

Electronic Supplementary Information (ESI) for

Heterogeneously catalyzed selective aerobic oxidative cross-coupling of terminal alkynes and amides with simple copper(II) hydroxide

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Experimental details

General: GC analyses were performed on Shimadzu GC-2014 with a FID detector equipped with a Rtx-200 capillary column. Mass spectra were recorded on Shimadzu GCMS-QP2010 equipped with a TC-5HT capillary column at an ionization voltage of 70 eV. Liquid-state NMR spectra were recorded on JEOL JNM-EX-270. ^1H and ^{13}C NMR spectra were measured at 270 and 67.8 MHz, respectively. Copper salts, bases, substrates, and solvents were commercially obtained from TCI, Wako, or Aldrich (reagent grade), and purified prior to the use, if necessary.^{S1} Supported copper hydroxide catalysts, $\text{Cu}(\text{OH})_x/\text{TiO}_2$ and $\text{Cu}(\text{OH})_x/\text{Al}_2\text{O}_3$, were prepared according to the literature procedure (see below).¹⁰

Preparation of supported copper hydroxide catalysts:¹⁰ The aqueous solution (60 mL) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.085 g, 8.3 mM) containing the TiO_2 (or Al_2O_3) powder (2.0 g) calcined at 550 °C was vigorously stirred at room temperature. After 15 min, the pH of the solution was quickly adjusted to 12 by addition of an aqueous solution of NaOH (1.0 M, base treatment) and the resulting slurry was further stirred for 24 h. The solid was then filtered off, washed with a large amount of water, and dried in vacuo to afford 2.0 g of $\text{Cu}(\text{OH})_x/\text{TiO}_2$ (or $\text{Cu}(\text{OH})_x/\text{Al}_2\text{O}_3$) as a light blue powder. The content of copper was 1.6 wt%. The content of water was ca. 10 wt%.

Typical procedure for cross-coupling of terminal alkynes and amides: Into a Pyrex-glass screw cap vial (volume: ca. 20 mL) were successively placed $\text{Cu}(\text{OH})_2$ (5 mol% with respect to an alkyne), a base (5–20 mol%), an alkyne (0.1 mmol), an amide (2–3 equivalents with respect to an alkyne), and mesitylene (1 mL). A Teflon-coated magnetic stir bar was added, and the reaction mixture was vigorously stirred at 100–120 °C, under 1 atm of air. After the reaction was completed, an internal standard (biphenyl) was added to the reaction mixture, and the conversion of an alkyne and the product yield were analyzed by gas chromatography. As for the isolation of products (ynamides), an internal standard was not added, and the crude reaction mixture was directly subjected to column chromatography on silica gel (Silica Gel 60N (63–210 μm), Kanto Chemical, 2.5 cm ID×15 cm length, initial: *n*-hexane only, after mesitylene, an alkyne and a diyne byproduct were eluted: *n*-hexane/ethyl acetate = 9/1 to 3/2 (v/v)), giving the pure ynamide. The isolated products were identified by GC-MS and ^1H and ^{13}C NMR.

Spectral data of ynamides

3aa (CAS registry number: 888329-88-2)

3-(phenylethynyl)oxazolidin-2-one (3aa): This compound has been reported previously, and the analytical data were identical to the literature ones.⁹

3ba

3-(*o*-tolylethynyl)oxazolidin-2-one (3ba): Solid. ¹H NMR (270 MHz, CDCl₃, TMS): δ 2.44 (s, 3H), 3.99–4.05 (m, 2H), 4.46–4.52 (m, 2H), 7.08–7.26 (m, 3H), 7.38–7.41 (m, 1H). ¹³C{¹H} NMR (67.8 MHz, CDCl₃, TMS): δ 20.69, 47.12, 62.95, 70.12, 82.68, 121.94, 125.50, 128.12, 129.39, 131.62, 139.90, 155.81. MS (EI): *m/z* (%) : 201 (57) [*M*⁺], 156 (16), 142 (11), 129 (24), 128 (16), 116 (13), 115 (100), 103 (10), 102 (24), 77 (10), 58 (10).

