Copper-Catalyzed Tandem [2,3]-Rearrangement and 6π -3-Azatriene

Electrocyclization in (*E*)-*O*-Propargylic α,β -Unsaturated Oximes

Itaru Nakamura,* Dong Zhang and Masahiro Terada

Research and Analytical Center for Giant Molecules, Graduate School of Science, Tohoku University, Sendai 980-8578, Japan, Department of Chemistry, Graduate School of Science, Tohoku University Sendai 980-8578, Japan

(Supplementary Information)

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1. Complete reference 5b.

Marion, N.; Lemire, G.; Correa, A.; Costabile, C.; Ramn, R. S.; Moreau, X.; de Frmont, P.; Dahmane, R.; Hours, A.; Lesage, D.; Tabet, J.-C.; Goddard, J.-P.; Gandon, V.; Cavallo, L.; Fensterbank, L.; Malacria, M.; Nolan, S. P. *Chem. Eur. J.* **2009**, *15*, 3243.

2. General.

^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-500 (500 MHz for ^1H and 125 MHz for ^{13}C) spectrometer and JEOL ECA-600 (600 MHz for ^1H and 150 MHz for ^{13}C) spectrometer. Chemical shifts are reported in ppm relative to TMS (for ^1H , δ 0.00), and CDCl_3 (for ^{13}C , δ 77.00). ^1H NMR data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, q = quartet, quint = quintet, sext = sextet, br = broad, m = multiplet) and coupling constants (Hz). Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer. High-resolution mass spectra analysis was performed on a Bruker Daltonics APEX III FT-ICR-MS spectrometer at the Instrumental Analysis Center for Chemistry, Graduate School of Science, Tohoku University. X-ray crystallographic data was obtained by Rigaku / MSC Saturn Cu-CCD device at Research and Analytical Center for Giant Molecules, Graduate School of Science, Tohoku University. Flash column chromatography was performed with Kanto Chemical silica gel 60N (spherical, neutral, 40-50 μm). Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 F_{254}). All reactions were carried out under Argon atmosphere. $\text{CuBr}(\text{PPh}_3)_3$ was prepared according to procedure reported previously.¹ DMSO dehydrated was purchased from Wako Pure Chemical Industries Ltd.

(1) Venkataraman, D.; Allen, D. V. *J. Org. Chem.* **2003**, *68*, 4590-4593

3. Optimization of Reaction Conditions.

Table S1. Optimization of Reaction Conditions (Ligand and Halogen Effect)

Entry	Catalyst (mol%)	Time / h	Yield 2a %	Yield 3a / %
1	CuBr (10), PPh_3 (40)	17	68	9
2	CuBr (10), (<i>p</i> - $\text{F}_3\text{CC}_6\text{H}_4$) $_3\text{P}$ (40)	2	17	7
3	CuBr (10), (<i>p</i> - MeOC_6H_4) $_3\text{P}$ (40)	16	48	4
4	CuCl (10), PPh_3 (40)	24	62	11
5	CuI (10), PPh_3 (40)	9	66	8
6 ^a	$\text{CuBr}(\text{PPh}_3)_3$ (10), PPh_3 (10)	2	75 (70)	trace

^a The reaction was carried out in DMSO at 120 $^\circ\text{C}$.

To avoid rapid decomposition of **1** by CuBr (Table 1, entry 4), $\text{CuBr}(\text{PPh}_3)_3$ was chosen as the catalyst.

4. Representative Procedure for the Synthesis of (*E*)-1a and (*Z*)-1a

(a) ***O*-(1,3-Diphenylprop-2-yn-1-yl)hydroxylamine (S2).** 1,3-Diphenylprop-2-yn-1-ol (**S1**) was prepared in accordance with the literature method.² To a stirred solution of **S1** (3.28 g, 15.7 mmol), PPh₃ (4.51 g, 17.2 mmol) and *N*-hydroxyphthalimide (2.78 g, 17.2 mmol) in THF (60 mL) at 0 °C was added diisopropyl azodicarboxylate (DIAD, 3.38 mL, 17.2 mmol) dropwise and stirred for 12 h at room temperature. Next, hydrazine monohydrate (1.6 mL) was added slowly to the reaction mixture and further stirred for 1 h at the same temperature. The mixture was then diluted with H₂O, extracted with ether, and the organic phase was washed with water and brine and dried over Na₂SO₄. After filtration, solvent was removed under reduced pressure and the residue was purified by flash column chromatography (hexane/EtOAc = 5/1 as eluent) to give **S2** (2.77 g, 79%). ¹H NMR (500 MHz, CDCl₃) δ 5.52 (brs, 2H), 5.59 (s, 1H), 7.29 – 7.43 (m, 6H), 7.50 – 7.52 (m, 2H), 7.59 – 7.61 (m, 2H). ¹³C NMR (125 MHz, CDCl₃) δ 77.23, 86.16, 87.81, 122.30, 128.03, 128.25, 128.61A, 128.79, 131.84, 137.20. IR (neat) 3317, 3244, 3060, 3031, 2878, 2223, 1954, 1890, 1812, 1577, 1454, 1443, 1303, 1177, 1027, 1009, 950, 916 cm⁻¹.

(2) Engel, D. A.; Dudley, G. B. *Org. Lett.* **2006**, 8, 4027-4029.

