(1-(benzyl(methyl)amino)-4-(diisopropylamino)but-2-yn-1-yl)benzaldehyde (6p). Light yellow oil (117mg, 62% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 7.86 (d, *J* = 8 Hz, 2H), 7.79 (d, *J* = 8 Hz, 2H), 7.39–7.30 (m, 4H), 7.24 (d, *J* = 8 Hz, 1H), 4.72 (s, 1H), 3.68–3.65 (m, 3H), 3.59 (d, *J* = 12 Hz, 1H), 3.35–3.26 (m, 2H), 2.16 (s, 3H), 1.19 (d, *J* = 4 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.9, 146.7, 139.0, 135.7, 129.5, 128.9, 128.9, 128.4, 127.2, 88.3, 77.3, 59.1, 59.0, 48.4, 38.1, 34.2, 29.7, 20.8, 20.8; HRMS (ESI) m/z calcd for $C_{25}H_{32}N_2O$ $[M + H]^+$ 377.2587, found 377.2586.



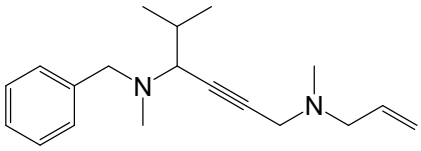
3-(1-(benzyl(methyl)amino)-4-(diisopropylamino)but-2-yn-1-yl)benzaldehyde (6q). Light yellow oil (128mg, 68% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.14 (s, 1H), 7.88 (d, *J* = 8 Hz, 1H), 7.79 (d, *J* = 8 Hz, 1H), 7.50 (t, *J* = 6 Hz, 1H), 7.38 (d, *J* = 8 Hz, 2H), 7.33 (t, *J* = 6 Hz, 2H), 7.26–7.23 (m, 1H), 4.74 (s, 1H), 3.70–3.65 (m, 3H), 3.59 (d, *J* = 12 Hz, 1H), 3.38–3.28 (m, 1H), 2.16 (s, 3H), 1.20 (d, *J* = 8 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2, 141.0, 139.0, 136.4, 134.4, 129.8, 128.9, 128.7, 128.6, 128.3, 127.2, 88.2, 77.6, 59.0, 58.8, 48.5, 38.0, 34.2, 29.7, 20.8; HRMS (ESI) m/z calcd for $C_{25}H_{32}N_2O$ $[M + H]^+$ 377.2587, found 377.2586.



***N*⁴-benzyl-*N*¹,*N*¹-diethyl-*N*⁴,5-dimethylhex-2-yne-1,4-diamine (7a).** Light yellow oil (133mg, 93% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 4H), 7.25–7.20 (m, 1H), 3.65 (d, *J* = 12 Hz, 1H), 3.55 (d, *J* = 4 Hz, 2H), 3.45 (d, *J* = 12 Hz, 1H), 2.90 (d, *J* = 12 Hz, 1H), 2.63–2.58 (m, 4H), 2.16 (s, 3H), 1.85–1.76 (m, 1H), 1.11 (t, *J* = 8 Hz, 6H), 1.01 (t, *J* = 8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 128.8, 128.1, 126.8, 81.8, 79.7, 63.0, 59.5, 47.3, 40.7, 37.7, 31.1, 29.7, 20.8, 19.7, 12.7; HRMS (ESI) m/z calcd for $C_{19}H_{30}N_2$ $[M + H]^+$ 287.2482, found 287.2481.

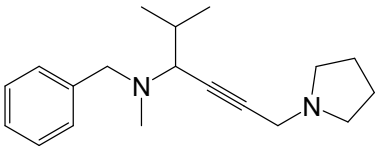


***N*¹,*N*¹-diallyl-*N*⁴-benzyl-*N*⁴,5-dimethylhex-2-yne-1,4-diamine (7b).** Light yellow oil (140mg, 90% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.28 (m, 4H), 7.25–7.21 (m, 1H), 5.92–5.82 (m, 2H), 5.29–5.24 (m, 2H), 5.19–5.16 (m, 2H), 3.67 (d, *J* = 12 Hz, 1H), 3.50–3.45 (m, 3H), 3.19 (d, *J* = 8 Hz, 4H), 2.92 (d, *J* = 8 Hz, 1H), 2.18 (s, 3H), 1.87–1.78 (m, 1H), 1.05–1.01 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 135.5, 128.8, 128.2, 126.8, 118.0, 82.3, 79.8, 63.0, 59.5, 56.6, 41.6, 37.7, 31.2, 20.9, 19.7; HRMS (ESI) m/z calcd for $C_{21}H_{30}N_2$ $[M + H]^+$ 311.2482, found 311.2482.

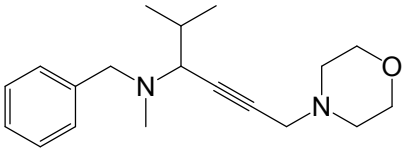


***N*¹-allyl-*N*⁴-benzyl-*N*¹,*N*⁴,5-trimethylhex-2-yne-1,4-diamine (7c).** Light yellow oil (131mg, 92% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.30 (m, 4H), 7.26–7.21 (m, 1H), 5.93–5.82 (m, 1H), 5.27–5.22 (m, 1H), 5.18–5.16 (m, 1H), 3.66 (d, *J* = 12 Hz, 1H), 3.48–3.44 (m, 3H), 3.12 (d, *J* = 8 Hz, 2H), 2.92 (d, *J* = 8 Hz, 1H), 2.36 (s, 3H), 2.18 (s, 3H), 1.87–1.78 (m, 1H), 1.04–1.00 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 135.5, 128.8, 128.1, 126.8, 117.9, 82.3, 80.1, 63.0, 59.5, 58.9, 45.3, 41.7, 37.7,

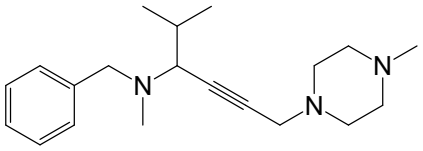
31.1, 29.7, 20.8, 19.7; HRMS (ESI) m/z calcd for $C_{19}H_{28}N_2$ $[M + H]^+$ 285.2325, found 285.2325.



N-benzyl-N,2-dimethyl-6-(pyrrolidin-1-yl)hex-4-yn-3-amine (7d). Light yellow oil (125mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 4H), 7.26–7.20 (m, 1H), 3.64 (d, *J* = 16 Hz, 1H), 3.52 (d, *J* = 2 Hz, 2H), 3.45 (d, *J* = 12 Hz, 1H), 2.91 (d, *J* = 12 Hz, 1H), 2.68 (s, 4H), 2.16 (s, 3H), 1.84 (s, 5H), 1.01 (t, *J* = 8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 128.8, 128.1, 126.8, 81.3, 81.1, 63.1, 59.4, 52.4, 43.3, 37.7, 31.0, 29.7, 23.9, 20.8, 19.7; HRMS (ESI) m/z calcd for $C_{19}H_{28}N_2$ $[M + H]^+$ 285.2325, found 285.2324.

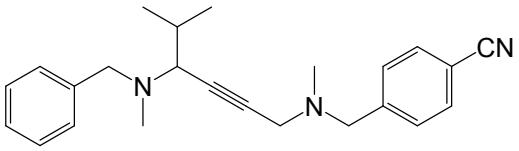


N-benzyl-N,2-dimethyl-6-morpholinohex-4-yn-3-amine (7e). Light yellow oil (120mg, 80% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 4H), 7.26–7.20 (m, 1H), 3.76 (t, *J* = 4 Hz, 4H), 3.65 (d, *J* = 12 Hz, 1H), 3.46 (d, *J* = 12 Hz, 1H), 3.41 (d, *J* = 2 Hz, 2H), 2.92 (d, *J* = 12 Hz, 1H), 2.60 (t, *J* = 6 Hz, 4H), 2.17 (s, 3H), 1.87–1.78 (m, 1H), 1.02 (t, *J* = 6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.7, 128.8, 128.2, 126.8, 82.6, 80.0, 66.9, 63.0, 59.5, 52.3, 47.6, 37.7, 31.0, 29.7, 20.9, 19.7; HRMS (ESI) m/z calcd for $C_{19}H_{28}N_2O$ $[M + H]^+$ 301.2274, found 301.2273.

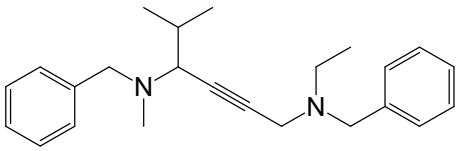


N-benzyl-N,2-dimethyl-6-(4-methylpiperazin-1-yl)hex-4-yn-3-amine (7f). Light yellow oil (136mg, 87% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 4H), 7.26–7.20 (m, 1H), 3.64 (d, *J* = 12 Hz, 1H), 3.46–3.41 (m, 3H), 2.91 (d, *J* = 12 Hz,

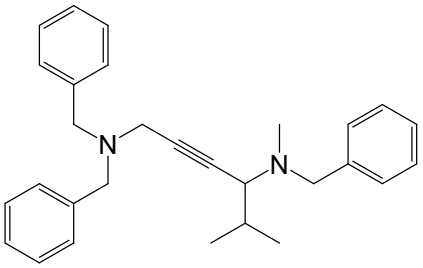
1H), 2.65–2.51 (m, 8H), 2.30 (s, 3H), 2.16 (s, 3H), 1.86–1.77 (m, 1H), 1.01 (t, J = 8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.7, 128.8, 128.1, 126.8, 82.3, 80.4, 63.1, 59.4, 55.1, 51.9, 47.2, 46.0, 37.7, 31.0, 20.9, 19.7; HRMS (ESI) m/z calcd for $C_{20}H_{31}N_3$ $[M + H]^+$ 314.2591, found 314.2593.



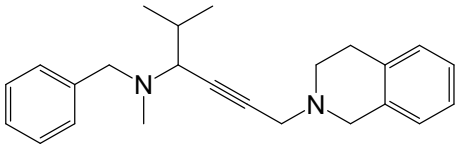
4-(((4-(benzyl(methyl)amino)-5-methylhex-2-yn-1-yl)(methyl)amino)methyl)benzonitrile (7g). Light yellow oil (140mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 12 Hz, 2H), 7.48 (d, J = 8 Hz, 2H), 7.36–7.29 (m, 4H), 7.25–7.22 (m, 1H), 3.70–3.66 (m, 3H), 3.49 (d, J = 12 Hz, 1H), 3.41 (d, J = 2 Hz, 2H), 2.96 (d, J = 12 Hz, 1H), 2.37 (s, 3H), 2.20 (s, 3H), 1.88–1.80 (m, 1H), 1.07–1.02 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 139.6, 132.2, 129.6, 128.8, 128.2, 126.9, 118.9, 111.1, 82.9, 79.7, 63.0, 59.6, 45.5, 42.1, 37.8, 31.1, 20.9, 19.8; HRMS (ESI) m/z calcd for $C_{24}H_{29}N_3$ $[M + H]^+$ 360.2434, found 360.2434.



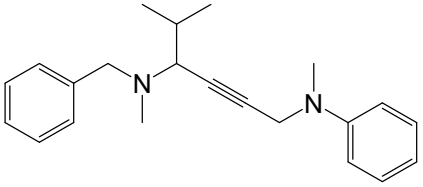
N^1,N^4-dibenzyl-N^1-ethyl-N^4,5-dimethylhex-2-yne-1,4-diamine (7h). Light yellow oil (157mg, 90% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.30 (m, 8H), 7.29–7.22 (m, 2H), 3.70–3.67 (m, 3H), 3.50 (d, J = 12 Hz, 1H), 3.44 (d, J = 4 Hz, 2H), 2.95 (d, J = 12 Hz, 1H), 2.68–2.63 (m, 2H), 2.21 (s, 3H), 1.89–1.80 (m, 1H), 1.15 (t, J = 6 Hz, 3H), 1.07–1.02 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 139.0, 129.2, 128.8, 128.3, 128.2, 127.1, 126.8, 82.2, 79.9, 63.0, 59.5, 57.8, 53.4, 47.5, 41.0, 37.8, 31.2, 21.0, 19.8, 12.9; HRMS (ESI) m/z calcd for $C_{24}H_{32}N_2$ $[M + H]^+$ 349.2638, found 349.2638.



***N*[1],*N*[1],*N*[4]-tribenzyl-*N*[4],5-dimethylhex-2-yne-1,4-diamine (7i).** Light yellow oil (174mg, 85% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.30 (m, 12H), 7.27–7.24 (m, 3H), 3.77–3.71 (m, 5H), 3.55 (d, *J* = 12 Hz, 1H), 3.36 (d, *J* = 4 Hz, 2H), 2.99 (d, *J* = 8 Hz, 1H), 2.25 (s, 3H), 1.93–1.84 (m, 1H), 1.10 (d, *J* = 4 Hz, 3H), 1.06 (d, *J* = 4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.8, 139.1, 129.1, 128.8, 128.3, 128.2, 127.1, 126.8, 82.5, 80.1, 63.1, 59.6, 57.7, 41.4, 37.8, 31.2, 29.7, 21.0, 19.8; HRMS (ESI) m/z calcd for $C_{29}H_{34}N_2$ $[M + H]^+$ 411.2795, found 411.2796.

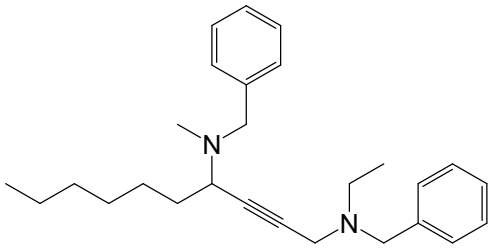


***N*-benzyl-6-(3,4-dihydroisoquinolin-2(1H)-yl)-N,2-dimethylhex-4-yn-3-amine (7j).** Light yellow oil (161mg, 93% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8 Hz, 2H), 7.37 (t, *J* = 8 Hz, 2H), 7.31–7.28 (m, 1H), 7.22–7.17 (m, 3H), 7.14–7.13 (m, 1H), 3.89 (s, 2H), 3.75–3.70 (m, 3H), 3.56 (d, *J* = 12 Hz, 1H), 3.06–2.95 (m, 5H), 2.25 (s, 3H), 1.95–1.86 (m, 1H), 1.12–1.08 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.7, 134.8, 134.0, 128.9, 128.8, 128.2, 126.9, 126.7, 126.2, 125.7, 82.5, 80.3, 63.1, 59.5, 54.5, 49.8, 47.2, 37.8, 31.1, 29.4, 21.0, 19.8; HRMS (ESI) m/z calcd for $C_{24}H_{30}N_2$ $[M + H]^+$ 347.2482, found 347.2481.

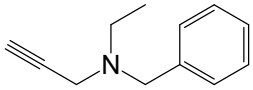


***N*[4]-benzyl-*N*[1],*N*[4],5-trimethyl-*N*[1]-phenylhex-2-yne-1,4-diamine (7k).** Light yellow oil (111mg, 69% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.19 (m, 7H), 6.90 (d, *J* = 8

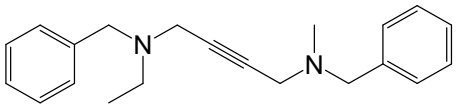
Hz, 2H), 6.80 (t, *J* = 8 Hz, 1H), 4.12 (s, 2H), 3.48 (d, *J* = 12 Hz, 1H), 3.25 (d, *J* = 12 Hz, 1H), 2.98 (s, 3H), 2.81 (d, *J* = 8 Hz, 1H), 2.03 (s, 3H), 1.77–1.68 (m, 1H), 0.95–0.93 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.5, 139.7, 129.0, 128.9, 128.1, 126.8, 118.3, 114.8, 81.2, 81.0, 62.9, 59.2, 43.0, 38.8, 37.6, 30.9, 20.8, 19.7; HRMS (ESI) m/z calcd for $C_{22}H_{28}N_2$ $[M + H]^+$ 321.2325, found 321.2325.



***N*^{1},*N*^{4}-dibenzyl-*N*^{1}-ethyl-*N*^{4}-methyldec-2-yne-1,4-diamine (7m).** Light yellow oil (107mg, 55% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.29 (m, 8H), 7.26–7.22 (m, 2H), 3.70 (d, *J* = 12 Hz, 3H), 3.50 (d, *J* = 8 Hz, 1H), 3.45–3.42 (m, 3H), 2.67–2.62 (m, 2H), 2.24 (s, 3H), 1.72–1.64 (m, 2H), 1.51–1.40 (m, 2H), 1.29 (s, 6H), 1.14 (t, *J* = 8 Hz, 3H), 0.88 (d, *J* = 4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.5, 139.0, 129.2, 129.0, 128.3, 128.2, 127.1, 126.9, 82.9, 79.4, 59.3, 57.8, 55.7, 47.5, 41.1, 37.9, 34.3, 31.9, 29.0, 26.6, 22.7, 14.1, 12.9; HRMS (ESI) m/z calcd for $C_{27}H_{38}N_2$ $[M + H]^+$ 391.3108, found 391.3110.

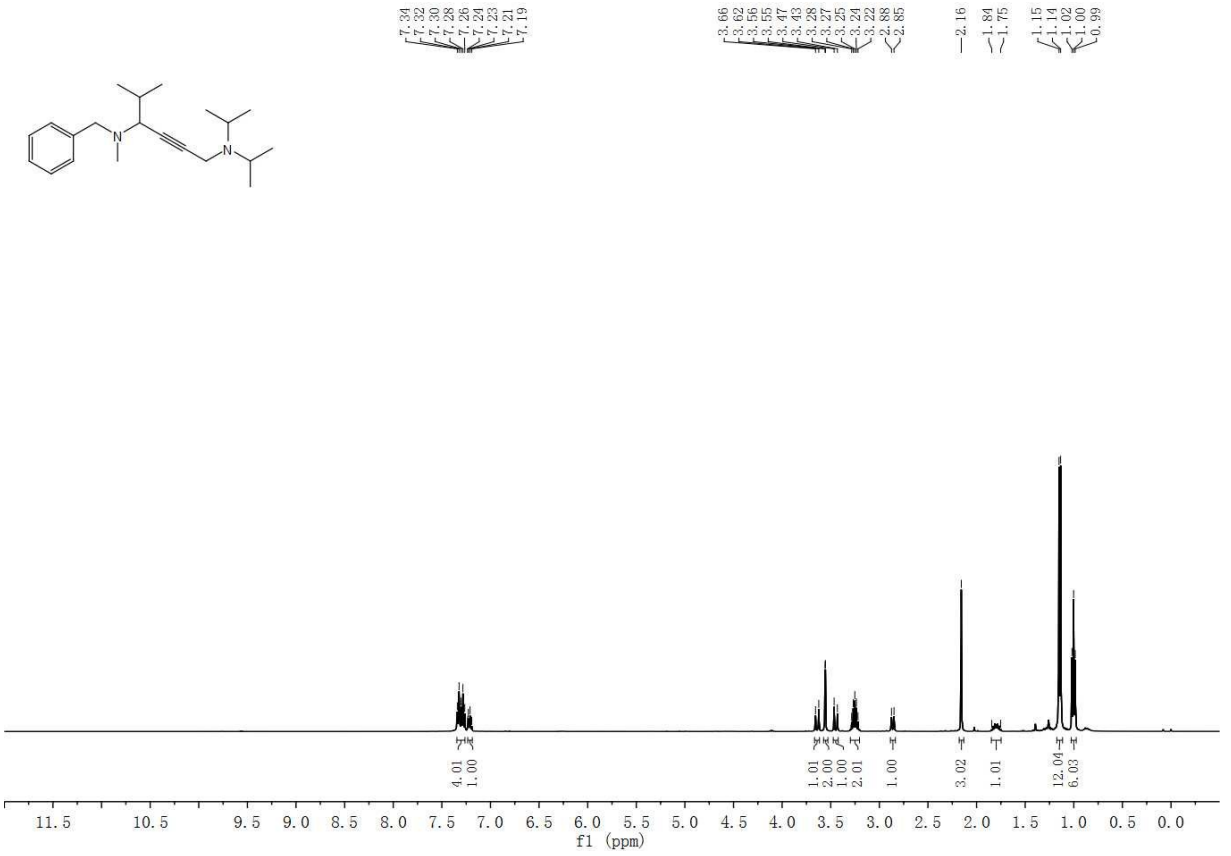


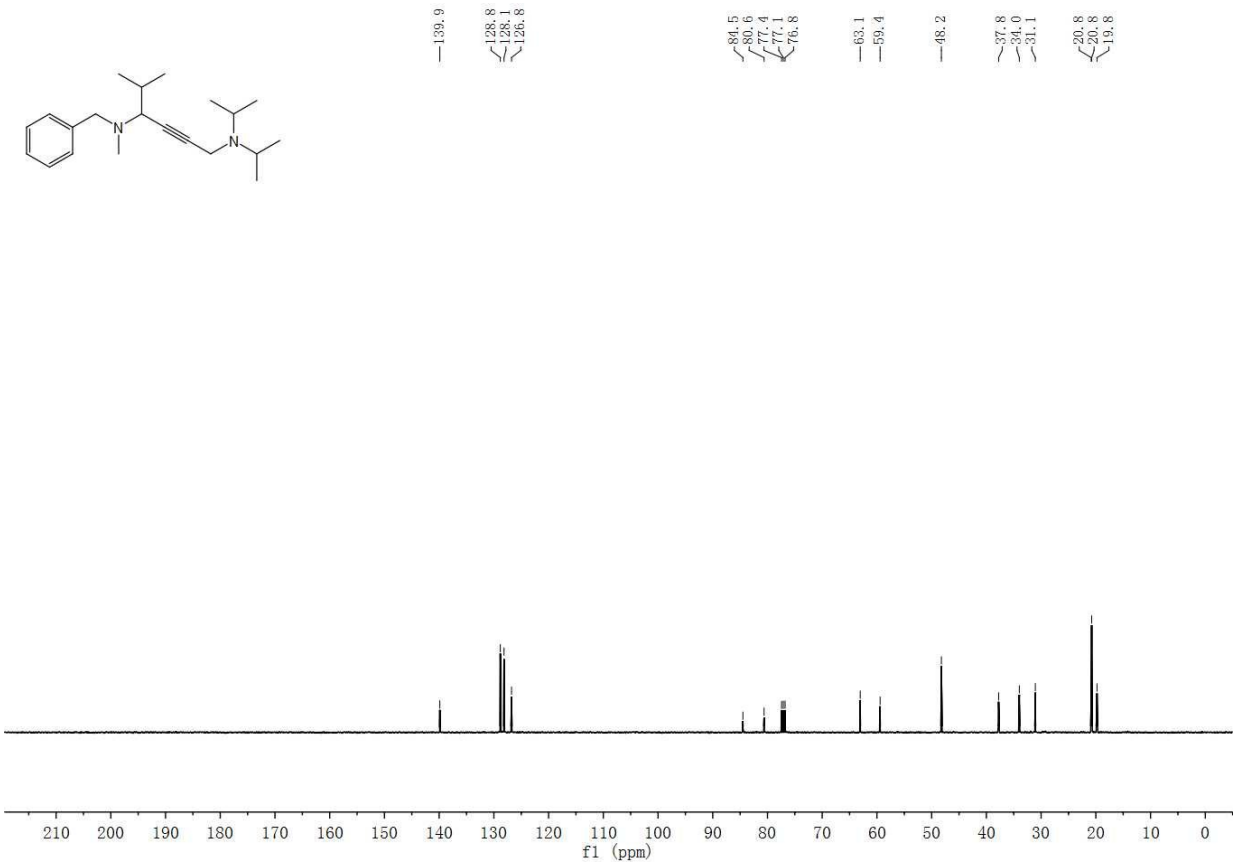
***N*-benzyl-*N*-ethylprop-2-yn-1-amine (9b).** Light yellow oil (30%–74% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8 Hz, 2H), 7.37 (t, *J* = 8 Hz, 2H), 7.32–7.29 (m, 1H), 3.69 (s, 2H), 3.40 (d, *J* = 4 Hz, 2H), 2.70–2.65 (m, 2H), 2.28 (t, *J* = 4 Hz, 1H), 1.18 (t, *J* = 8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 129.2, 128.3, 127.1, 78.6, 73.0, 57.6, 47.4, 40.9, 12.8; MS (ESI) m/z: 174.3 $[M + H]^+$.



