The First Silver-Catalyzed Three-Component-Coupling of Aldehyde, Alkyne, and Amines

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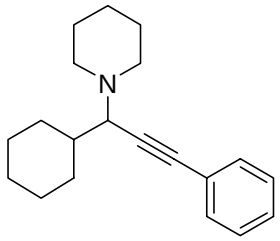
Supporting Information

All experiments were carried out under an inert atmosphere of nitrogen. Water was deoxygenated by nitrogen. Flash column chromatography was performed over SORBENT silica gel 30-60μm. ^{1}H-NMR and ^{13}C-NMR spectra were acquired by Varian 400 MHz and 100 MHz, respectively, and referenced to the internal solvent signals. IR spectra were recorded by Thermo-Nicolet Interferometer. GC/MS data were obtained by HP 5890 Series II Gas Chromatograph & HP5989A Mass Spectrometer. HRMS were made by Bin Xin of Institute of Chemistry, CAS.

A representative procedure: A mixture of AgI (7 mg, 0.03 mmol), cyclohexylcarboxaldehyde (244 μL, 2.0 mmol), piperidine (210 μL, 2.2 mmol), phenylacetylene (300 μL, 3 mmol) in water (1 mL) was stirred at 100ºC oil-bath for 2 h under N_2. The reaction mixture was cooled, extracted with ether (3x15 mL) and dried over $MgSO_4$. Analysis of the crude mixture by ^{1}H NMR showed a quantitative conversion of aldehyde. The product was isolated by flash chromatography on silica gel (eluent: hexane-EtOAc) to give the propargyl amine in almost quantitative yield (540mg, 96%).



1-(1-Cyclohexyl-3-phenyl-2-propynyl]piperidine.

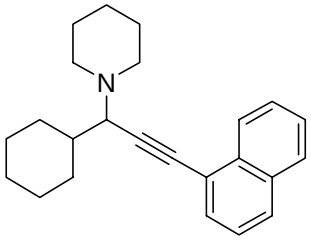
IR (neat, cm^{-1}): 3055(m), 2930(s), 2852(s), 2750(s), 1598(s), 1489(s), 1443(s), 1318(s), 1156(s), 1103(s), 890(m), 755(s), 691(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.45-7.41(m, 2H), 7.31-7.25(m, 3H), 3.10(d, *J*=10.0Hz, 1H), 2.66-2.58(m, 2H), 2.44-2.34(m, 2H), 2.14-1.98(m, 2H), 1.80-1.70(m, 2H), 1.70-1.48(m, 6H), 1.48-1.36(m, 2H), 1.34-1.10(m, 3H), 1.08-0.86(m, 2H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ131.94, 128.41, 127.84, 123.99, 87.99, 86.34, 64.59, 39.79, 31.56, 30.66, 27.03, 26.50, 26.33, 24.94;

GCMS *m/z* (relative intensity): 280[(M^+-1), 0.5], 241(1), 198(100), 141(2), 115(19);

HRMS calcd for $C_{20}H_{28}N$ (M+1) 282.2216, found 282.2216.



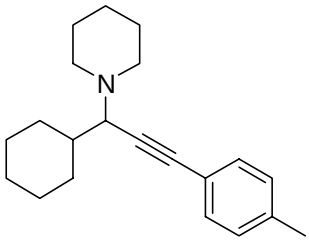
1-[1-Cyclohexyl-3-(1-naphathyl)-2-propynyl]piperidine.

IR (neat, cm^{-1}): 3057(m), 2929(s), 2850(s), 2801(m), 2207(w), 1586(m), 1448(s), 1443(s), 1394(s), 1156(s), 1103(s), 797(m), 772(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ8.35(d, *J*=8.0Hz, 1H), 7.82(d, *J*=7.6Hz, 1H), 7.78(d, *J*=8.0Hz, 1H), 7.66(dd, J_1=6.8 Hz, J_2=1.2Hz 1H), 7.58-7.52(m, 1H), 7.52-7.47(m, 1H), 7.42-7.37(m, 1H), 3.25(d, *J*=10.4Hz, 1H), 2.75-2.67(m, 2H), 2.53-2.44(m, 2H), 2.24-2.16(m, 1H), 2.11-2.04(m, 1H), 1.82-1.52(m, 6H), 1.48-1.40(m, 2H), 1.34-0.92(m, 5H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ 133.71, 133.52, 130.73, 128.55, 128.34, 126.86, 126.68, 126.53, 125.53, 121.84, 93.22, 84.42, 65.03, 51.17, 40.08, 31.87, 30.80, 27.15, 26.67, 26.64, 26.44, 25.13;

GCMS *m/z* (relative intensity): 330[(M^+-1), 0.5], 300(0.5), 248(100), 165(31), 152(9).