(b) **Cinnamaldehyde *O*-(1,3-diphenylprop-2-yn-1-yl) oxime ((*E*)-1a and (*Z*)-1a).** Hydroxylamine **S2** (5 mmol) was dissolved in THF (10 mL). Cinnamaldehyde (5 mmol) was added at room temperature and the reaction mixture was heated to 65 °C for 2 h. The solvent was then removed under reduced pressure and the residue was purified by flash column chromatography (Hexane/CH₂Cl₂ = 3/1 as eluent) to give (*E*)-1a (42%) and (*Z*)-1a (32%).

For preparation of **1j**: (*E*)-1j (60%) and (*Z*)-1a (33%).

5. Analytical Data of 1.

(1*E*, 2*E*)-Cinnamaldehyde *O*-(1,3-diphenylprop-2-yn-1-yl) oxime ((*E*)-1a). ¹H NMR (500 MHz, CDCl₃) δ 6.09 (s, 1H), 6.79 (d, *J* = 16.0 Hz, 1H), 6.87 (dd, *J* = 16.0 Hz, *J* = 9.5 Hz, 1H), 7.27 – 7.44 (m, 11H), 7.50 – 7.52 (m, 2H), 7.65 (d, *J* = 3.5 Hz, 2H), 7.97 (d, *J* = 9.5 Hz, 1H), ¹³C NMR (125 MHz, CDCl₃) δ 76.07,

86.66, 87.84, 121.82, 122.48, 126.95, 128.00, 128.20, 128.56, 128.77 (2C), 128.87, 131.93, 135.91, 137.64, 139.20, 151.80. IR (neat) 3060, 3032, 2893, 2227, 1627, 1598, 1489, 1450, 1300, 1161, 1014, 996, 970, 933 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 360.1359, found. 360.1358.

(1E, 2Z)-Cinnamaldehyde O-(1,3-diphenylprop-2-yn-1-yl) oxime ((Z)-1a). ^1H NMR (500 MHz CDCl_3) δ 6.13 (s, 1H), 6.83 (d, $J = 16.0$ Hz, 1H), 7.27-7.38 (m, 9H), 7.40-7.43 (m, 2H), 7.47-7.52 (m, 4H), 7.66 (d, $J = 7.0$ Hz, 2H). ^{13}C NMR (125 MHz, CDCl_3) δ 76.06, 86.92, 87.65, 116.52, 122.54, 127.58, 127.97, 128.19, 128.51, 128.53, 128.64, 128.73, 129.36, 131.96, 135.71, 137.96, 140.45, 149.09. IR (neat) 3060, 3030, 2895, 2228, 1624, 1598, 1489, 1449, 1342, 1294, 1136, 1071, 1091, 996, 970, 920, 889 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 360.1359, found. 360.1358.

(E)-Acrylaldehyde O-(1,3-diphenylprop-2-yn-1-yl) oxime ((E)-1b). ^1H NMR (500 MHz, CDCl_3) δ 5.54 (d, $J = 18.0$ Hz, 1H), 5.57 (d, $J = 11.0$ Hz, 1H), 6.05 (s, 1H), 6.46 (m, 1H), 7.28-7.33 (m, 3H), 7.34-7.42 (m, 3H), 7.48-7.50 (m, 2H), 7.62 (d, $J = 7.0$ Hz, 2H), 7.81 (d, $J = 10.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 76.01, 86.59, 87.80, 122.47, 124.60, 127.97, 128.19, 128.53, 128.57, 128.75, 130.60, 131.90, 137.58, 151.81. IR (neat) 3062, 3032, 2228, 1597, 1489, 1454, 1443, 1419, 1297, 1275, 1190, 1016, 995, 976, 926 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 284.1046, found. 284.1045.

(1E, 2E)-But-2-enal O-(1,3-diphenylprop-2-yn-1-yl) oxime ((E)-1c). ^1H NMR (500 MHz, CDCl_3) δ 1.83 (d, $J = 6.5$ Hz, 3H), 5.99-6.06 (m, 2H), 6.15-6.20 (m, 1H), 7.27-7.31 (m, 3H), 7.32-7.41 (m, 3H), 7.47-7.50 (m, 2H), 7.60-7.62 (m, 2H), 7.78 (d, $J = 9.5$ Hz). ^{13}C NMR (125 MHz, CDCl_3) δ 18.50, 75.70, 86.83, 87.60, 122.55, 125.10, 127.94, 128.16, 128.49 (2C), 128.64, 131.90, 137.77, 138.06, 151.37. IR (neat) 3032, 2228, 1649, 1597, 1489, 1453, 1443, 1301, 1277, 1015, 972, 905 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 298.1202, found. 298.1201.

(1E, 2E)-Hex-2-enal O-(1,3-diphenylprop-2-yn-1-yl) oxime ((E)-1d). ^1H NMR (500 MHz, CDCl_3) δ 0.90 (t, $J = 7.5$ Hz, 3H), 1.44 (sext, $J = 7.0$ Hz, 2H), 1.45 (q, $J = 7.0$ Hz, 2H), 5.99-6.05 (m, 2H), 6.16 (dd, $J = 15.5$ Hz, $J = 9.5$ Hz, 1H), 7.28-7.33 (m, 3H), 7.34-7.41 (m, 3H), 7.48-7.50 (m, 2H), 7.62 (d, $J = 7.5$ Hz, 2H), 7.79 (d, $J = 9.5$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.62, 21.74, 34.84, 75.73, 86.88, 87.62, 122.58, 123.83, 127.96, 128.18, 128.51 (2C), 128.66, 131.92, 137.81, 143.22, 151.88. IR (neat) 3062, 3032, 2959, 2929, 2871, 2228, 1646, 1598, 1489, 1454, 1443, 1303, 1015, 975, 925 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 326.1515, found. 326.1514.