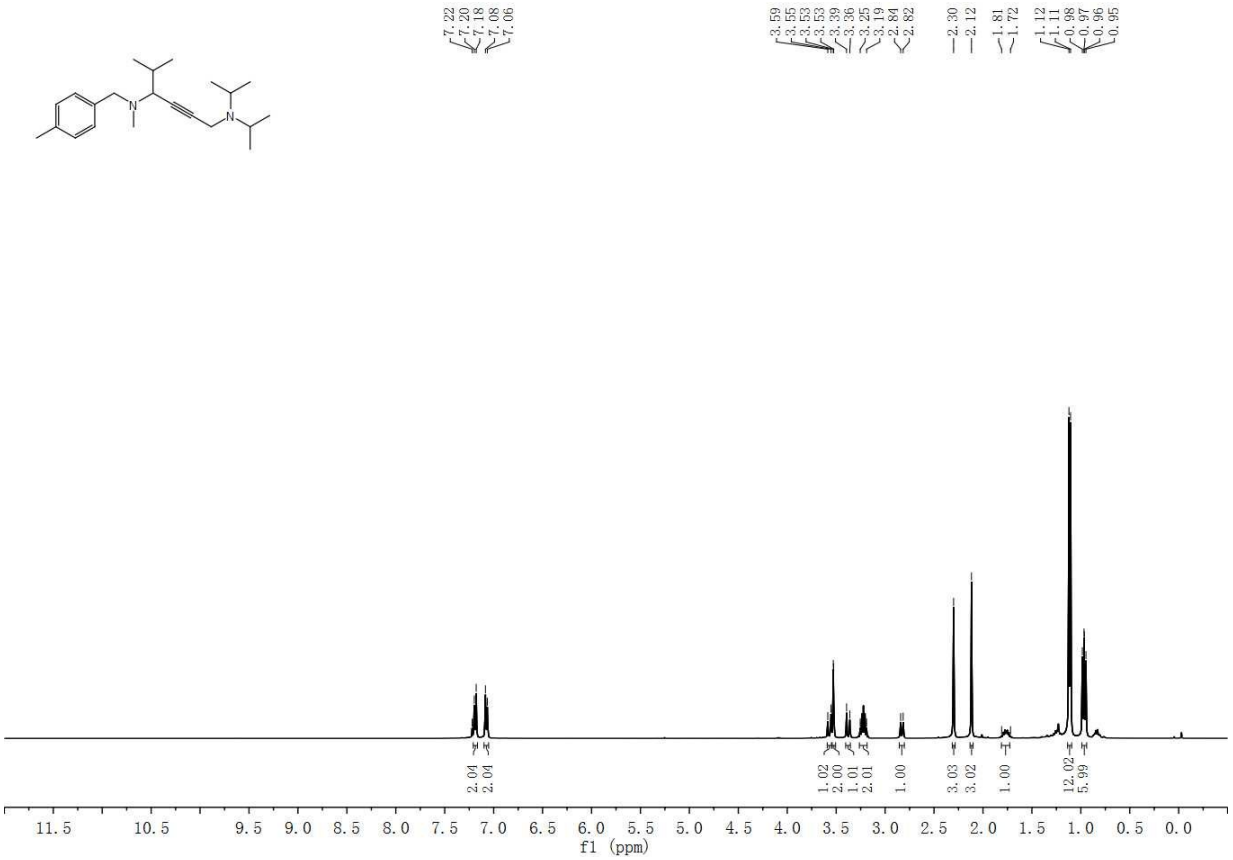
N^1,N^4-dibenzyl-N^1-ethyl-N^4-methylbut-2-yne-1,4-diamine (10). Light yellow oil (132mg, 86% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.36 (m, 8H), 7.35–7.28 (m, 2H), 3.72 (s, 2H), 3.66 (s, 2H), 3.45–3.41 (m, 4H), 2.72–2.67 (m, 2H), 2.42 (s, 3H), 1.19 (t, *J* = 6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 138.6, 129.2, 129.2, 128.3, 128.3, 127.2, 127.1, 80.0, 79.7, 60.2, 57.9, 47.5, 45.3, 42.0, 41.2, 29.7, 12.9; HRMS (ESI) m/z calcd for $C_{21}H_{26}N_2$ $[M + H]^+$ 307.2169, found 307.2168.

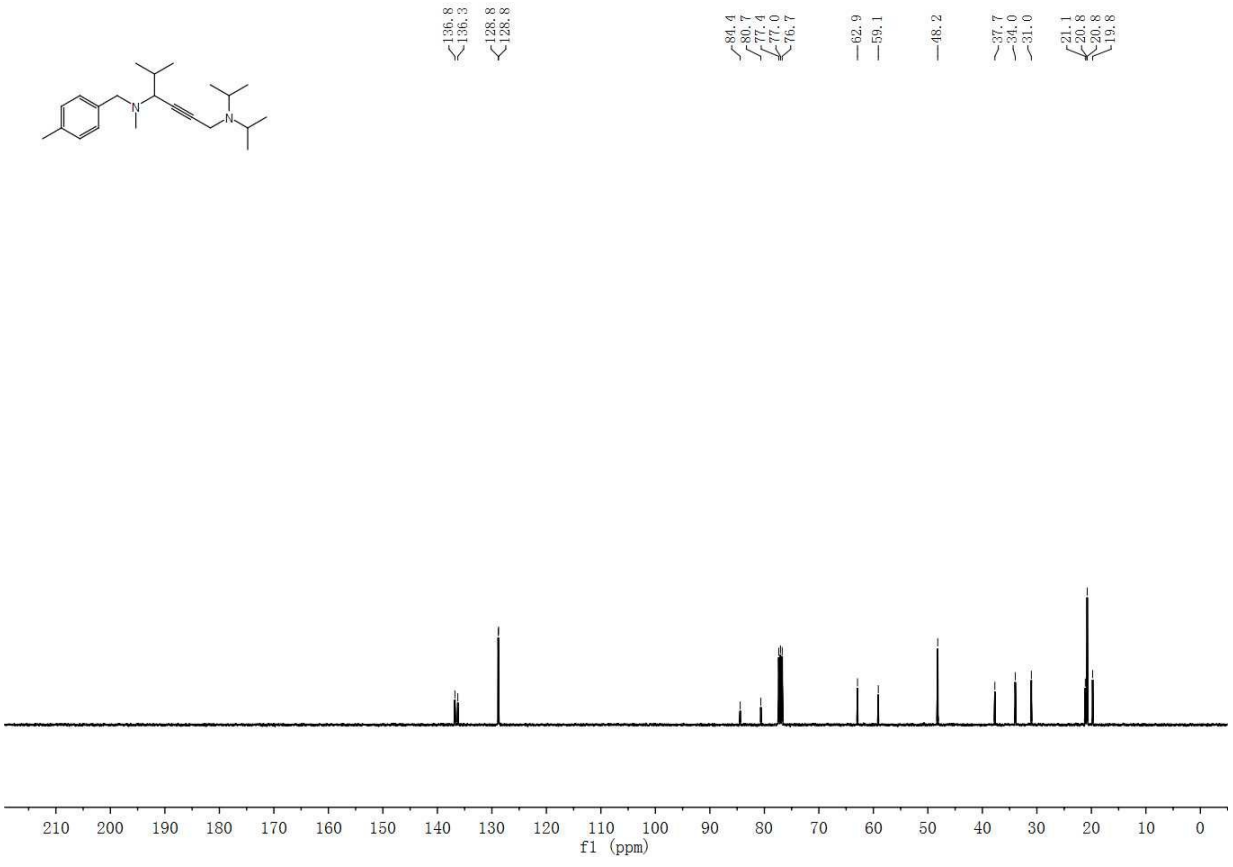
N^4-benzyl-N^1,N^1-diisopropyl-N^4,5-dimethylhex-2-yne-1,4-diamine (6a).



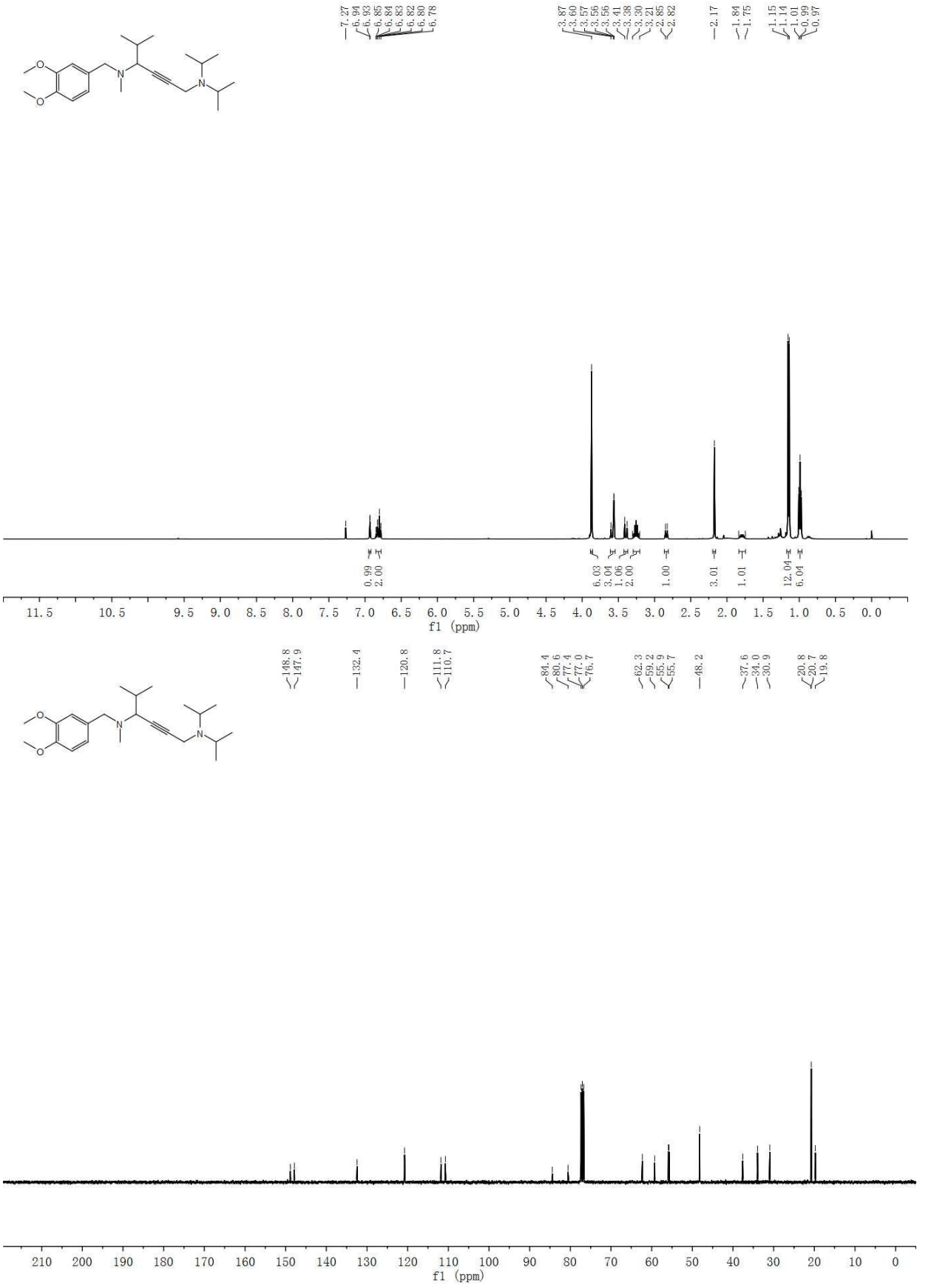


***N*[1],*N*[1]-diisopropyl-*N*[4],5-dimethyl-*N*[4]-(4-methylbenzyl)hex-2-yne-1,4-diamine (6b).**

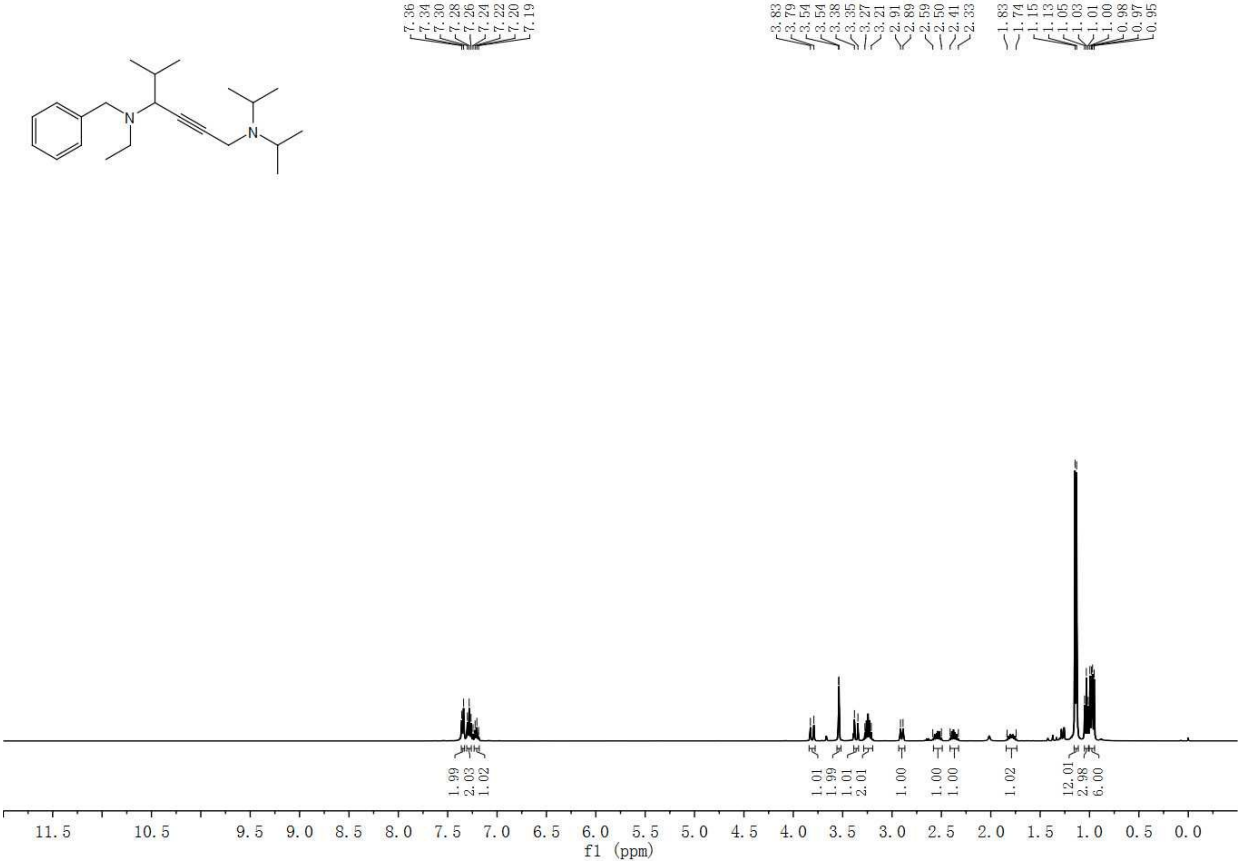


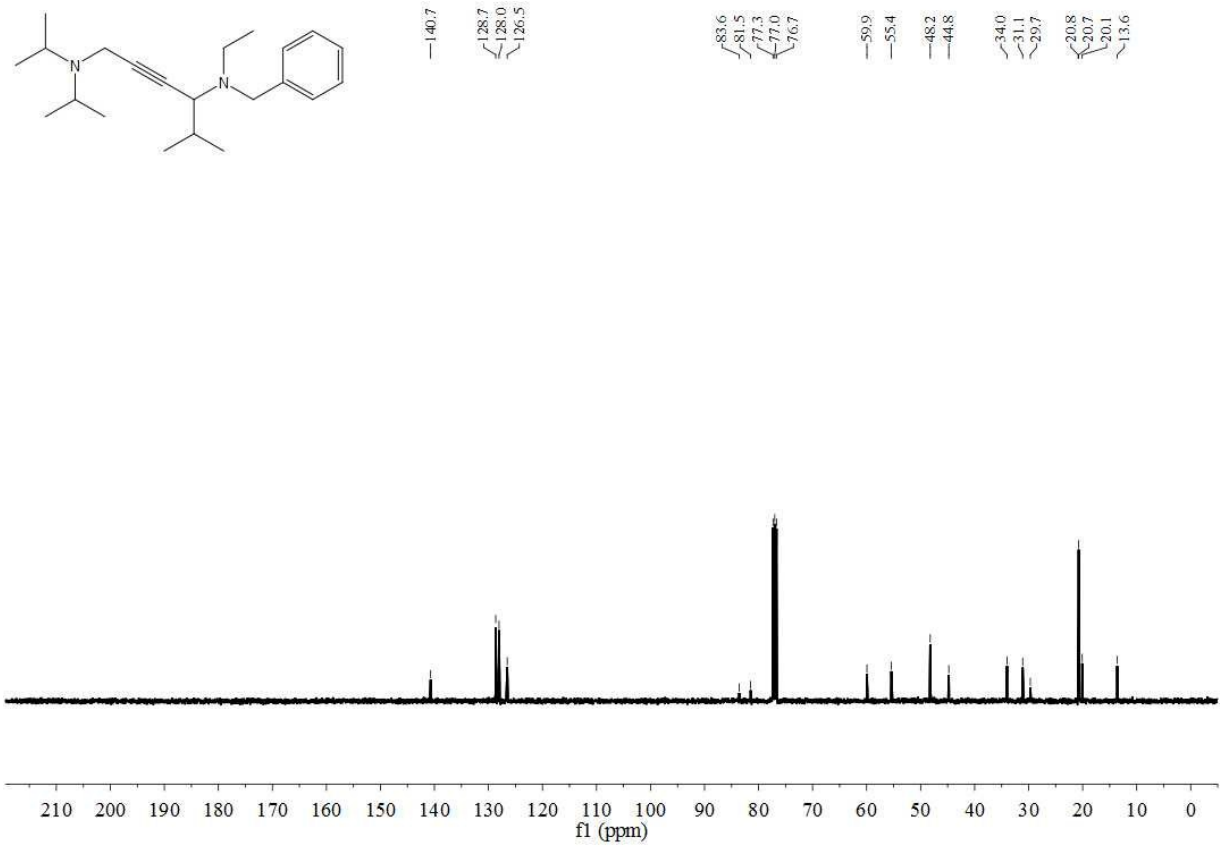


N^4-(3,4-dimethoxybenzyl)-N^1,N^1-diisopropyl-N^4,5-dimethylhex-2-yne-1,4-diamine (6c).

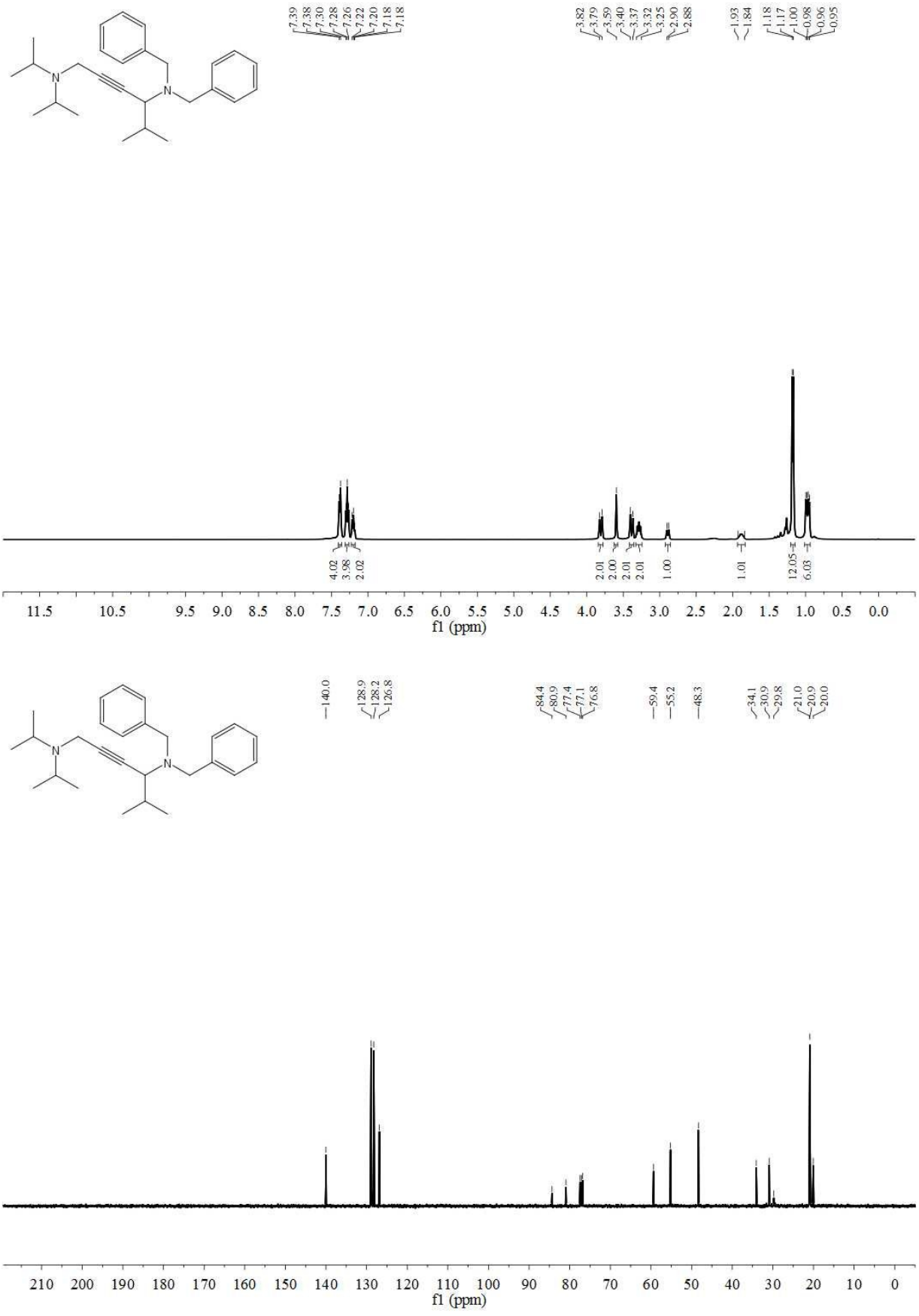


N^4-benzyl-N^4-ethyl-N^1,N^1-diisopropyl-5-methylhex-2-yne-1,4-diamine (6d).