3ca (CAS registry number: 1221282-86-5)

3-(*m*-tolylethynyl)oxazolidin-2-one (3ca): This compound has been reported previously, and the analytical data were identical to the literature ones.⁵

3da (CAS registry number: 1221282-84-3)

3-(*p*-tolylethynyl)oxazolidin-2-one (3da): This compound has been reported previously, and the analytical data were identical to the literature ones.⁵

3ea (CAS registry number: 1311313-26-4)

3-((4-fluorophenyl)ethynyl)oxazolidin-2-one (3ea): This compound has been reported previously, and the analytical data were identical to the literature ones.^{2j}

3fa

3-((4-chlorophenyl)ethynyl)oxazolidin-2-one (3fa): Solid. ¹H NMR (270 MHz, CDCl₃, TMS): δ 3.98–4.04 (m, 2H), 4.49–4.55 (m, 2H), 7.26–7.30 (m, 2H), 7.34–7.40 (m, 2H). ¹³C{¹H} NMR (67.8 MHz, CDCl₃, TMS): δ 46.93, 63.05, 70.24, 79.78, 120.67, 128.63, 132.73, 134.19, 155.75. MS (EI): *m/z* (%) : 223 (33), 222 (13), 221 (100) [*M*⁺], 179 (11), 177 (36), 164 (18), 162 (57), 151 (32), 150 (15), 149 (43), 142 (14), 127 (11), 126 (15), 116 (12), 115 (59), 114 (85), 98 (10), 89 (11), 88 (21), 87 (21), 75 (13), 73 (17), 63 (16), 62 (10).

3ga

3-((4-fluorophenyl)ethynyl)oxazolidin-2-one (3ga): This compound has been reported previously, and the analytical data were identical to the literature ones.⁶

3ha

3-((3-chlorophenyl)ethynyl)oxazolidin-2-one (3ha): Solid. ¹H NMR (270 MHz, CDCl₃, TMS): δ 3.98–4.04 (m, 2H), 4.47–4.53 (m, 2H), 7.20–7.33 (m, 3H), 7.41–7.43 (m, 1H). ¹³C{¹H} NMR (67.8 MHz, CDCl₃, TMS): δ 46.88, 63.08, 70.10, 80.07, 123.93, 128.34, 129.49, 129.51, 131.17, 134.07, 155.68. MS (EI): *m/z* (%) : 223 (33), 222 (13), 221 (100) [*M*⁺], 179 (13), 177 (39), 176 (10), 164 (24), 162 (74), 151 (29), 149 (31), 142 (12), 127 (12), 126 (14), 116 (16), 115 (58), 114 (80), 88 (19), 87 (16), 75 (12), 63 (14).

3ia

3-((4-(trifluoromethyl)phenyl)ethynyl)oxazolidin-2-one (3ia): Solid. ¹H NMR (270 MHz, CDCl₃, TMS): δ 4.01–4.07 (m, 2H), 4.49–4.55 (m, 2H), 7.50–7.58 (m, 4H). ¹³C{¹H} NMR (67.8 MHz, CDCl₃, TMS): δ 46.86, 63.14, 70.40, 81.33, 114.14, 117.86, 121.87, 125.13, 125.18, 125.24, 125.30, 125.87, 125.15, 126.18, 129.03, 129.42, 129.90, 130.13, 131.32, 137.50, 155.62. MS (EI): *m/z* (%) : 256 (14), 255 (100) [*M*⁺], 236 (11), 211 (58), 210 (15), 197 (12), 196 (96), 185 (17), 183 (41), 176 (12), 163 (13), 145 (10), 142 (14), 133 (14), 115 (20), 114 (12), 88 (10), 81 (19).

3ja

3-((3-methoxyphenyl)ethynyl)oxazolidin-2-one (3ja): Solid. ¹H NMR (270 MHz, CDCl₃, TMS): δ 3.79 (s, 3H), 3.98–4.04 (m, 2H), 4.46–4.51 (m, 2H), 6.8–6.88 (m, 1H), 6.96–6.98 (m, 1H), 7.01–7.05 (m, 1H), 7.18–7.27 (m, 1H). ¹³C{¹H} NMR (67.8 MHz, CDCl₃, TMS): δ 46.98, 55.25, 63.02, 71.15, 78.75, 114.80, 116.20, 123.13, 123.95, 129.32, 155.84, 159.26. MS (EI): *m/z* (%) : 218 (13), 217 (100) [*M*⁺], 173 (35), 158 (33), 146 (10), 145 (19), 143 (14), 130 (24), 116 (22), 115 (24), 103 (15), 102 (19), 90 (13), 89 (12), 88 (12), 77 (11), 76 (14), 75 (16), 51 (11).

3ka

3-(naphthalene-1-ylethynyl)oxazolidin-2-one (3ka): Solid. ¹H NMR (270 MHz, CDCl₃, TMS): δ 4.04–4.10 (m, 2H), 4.48–4.53 (m, 2H), 7.38–7.67 (m, 4H), 7.79–7.85 (m, 2H), 8.33 (dd, *J* = 8.1 and 0.8 Hz, 1H). ¹³C{¹H} NMR (67.8 MHz, CDCl₃, TMS): δ 47.07, 63.06, 69.53, 83.59, 119.84, 125.13, 126.06, 126.40, 126.81, 128.20, 128.51, 129.90, 132.96, 133.10, 155.87. MS (EI): *m/z* (%) :

238 (16), 237 (100) [M^+], 193 (19), 192 (12), 178 (33), 166 (18), 165 (71), 164 (39), 152 (12), 151 (31), 150 (11), 139 (13), 138 (18), 97 (13), 89 (17), 76 (14).