(E)-Methacrylaldehyde O-(1,3-diphenylprop-2-yn-1-yl) oxime ((E)-1e). ^1H NMR (500 MHz, CDCl_3) δ 1.93 (s, 3H), 5.21 (s, 1H), 5.34 (s, 1H), 6.08 (s, 1H), 7.28-7.31 (m, 3H), 7.34-7.42 (m, 3H), 7.47-7.51 (m, 2H), 7.63 (d, $J = 7.0$ Hz, 2H), 7.82 (s, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 17.26, 76.01, 86.80, 87.60, 122.24, 122.57, 128.04, 128.20, 128.46, 128.50, 128.67, 131.85, 137.79, 138.85, 152.53. IR (neat) 3391, 3059, 3027, 2921, 1604, 1562, 1494, 1472, 1452, 1388, 1313, 1229, 1155, 1038, 1014, 846 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 298.1202, found. 298.1201.

(E)-Cyclohex-1-enecarbaldehyde O-(1,3-diphenylprop-2-yn-1-yl) oxime ((E)-1f). ^1H NMR (500 MHz, CDCl_3) δ 1.63-1.64 (m, 4H), 2.15 (s, 2H), 2.23-2.32 (m, 2H), 5.97 (s, 1H), 6.04 (s, 1H), 7.30-7.41 (m, 6H), 7.48-7.50 (m, 2H), 7.63 (d, $J = 7.5$ Hz, 2H), 7.73 (s, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 21.82, 22.20, 23.48, 25.99, 75.68, 87.07, 87.40, 122.69, 128.03, 128.17, 128.43 (2C), 128.56, 131.88, 133.01, 136.22, 138.02, 153.16. IR (neat) 3062, 3032, 2930, 2859, 1638, 1597, 1489, 1452, 1299, 1188, 1018, 939, 906 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 338.1515, found. 338.1512.

(E)-Acrylaldehyde O-[3-(4-methoxyphenyl)-1-phenylprop-2-yn-1-yl] oxime ((E)-1g). ^1H NMR (500 MHz, CDCl_3) δ 3.80 (s, 3H), 5.52-5.57 (m, 2H), 6.04 (s, 1H), 6.42-6.50 (m, 1H), 6.83 (d, $J = 9.0$ Hz, 2H), 7.34-7.45 (m, 5H), 7.62 (d, $J = 7.0$ Hz, 2H), 7.81 (d, $J = 10.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 55.25, 76.12, 85.18, 87.82, 113.82, 114.54, 124.51, 127.95, 128.50, 128.67, 130.65, 133.41, 137.81, 151.75, 159.81. IR (neat) 2836, 2226, 1605, 1509, 1455, 1290, 1247, 1172, 1031, 928, 832 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 314.1151, found. 314.1151.

(E)-Acrylaldehyde O-[1-phenyl-3-(4-trifluoromethyl)phenyl]prop-2-yn-1-yl] oxime ((E)-1h). ^1H NMR (500 MHz, CDCl_3) δ 5.54-5.60 (m, 2H), 6.06 (s, 1H), 6.42-6.50 (m, 1H), 7.36-7.43 (m, 3H), 7.56-7.61 (m, 6H), 7.82 (d, $J = 10.0$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 75.83, 86.28, 89.18, 123.84 (q, $J = 273.0$ Hz), 124.89, 125.15 (q, $J = 3.8$ Hz), 126.27, 127.92, 128.63, 128.93, 130.31 (q, $J = 33.0$ Hz), 130.47, 132.14, 137.12, 152.01. IR (neat) 3065, 3034, 2896, 1615, 1494, 1455, 1404, 1322, 1167, 1127, 1068, 1018, 929, 842 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 352.0920, found. 352.0919.

(E)-Acrylaldehyde O-(1-phenylprop-2-yn-1-yl) oxime ((E)-1i) ^1H NMR (500 MHz, CDCl_3) δ 2.70-2.71 (m, 1H), 5.52-5.59 (m, 2H), 5.83 (s, 1H), 6.41-6.49 (m, 1H), 7.34-7.41 (m, 3H), 7.56 (d, $J = 7.5$ Hz), 7.79 (d, $J = 10.0$ Hz). ^{13}C NMR (125 MHz, CDCl_3) δ 75.15, 75.93, 81.29, 124.86, 127.86, 128.53, 128.87, 130.45, 136.79, 152.02. IR (neat) 3288, 2121, 1495, 1454, 1419, 1269, 1192, 1018, 993, 970, 924 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 352.0920, found. 352.0919.

(E)-Acrylaldehyde O-(1-phenylhex-2-yn-1-yl) oxime ((E)-1j). ^1H NMR (500 MHz, CDCl_3) δ 0.99 (t, $J = 7.5$ Hz, 3H), 1.58 (sext, $J = 7.5$ Hz, 2H), 2.28 (t, $J = 7.5$ Hz, 2H), 5.49-5.55 (m, 2H), 5.83 (s, 1H), 6.40-6.48 (m, 1H), 7.31-7.38 (m, 3H), 7.54 (d, $J = 7.5$ Hz, 2H), 7.77 (d, $J = 9.5$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.47, 20.92, 21.95, 75.83, 77.72, 88.88, 124.29, 127.86, 128.37, 128.49, 130.70, 138.15, 151.54. IR (neat) 3090, 3064, 3032, 2963, 2933, 2233, 1494, 1454, 1419, 1272, 1137, 991, 932 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 250.1202, found. 250.1202.