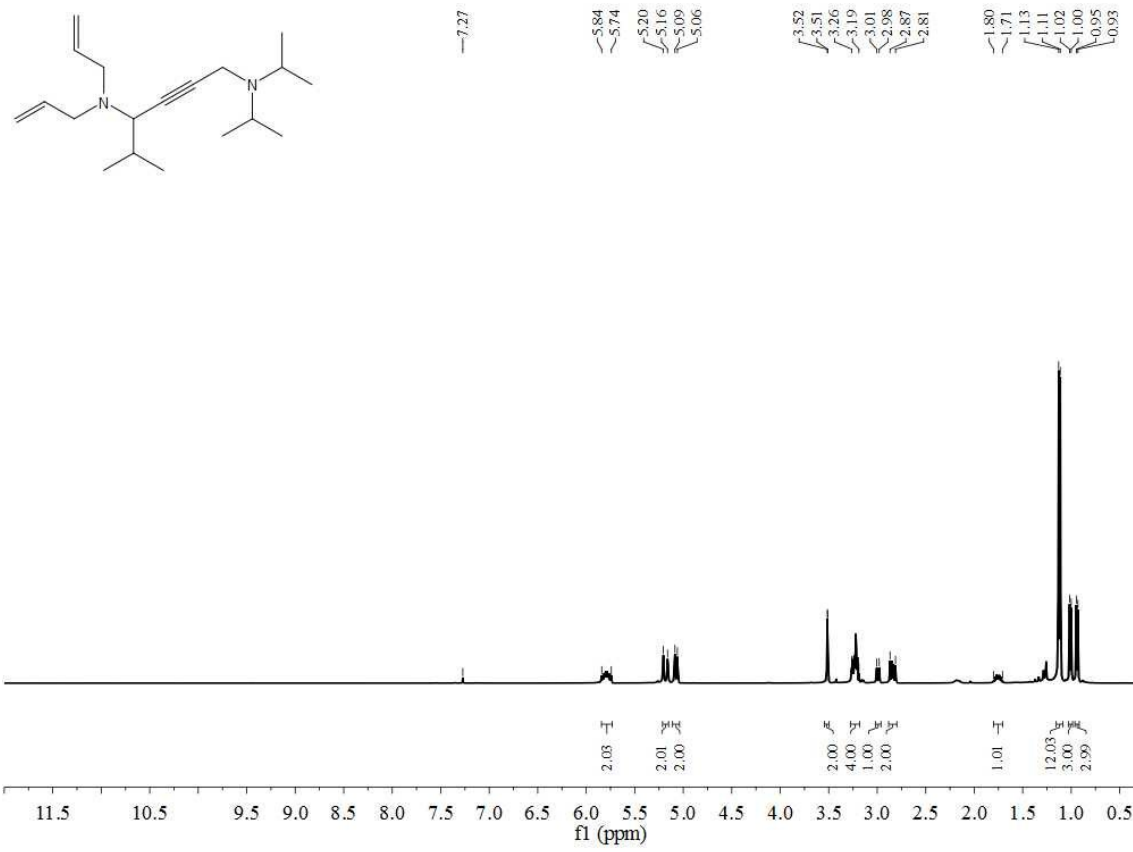


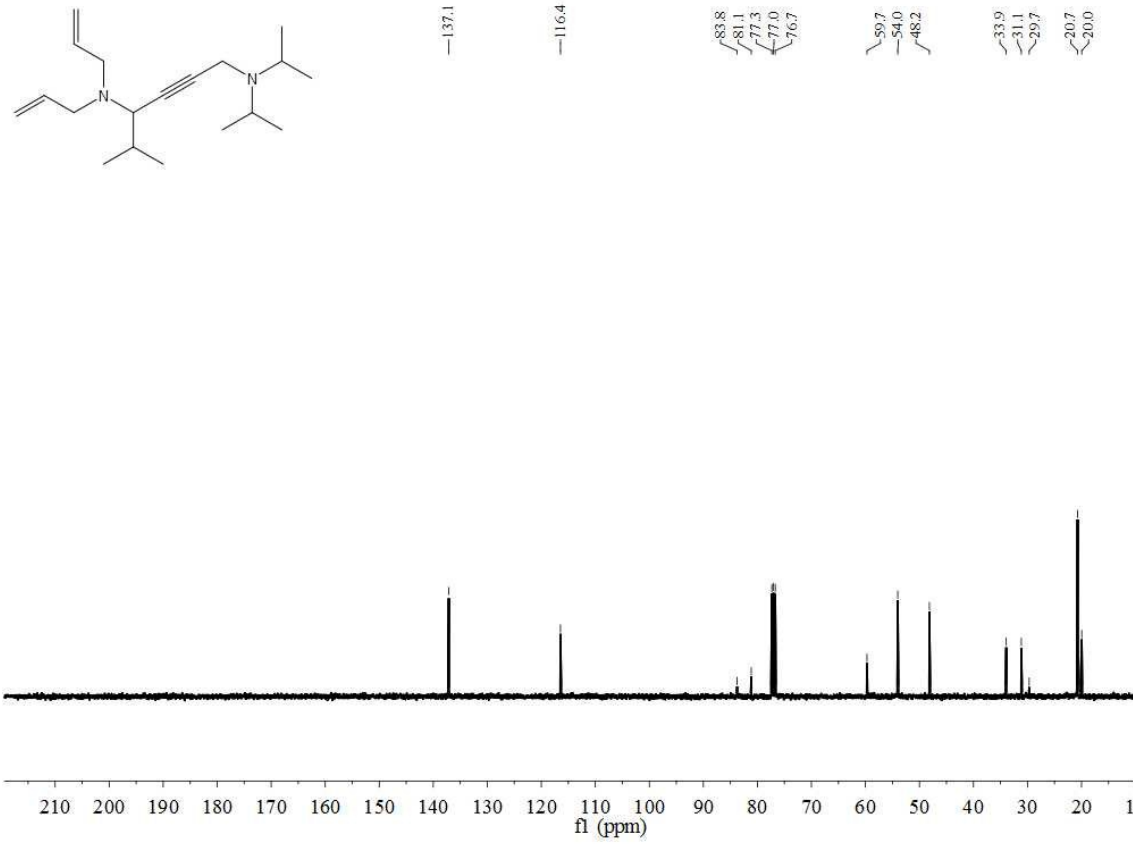


N^4,N^4-dibenzyl-N^1,N^1-diisopropyl-5-methylhex-2-yne-1,4-diamine (6e).

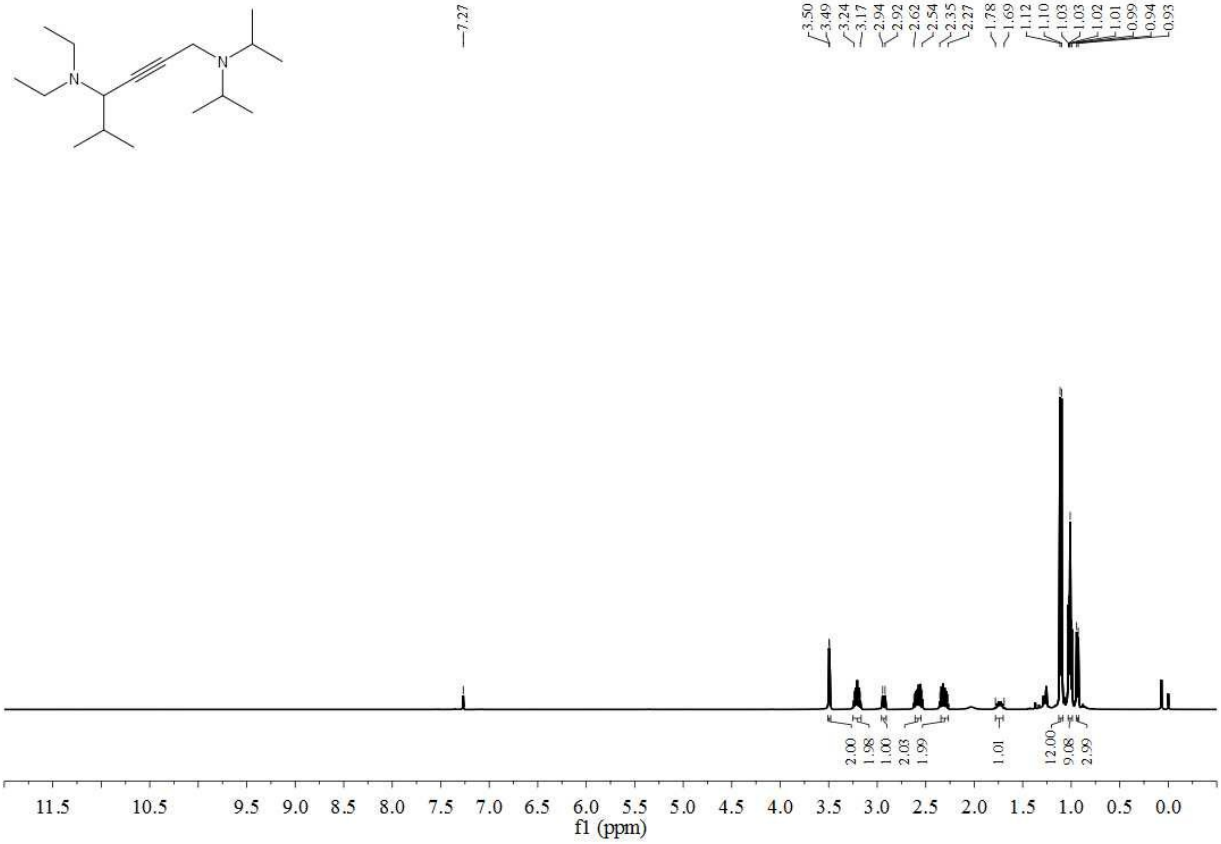


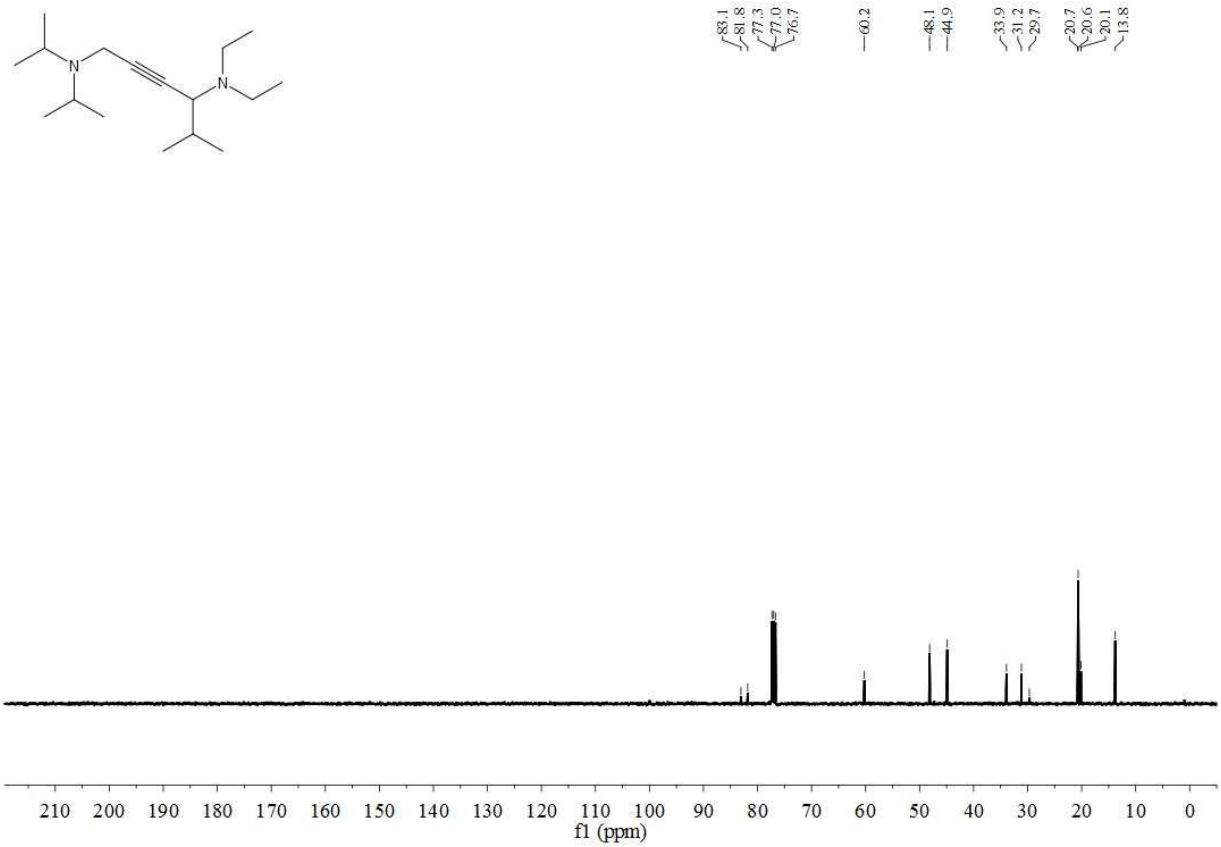
N⁴,N⁴-diallyl-N¹,N¹-diisopropyl-5-methylhex-2-yne-1,4-diamine (6f).



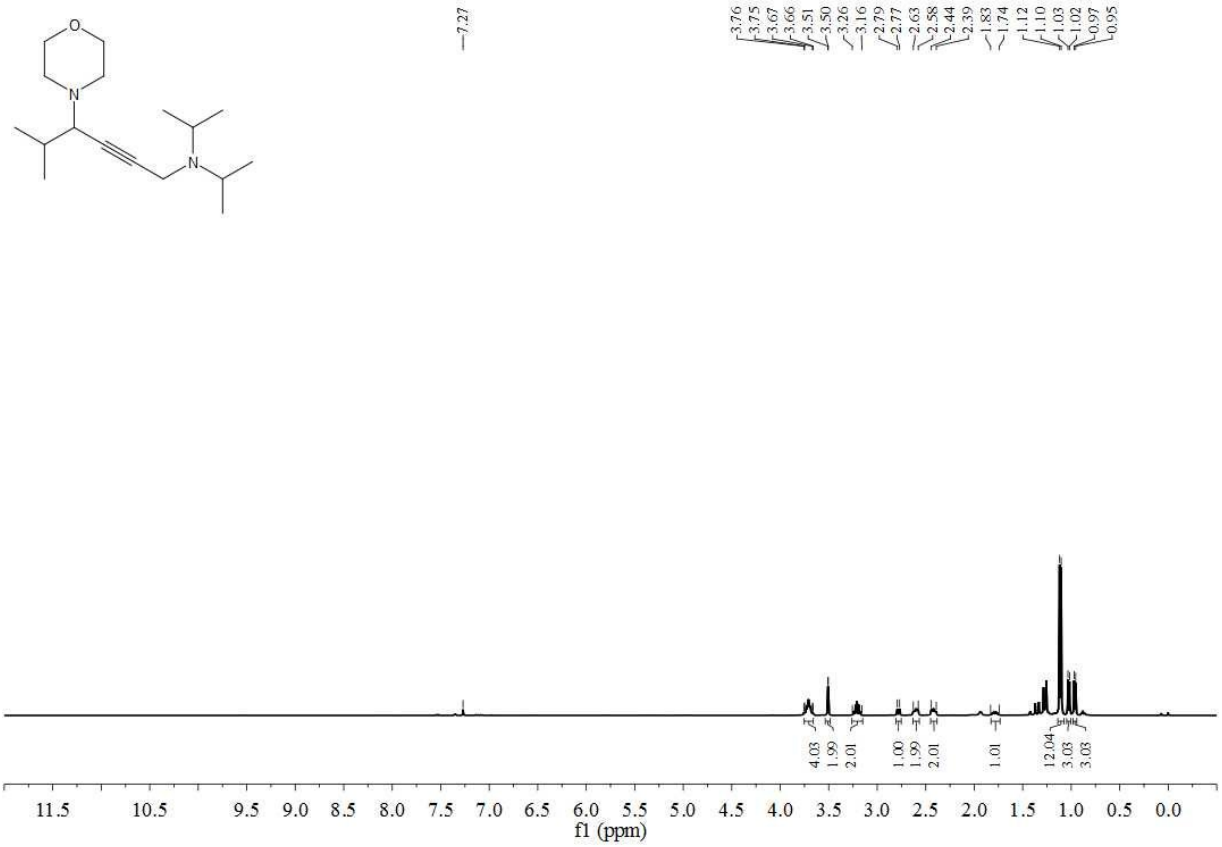


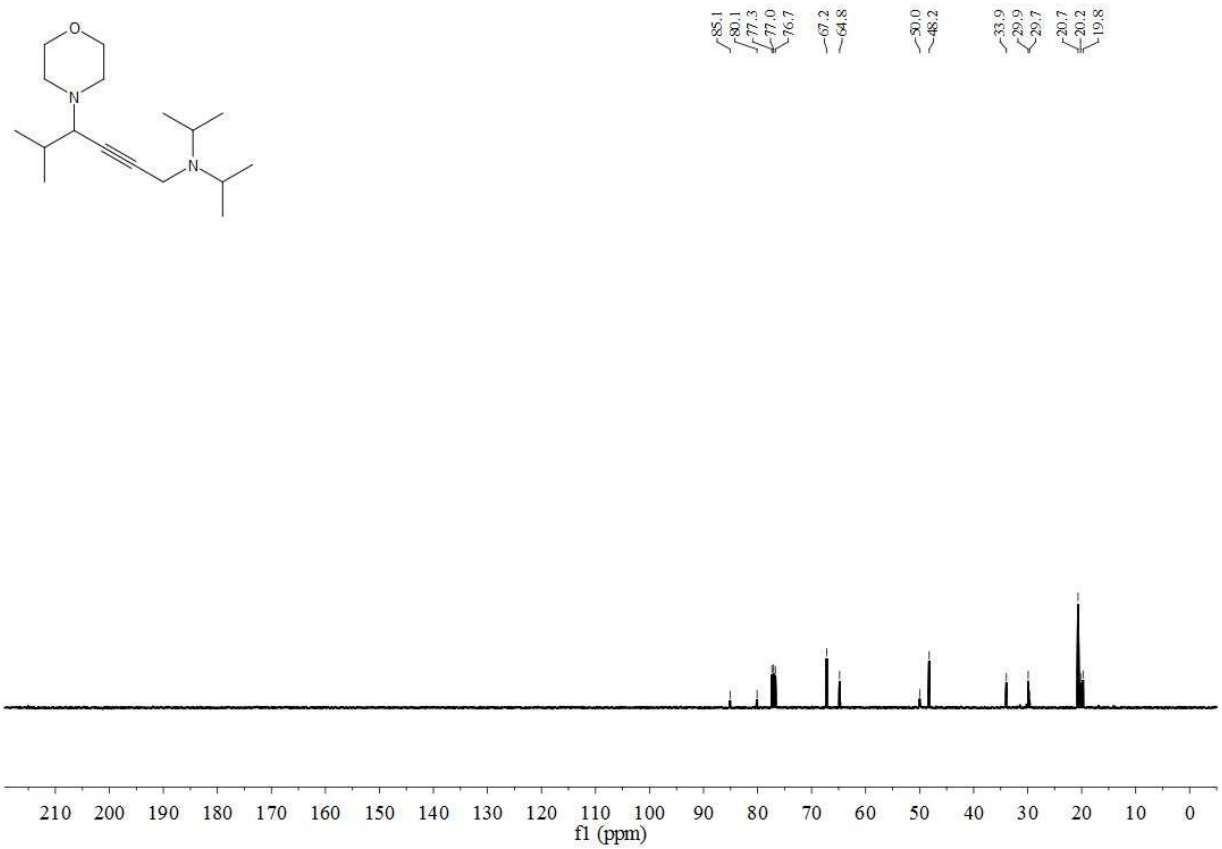
N⁴,N⁴-diethyl-N¹,N¹-diisopropyl-5-methylhex-2-yne-1,4-diamine (6g).