3la

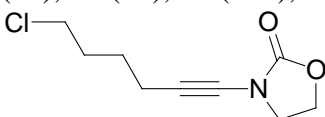
3-(thiophen-3-ylethynyl)oxazolidin-2-one (3la): Solid. ^1H NMR (270 MHz, CDCl_3 , TMS): δ 3.96–4.02 (m, 2H), 4.45–4.51 (m, 2H), 7.12 (dd, $J = 4.9$ and 1.1 Hz, 1H), 7.25–7.28 (m, 1H), 7.46 (dd, $J = 3.0$ and 1.1 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (67.8 MHz, CDCl_3 , TMS): δ 46.98, 63.02, 66.34, 78.32, 120.85, 125.28, 129.15, 130.04, 155.91. MS (EI): m/z (%) : 194 (11), 193 (100) [M^+], 149 (24), 148 (17), 134 (50), 123 (15), 122 (28), 121 (58), 96 (10), 95 (14), 94 (28), 70 (12), 69 (10), 63 (10).

3ma

3-(cyclohexenylethynyl)oxazolidin-2-one (3ma): Oil. ^1H NMR (270 MHz, CDCl_3 , TMS): δ 1.53–1.69 (m, 4H), 2.05–2.16 (m, 4H), 3.89–3.95 (m, 2H), 4.41–4.47 (m, 2H), 6.10–6.14 (m, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (67.8 MHz, CDCl_3 , TMS): δ 21.38, 22.24, 25.63, 29.33, 47.08, 62.85, 72.62, 76.39, 119.41, 135.35, 156.02. MS (EI): m/z (%) : 192 (13), 191 (100) [M^+], 163 (14), 146 (20), 135 (11), 132 (16), 119 (28), 118 (24), 117 (12), 108 (12), 105 (31), 104 (66), 103 (10), 92 (21), 91 (45), 80 (14), 79 (27), 78 (23), 77 (40), 65 (19), 64 (16), 55 (12), 51 (14).

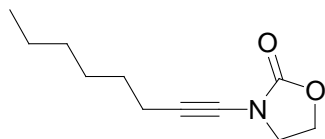
3na

3-(3-(dimethylamino)prop-1-ynyl)oxazolidin-2-one (3na): Oil. ^1H NMR (270 MHz, CDCl_3 , TMS): δ 2.30 (s, 6H), 3.39 (s, 2H), 3.89–3.95 (m, 2H), 4.42–4.47 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (67.8 MHz, CDCl_3 , TMS): δ 44.05, 46.85, 47.83, 62.86, 66.24, 74.66, 156.29. MS (EI): m/z (%) : 168 (76) [M^+], 167 (79), 125 (14), 124 (30), 123 (10), 96 (38), 95 (16), 82 (56), 81 (90), 80 (94), 68 (13), 67 (21), 66 (14), 58 (37), 56 (17), 55 (15), 54 (59), 53 (100), 52 (45).



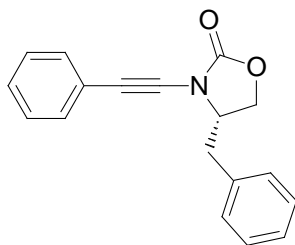
3oa (CAS registry number: 1262669-87-3)

3-(6-chlorohex-1-ynyl)oxazolidin-2-one (3oa): This compound has been reported previously, and the analytical data were identical to the literature ones.^{S2}



3pa (CAS registry number: 888329-96-2)

3-(oct-1-ynyl)oxazolidin-2-one (3pa): This compound has been reported previously, and the analytical data were identical to the literature ones.⁹



3ab (CAS registry number: 888329-89-3)

(S)-4-benzyl-3-(phenylethynyl)oxazolidin-2-one (3ab): This compound has been reported previously, and the analytical data were identical to the literature ones.⁹

3ac (CAS registry number: 950747-29-2)

3-(phenylethynyl)-1,3-oxazetidin-2-one (3ac): This compound has been reported previously, and the analytical data were identical to the literature ones.⁹

3ad (CAS registry number: 1005500-77-5)

N,4-dimethyl-N-(phenylethynyl)benzenesulfonamide: This compound has been reported previously, and the analytical data were identical to the literature ones.⁹

Additional references

- S1 *Purification of Laboratory Chemicals*, 3rd ed. (Eds.: D. D. Perrin, W. L. F. Armarego), Pergamon Press, Oxford, 1988.
- S2 P. W. Davies, A. Cremonesi and N. Martin, *Chem. Commun.*, 2011, **47**, 379.