(E)-Acrylaldehyde O-[1-phenyl-6-(triisopropylsilyloxy)hex-2-yn-1-yl] oxime ((E)-1k). ^1H NMR (500 MHz, CDCl_3) δ 1.02-1.09 (m, 21H), 1.78 (quint, $J = 6.5$ Hz, 2H), 2.41-2.44 (m, 2H), 3.76 (t, $J = 6.5$ Hz, 2H), 5.50-5.56 (m, 2H), 5.81 (s, 1H), 6.40-6.48 (m, 1H), 7.31-7.38 (m, 3H), 7.53 (d, $J = 6.5$ Hz, 2H), 7.77 (d, $J = 10.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 11.94, 15.47, 17.99, 31.72, 61.86, 75.83, 77.70, 88.64,

124.33, 127.84, 128.39, 128.51, 130.71, 138.13, 151.56. IR (neat) 2941, 2892, 2864, 2232, 1494, 1462, 1383, 1105, 994, 934, 882 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 422.2486, found. 422.2484.

(E)-Acrylaldehyde O-[3-(cyclohexyl)-1-phenylprop-2-yn-1-yl] oxime ((E)-1l). ^1H NMR (500 MHz, CDCl_3) δ 1.26-1.36 (m, 3H), 1.48-1.52 (m, 3H), 1.70-1.72 (m, 2H), 1.81-1.84 (m, 2H), 2.49 (s, 1H), 5.49-5.55 (m, 2H), 5.84 (d, $J = 2.0$ Hz, 1H), 6.40-6.48 (m, 1H), 7.31-7.38 (m, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 24.78, 25.85, 29.19, 32.42, 32.46, 75.87, 77.47, 93.03, 124.21, 127.92, 128.34, 128.46, 130.73, 138.24, 151.48. IR (neat) 3032, 2928, 2853, 1495, 1449, 1418, 1292, 1270, 988, 952, 933 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 290.1515, found. 290.1514.

(E)-Acrylaldehyde O-[4-(4-dimethyl)-1-phenylpent-2-yn-1-yl] oxime ((E)-1m). ^1H NMR (500 MHz, CDCl_3) δ 1.27 (s, 9H), 5.49-5.55 (m, 2H), 5.82 (s, 1H), 6.40-6.47 (m, 1H), 7.31-7.38 (m, 3H), 7.54 (d, $J = 7.5$ Hz, 2H), 7.76 (d, $J = 10.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 27.58, 30.85, 75.82, 75.91, 97.10, 124.17, 127.95, 128.34, 128.44, 130.73, 138.29, 151.43. IR (neat) 2968, 2240, 1494, 1475, 1454, 1419, 1362, 1273, 990, 931 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 264.1359, found. 264.1358.

(E)-Acrylaldehyde O-[1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-yl] oxime ((E)-1n). ^1H NMR (500 MHz, CDCl_3) δ 3.82 (s, 3H), 3.51-3.57 (m, 2H), 6.00 (s, 1H), 6.24-6.50 (m, 1H), 6.93 (d, $J = 8.5$ Hz, 2H), 7.30-7.31 (m, 3H), 7.49-7.50 (m, 2H), 7.56 (d, $J = 9.0$ Hz, 2H), 7.79 (d, $J = 10.0$ Hz, 1H). IR (neat) 2835, 2227, 1610, 1510, 1489, 1461, 1303, 1247, 1172, 975, 923, 829 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 314.1151, found. 314.1150.

(E)-Acrylaldehyde O-[1-(4-trifluoromethylphenyl)-3-phenylprop-2-yn-1-yl] oxime ((E)-1o). ^1H NMR (500 MHz, CDCl_3) δ 5.55-5.61 (m, 2H), 6.09 (s, 1H), 6.40-6.48 (m, 1H), 7.28-7.34 (m, 3H), 7.48-7.51 (m, 2H), 7.66 (d, $J = 8.0$ Hz, 2H), 7.73 (d, $J = 8.0$ Hz, 2H), 7.83 (d, $J = 10.0$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 75.15, 85.69, 88.40, 122.07, 124.01 (q, $J = 273.0$ Hz), 124.92, 125.09, 125.52 (q, $J = 3.8$ Hz), 128.16, 128.28, 128.83, 130.34, 130.75 (q, $J = 33.0$ Hz), 131.91, 141.71, 152.18. IR (neat) 3062, 2900, 2230, 1620, 1598, 1490, 1443, 1417, 1322, 1164, 1123, 1109, 1066, 1018, 925 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 352.0920, found. 352.0919.

(E)-Acrylaldehyde O-(1-phenylhex-1-yn-3-yl) oxime ((E)-1p). ^1H NMR (500 MHz, CDCl_3) δ 0.99 (t, $J = 8.0$ Hz, 3H), 1.57 (sext, $J = 8.0$ Hz, 2H), 1.82-1.96 (m, 2H), 5.00 (t, $J = 6.0$ Hz, 1H), 5.52-5.57 (m, 2H), 6.43-6.51 (m, 1H), 7.26-7.29 (m, 3H), 7.44-7.47 (m, 2H), 7.78 (d, $J = 10.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.80, 18.47, 36.64, 73.97, 85.76, 87.93, 122.73, 124.13, 124.14, 128.13, 128.28, 130.75, 131.84, 151.17. IR (neat) 2959, 2873, 1627, 1598, 1489, 1465, 1443, 1419, 1341, 1109, 1062, 1003, 992, 931 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 250.1202, found. 250.1203.