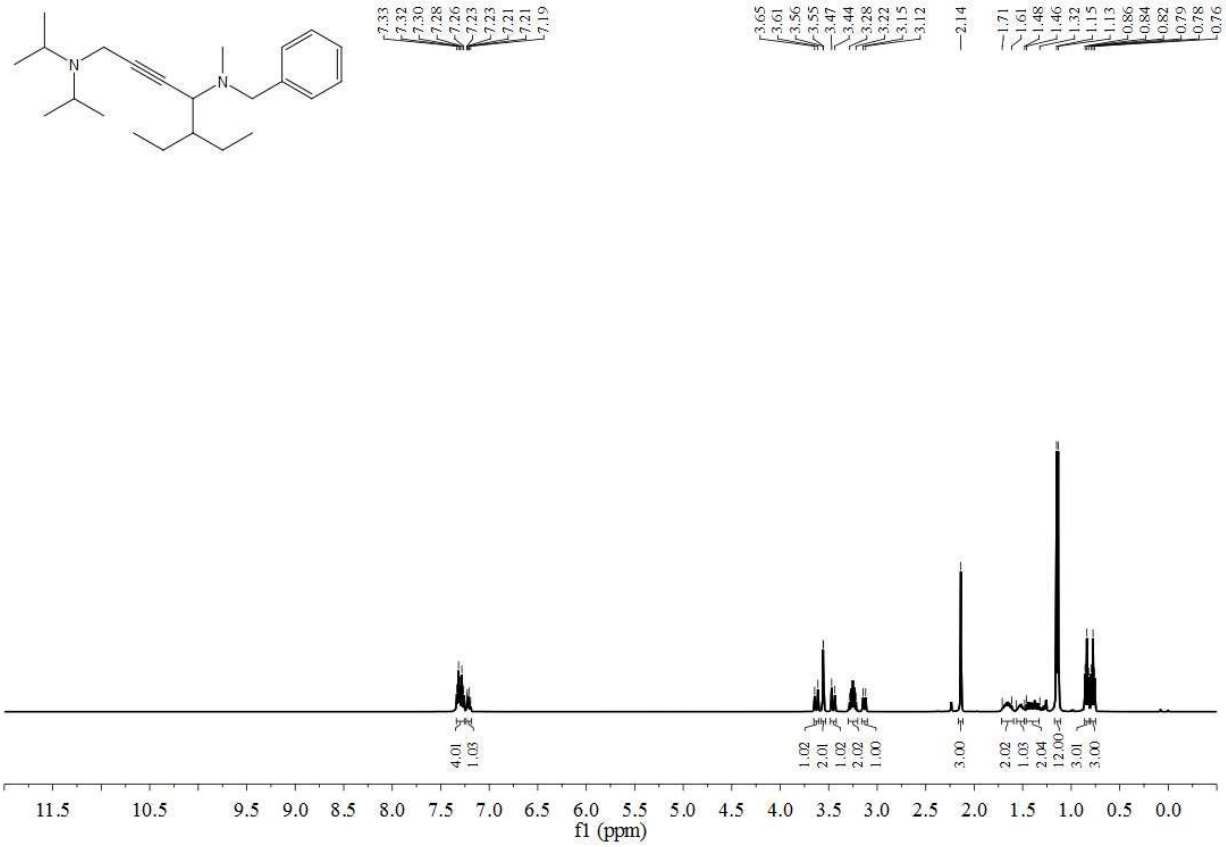


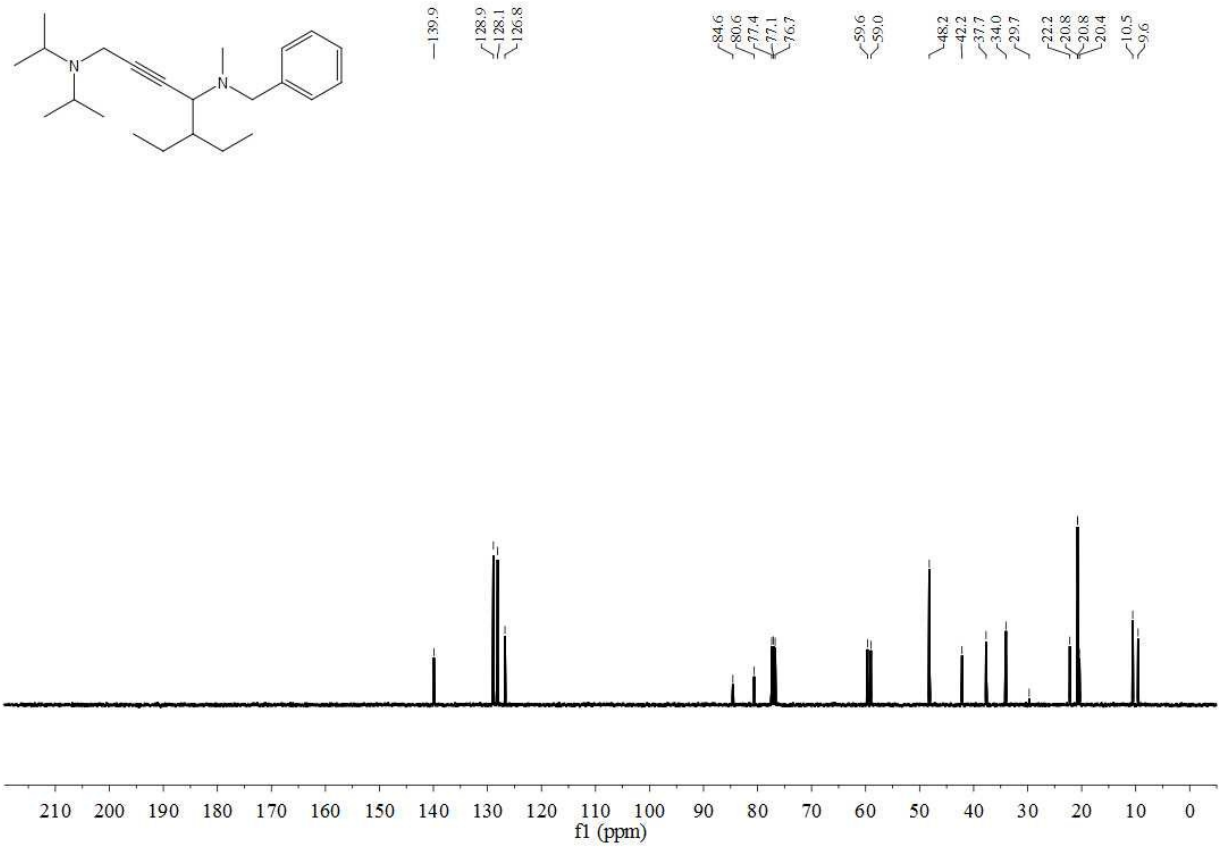
N,N-diisopropyl-5-methyl-4-morpholinohex-2-yn-1-amine (6h).



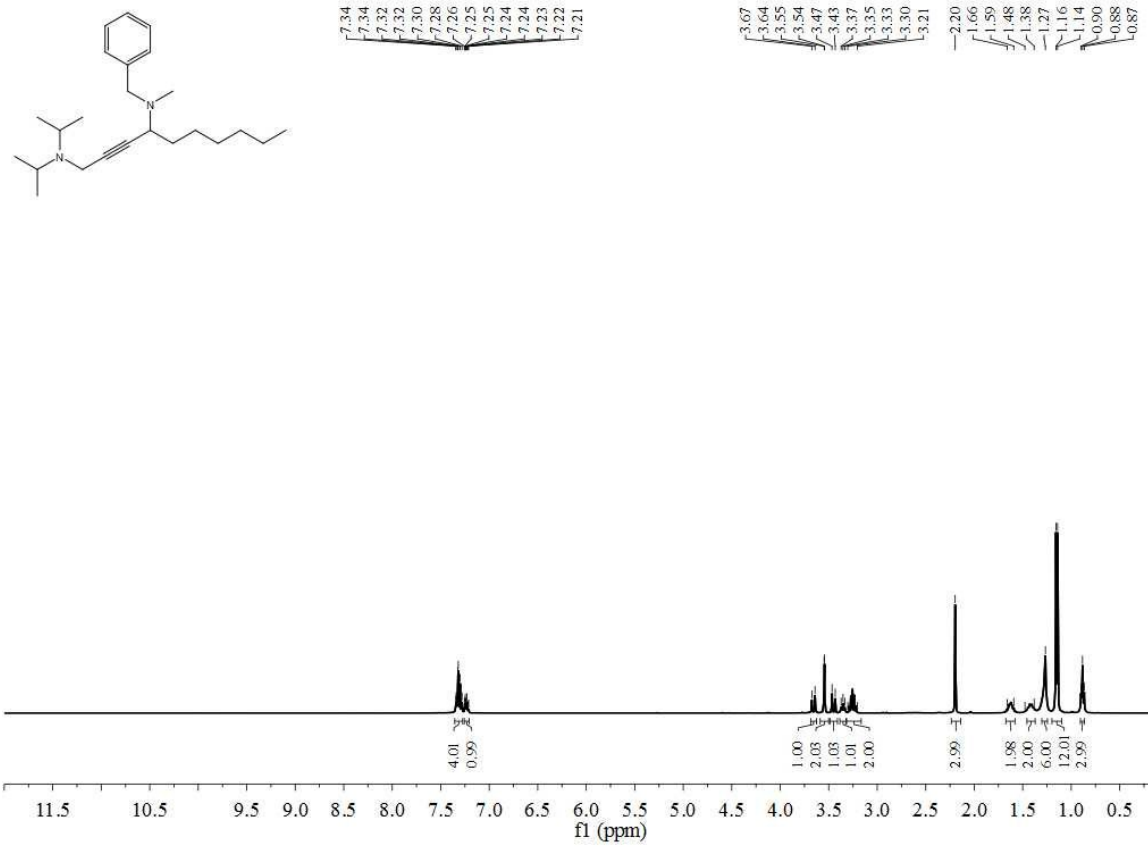


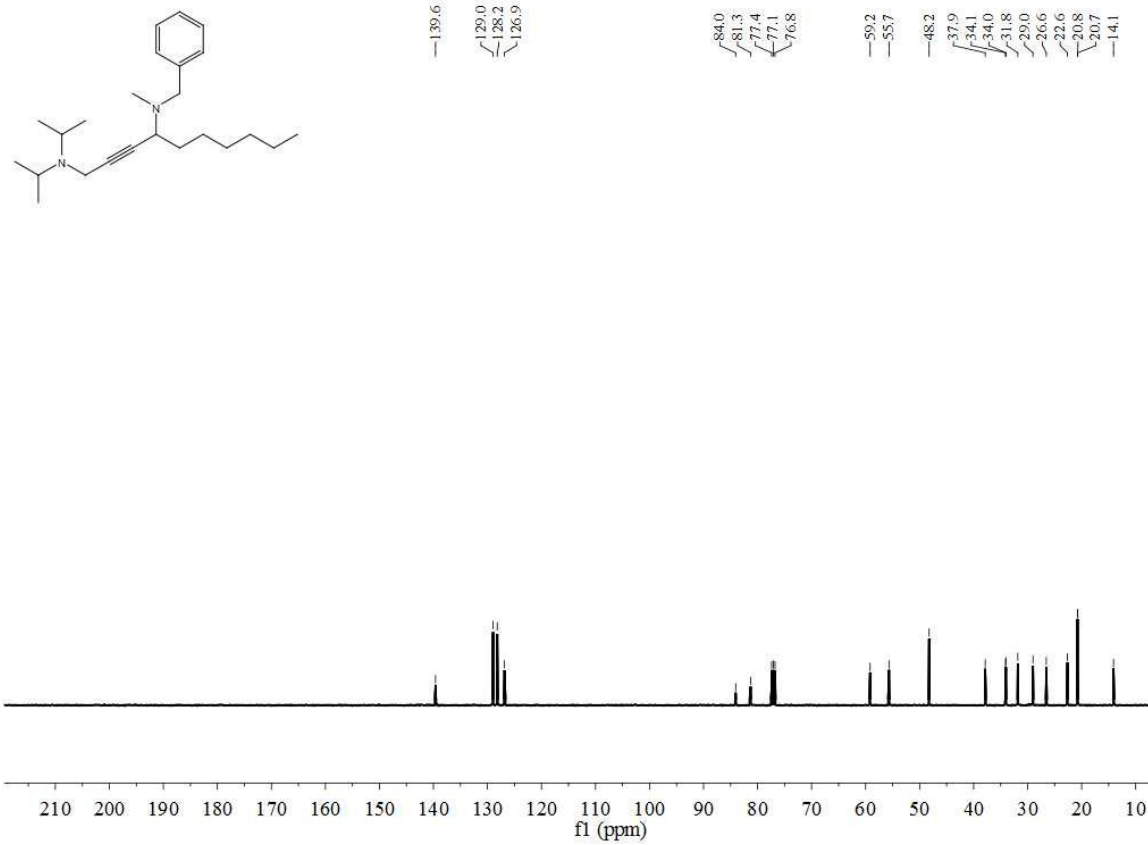
***N*⁴-benzyl-5-ethyl-*N*¹,*N*¹-diisopropyl-*N*⁴-methylhept-2-yne-1,4-diamine (6i).**



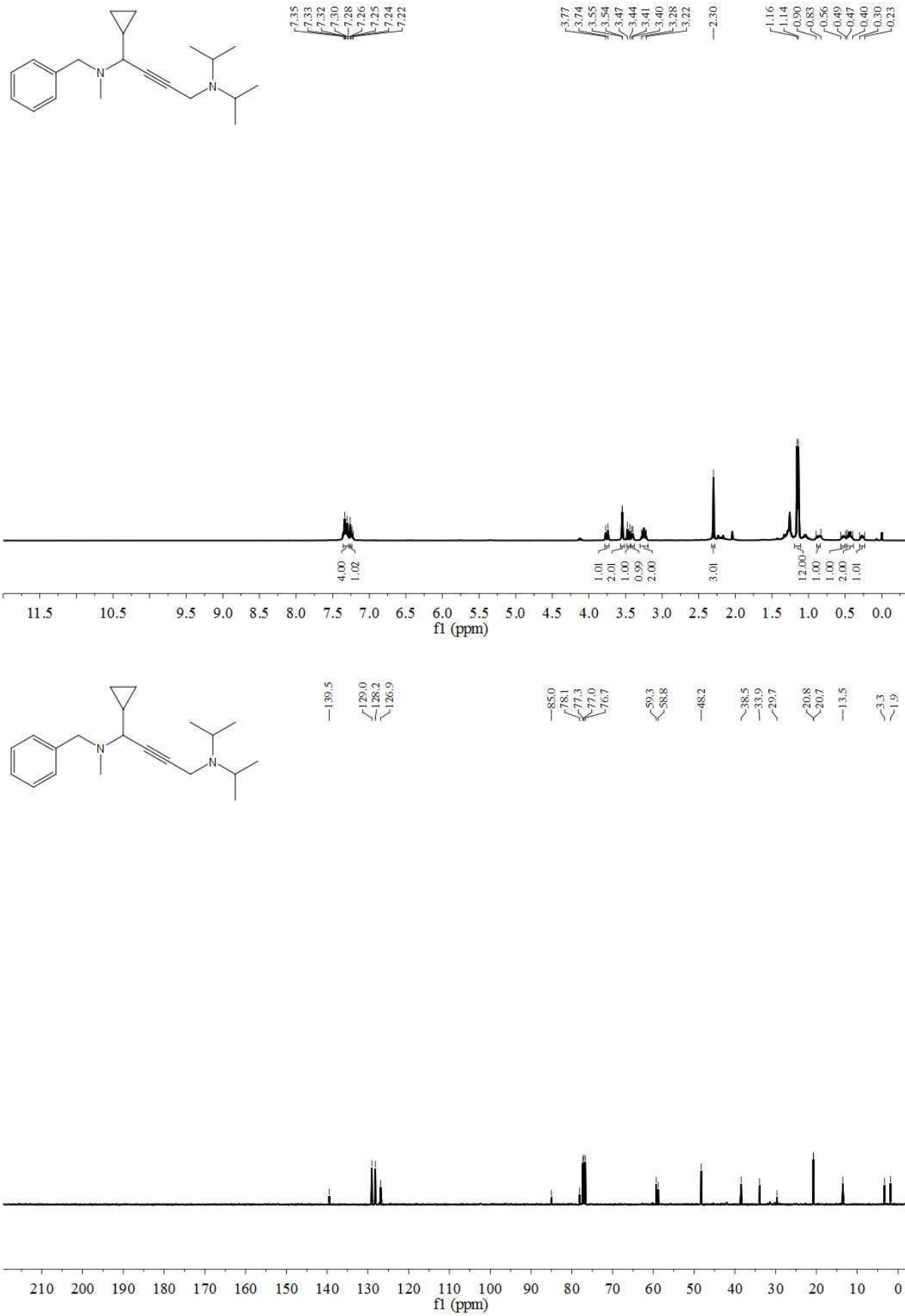


N*^{4}*-benzyl-N*^{1}*,N*^{1}*-diisopropyl-N*^{4}*-methyldec-2-yne-1,4-diamine (6j).

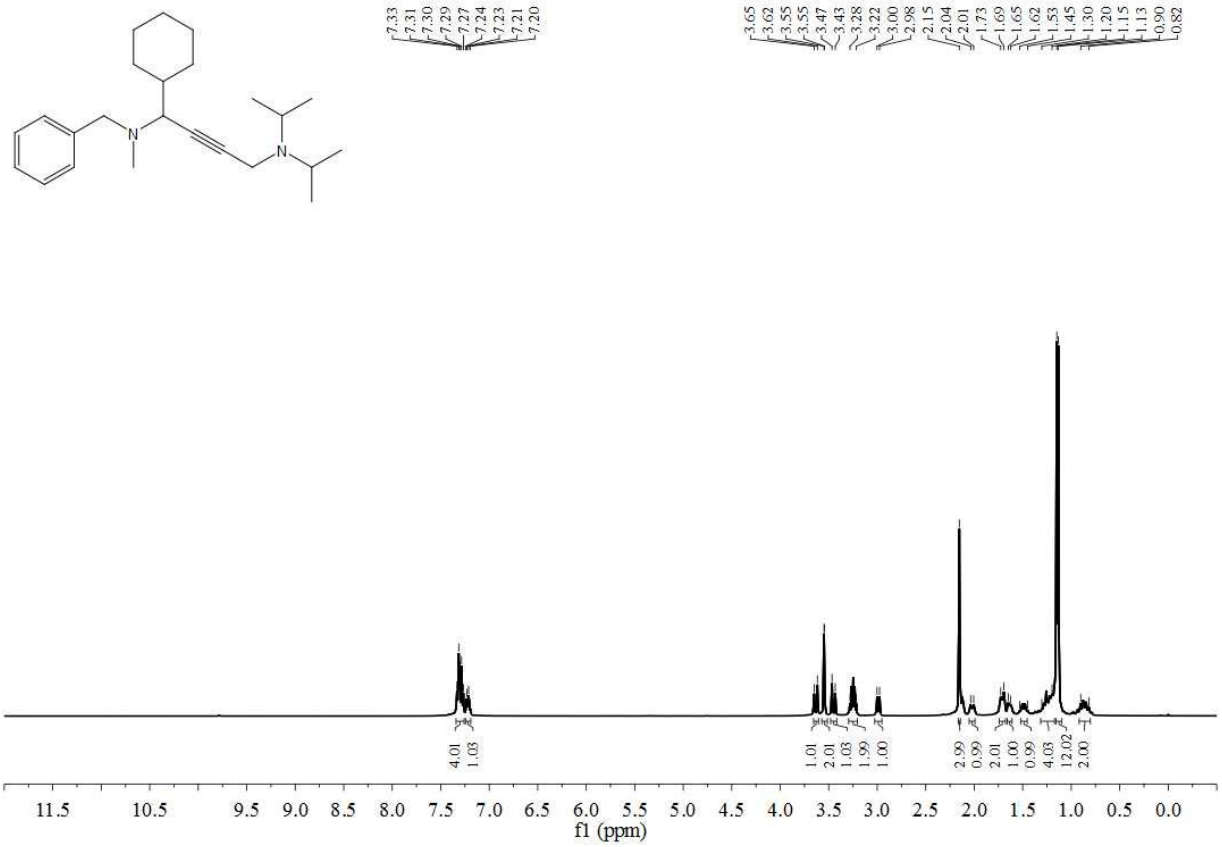


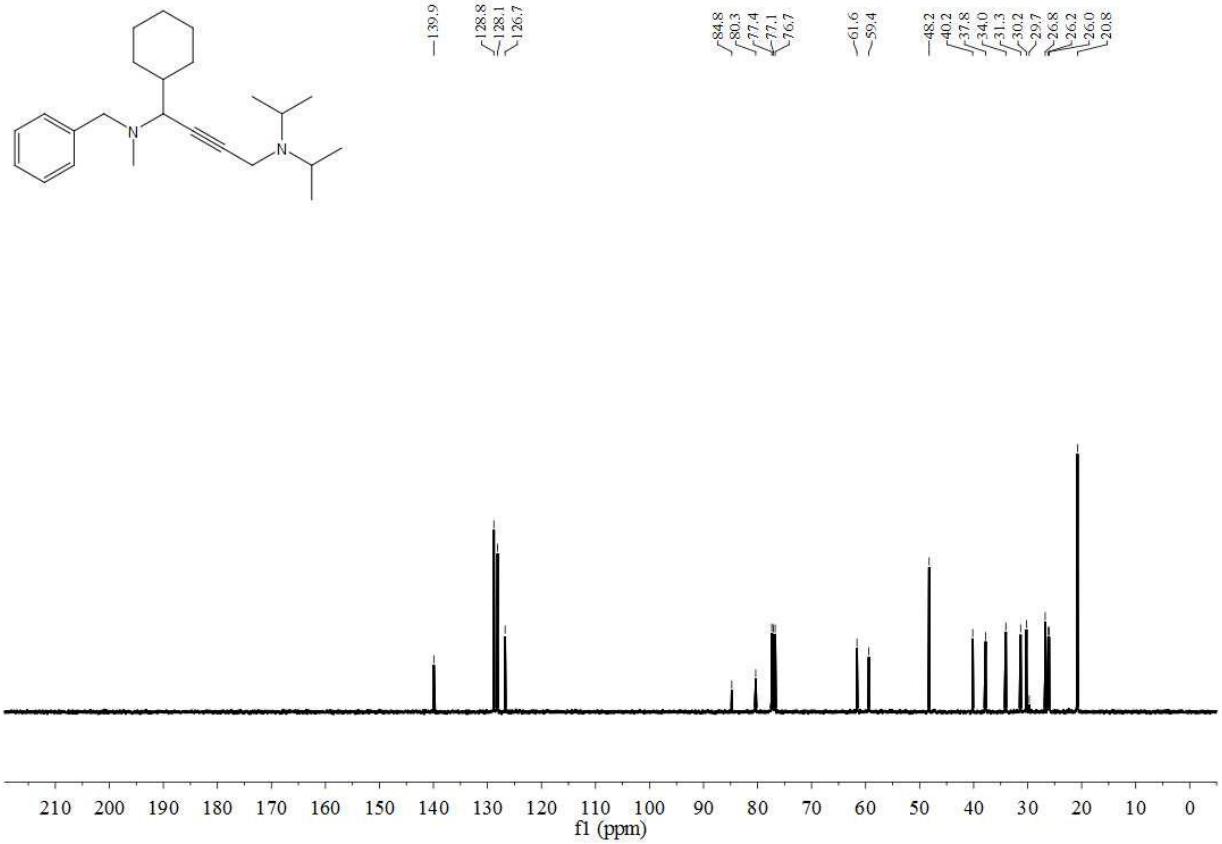


N*[1]*-benzyl-1-cyclopropyl-N*[4]*,N*[4]*-diisopropyl-N*[1]*-methylbut-2-yne-1,4-diamine (6k).