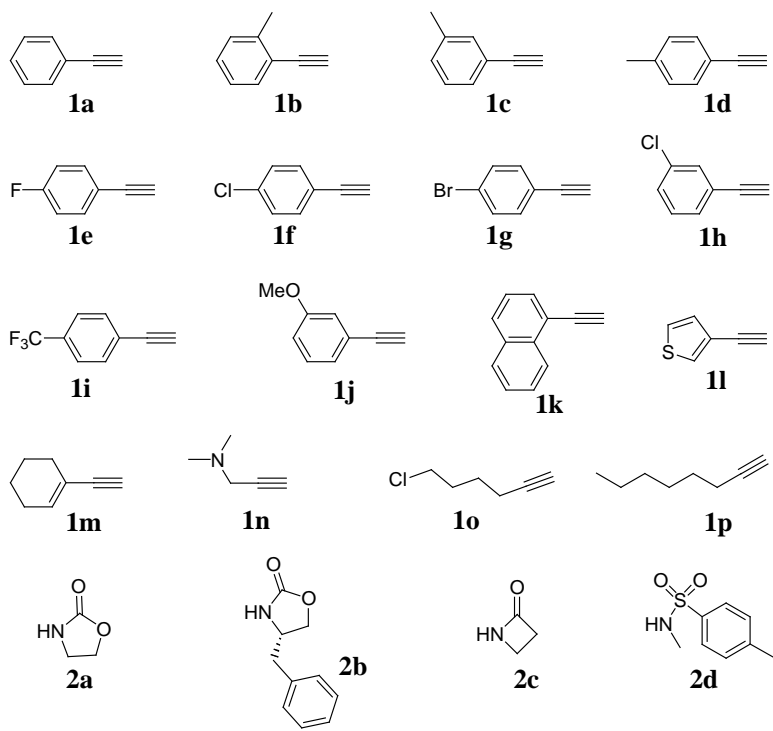
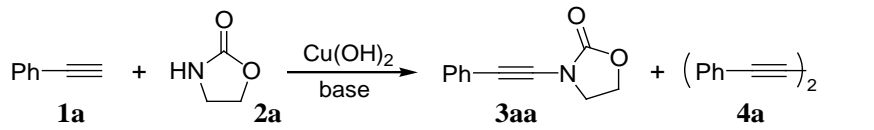


Fig. S1. Terminal alkynes and amides used in this study.

Table S1 Solvent screening^a

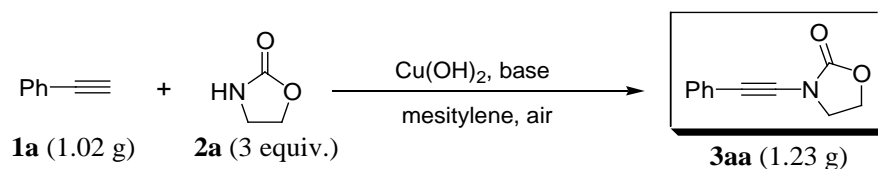


$\text{Ph-C}\equiv\text{C-H} + \text{HN-CO-O} \xrightarrow[\text{base}]{\text{Cu(OH)}_2} \text{Ph-C}\equiv\text{C-N-CO-O} + (\text{Ph-C}\equiv\text{C})_2$

1a **2a** **3aa** **4a**

Entry	Solvent	Conv. of 1a (%)	Yield (%)	
			3aa	4a
1	Mesitylene	76	75	1
2 ^b	Mesitylene	5	nd	nd
3	1,2-Dichloroethane	<1	nd	nd
4	1,4-Dioxane	<1	nd	nd
5	Ethyl acetate	<1	nd	nd
6	2-Propanol	<1	nd	nd
7	Acetonitrile	<1	nd	nd
8	DMSO	<1	nd	nd
9	DMF	6	2	nd

^a Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), Cu(OH)₂ (Cu: 5 mol%), K₂CO₃ (5 mol%), solvent (1 mL), 100 °C, under air (1 atm), 0.5 h. Conversions and yields (based on **1a**) were determined by GC using biphenyl as an internal standard. nd = not detected. ^b The reaction was carried out under Ar atmosphere.



Scheme S1. Gram-scale cross-coupling of **1a** and **2a**. Reaction conditions: **1a** (1.02 g), **2a** (3 equiv. with respect to **1a**), Cu(OH)₂ (Cu: 5 mol%), K₂CO₃ (2.5 mol%), mesitylene (100 mL), 100 °C, under air (1 atm), 11 h. After the reaction was completed, the crude reaction mixture was directly subjected to column chromatography on silica gel, giving 1.23 g of **3aa** (66% isolated yield).