(E)-Acrylaldehyde O-(1-cyclohexyl-3-phenylprop-2-yn-1-yl) oxime ((E)-1q). ^1H NMR (500 MHz,

CDCl₃) δ 1.19-1.32 (m, 5H), 1.69 (d, J = 12.0 Hz, 1H), 1.79-1.95 (m, 5H), 4.81 (d, J = 5.5 Hz, 1H), 5.53 (d, J = 15.0 Hz, 1H), 5.56 (d, J = 8.0 Hz, 1H), 6.43-6.51 (m, 1H), 7.29-7.30 (m, 3H), 7.45-7.47 (m, 2H), 7.79 (d, J = 10.0 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 25.84, 25.93, 26.38, 28.09, 28.99, 41.75, 76.75, 86.60, 86.91, 122.84, 124.04, 128.13, 128.24, 130.79, 131.87, 151.08. IR (neat) 2925, 2852, 2227, 1597, 1489, 1449, 1419, 1336, 1013, 990, 931 cm⁻¹. HRMS (ESI) calcd. for (M+Na)⁺ 290.1515, found. 290.1515.

6. Representative Procedure for the Copper-Catalyzed Synthesis of 2a.

To a mixture of CuBr(PPh₃)₃ (37.2 mg, 0.04 mmol), PPh₃ (10.5 mg, 0.04 mmol) and the oxime (E)-**1a** (134.8 mg, 0.40 mmol) in a pressure vial was added DMSO (0.8 mL) under argon atmosphere and the mixture was stirred at 120 °C for 2 h. The reaction mixture was passed through a pad of silica gel with CHCl₃. After removing solvents in vacuo, the residue was purified by flash column chromatography (CHCl₃/MeOH = 100/1 as eluent) to give **2a** (94.4 mg, 70%).

7. Analytical Data of 2.

3-Benzyl-2,4-diphenylpyridine N-oxide (2a). ¹H NMR (500 MHz, CDCl₃) δ 3.81 (s, 2H), 6.53-6.55 (m, 2H), 7.01-7.05 (m, 3H), 7.15-7.24 (m, 5H), 7.34-7.35 (m, 6H), 8.34 (d, J = 7.0 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 35.74, 125.88, 125.91, 127.98, 128.02, 128.13, 128.50, 128.54, 128.62, 128.79, 129.13, 132.32, 136.16, 137.74, 138.25, 139.29, 141.11, 150.74. IR (neat) 3057, 3022, 2959, 2925, 2858, 1728, 1600, 1493, 1445, 1423, 1264, 1119, 1072, 1041, 862 cm⁻¹. HRMS (ESI) calcd. for (M+Na)⁺ 360.1359, found. 360.1358.

3-Benzyl-2-phenylpyridine N-oxide (2b). ¹H NMR (500 MHz, CDCl₃) δ 3.73 (s, 2H), 6.91 (d, J = 7.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 1H), 7.16-7.29 (m, 6H), 7.42-7.48 (m, 3H), 8.25 (d, J = 6.0 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 38.56, 124.02, 126.60, 127.16, 128.56, 128.73, 128.76, 129.03, 129.26, 131.83, 137.99, 138.59, 139.10, 150.10. IR (neat) 3391, 3061, 3027, 2923, 2853, 1602, 1494, 1467, 1444, 1418, 1261, 1233, 1075, 1014, 997 cm⁻¹. HRMS (ESI) calcd. for (M+Na)⁺ 284.1046, found. 284.1044.

3-Benzyl-4-methyl-2-phenylpyridine N-oxide (2c). ¹H NMR (500 MHz, CDCl₃) δ 2.19 (s, 3H), 3.79 (s, 2H), 6.86 (d, J = 7.5 Hz, 2H), 7.10 (d, J = 6.5 Hz, 1H), 7.15-7.25 (m, 5H), 7.36-7.39 (m, 3H), 8.24 (d, J = 7.0 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃) δ 19.40, 35.79, 126.15, 126.29, 127.64, 128.52, 128.59, 128.84,

129.01, 132.47, 136.33, 137.00, 137.68, 138.13, 150.27. IR (neat) 3057, 3027, 1602, 1494, 1438, 1255, 1233, 1099, 1030, 820 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 298.1202, found. 298.1202.

3-Benzyl-2-phenyl-4-propylpyridine *N*-oxide (2d). ^1H NMR (500 MHz, CDCl_3) δ 0.83 (t, $J = 7.5$ Hz, 3H), 1.47 (sext, $J = 7.5$ Hz, 2H), 2.41 (t, $J = 7.5$ Hz, 2H), 3.74 (s, 2H), 6.75 (d, $J = 7.0$ Hz, 2H), 7.05-7.13 (m, 6H), 7.28 (t, $J = 3.5$ Hz, 3H), 8.19 (d, $J = 6.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.82, 22.86, 34.10, 35.11, 124.88, 126.20, 127.65, 128.39, 128.50, 128.72, 128.94, 132.60, 135.90, 137.74, 138.70, 141.13, 150.31. IR (neat) 3381, 3059, 3026, 2960, 2870, 1601, 1494, 1446, 1256, 1027 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 326.1515, found. 326.1513.