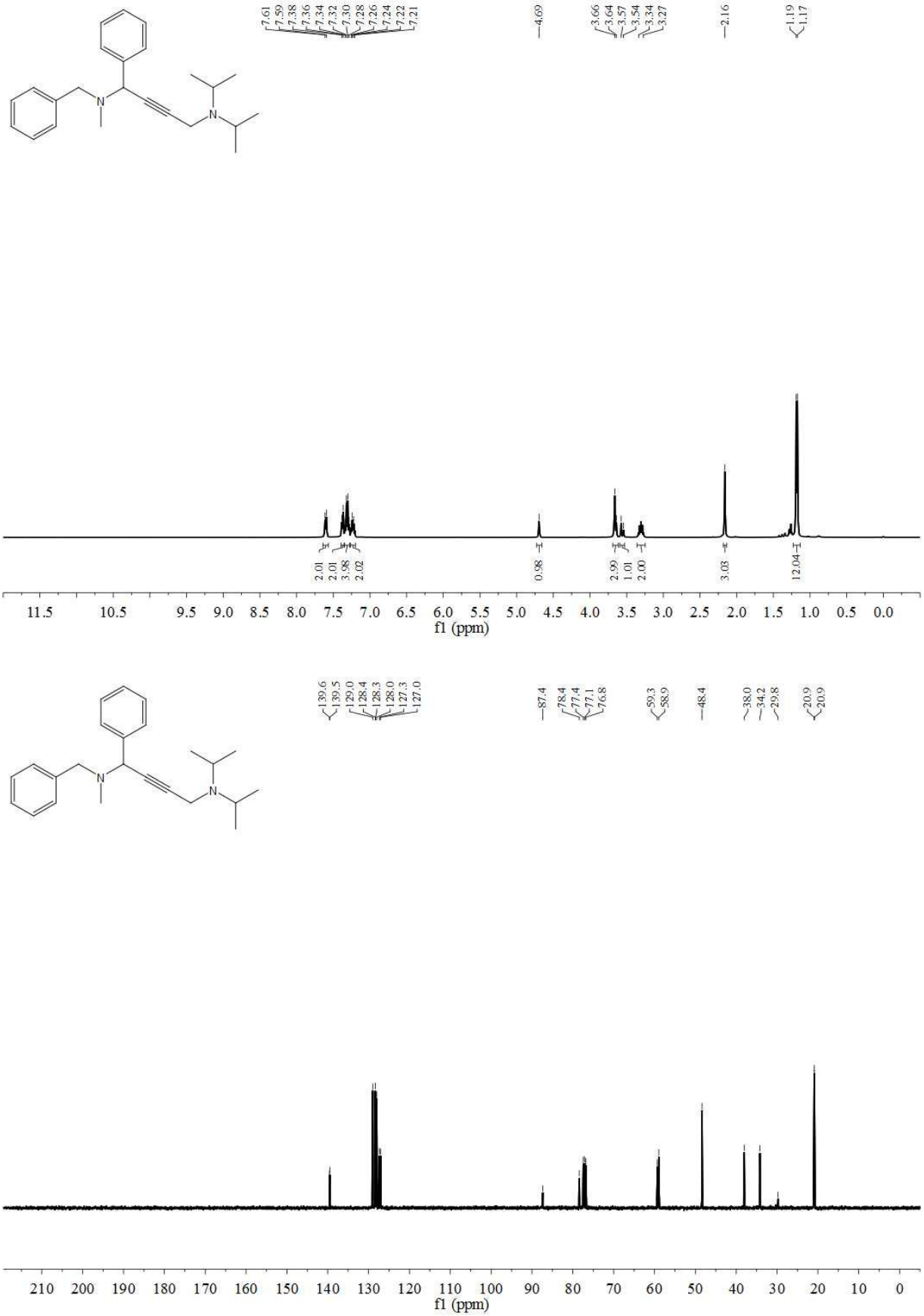


N*[1]*-benzyl-1-cyclohexyl-N*[4]*,N*[4]*-diisopropyl-N*[1]*-methylbut-2-yne-1,4-diamine (6l).

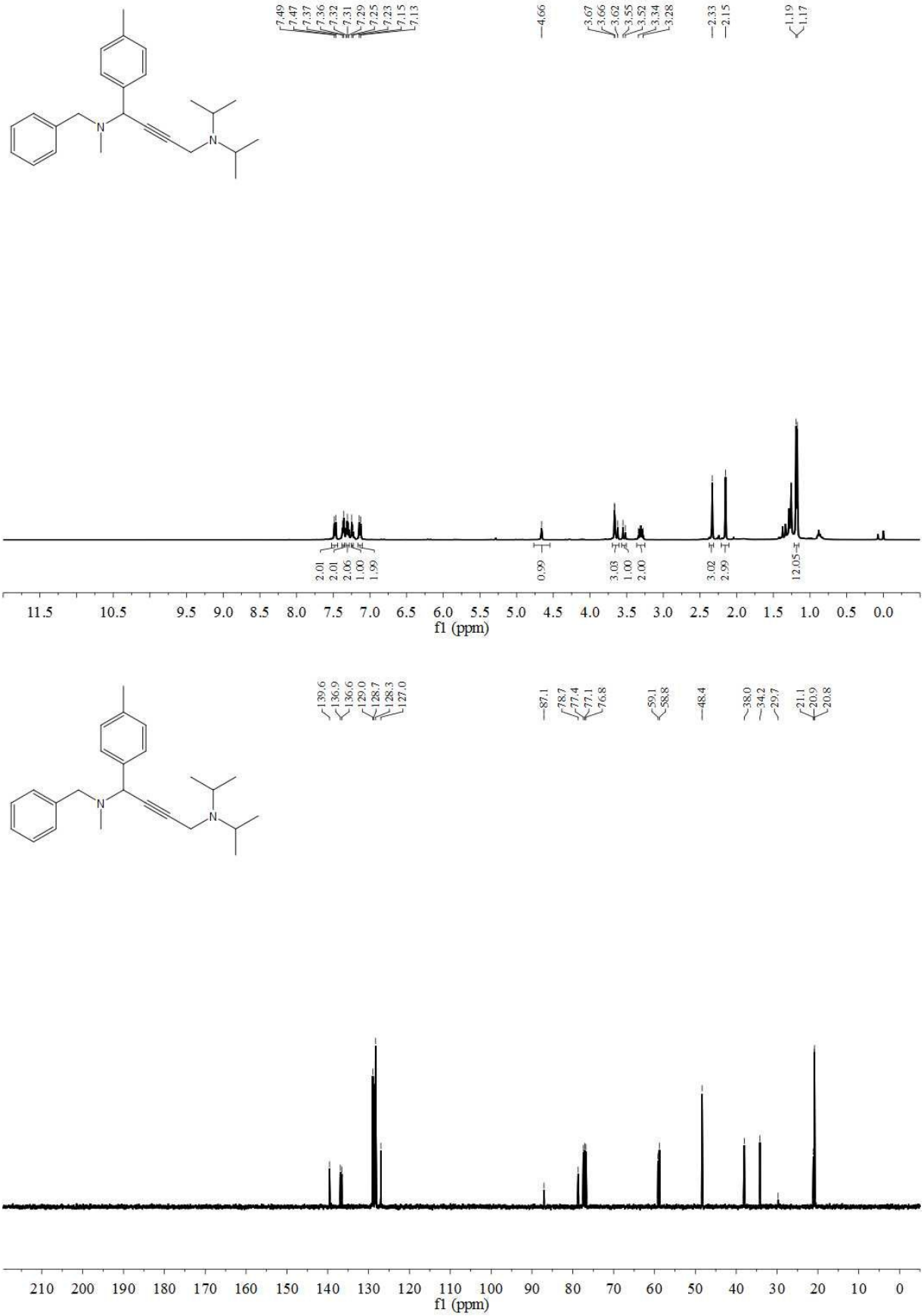




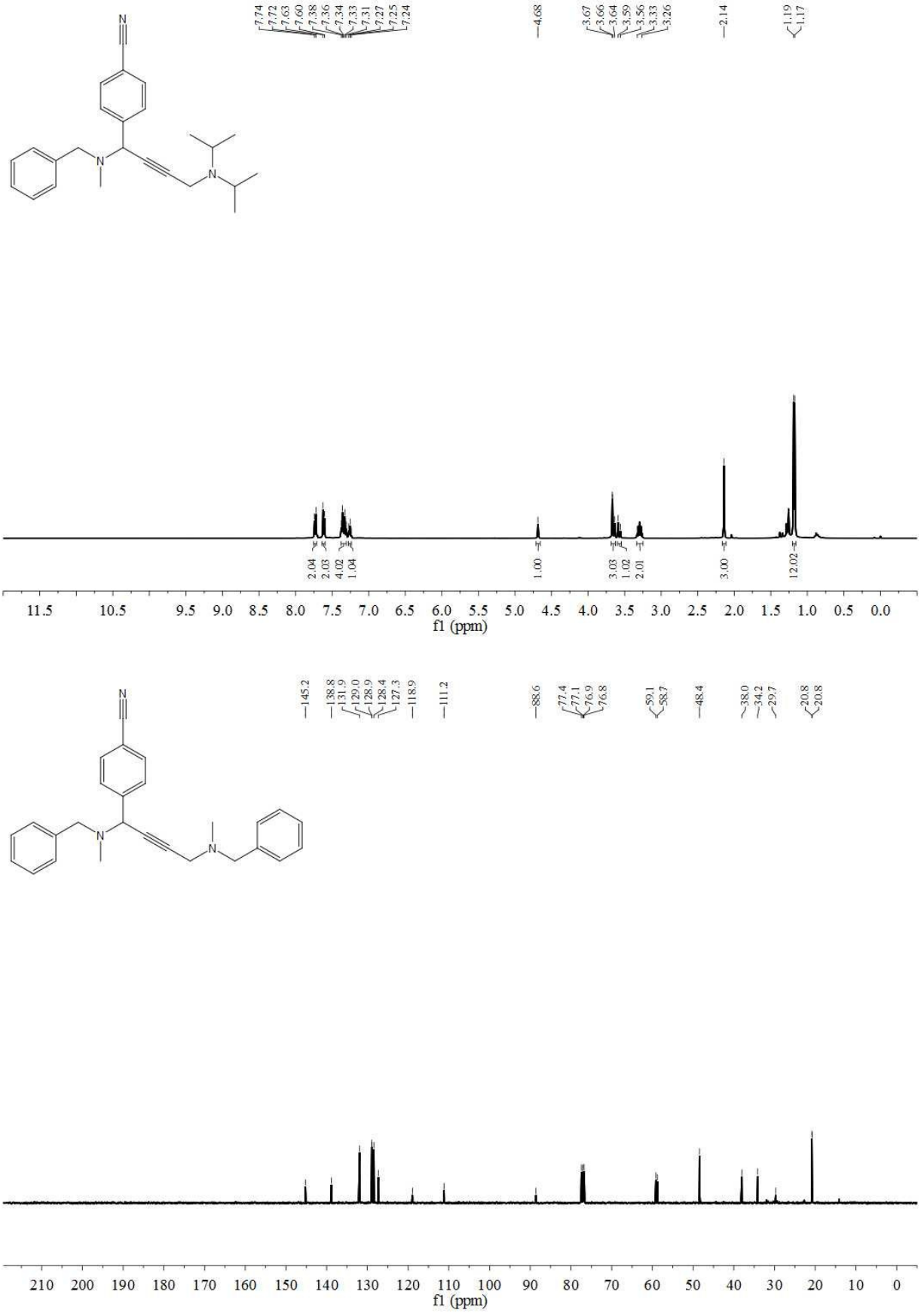
N^1-benzyl-N^4,N^4-diisopropyl-N^1-methyl-1-phenylbut-2-yne-1,4-diamine (6m).



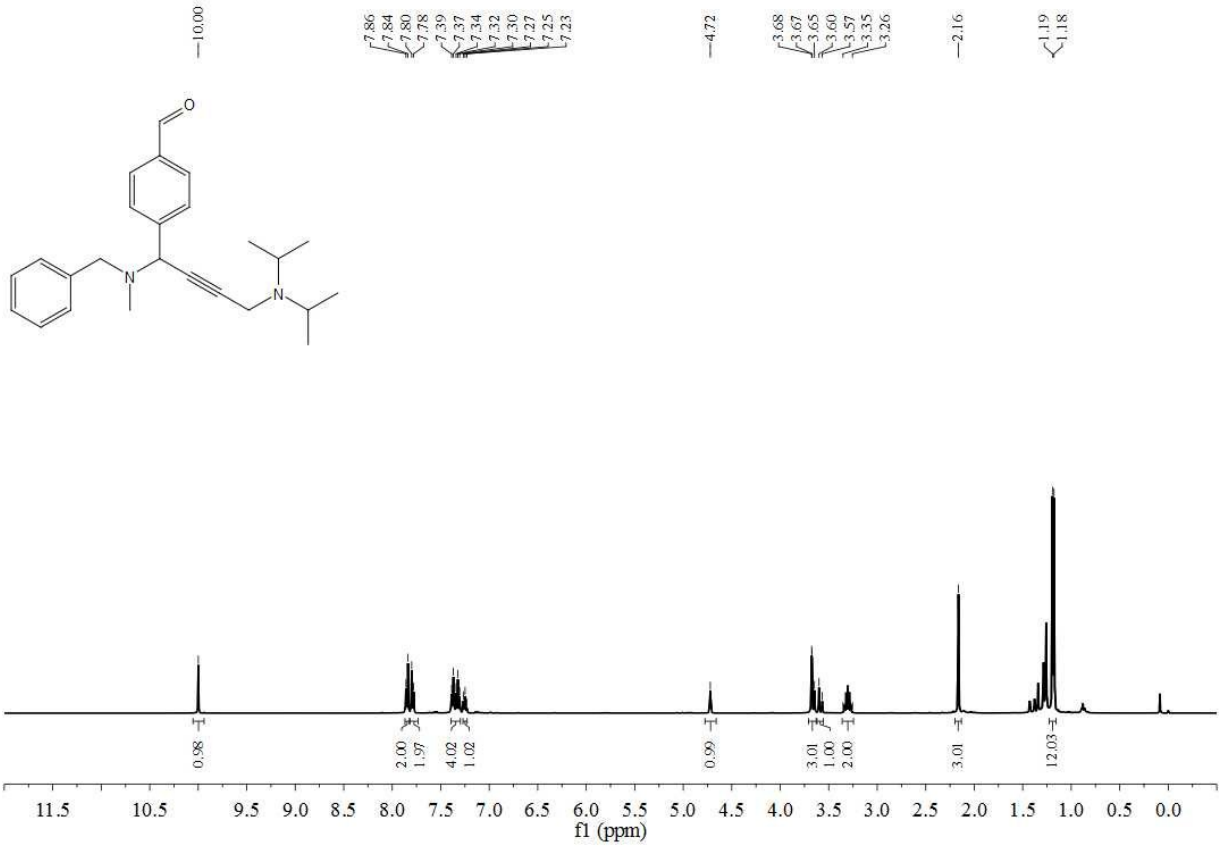
N^1-benzyl-N^4,N^4-diisopropyl-N^1-methyl-1-(p-tolyl)but-2-yne-1,4-diamine (6n).

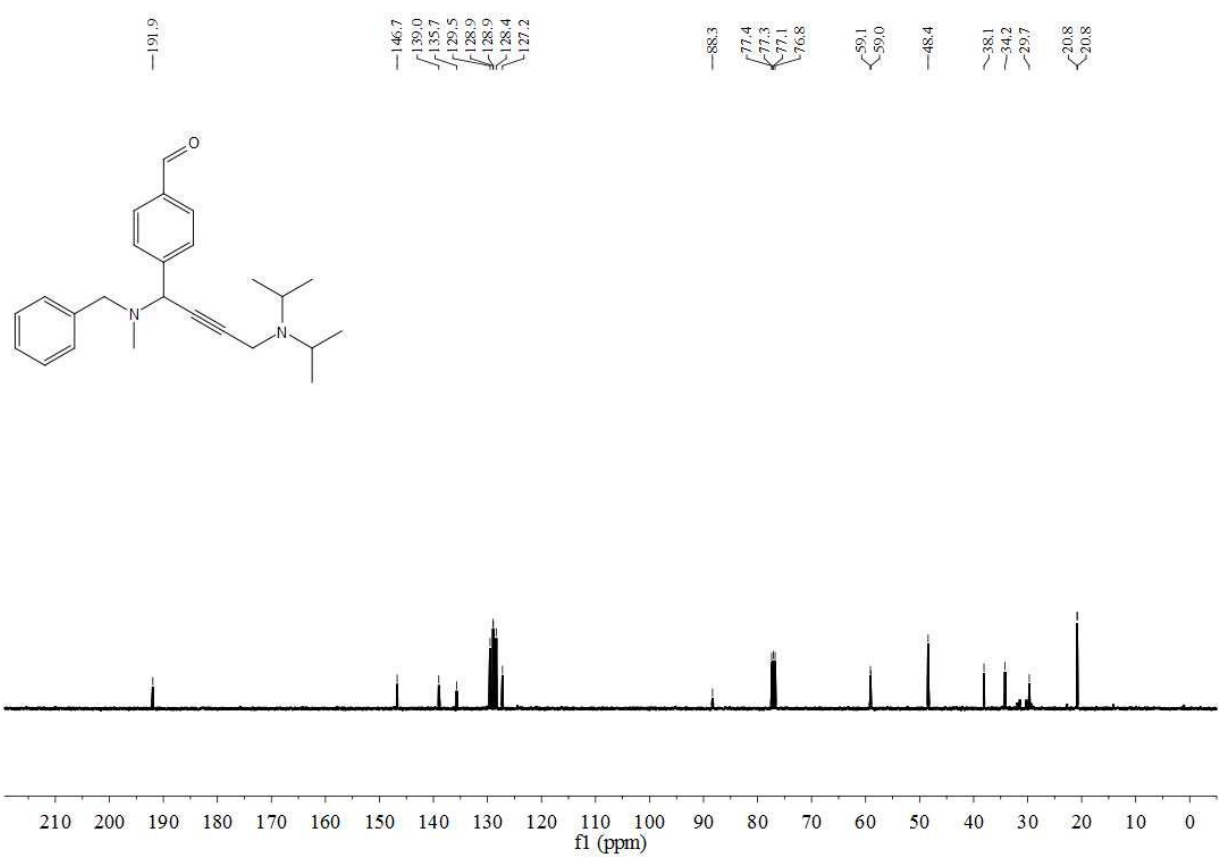


4-(1-(benzyl(methyl)amino)-4-(diisopropylamino)but-2-yn-1-yl)benzonitrile (6o).

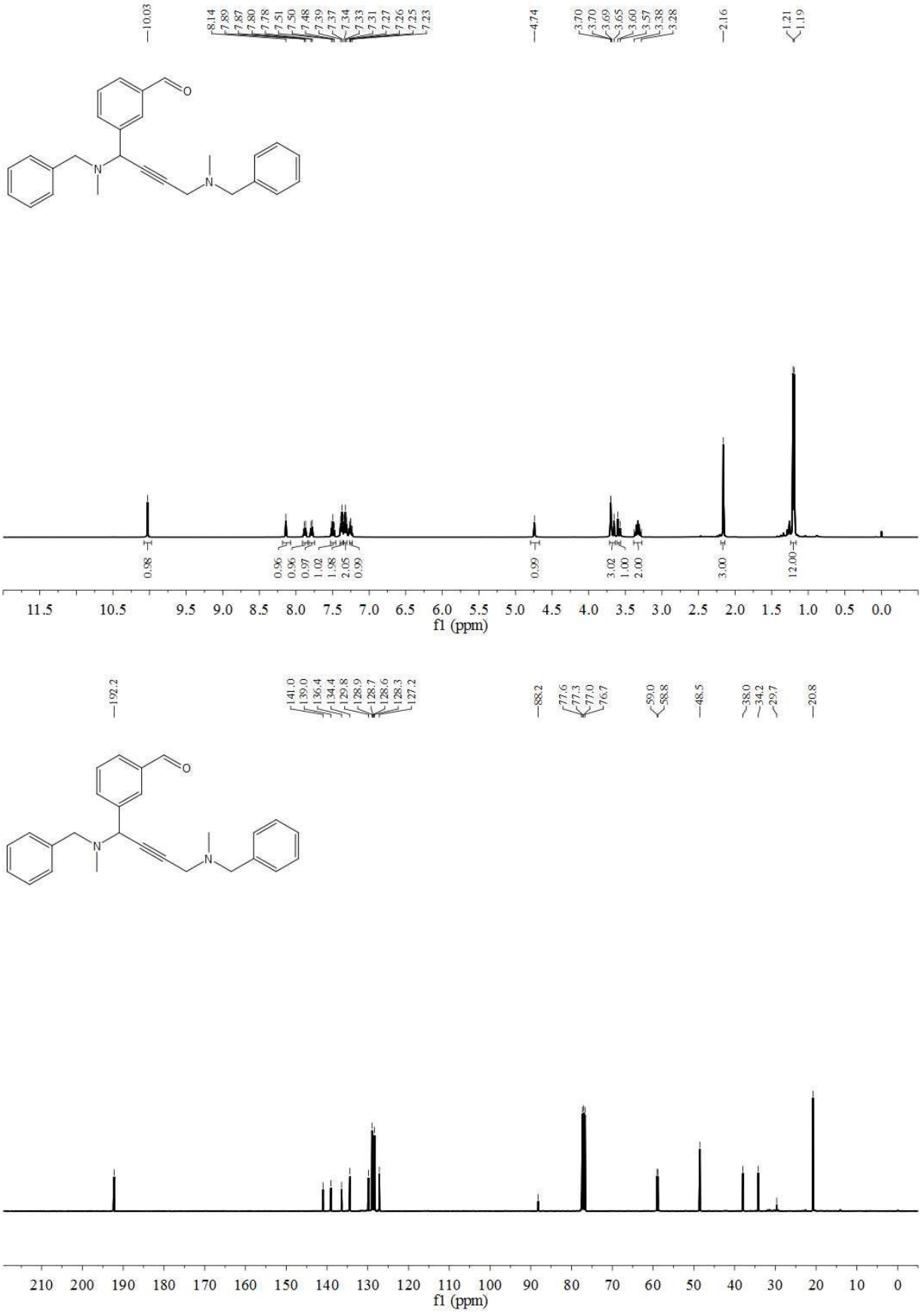


4-(1-(benzyl(methyl)amino)-4-(diisopropylamino)but-2-yn-1-yl)benzaldehyde (6p).

