Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

for

Angew. Chem. Int. Ed. Z52317

69451 Weinheim, Germany

Base-Induced Condensation of α-Chloro Oxime Derivatives Furnishes Alkynes

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Instrumentation and Materials

^{1}H NMR (300 MHz) and ^{13}C NMR (75.3 MHz) spectra were taken on Varian GEMINI 300 and Mercury 300 spectrometers. ^{1}H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ with tetramethylsilane as an internal standard. IR spectra were recorded on JASCO IR-810 and SHIMADZU FTIR-8200PC spectrometers. Mass spectra were determined on a JEOL Mstation 700 spectrometer. Silica gel (Wakogel 200 mesh) was used for column chromatography. The analyses were carried out at the Elemental Analysis Center of Kyoto University. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl before use.

General Procedure

The reaction of α-chloro oxime ethers (Method B)

To a solution of freshly prepared $MgBr_2$ (0.5 mmol)[1] in THF (1 mL) was added a solution of LDA (2.5 mmol) in THF (4 mL) at –78 °C. To the resulting mixture was added **1c** (218.1 mg, 1.0 mmol) dropwise at –78 °C. The reaction mixture was stirred for 3 h. After quenching the reaction with saturated aq. NH_4Cl, the mixture was extracted with hexane/ethyl acetate (10/1). The combined oraganic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Purification by chromatography on a silica gel column afforded the corresponding alkynyl oxime ether **7c** (106.5 mg, 0.35 mmol).

[1] Magnesium bromide was prepared by mixing BuMgBr (0.5 mL, 1.0 M solution in THF, 0.5 mmol) and allyl bromide (0.6 mmol). THF and remaining allyl bromide were removed under reduced pressure before use.

The reaction of α-chloro oxime ethers with α-chloro oxime *p*-toluenesulfonates

To a solution of LDA (2.50 mmol) in THF (3 mL) was added a solution of **1c** (109.0 mg, 0.50 mmol) in THF (2 mL) dropwise at –78 °C, and the mixture was stirred at –78 °C for 15 min. To the resulting mixture was added **14a** (178.1 mg, 0.55 mmol) in THF (2 mL) at –78 °C. The color of the reaction mixture turned black accopanied with exothermicity. The reaction mixture was stirred for 3 h. After quenching the reaction with saturated aq. NH_4Cl, the mixture was extracted with hexane/ethyl acetate (10/1). The combined oraganic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Purification by chromatography on a silica gel column afforded the corresponding alkynyl oxime ether **13ca** (87.7 mg, 0.33 mmol).

Compound Data

(4-Methyl-3-phenyl-1-azabicyclo[1.1.0]but-2-yl)phenylmethanone *O*-methyloxime (5b): IR (neat) 3063, 2966, 1591, 1495, 1445, 1398, 1367, 1184, 1047 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (d, *J* = 5.4 Hz, 3H), 2.22 (q, *J* = 5.4 Hz, 1H), 3.69 (s, 1H), 4.02 (s, 3H), 7.34–7.43 (m, 6H), 7.51–7.55 (m, 2H), 7.80–7.86 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.58, 43.39, 60.58, 61.42, 62.59, 126.07, 128.33, 128.41, 128.42, 128.98, 129.39, 132.43, 134.91, 152.04. HRMS (*m*/*z*) Found: 278.1426. Calcd for $C_{18}H_{18}N_2O$: 278.1419.

1,3-Diphenylpropynone *O*-methyloxime (7a): IR (neat) 2924, 2855, 2214, 1539, 1445, 1377, 1331, 1051 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.13 (s, 3H), 7.36–7.40 (m, 6H), 7.59–7.62 (m, 2H), 7.89–7.92 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 63.12, 79.42, 101.16, 121.76, 126.48, 128.41, 128.42, 129.52, 129.66, 132.15, 133.57, 139.90. Found: C, 81.60; H, 5.71%. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57%.