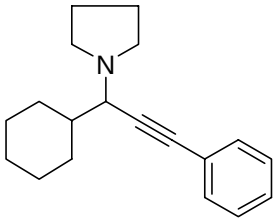
1-[1-Cyclohexyl-3-(4-methylphenyl)-2-propynyl]piperidine.

IR (neat, cm^{-1}): 3026(m), 2930(s), 2852(s), 2750(s), 2180(w), 1509(s), 1449(s), 1317(s), 1262(s), 1156(s), 1103(s), 996(m), 815(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.31(d, *J*=8.0Hz, 2H), 7.08(d, *J*=8.0Hz, 2H), 3.07(d, *J*=10.0Hz, 1H), 2.64-2.56(m, 2H), 2.42-2.34(m, 2H), 2.32(s, 3H), 2.12-1.96(m, 2H), 1.78-1.68(m, 2H), 1.65-1.47(m, 6H), 1.46-1.36(m, 2H), 1.32-1.10(m, 3H), 1.07-0.85(m, 2H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ 137.78, 131.85, 129.17, 121.00, 87.15, 86.42, 64.68, 51.00, 39.87, 31.63, 30.71, 27.12, 26.59, 26.58, 26.41, 25.03, 21.67;

GCMS *m/z* (relative intensity): 294[(M^+-1), 0.5], 252(1), 212(100), 129(19), 115(5).



1-[1-Cyclohexyl-3-(4-methylphenyl)-2-propynyl]pyrrodine.

IR (neat, cm^{-1}): 3055(m), 2925(s), 2852(s), 2193(w), 1598(s), 1489(s), 1448(s), 1260(s), 1130(s), 755(s), 691(s);

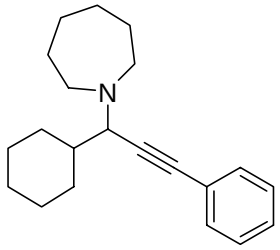
^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.46-7.41(m, 2H), 7.31-7.25(m, 3H), 3.36(d, *J*=10.4Hz, 1H), 2.81-2.71(m, 2H), 2.70-2.62(m, 2H), 2.14-2.06(m, 2H), 2.01-

1.93(m, 2H), 1.84-1.73(m, 4H), 1.72-1.64(m, 1H), 1.64-1.53(m, 1H), 1.31-0.86(m, 5H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ131.94, 128.43, 127.95, 123.87, 88.06, 86.02, 61.47, 50.26, 41.56, 30.93, 30.52, 26.94, 26.48, 26.46, 23.77;

GCMS *m/z* (relative intensity): 268[(M^+-1), 0.5], 184(100), 128(6), 115(31);

HRMS calcd for $C_{19}H_{26}N$ (M+1) 268.2060, found 268.2059.



1-[1-Cyclohexyl-3-(4-methylphenyl)-2-propynyl]hexamethylamine.

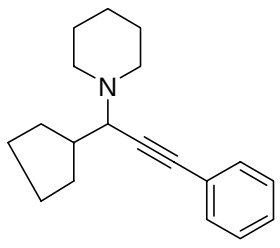
IR (neat, cm^{-1}): 3078(m), 2923(s), 2850(s), 2755(m), 2200(w), 1598(s), 1489(s), 1448(s), 1316(s), 1160(s), 1119(s), 755(s), 691(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.46-7.41(m, 2H), 7.32-7.26(m, 3H), 3.18(d, *J*=10.0Hz, 1H), 2.86-2.77(m, 2H), 2.64-2.54(m, 2H), 2.23-2.08(m, 2H), 1.84-1.73(m, 2H), 1.73-1.59(m, 8H), 1.59-1.48(m, 1H), 1.37-1.14(m, 3H), 1.08-0.88(m, 2H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ131.94, 128.41, 127.77, 124.17, 89.15, 85.13, 65.49, 52.87, 41.04, 31.44, 30.92, 29.56, 27.40, 27.10, 26.54, 26.35;

GCMS *m/z* (relative intensity): 294[(M^+-1), 0.5], 212(100), 128(4), 115(16);

HRMS calcd for $C_{21}H_{30}N$ (M+1) 296.2373, found 296.2373.