3-Benzyl-5-methyl-2-phenylpyridine *N*-oxide (2e). ^1H NMR (500 MHz, CDCl_3) δ 2.26 (s, 3H), 3.70 (s, 2H), 6.90-6.92 (m, 3H), 7.17-7.28 (m, 5H), 7.39-7.46 (m, 3H), 8.13 (s, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 18.07, 38.40, 126.49, 128.48, 128.55, 128.64, 128.67, 128.83, 129.45, 131.85, 134.44, 137.88, 138.18, 138.73, 147.20. IR (neat) 3393, 3060, 3027, 1604, 1562, 1494, 1471, 1452, 1388, 1312, 1298, 1228, 1154, 1037, 1013, 844 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 298.1202, found. 298.1202.

4-Benzyl-3-phenyl-5,6,7,8-tetrahydroisoquinoline *N*-oxide (2f). ^1H NMR (500 MHz, CDCl_3) δ 1.76-1.77 (m, 4H), 2.48 (s, 2H), 2.74 (s, 2H), 3.77 (s, 2H), 6.87 (d, $J = 7.5$ Hz, 2H), 7.15-7.24 (m, 5H), 7.35-7.36 (m, 3H), 8.14 (s, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 21.66, 22.39, 26.04, 26.75, 35.15, 126.18, 127.58, 128.49, 128.52, 128.66, 129.23, 132.71, 134.68, 135.46, 136.58, 137.67, 138.37, 147.82. IR (neat) 3396, 3061, 3027, 2937, 2861, 1602, 1494, 1461, 1451, 1408, 1357, 1282, 1261, 1204, 1130, 1076, 1034, 975 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 338.1515, found. 338.1515.

3-Benzyl-2-(4-methoxyphenyl)pyridine *N*-oxide (2g). ^1H NMR (500 MHz, CDCl_3) δ 3.76 (s, 2H), 3.85 (s, 3H), 6.93 (d, $J = 7.5$ Hz, 2H), 6.99 (d, $J = 8.5$ Hz, 2H), 7.08 (d, $J = 7.5$ Hz, 1H), 7.13-7.26 (m, 6H), 8.25 (d, $J = 6.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 38.65, 55.25, 114.26, 123.79, 123.88, 126.56, 127.14, 128.55, 128.71, 130.68, 137.95, 138.76, 139.29, 149.96, 159.96. IR (neat) 3382, 3060, 3027, 2835, 1610, 1518, 1494, 1468, 1454, 1422, 1294, 1248, 1233, 1177, 1020, 829 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 314.1151, found. 314.1152.

3-Benzyl-2-[4-(trifluoromethyl)phenyl]pyridine *N*-oxide (2h). ^1H NMR (500 MHz, CDCl_3) δ 3.72 (s, 2H), 6.88 (d, $J = 7.0$ Hz, 2H), 7.15 (d, $J = 7.5$ Hz, 1H), 7.18-7.26 (m, 5H), 7.39 (d, $J = 8.0$ Hz, 2H), 7.71 (d, $J = 8.0$ Hz, 2H). ^{13}C NMR (150 MHz, CDCl_3) δ 38.55, 123.87 (q, $J = 273.0$ Hz), 124.62, 125.75, (q, $J = 3.8$ Hz), 126.80, 127.44, 128.59, 128.67, 129.13, 131.09 (q, $J = 33.0$ Hz), 135.51, 138.11 (2C), 139.01, 148.65. IR (neat) 3424, 1417, 1403, 1322, 1253, 1228, 1159, 1126, 1107, 1067, 1009, 841 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 352.0920, found. 352.0919.

3-Benzylpyridine *N*-oxide (2i). ^1H NMR (500 MHz, CDCl_3) δ 3.93 (s, 2H), 7.09 (d, $J = 8.5$ Hz, 1H), 7.16-7.20 (m, 3H), 7.25-7.28 (m, 1H), 7.33 (t, $J = 7.5$ Hz, 2H), 8.07 (s, 2H). ^{13}C NMR (125 MHz, CDCl_3)

δ 38.67, 125.52, 126.55, 127.07, 128.88, 128.94, 137.05, 137.73, 139.40, 140.42. IR (neat) 3392, 3060, 3027, 2919, 1599, 1563, 1494, 1482, 1261, 1156, 1075, 1015, 969 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 208.0733, found. 208.0733.

3-Benzyl-2-propylpyridine *N*-oxide (2j). ^1H NMR (500 MHz, CDCl_3) δ 0.99 (t, $J = 7.5$ Hz, 3H), 1.60 (sext, $J = 7.5$ Hz, 2H), 2.94 (t, $J = 7.5$ Hz, 2H), 4.02 (s, 2H), 6.96 (d, $J = 8.0$ Hz, 1H), 7.03 (t, $J = 6.5$ Hz, 1H), 7.11 (d, $J = 7.0$ Hz, 2H), 7.23-7.26 (m, 1H), 7.30-7.33 (m, 2H), 8.17 (d, $J = 6.5$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 14.36, 19.14, 29.36, 38.37, 122.29, 126.80, 127.25, 128.65, 128.77, 137.67, 137.92, 138.36, 152.30. IR (neat) 3400, 2961, 2929, 2870, 1494, 1478, 1454, 1423, 1253, 1201, 1097 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 250.1202, found. 250.1202.

3-Benzyl-2-[3-(triisopropylsilyloxy)propyl]pyridine *N*-oxide (2k). ^1H NMR (500 MHz, CDCl_3) δ 1.04-1.13 (m, 21H), 1.85-1.90 (m, 2H), 3.10 (t, $J = 8.0$ Hz, 2H), 3.76 (t, $J = 5.5$ Hz, 2H), 4.07 (s, 2H), 6.96 (d, $J = 8.0$ Hz, 1H), 7.03 (t, $J = 6.5$ Hz, 1H), 7.11 (d, $J = 8.0$ Hz, 2H), 7.23 (t, $J = 7.5$ Hz, 1H), 7.28-7.32 (m, 2H), 8.16 (d, $J = 6.5$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 11.97, 18.02, 24.27, 28.83, 38.07, 62.93, 122.36, 126.70, 127.22, 128.68, 128.71, 137.84, 137.95, 138.37, 152.16. IR (neat) 3062, 3028, 2940, 2863, 1462, 1425, 1382, 1263, 1183, 1101, 996, 882 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 422.2486, found. 422.2485.