1,3-Bis-(4-methoxyphenyl)propynone *O*-methyloxime (7b): IR (neat) 2936, 2837, 2193, 1605, 1506, 1464, 1339, 1294, 1252, 1171, 1045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.84 (s, 6H), 4.11 (s, 3H),

6.90 (d, *J* = 9.0 Hz, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 7.56 (d, *J* = 9.0 Hz, 2H), 7.85 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 55.37, 55.37, 62.91, 78.67, 101.21, 113.69, 113.75, 113.99, 126.31, 127.81, 133.70, 139.61, 160.39, 160.64. Found: C, 72.98; H, 5.83%. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80%.

1,3-Bis-(4-chlorophenyl)propynone *O*-methyloxime (7c): IR (nujol) 2214, 1580, 1535, 1489, 1396, 1332, 1092, 1057, 1014 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.14 (s, 3H), 7.37 (d, *J* = 9.0 Hz, 2H), 7.37 (d, *J* = 9.0 Hz, 2H), 7.54 (d, *J* = 9.0 Hz, 2H), 7.83 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 63.32, 79.83, 100.13, 119.93, 127.56, 128.56, 128.80, 131.76, 133.25, 135.62, 135.78, 138.52. Found: C, 62.91; H, 3.76%. Calcd for $C_{16}H_{11}NOCl_2$: C, 63.18; H, 3.64%.

1,3-Bis-(4-bromophenyl)propynone *O*-methyloxime (7d): IR (nujol) 2216, 1531, 1485, 1394, 1337, 1059 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.13 (s, 3H), 7.45 (d, *J* = 8.7 Hz, 2H), 7.52 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.7 Hz, 2H), 7.75 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 63.34, 79.92, 100.20, 120.37, 123.97, 124.12, 127.80, 131.50, 131.72, 132.20, 133.39, 138.59. Found: C, 48.61; H, 3.00%. Calcd for $C_{16}H_{11}NOBr_2$: C, 48.89; H, 2.82%.

1,3-Bis-2-naphthylpropynone *O*-methyloxime (7e): IR (nujol) 2197, 1356, 1310, 1047 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.24 (s, 3H), 7.50–7.57 (m, 4H), 7.71 (dd, *J* = 1.5, 8.4 Hz, 1H), 7.86–7.89 (m, 5H), 7.95 (dd, *J* = 3.6, 6.0 Hz, 1H), 8.11–8.14 (m, 1H), 8.23 (s, 1H), 8.42 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 63.29, 79.68, 101.63, 118.97, 122.99, 126.33, 126.71, 126.71, 127.07, 127.24, 127.64, 127.75, 127.93, 128.02, 128.11, 128.24, 128.57, 131.02, 132.57, 132.72, 132.96, 133.28, 133.89, 139.87. Found: C, 85.82; H, 5.04%. Calcd for $C_{24}H_{17}NO$: C, 85.95; H, 5.11%.

2-Chloro-1,4-diphenylbutane-1,4-dione bis(*O*-methyloxime) (8a): IR (neat) 2937, 2820, 1497, 1462, 1445, 1331, 1049 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.44 (dd, *J* = 6.9, 14.1 Hz, 1H), 3.55 (dd, *J* = 8.4, 14.1 Hz, 1H), 3.945 (s, 3H), 3.954 (s, 3H), 5.85 (dd, *J* = 6.9, 8.4 Hz, 1H), 7.35–7.40 (m, 6H),

7.56–7.59 (m, 2H), 7.61–7.64 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 32.92, 48.18, 62.05, 62.46, 126.61, 127.83, 128.24, 128.39, 129.20, 129.22, 133.59, 135.16, 154.15, 155.55. HRMS (*m*/*z*) Found: 330.1130. Calcd for $C_{18}H_{19}ClN_2O_2$: 330.1135.