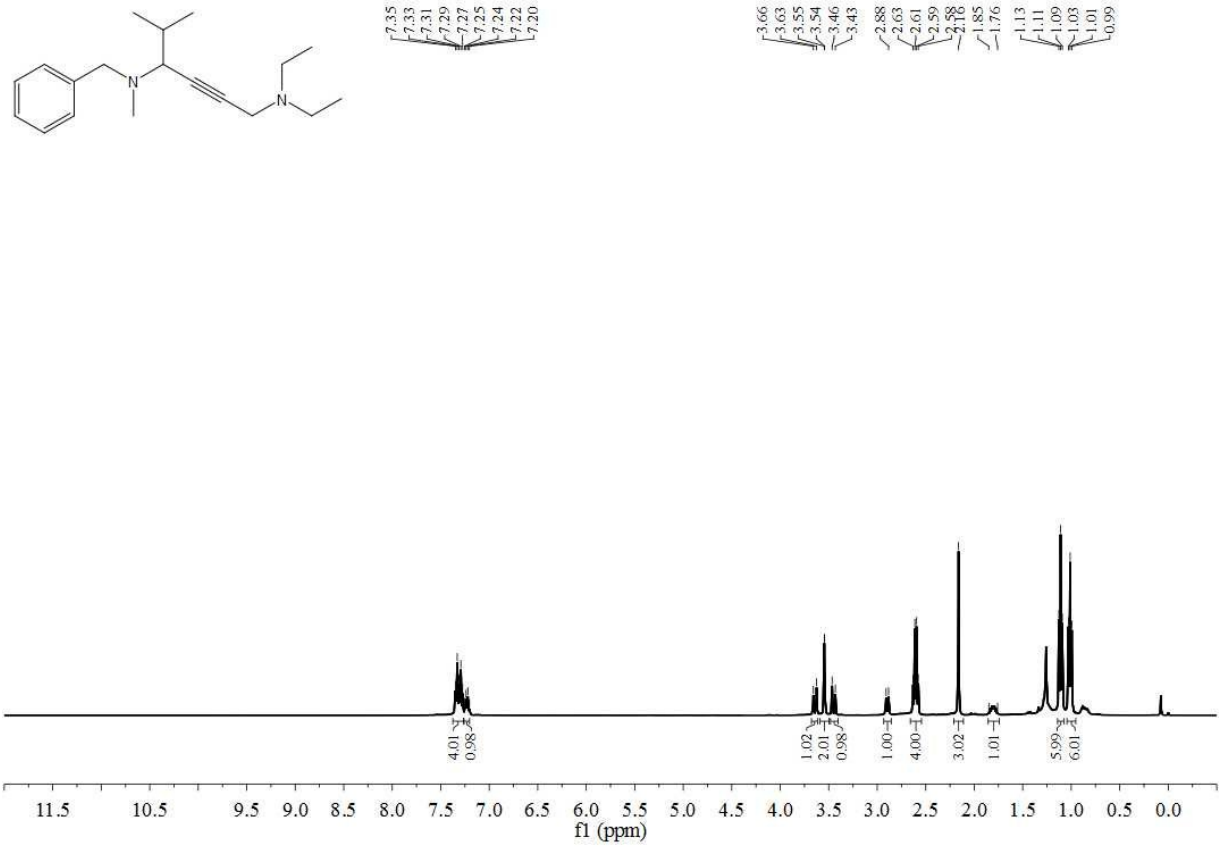


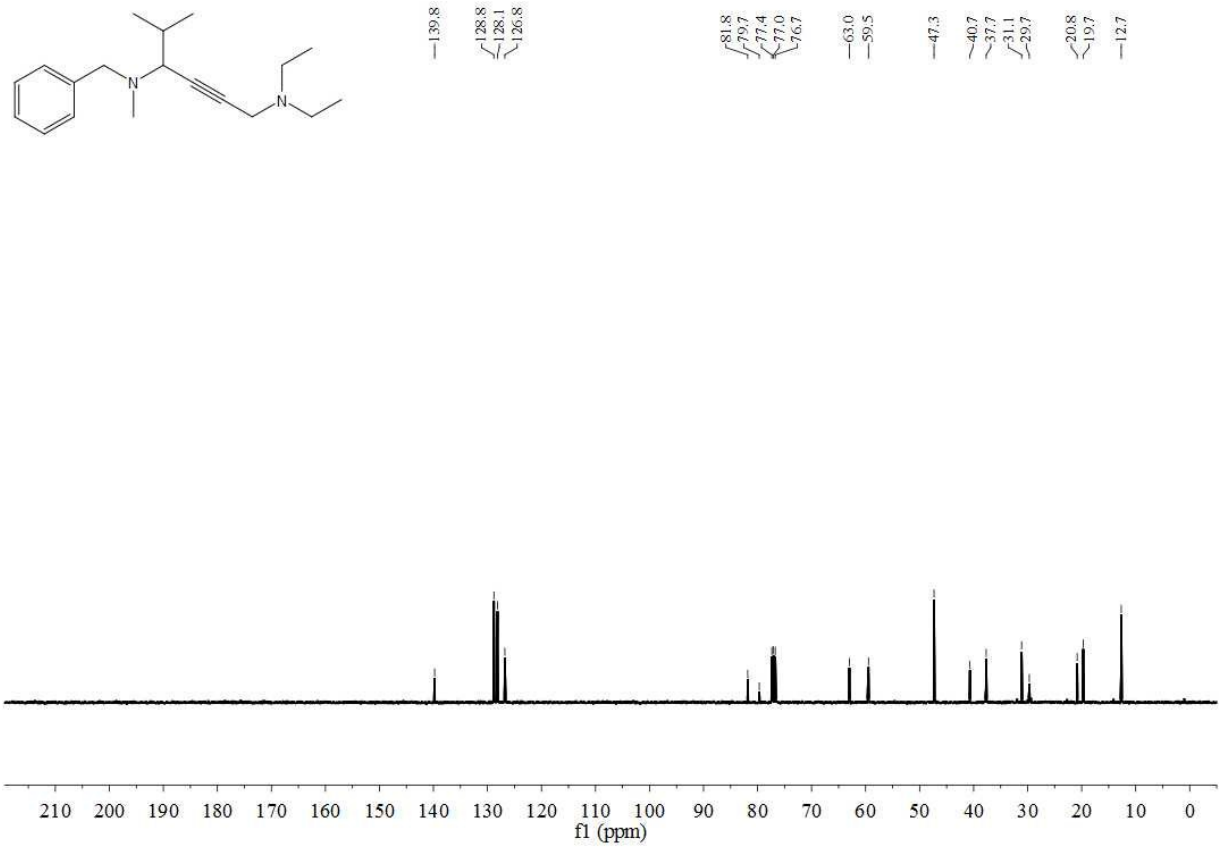


3-(1-(benzyl(methyl)amino)-4-(diisopropylamino)but-2-yn-1-yl)benzaldehyde (6q).

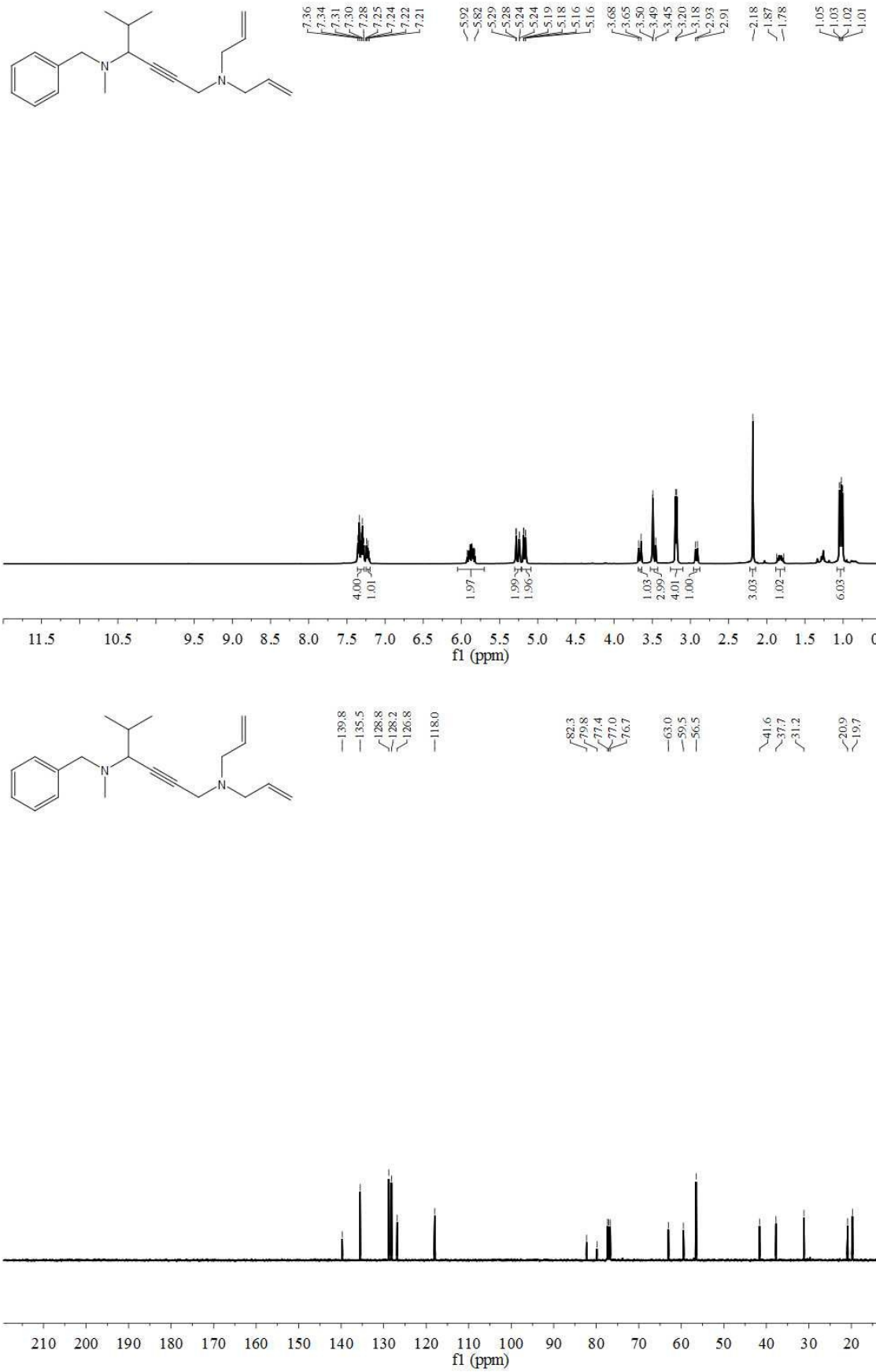


***N*⁴-benzyl-*N*¹,*N*¹-diethyl-*N*⁴,5-dimethylhex-2-yne-1,4-diamine (7a).**

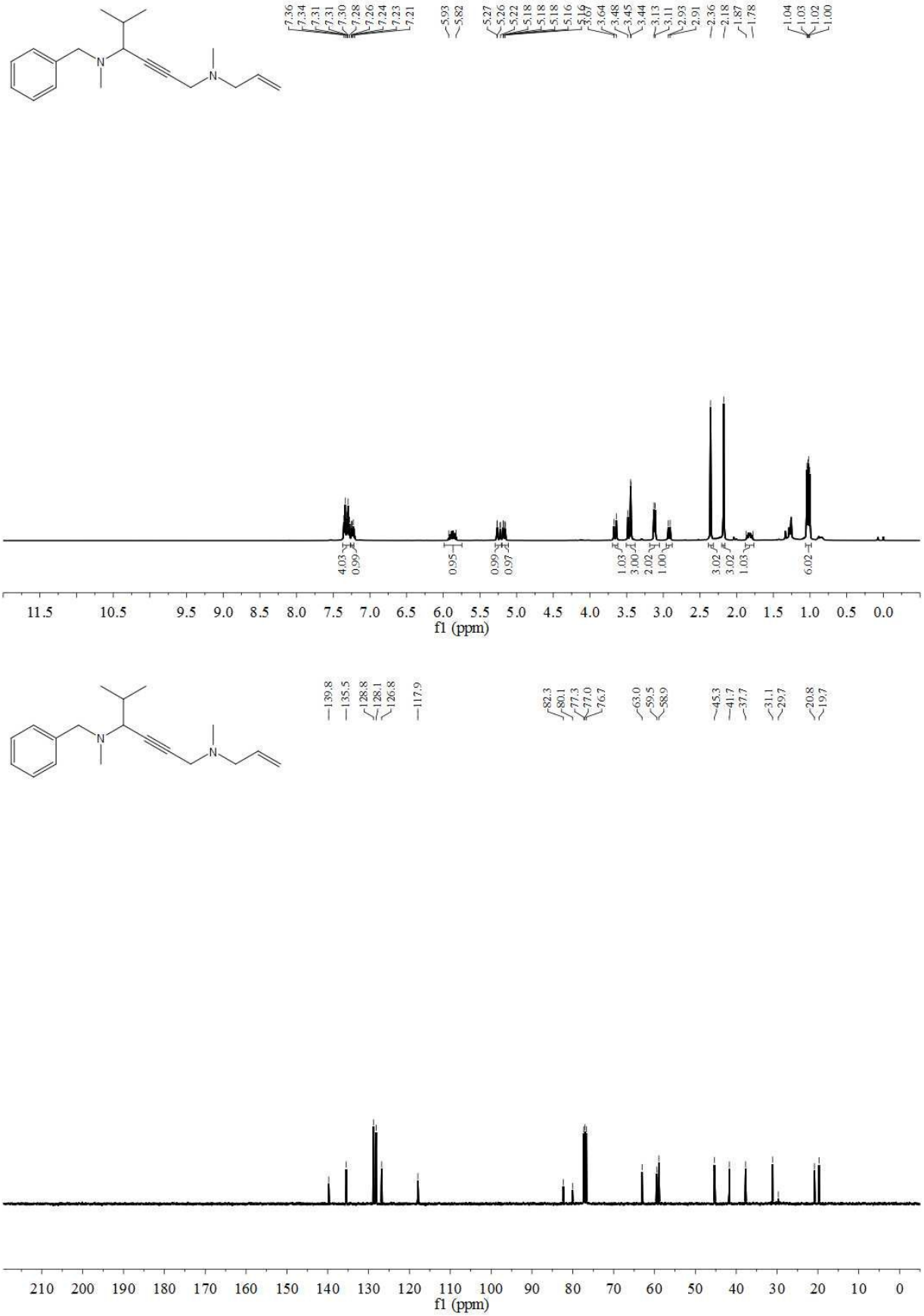




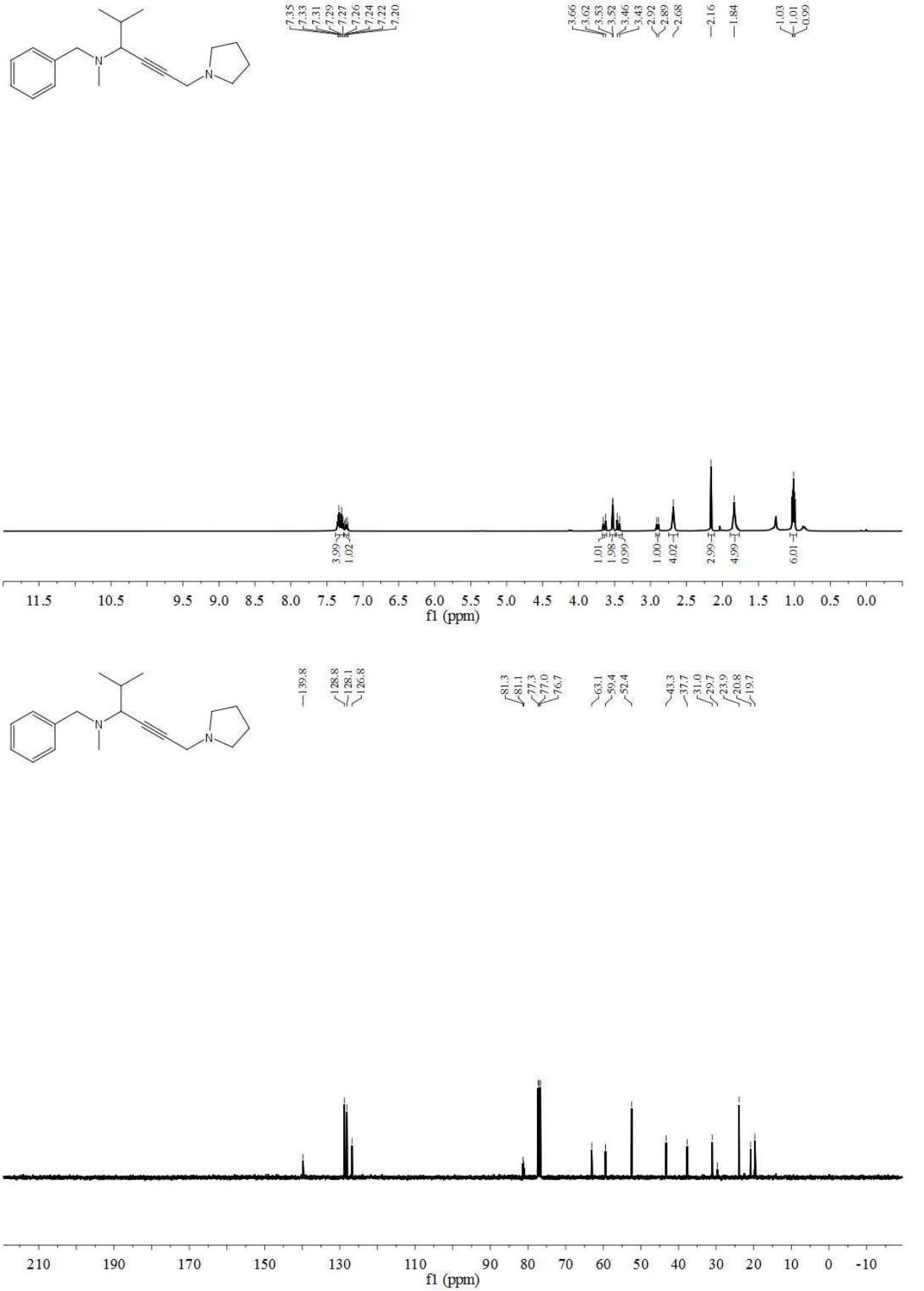
***N*[1],*N*[1]-diallyl-*N*[4]-benzyl-*N*[4],5-dimethylhex-2-yne-1,4-diamine (7b).**



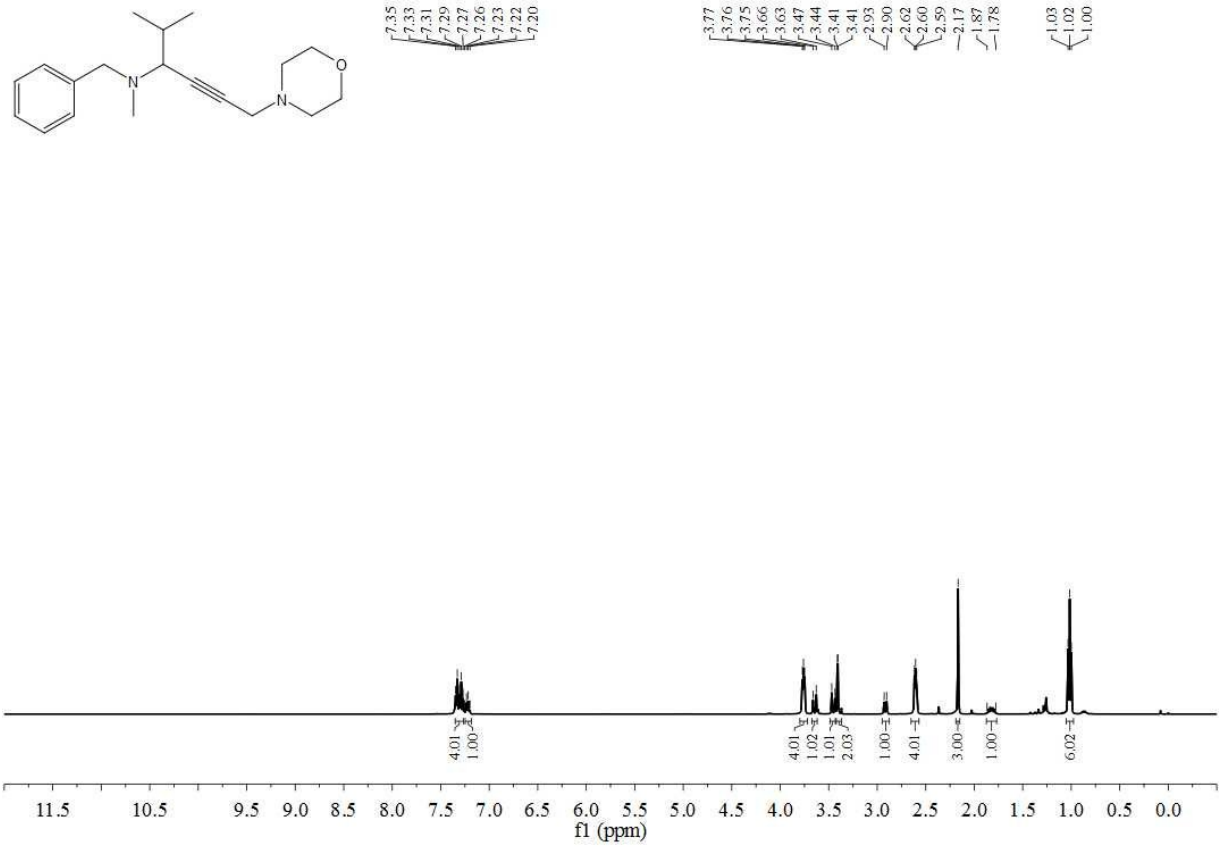
N*[1]*-allyl-N*[4]*-benzyl-N*[1]*,N*[4]*,5-trimethylhex-2-yne-1,4-diamine (7c).