3-Benzyl-2-cyclohexylpyridine *N*-oxide (2l). ^1H NMR (500 MHz, CDCl_3) δ 1.10–1.30 (m, 4H), 1.61-1.81 (m, 4H), 2.68 (brs, 2H), 2.88 (brs, 1H), 4.01 (brs, 2H), 7.02-7.10 (m, 4H), 7.22-7.31 (m, 3H), 8.09 (brs, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 25.16, 25.61, 26.68, 39.81, 41.00, 122.39, 126.72, 128.01, 128.52, 128.70, 137.60, 138.91, 139.93, 154.49. IR (neat) 2921, 2849, 1602, 1494, 1452, 1423, 1278, 1252, 1207, 1134, 1015, 894 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 290.1515, found. 290.1515.

3-(4-Methoxybenzyl)-2-phenylpyridine *N*-oxide (2n). ^1H NMR (500 MHz, CDCl_3) δ 3.66 (s, 2H), 3.77 (s, 3H), 6.78 (d, $J = 8.5$ Hz, 2H), 6.83 (d, $J = 8.5$ Hz, 2H), 7.08 (d, $J = 8.0$, 1H), 7.15-7.18 (m, 1H), 7.26-7.30 (m, 2H), 7.42-7.49 (m, 3H), 8.25 (d, $J = 6.0$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 37.70, 55.21, 113.95, 123.99, 127.04, 128.76, 129.00, 129.27, 129.73, 130.59, 131.88, 137.87, 139.54, 149.93, 158.27. IR (neat) 3061, 2998, 2953, 2834, 1610, 1585, 1510, 1462, 1440, 1423, 1300, 1261, 1243, 1175, 1032, 1012 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 314.1151, found. 314.1151.

3-Butyl-2-phenylpyridine *N*-oxide (2p). ^1H NMR (500 MHz, CDCl_3) δ 0.69 (t, $J = 7.5$ Hz, 3H), 1.11 (sext, $J = 7.5$ Hz, 2H), 1.33 (quint, $J = 7.5$ Hz, 2H), 2.29 (t, $J = 7.5$ Hz, 2H), 7.26 (d, $J = 7.5$ Hz, 2H), 7.36-7.44 (m, 3H), 8.15 (d, $J = 5.5$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 13.55, 22.12, 32.16, 32.37, 123.93, 126.44, 128.63, 128.82, 129.18, 132.08, 137.47, 140.65, 149.67. IR (neat) 3066, 2953, 2923, 2866, 1467, 1427, 1272, 1242, 1012, 814 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 250.1202, found. 250.1202.

3-Cyclohexyl-2-phenylpyridine *N*-oxide (2q). ^1H NMR (500 MHz, CDCl_3) δ 0.71-0.78 (m, 2H),

1.03-1.13 (m, 3H), 1.31- 1.35 (m, 1H), 1.47 (d, $J = 12.5$ Hz, 2H), 1.59-1.62 (m, 3H), 2.27 (d, $J = 7.5$ Hz, 2H), 7.16-7.19 (m, 2H), 7.31 (d, $J = 7.5$ Hz, 2H), 7.43-7.51 (m, 3H), 8.23 (d, $J = 5.5$ Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 26.05, 26.15, 32.86, 38.64, 40.03, 123.66, 127.10, 128.60, 128.79, 129.40, 132.23, 137.54, 139.26, 150.12. IR (neat) 3062, 2920, 2847, 1466, 1447, 1418, 1267, 1233, 1014 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 290.1515, found. 290.1515.

8. Representative Procedure for the Copper-Catalyzed Synthesis of **3a**.

To a mixture of $\text{CuBr(PPh}_3)_3$ (37.2 mg, 0.04 mmol), and the oxime **(Z)-1a** (134.8 mg, 0.40 mmol) in a pressure vial was added MeCN (0.8 mL) under argon atmosphere and the mixture was stirred at 100 $^\circ\text{C}$ for 7 h. The reaction mixture was passed through a pad of silica gel with EtOAc. After removing solvents in vacuo, the residue was purified by flash column chromatography (Hexane/ EtOAc = 5/1 as eluent) to give **3a** (113.5 mg, 84%).

9. Analytical Data of **3a**.

(Z)-3,5-Diphenyl-4-[(E)-3-phenylallylidene]-4,5-dihydroisoxazole (3a). ^1H NMR (500 MHz, CDCl_3) δ 6.02 (s, 1H), 6.52 (dd, $J = 15.5$ Hz, $J = 11.0$ Hz, 1H), 6.65 (d, $J = 15.5$ Hz, 1H), 6.71 (d, $J = 11.0$ Hz, 1H), 7.18-7.27 (m, 5H), 7.40-7.52 (m, 8H), 8.14 (d, $J = 7.5$ Hz, 2H). ^{13}C NMR (125 MHz, CDCl_3) δ 85.66, 117.02, 124.08, 126.34, 126.38, 127.11, 127.96, 128.67, 128.80, 129.18, 129.80, 130.28, 131.75, 131.90, 134.06, 136.77, 149.14. IR (neat) 3058, 3027, 1671, 1540, 1489, 1448, 1416, 1256, 961 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 360.1359, found. 360.1358.