3-(4-Chlorophenyl)-1-phenylpropynone *O*-methyloxime (13ac): IR (neat) 2936, 2897, 2214, 1585, 1537, 1489, 1445, 1339, 1184, 1092, 1047 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.14 (s, 3H), 7.35–7.42 (m, 5H), 7.54–7.57 (m, 2H), 7.88–7.91 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 63.20, 80.24, 99.77, 120.13, 126.32, 128.34, 128.74, 129.64, 133.24, 135.59, 139.54, 148.25. Found: C, 71.25; H, 4.72%. Calcd for $C_{16}H_{12}NOCl$: C, 71.25; H, 4.48%.

4-Methyl-1-phenylpent-2-yn-1-one *O*-methyoxime (13al): IR (neat) 2872, 2222, 1545, 1445, 1331, 1053 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (d, *J* = 6.9 Hz, 6H), 2.92 (septet, *J* = 6.9 Hz, 1H), 4.09 (s, 3H), 7.35–7.39 (m, 3H), 7.82–7.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.62, 22.66, 62.94, 70.57, 108.88, 126.35, 128.17, 129.35, 133.83, 140.01. Found: C, 77.86; H, 7.54%. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51%.

1-(4-Methoxyphenyl)-3-phenylpropynone *O*-mehtyloxime (13ba): IR (nujol) 1585, 1512, 1342, 1256, 1175, 1032 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3H), 4.12 (s, 3H), 6.93 (d, *J* = 9.0 Hz, 2H), 7.38–7.40 (m, 3H), 7.60–7.63 (m, 2H), 7.86 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 55.38, 62.98, 79.53, 100.75, 113.73, 121.73, 126.13, 127.80, 128.31, 129.35, 132.02, 139.40, 160.71. Found: C, 76.98; H, 5.72%. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70%.

1-(4-Chlorophenyl)-3-phenylpropynone *O*-methyloxime (13ca): IR (neat) 2936, 2897, 2212, 1597, 1580, 1533, 1489, 1443, 1398, 1333, 1175, 1094, 1051 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.14 (s, 3H), 7.36–7.41 (m, 5H), 7.62 (dd, *J* = 1.8, 7.8 Hz, 2H), 7.86 (d, *J* = 6.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 63.26, 78.99, 101.45, 121.44, 127.60, 128.37, 128.51, 129.56, 131.96, 132.04, 135.50, 138.72. Found: C, 71.37; H, 4.76%. Calcd for $C_{16}H_{12}NOCl$: C, 71.25; H, 4.48%.

1,5-Diphenylpent-1-en-4-yn-3-one *O*-mehtyloxime (13fa): IR (neat) 2934, 2855, 2203, 1574, 1531, 1489, 1448, 1342, 1175, 1051 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.09 (s, 3H), 6.93 (d, *J* = 15.6 Hz, 1H), 7.24–7.42 (m, 7H), 7.50–7.52 (m, 2H), 7.62–7.65 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 63.04, 77.76, 100.86, 121.55, 123.20, 126.99, 128.36, 128.56, 128.67, 129.46, 132.04, 135.91, 136.10, 141.28. Found: C, 82.89; H, 6.07%. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79%.

4,4-Dimethyl-1-phenylpent-1-yn-3-one *O*-methyloxime (13ga, 92/8 diastereomer mixture): IR (neat) 2968, 2210, 1491, 1460, 1364, 1115, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (s, 8.28H), 1.34 (s, 0.72H), 3.96 (s, 0.24H), 3.97 (s, 2.76H), 7.32–7.37 (m, 3H), 7.51–7.55 (m, 2H); ^{13}C NMR ($CDCl_3$) For major isomer: δ 28.26, 37.05, 62.30, 79.31, 100.28, 121.97, 128.67, 129.07, 131.90, 148.96, for minor isomer: δ 28.12, 37.42, 62.59, 84.93, 90.65, 122.29, 128.19, 128.22, 131.72, 152.54. Found: C, 78.35; H, 8.06%. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96%.