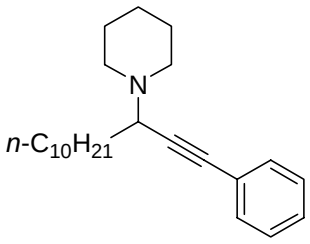
1-(1-Cyclopentyl-3-phenyl-2-propynyl)piperidine.

IR (neat, cm^{-1}): 3054(m), 2934(s), 2749(m), 1957(m), 1598(s), 1489(s), 1442(s), 1322(s), 1117(s), 754(s), 690(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm) δ 7.45-7.43(m, 2H), 7,29-7,27(m, 3H), 3.22(d, *J*=9.2Hz, 1H), 2.68-2.63(m, 2H), 2.45-2.39(m, 2H), 2.28-2.20(m, 1H), 1.90-1.74(m, 2H), 1.65-1.52(m, 7H), 1.51-1.40(m, 5H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm) δ 131.96, 128.41, 127.68, 124.00, 88.32, 85.76, 63.99, 42.63, 31.10, 30.65, 26.51, 25.67, 25.53, 24.91;

GCMS *m/z* (relative intensity): 266[(M^+-1), 0.5], 238(0.5), 224(0.5), 198(100), 141(2), 115(20).



1-(1-decyl-3-Phenyl-2-propynyl)piperidine.

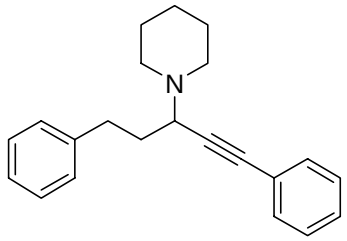
IR (neat, cm^{-1}): 2928(s), 2854(s), 2750(w), 1598(m), 1489(s), 1325(m), 1156(s), 1099(s), 755(s), 691(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.44-7.39(m, 2H), 7.31-7.25(m, 3H), 3.46(dd, J_1=8.0Hz, J_2=7.6 Hz, 1H), 2.72-2.62(m, 2H), 2.50-2.40(m, 2H), 1.78-1.48(m, 10H), 1.48-1.18(m, 14H), 0.86(t, *J*=6.8Hz, 3H);

^{13}C-NMR ($CDCl_3$, 400MHz, ppm): δ 131.93, 128.39, 127.93, 123.84, 88.46, 85.80, 58.85, 50.78, 33.71, 32.13, 29.83, 29.83, 29.77, 29.64, 29.57, 27.12, 26.43, 24.81, 22.90, 14.33;

GCMS *m/z* (relative intensity): 339(M^+, 1), 241(1), 198(100), 130(3), 115(9), 86(3), 84(4);

HRMS calcd for $C_{24}H_{38}N$ (M+1) 340.3000, found 340.2998.



1-[3-Phenyl-1-(2-phenylethyl)-2-propynyl]piperidine.

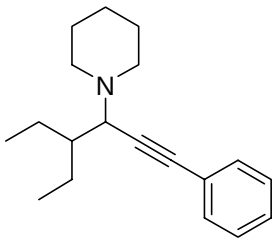
IR (neat, cm^{-1}): 3061(m), 2933(s), 2852(s), 2751(s), 1687(m), 1599(m), 1489(s), 1453(s), 1324(m), 1102(s), 755(s), 692(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.47-7.53(m, 2H), 7.34-7.20(m, 8H), 3.47(dd, J_2=8.0Hz, J_2=7.6Hz, 1H), 2.89-2.80(m, 1H), 2.80-2.71(m, 1H), 2.71-2.62(m, 2H), 2.51-2.42(m, 2H), 2.08-1.98(m, 2H), 1.70-1.52(m, 4H), 1.52-1.40(m, 2H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ142.11, 132.05, 128.94, 128.94, 128.64 (two signals overlap), 128.55, 128.16, 126.14, 123.79, 88.06, 86.35, 57.86, 50.85, 35.39, 33.19, 26.54, 24.91;

GCMS *m/z* (relative intensity): 303(M^+, 1), 198(100), 128(4), 115(21), 91(10), 65(2);

HRMS calcd for $C_{22}H_{26}N$ (M+1) 304.2060, found 304.2061.