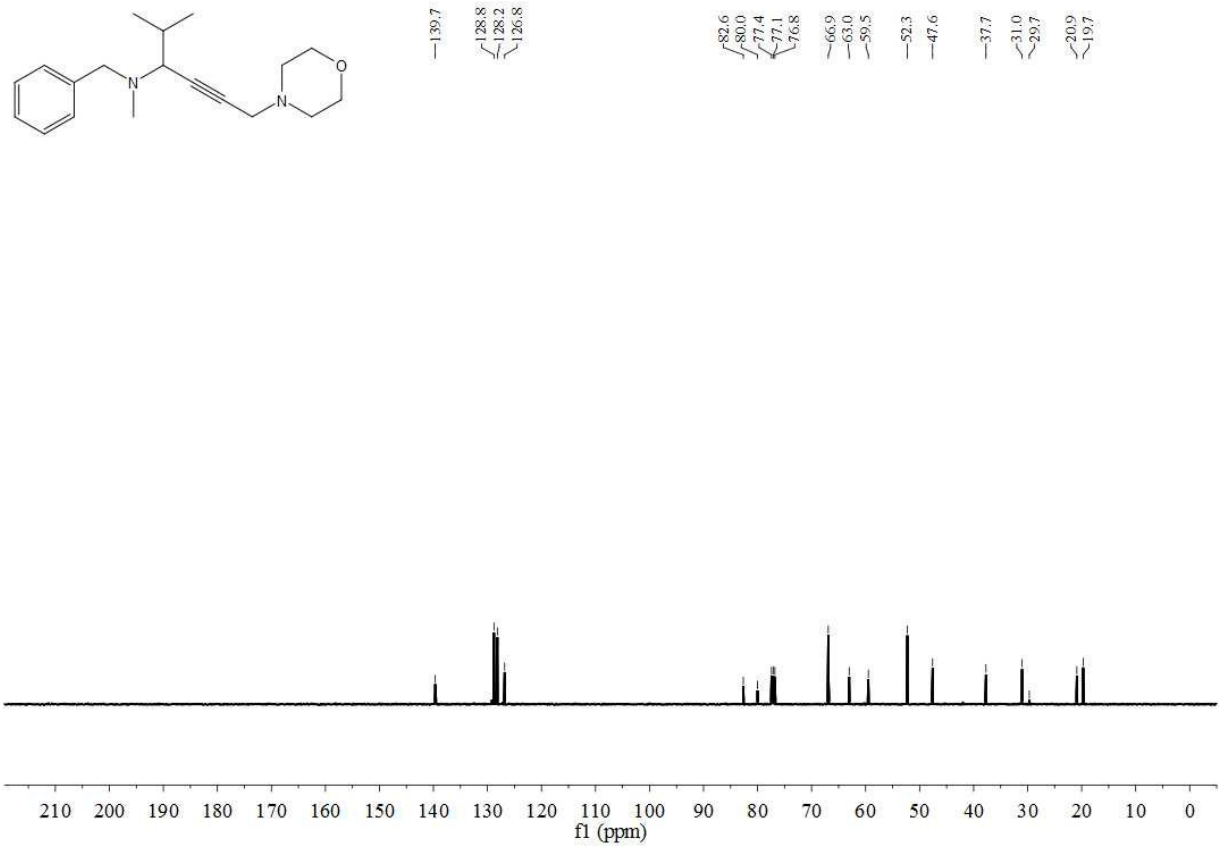


N-benzyl-N,2-dimethyl-6-(pyrrolidin-1-yl)hex-4-yn-3-amine (7d).

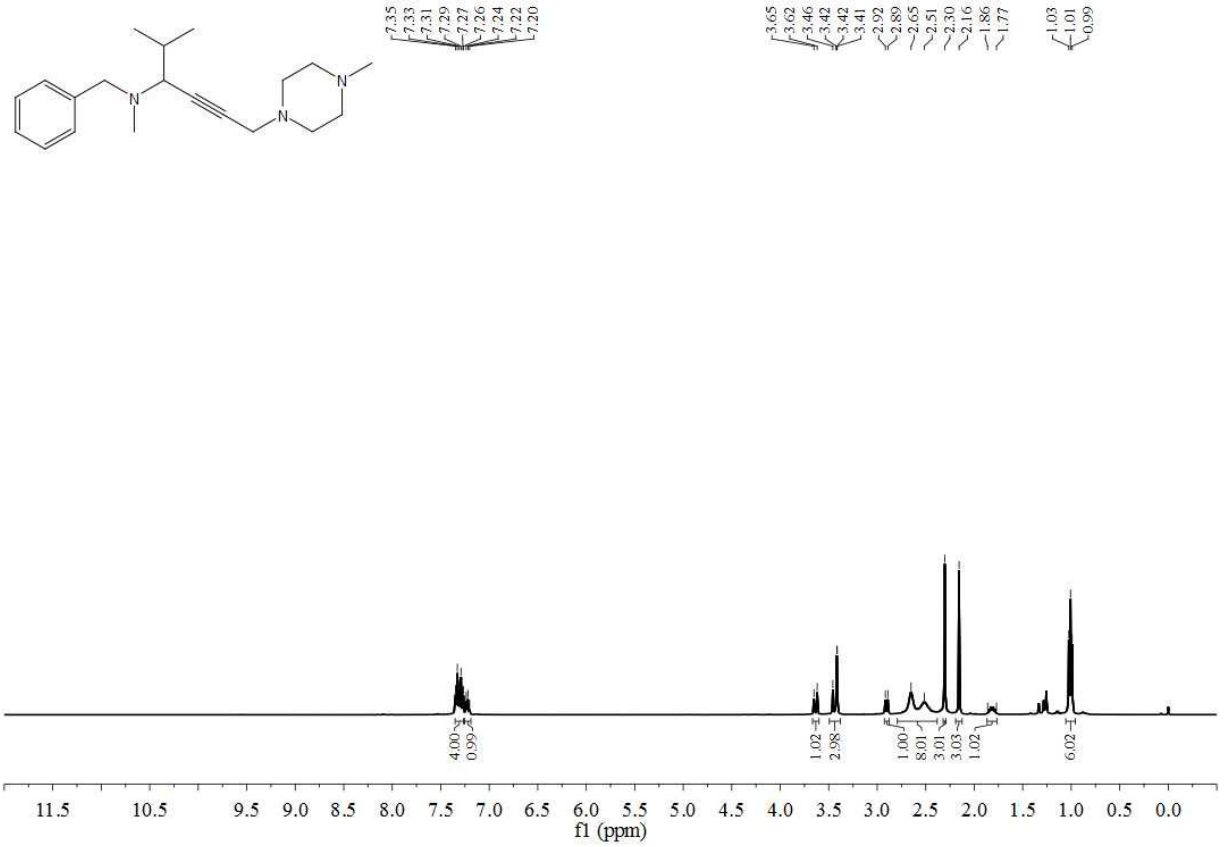


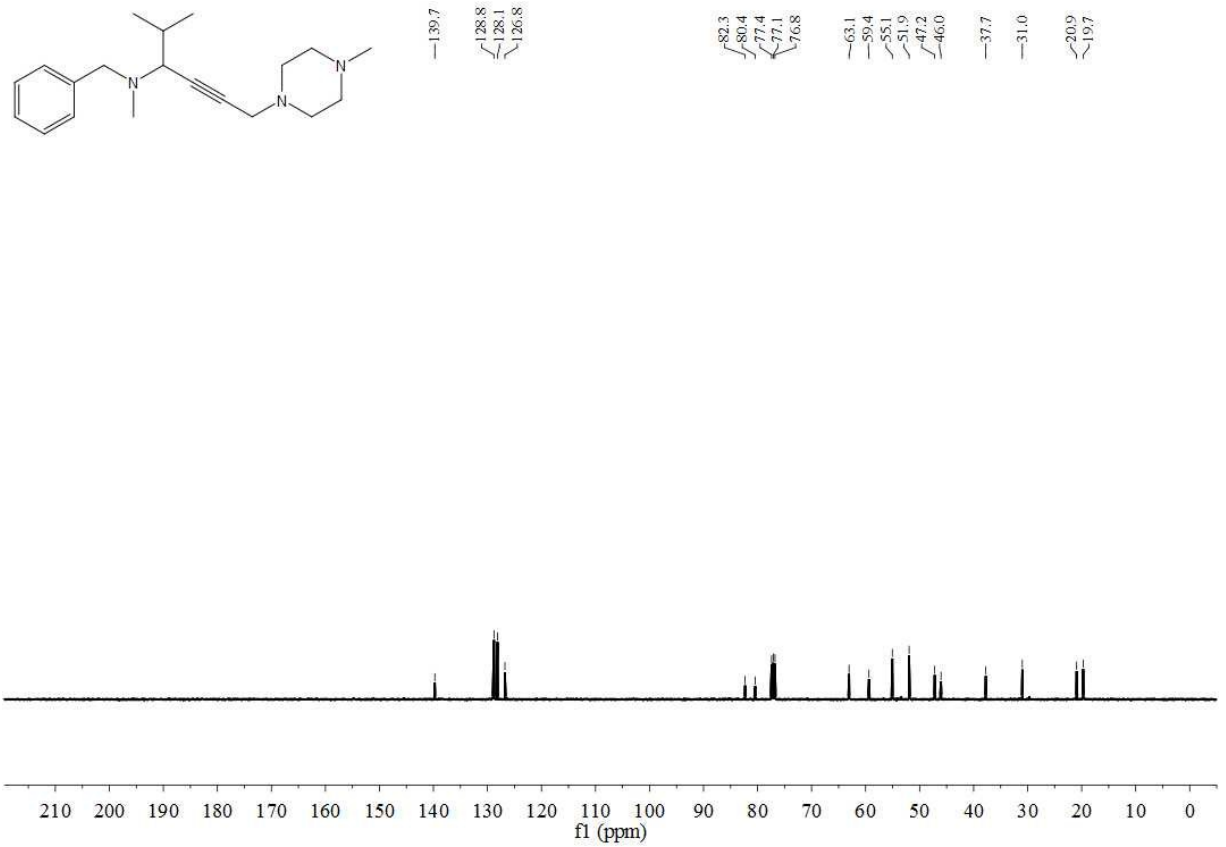
N-benzyl-N,2-dimethyl-6-morpholinohex-4-yn-3-amine (7e).



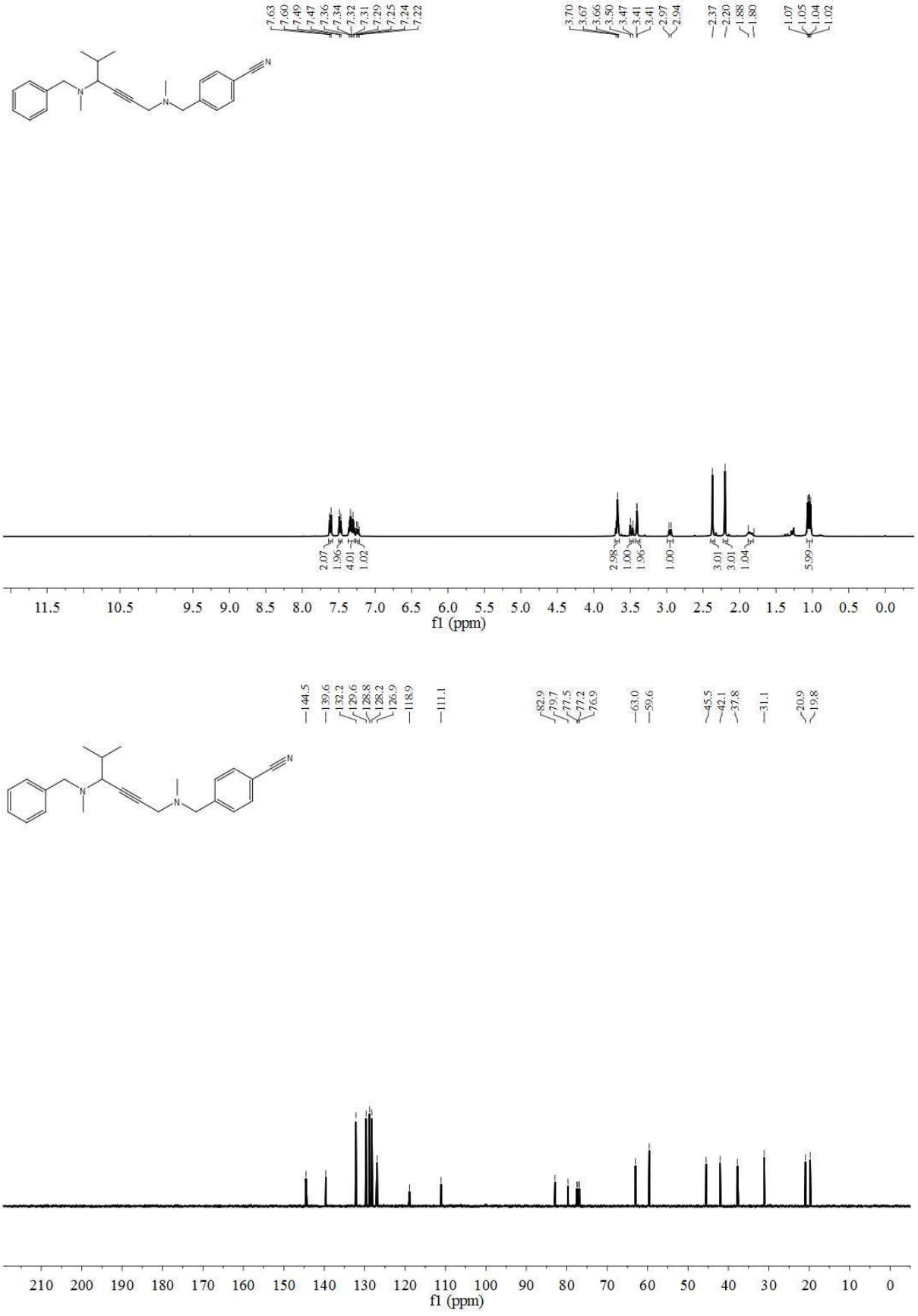


N-benzyl-N,2-dimethyl-6-(4-methylpiperazin-1-yl)hex-4-yn-3-amine (7f).

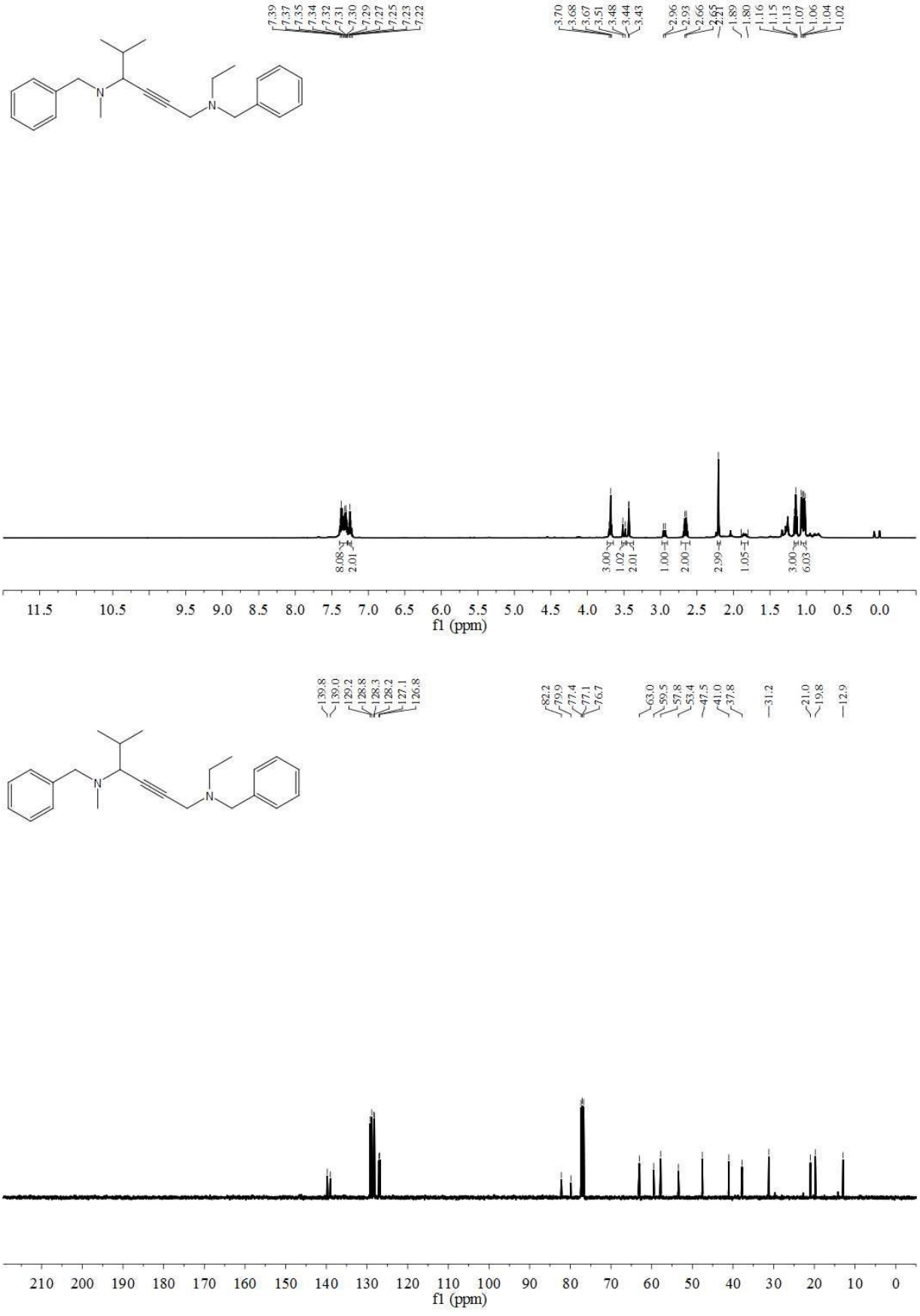




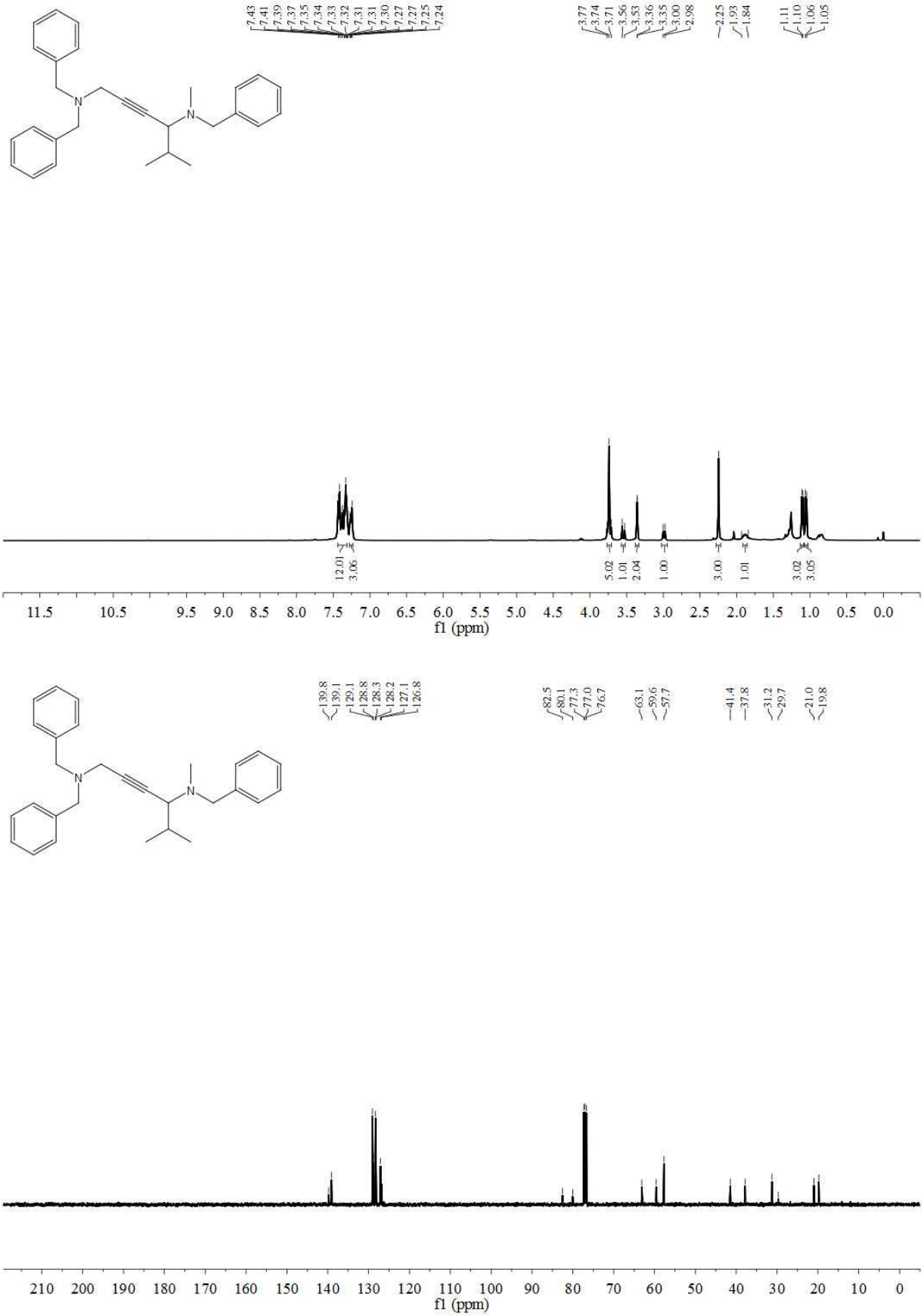
4-(((4-(benzyl(methyl)amino)-5-methylhex-2-yn-1-yl)(methyl)amino)methyl)benzonitrile (7g).