1-Cyclopentyl-3-phenylpropynone *O*-methyloxime (13ha): IR (neat) 2959, 2868, 2214, 1572, 1489, 1443, 1049 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.61–1.98 (m, 8H), 2.88 (quint, *J* = 8.1 Hz, 1H), 3.96 (s, 3H), 7.34–7.36 (m, 3H), 7.51–7.54 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 25.95, 31.08, 43.87, 62.24, 79.28, 99.77, 121.74, 128.22, 129.19, 131.98, 145.65. HRMS Found 227.1305. Calcd for $C_{15}H_{17}NO$ 227.1310.

1-Phenylundec-1-yn-3-one *O*-methyloxime (13ia): IR (neat) 2928, 2856, 2218, 1574, 1489, 1443, 1304, 1157, 1107, 1051 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (t, *J* = 6.9 Hz, 3H), 1.23–1.41 (m, 10H), 1.67 (tt, *J* = 6.9, 7.5 Hz, 2H), 2.39 (t, *J* = 7.5 Hz, 2H), 3.97 (s, 3H), 7.34–7.37 (m, 3H), 7.51–7.54 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.19, 22.74, 27.15, 28.99, 29.25, 29.36, 31.89, 34.39, 62.28, 80.32, 99.51, 121.72, 128.23, 129.22, 131.99, 141.90. Found: C, 79.47; H, 9.30%. Calcd for $C_{18}H_{25}NO$: C, 79.66; H, 9.28%.

2-Methyltridec-3-yn-5-one *O*-mehtyloxime (13il): IR (neat) 2928, 2856, 2216, 1585, 1466, 1321, 1271, 1103, 1057 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, *J* = 6.9 Hz, 3H), 1.24 (d, *J* = 6.9 Hz, 6H), 1.23–1.36 (m, 10H), 1.54–1.60 (m, 2H), 2.26 (t, *J* = 7.5 Hz, 2H), 2.80 (septet, *J* = 6.9 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 14.21, 21.44, 22.61, 22.75, 27.05, 28.95, 29.24, 29.37, 31.90, 34.63, 62.09, 71.45, 107.34, 142.41. Found: C, 75.60; H, 11.17%. Calcd for $C_{15}H_{27}NO$: C, 75.90; H, 11.46%.

4-Phenylbut-3-yn-2-one *O*-mehtyloxime (13ja): IR (neat) 2936, 2899, 2224, 2181, 1583, 1491, 1443, 1375, 1313, 1171, 1061 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.13 (s, 3H), 3.97 (s, 3H), 7.32–7.39 (m, 3H), 7.48–7.54 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.68, 62.29, 80.91, 99.03, 121.58, 128.23, 129.27, 131.95, 137.37. Found: C, 76.02; H, 6.54%. Calcd for $C_{11}H_{11}NO$: C,76.28; H, 6.40%.

1-Benzofuran-2-yl-3-phenylpropynone *O*-methyloxime (13ka, ca. 4/1 diastereomer mixture): IR (neat) 2939, 2208, 1531, 1450, 1306, 1254, 1159, 1045 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.22 (s, 2.4H), 4.23 (s, 0.6H), 7.22–7.29 (m, 2H), 7.33–7.47 (m, 4H), 7.56–7.70 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 63.69, 63.92, 77.87, 99.76, 109.16, 111.74, 113.84, 121.17, 121.42, 122.19, 123.26, 125.70, 125.87, 126.47, 127.65, 127.98, 128.25, 128.38, 129.10, 129.71, 132.08, 132.24, 149.80, 155.32. Found: C, 78.41; H, 5.03%. Calcd for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76%.

1,4-Diphenylbut-2-ene-1,4-dione bis(*O*-methyloxime): Mp 168 °C, IR (nujol) 1445, 1342, 1248, 1043 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.97 (s, 6H), 7.18 (s, 2H), 7.44–7.46 (m, 6H), 7.54–7.57 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 62.44, 127.02, 128.45, 128.97, 129.27, 134.35, 156.13. Found: C, 73.33; H, 6.27%. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16%.