1-[1-(1-Ethylpropyl)-3-phenyl-2-propynyl]piperidine.

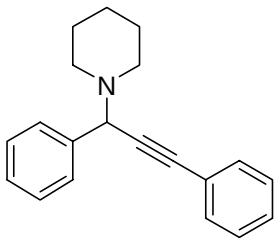
IR (neat, cm^{-1}): 3076(m), 2933(s), 2804(s), 2749(m), 1598(m), 1489(s), 1453(s), 1322(m), 1158(m), 1094(m), 755(s), 691(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.45-7.40(m, 2H), 7.32-7.25(m, 3H), 3.22(d, *J*=10.0Hz, 1H), 2.66-2.57(m, 2H), 2.44-2.35(m, 2H), 1.78-1.66(m, 1H), 1.66-1.50(m, 6H), 1.50-1.38(m, 4H), 0.90(t, *J*=7.6Hz, 3H), 0.84(t, *J*=7.6Hz, 3H);

^{13}C-NMR ($CDCl_3$, 400MHz, ppm): δ131.94, 128.42, 127.81, 124.11, 88.32, 86.12, 61.69, 61.63, 41.70, 26.58, 25.00, 22.64, 21.03, 10.96, 10.02;

GCMS *m/z* (relative intensity): 268[(M^+-1), 0.5], 241(1), 198(100), 141(2), 115(21), 86(1), 84(2);

HRMS calcd for $C_{19}H_{28}N$ (M+1) 270.2216, found 270.2216.



***N*-(1,3-Diphenyl-2-propynyl)piperidine. CA Registry Number: [1036-21-1]**

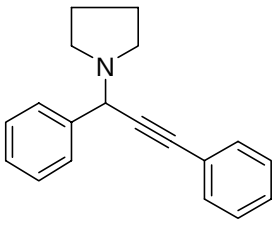
IR (neat, cm^{-1}): 3060(m), 2933(s), 2749(m), 1598(s), 1489(s), 1450(s), 1321(s), 1154(s), 756(s), 691(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.67-7.62(m, 2H), 7.55-7.50(m, 2H), 7.40-7.26(m, 6H), 4.81(s, 1H), 2.61-2.50(m, 4H), 1.70-1.50(m, 4H), 1.50-1.40(m, 2H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ 138.89, 132.05, 128.75, 128.50, 128.29 (two signals overlap), 127.66, 123.59, 88.01, 86.34, 62.63, 59.93, 26.44, 24.69;

GCMS *m/z* (relative intensity): 275(M^+, 27), 274(14), 232(7), 198(90), 191(100), 165(8), 115(10), 84(7);

HRMS calcd for $C_{20}H_{22}N$ (M+1) 276.1747, found 276.1748.



***N*-(1,3-Diphenyl-2-propynyl)pyrrolidine.**

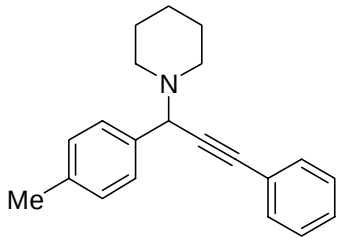
IR (neat, cm^{-1}): 3077(m), 2966(s), 2807(s), 2694(w), 1683(w), 1599(m), 1489(s), 1344(m), 1128(s), 1071(s), 756(s), 692(s) cm^{-1};

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.68-7.64(m, 2H), 7.57-7.51(m, 2H), 7.44-7.37(m, 2H), 7.37-7.30(m, 4H), 4.93(s, 1H), 2.80-2.68(m, 4H), 1.90-1.78(m, 4H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ 139.82, 132.09, 128.56 (three signals overlap), 128.38, 127.86, 123.51, 87.19, 87.01, 59.45, 59.36, 50.57, 23.76;

GCMS *m/z* (relative intensity): 261(M^+, 25), 274(13), 232(7), 198(100), 184(65), 165(8), 115(13), 70(4);

HRMS calcd for $C_{19}H_{20}N$ (M+1) 262.1590, found 262.1592.