10. Representative Procedure for the CuCl Catalyzed Synthesis of **4a**.

To a mixture of CuCl (3.96 mg, 0.04 mmol), and oxime **(E)-1a** (134.8 mg, 0.40 mmol) in a pressure vial

was added MeCN (0.8 mL) under argon atmosphere and the mixture was stirred at 60 °C for 2.5 h. The reaction mixture was passed through a pad of silica gel with EtOAc. After removing solvents in vacuo, the residue was purified by flash column chromatography (Hexane/ EtOAc = 5/1 as eluent) to give **4a** (48.5 mg, 36%).

11. Analytical Data of **4a**.

(E)-3-Benzylidene-2,4-diphenyl-3,4-dihydropyridine N-oxide (4a). ^1H NMR (500 MHz, CDCl_3) δ 4.83 (d, J = 6.0 Hz, 1H), 6.40 (dd, J = 7.5 Hz, J = 6.0 Hz, 1H), 6.77 (s, 1H), 6.88-6.91 (m, 5 H), 6.92-6.98 (m, 4H), 7.29-7.40 (m, 4H), 7.47-7.50 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3) δ 47.15, 124.87, 125.90, 127.04, 127.20, 127.35, 127.87, 127.98, 128.01, 128.49, 129.03, 129.06, 129.22, 130.30, 135.50, 137.18, 138.70. IR (neat) 3057, 3025, 1951, 1887, 1671, 1597, 1574, 1492, 1469, 1440, 1217, 1205 cm^{-1} . HRMS (ESI) calcd. for $(\text{M}+\text{Na})^+$ 360.1359, found. 360.1358.

Chemical structure: O=C1C(=C/C=C/c2ccccc2)C#CC1c3ccccc3

¹H NMR spectrum (CDCl₃) showing peaks from 6.0 to 7.9 ppm. Integration values are provided for several peaks: 0.93, 1.00, 1.00, 1.97, 2.00, and 0.93.

(*E*)-Acrylaldehyde *O*-(1,3-diphenylprop-2-yn-1-yl) oxime ((*E*)-1b).

(1*E*, 2*E*)-Hex-2-enal *O*-(1,3-diphenylprop-2-yn-1-yl) oxime ((*E*)-1d).

(E)-Methacrylaldehyde O-(1,3-diphenylprop-2-yn-1-yl) oxime ((E)-1e).

(*E*)-Cyclohex-1-enecarbaldehyde *O*-(1,3-diphenylprop-2-yn-1-yl) oxime ((*E*)-1f).

(*E*)-Acrylaldehyde *O*-[3-(4-methoxyphenyl)-1-phenylprop-2-yn-1-yl] oxime ((*E*)-1g).

(*E*)-Acrylaldehyde *O*-[1-phenyl-3-(4-trifluoromethyl)phenyl]prop-2-yn-1-yl] oxime ((*E*)-1h).

(*E*)-Acrylaldehyde *O*-(1-phenylprop-2-yn-1-yl) oxime ((*E*)-1i)

(*E*)-Acrylaldehyde *O*-(1-phenylhex-2-yn-1-yl) oxime ((*E*)-1j).

(*E*)-Acrylaldehyde *O*-[1-phenyl-6-(triisopropylsilyloxy)hex-2-yn-1-yl] oxime ((*E*)-1k).

(*E*)-Acrylaldehyde *O*-[3-(cyclohexyl)-1-phenylprop-2-yn-1-yl] oxime ((*E*)-11).

(*E*)-Acrylaldehyde *O*-[4-(4-dimethyl)-1-phenylpent-2-yn-1-yl] oxime ((*E*)-1m).

(*E*)-Acrylaldehyde *O*-[1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-yl] oxime ((*E*)-1n).

(E)-Acrylaldehyde O-(1-phenylhex-1-yn-3-yl) oxime ((E)-1p).

(*E*)-Acrylaldehyde *O*-(1-cyclohexyl-3-phenylprop-2-yn-1-yl) oxime ((*E*)-1q).

3-Benzyl-2,4-diphenylpyridine *N*-oxide (2a).

3-Benzyl-2-phenylpyridine *N*-oxide (2b).

3-Benzyl-4-methyl-2-phenylpyridine *N*-oxide (2c).

3-Benzyl-2-phenyl-4-propylpyridine *N*-oxide (2d).

3-Benzyl-5-methyl-2-phenylpyridine *N*-oxide (2e).

4-Benzyl-3-phenyl-5,6,7,8-tetrahydroisoquinoline *N*-oxide (2f).

3-Benzyl-2-(4-methoxyphenyl)pyridine *N*-oxide (2g).

3-Benzyl-2-[4-(trifluoromethyl)phenyl]pyridine *N*-oxide (2h).

3-Benzylpyridine *N*-oxide (2i).

3-Benzyl-2-propylpyridine *N*-oxide (2j).

3-Benzyl-2-[3-(triisopropylsilyloxy)propyl]pyridine *N*-oxide (2k).

3-Benzyl-2-cyclohexylpyridine *N*-oxide (2l).

3-(4-Methoxybenzyl)-2-phenylpyridine *N*-oxide (2n).

3-Butyl-2-phenylpyridine *N*-oxide (2p).

(Z)-3-Benzylidene-2,4-diphenyl-3,4-dihydropyridine N-oxide (4a).