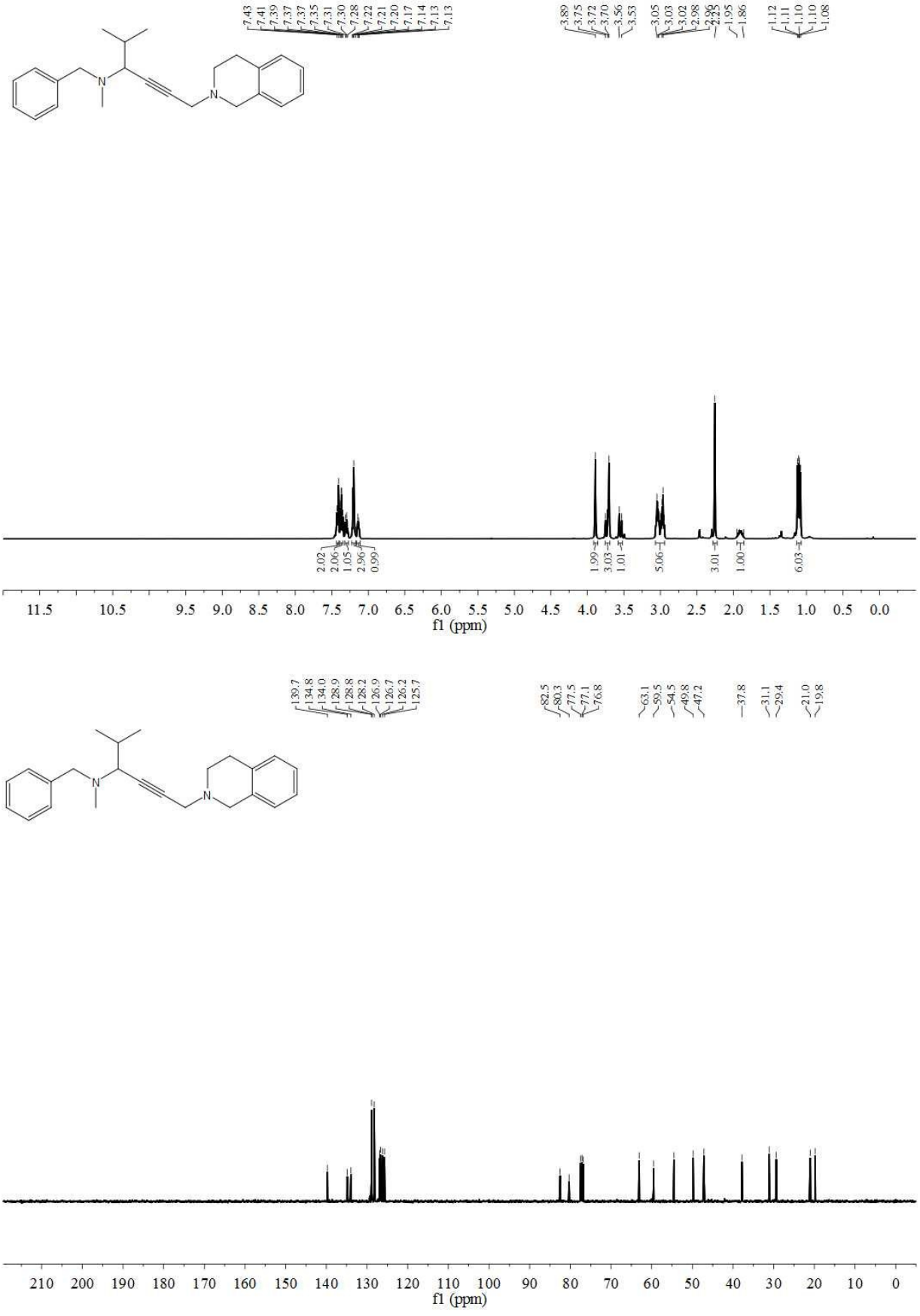
***N*[1],*N*[4]-dibenzyl-*N*[1]-ethyl-*N*[4],5-dimethylhex-2-yne-1,4-diamine (7h).**



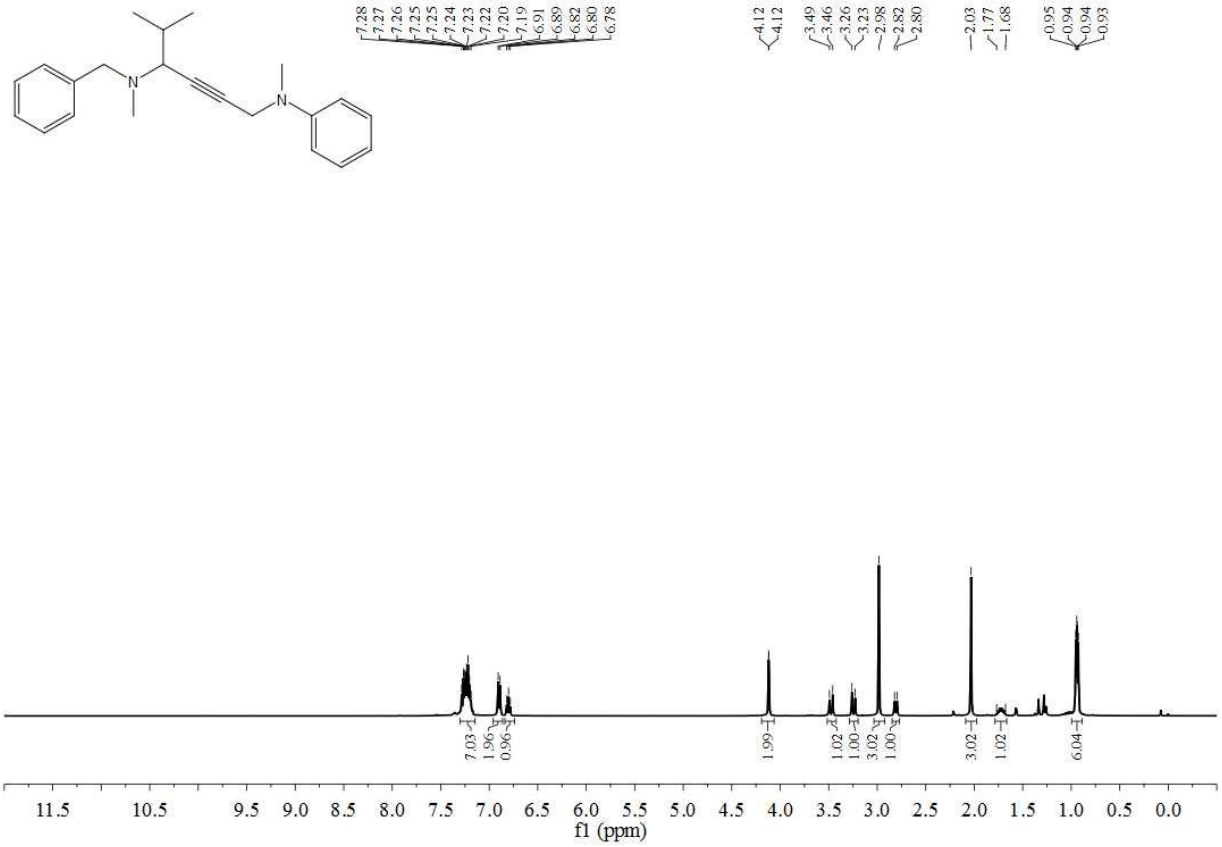
***N*[1],*N*[1],*N*[4]-tribenzyl-*N*[4],5-dimethylhex-2-yne-1,4-diamine (7i).**

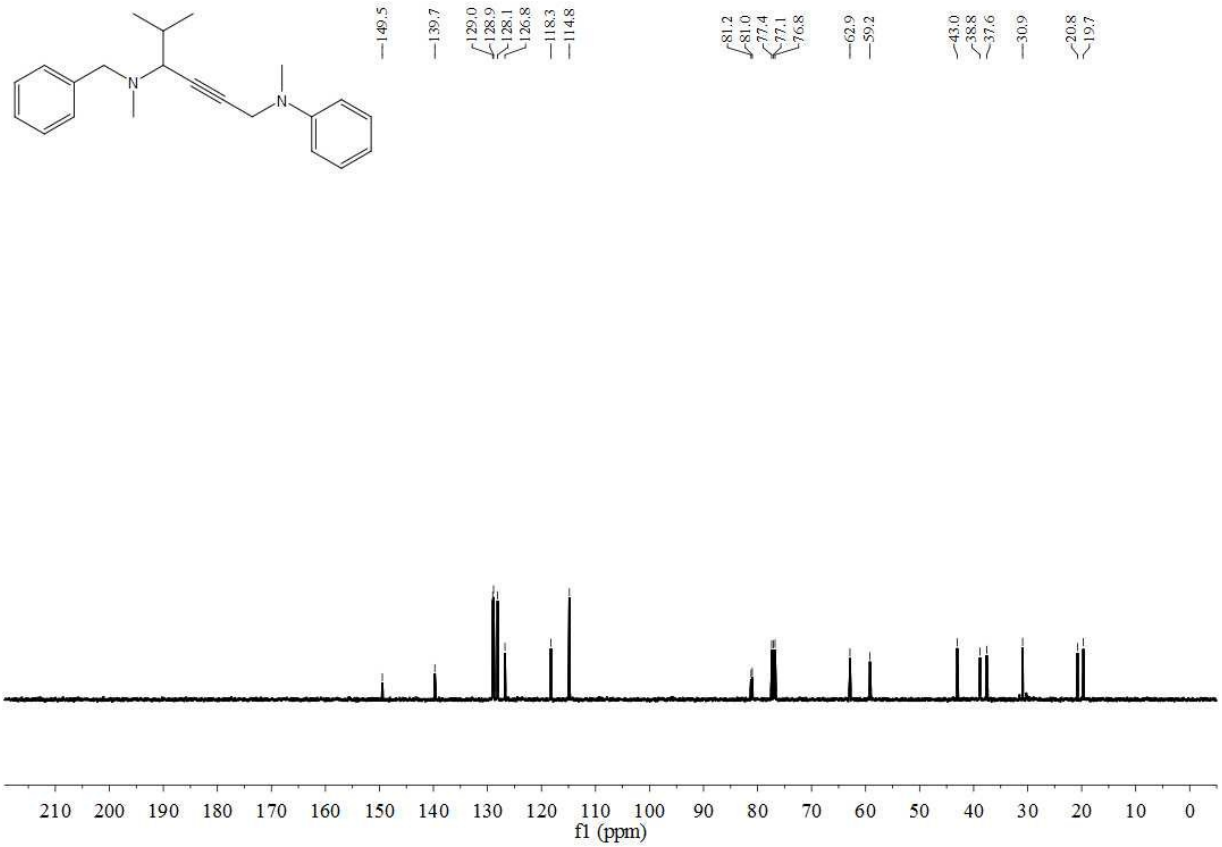


N-benzyl-6-(3,4-dihydroisoquinolin-2(1H)-yl)-N,2-dimethylhex-4-yn-3-amine (7j).

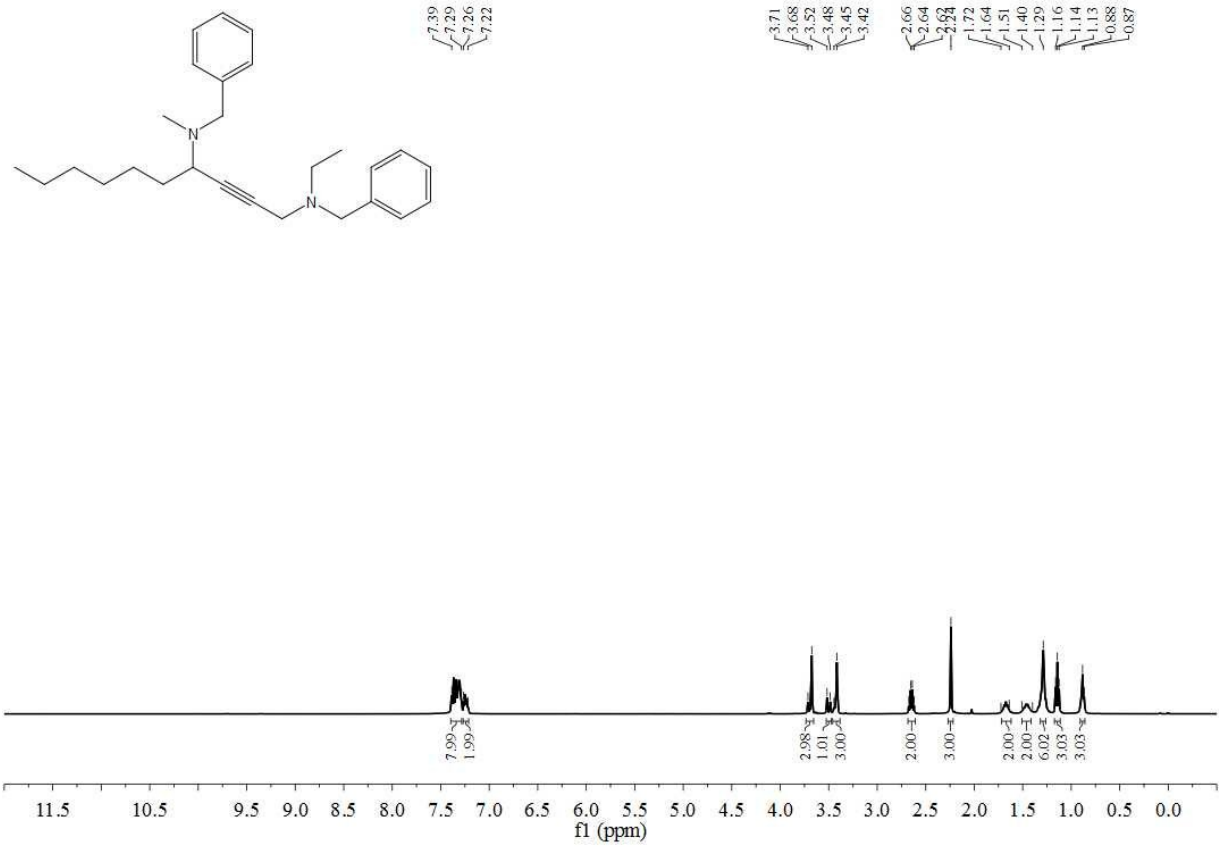


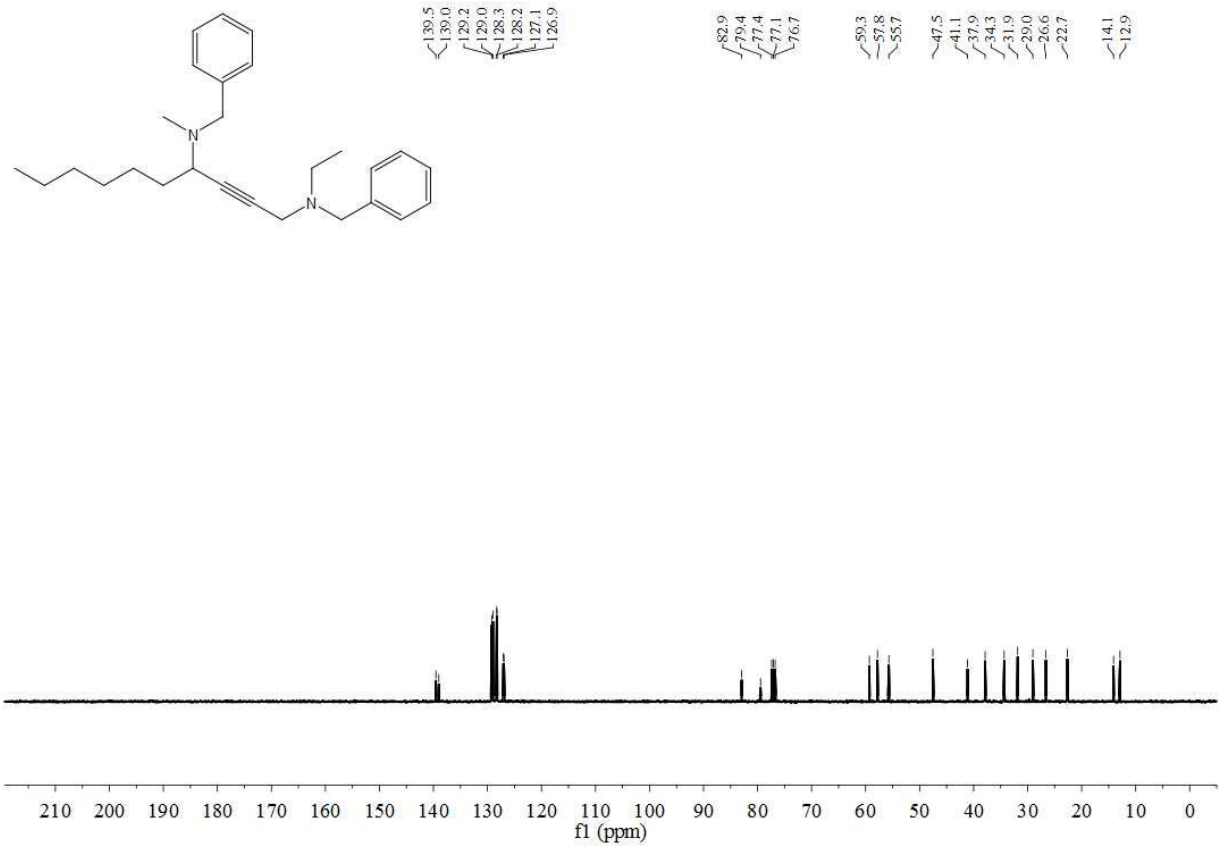
***N*⁴-benzyl-*N*¹,*N*⁴,5-trimethyl-*N*¹-phenylhex-2-yne-1,4-diamine (7k).**



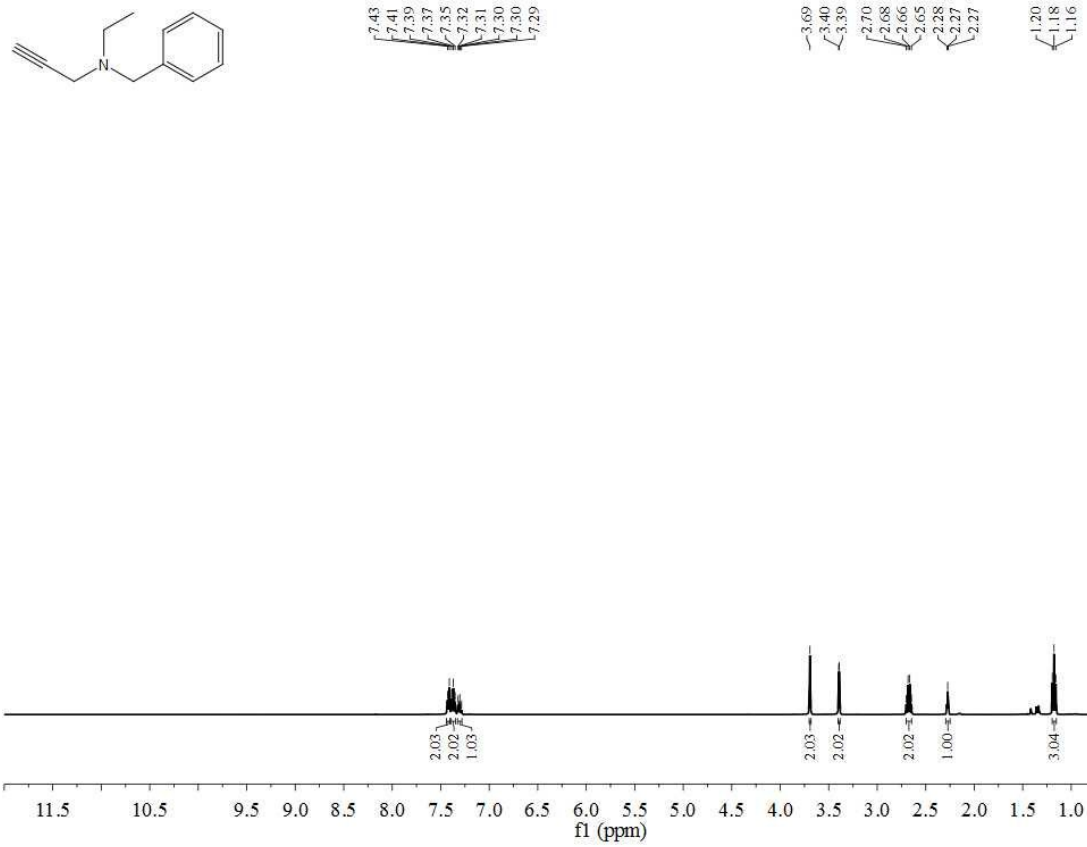


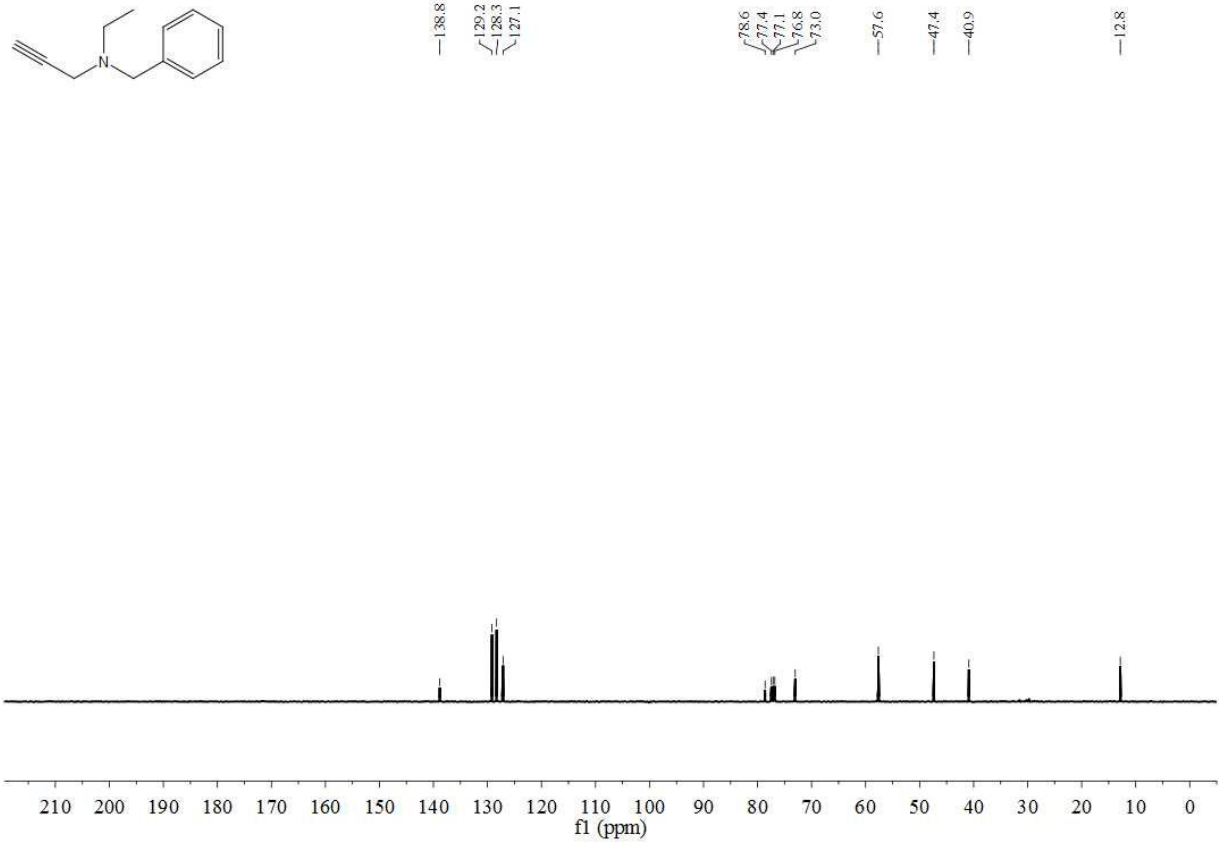
N^1,N^4-dibenzyl-N^1-ethyl-N^4-methyldec-2-yne-1,4-diamine (7m).





N-benzyl-N-ethylprop-2-yn-1-amine (9b).





N^1,N^4-dibenzyl-N^1-ethyl-N^4-methylbut-2-yne-1,4-diamine (10).