***N*-[1-(4-Methylphenyl)-3-phenyl-2-propynyl]piperidine.**

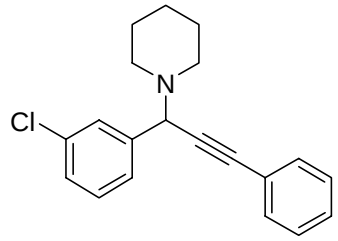
IR (neat, cm^{-1}): 2933(s), 2804(s), 2748(m), 1598(m), 1510(s), 1318(s), 1154(s), 1092(s), 847(m), 755(s), 691(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.61-7.56(m, 4H), 7.42-7.34(m, 3H), 7.23(d, *J*=8.0Hz, 2H), 4.83(s, 1H), 2.68-2.56(m, 4H), 2.42(s, 3H), 1.73-1.58(m, 4H), 1.58-1.45(m, 2H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ 137.36, 135.90, 132.10, 129.06, 128.77, 128.57, 128.30, 123.72, 87.92, 86.70, 62.48, 62.41, 50.99, 26.52, 24.80, 21.44;

GCMS *m/z* (relative intensity): 289(M^+, 22), 288(9), 205(100), 198(33), 189(8), 165(3), 115(7), 84(7);

HRMS calcd for $C_{21}H_{24}N$ (M+1) 290.1903, found 290.1906.



***N*-[1-(3-Chlorophenyl)-3-phenyl-2-propynyl]piperidine.**

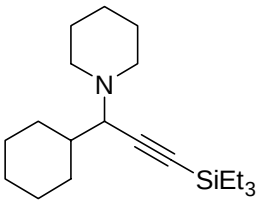
IR (neat, cm^{-1}): 3060(m), 2934(s), 2852(s), 2749(s), 1596(s), 1489(s), 1317(s), 1155(s), 1097(s), 862(m), 794(s), 754(s), 689(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 7.74-7.72(m, 1H), 7.62-7.55(m, 3H), 7.41-7.34(m, 3H), 7.34-7.29(m, 2H), 4.82(s, 1H), 2.65-2.55(m, 4H), 1.72-1.57(m, 4H), 1.57-1.47(m, 2H);

^{13}C-NMR ($CDCl_3$, 100MHz, ppm): δ 141.29, 134.37, 132.14, 129.61, 128.82, 128.76, 128.63, 128.54, 127.93, 126.89, 123.35, 88.68, 85.39, 62.22, 62.13, 50.97, 26.48, 24.69;

GCMS *m/z* (relative intensity): 311(M^+, 6), 309(M^+, 18), 308(8), 266(6), 227(19), 225(57), 198(100), 188(26), 115(12), 84(10);

HRMS calcd for $C_{20}H_{21}ClN$ (M+1) 310.1357, found 310.1350.



1-(1-cyclohexyl-3-triethylsilyl-2-propynyl]piperidine.

IR(neat, cm^{-1}): 3308(m), 2932(s), 2852(s), 2804(m), 2156(m), 1450(s), 1310(m), 1230(s), 1103(s), 999(s), 727(s);

^{1}H-NMR ($CDCl_3$, 400MHz, ppm): δ 2.88(d, *J*=9.6 Hz, 1H), 2.55-2.47(m, 2H), 2.33-2.25(m, 2H), 2.06-1.90(m, 2H), 1.76-1.34(m, 11H), 1.29-1.08(m, 3H), 0.98(t, *J*=8.0Hz, 9H), 0.96-0.79(m, 1H), 0.56(q, *J*=8.0Hz, 6H);

^{13}C-NMR ($CDCl_3$, 400MHz, ppm): δ 105.32, 86.86, 64.82, 50.55, 39.65, 31.44, 30.54, 27.01, 26.46, 26.46, 26.29, 24.97, 7.85, 4.88;

GCMS *m/z* (relative intensity): 318[(M^+-1), 0.5], 290(0.5), 236(100), 111(3), 84(5), 55(5).