Access to ynamides via CuO-mediated oxidative amidation of alkynes

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General considerations: All commercially available compounds were purchased from Aldrich, and all solvents were purified and dried according to standard methods prior to use. $^1$H and $^{13}$C NMR spectra were recorded on Bruker AV-400 MHz or DRX 500 MHz spectrometers and referenced to internal tetramethysilane. $^1$H NMR data are recorded as follows: chemical shift ($\delta$, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet, br = broad singlet, coupling constant(s) in Hz, integration). $^{13}$C NMR data are reported in terms of chemical shift ($\delta$, ppm). ESI-MS and HR-ESI-MS were determined with an API QSTAR Pulsar 1 spectrometer. EI-MS and ESI-MS were obtained on a Finnigan-4510 spectrometer and a Finnigan MAT 90 mass spectrometer, respectively. HR-ESIMS was recorded with an API QSTAR Pulsar 1 spectrometer. Optical rotations were obtained with a Horiba SEAP-300 polarimeter. Silica gel (200-300 mesh; Qingdao Marine Chemical Inc., Qingdao, China) was used for flash chromatography which was eluted with hexanes/ethyl acetate.

General procedures for the synthesis of ynamides: In a dry 25 mL round flask,
CuO (1.93 mmol), KCl (0.154 mmol), 4-PPY (0.154 mmol) and 2-oxazolidinones (3.85 mmol) were added to dry toluene (5 ML) under argon. The flask was placed in an oil-bath and added 4-ethynylanisole (0.77 mmol). Then, the reaction mixture was stirred for 36 hours at 80 °C. After the crude mixture was filtrated and concentrated under vacuum, the mixture was separated on a silica gel column using hexanes/ethyl acetate (2/1) as eluent to afford the ynamides.

Ynamide 3.\(^1\) colorless acicular crystal. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.38 (d, \(J = 8.8\) Hz, 2H), 6.83 (d, \(J = 8.8\) Hz, 2H), 4.49-4.56 (m, 2H), 4.00-3.97 (m, 2H), 3.80 (s, 3H).

Product 4.\(^2\) colorless acicular crystal. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.46 (d, \(J = 8.8\) Hz, 4H), 6.85 (d, \(J = 8.8\) Hz, 4H), 3.82 (s, 6H).

Ynamide 7.\(^1\) colorless acicular crystal. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.42 (d, \(J = 9.1\) Hz, 2H), 7.35-7.28 (m, 3H), 7.24-7.23 (m, 2H), 6.85 (d, \(J = 9.1\) Hz, 2H), 4.33 (m, 2H), 4.14 (m, 1H), 3.80 (s, 3H), 3.25 (dd, \(J = 14.0, 3.5\) Hz, 1H), 3.00 (m, 1H); [\(\alpha\)]\(^\text{b}\) +82.1 (c 3.01, CHCl\(_3\)).
Ynamide 8. colorless acicular crystal. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.39 (d, $J = 8.8$ Hz, 2H), 6.83 (d, $J = 8.8$ Hz, 2H), 4.42 (t, $J = 8.8$ Hz, 1H), 4.19 (d, $J = 8.8$, 6.0 Hz, 1H), 4.03 (m, 1H), 3.81 (s, 3H), 2.29 (m, 1H), 1.03 (d, $J = 6.6$ Hz, 3H), 1.02 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 159.6, 156.1, 133.4, 114.3, 113.9, 77.0, 71.9, 64.8, 62.1, 55.3, 29.2, 17.2, 15.2; HRMS: m/z (ESI) measured 260.1281 (calcd [M+H]$^+$ = 260.1286); $[\alpha]^\text{D} +28.2$ (c 2.57, CHCl$_3$).

Ynamide 9. colorless acicular crystal. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.39-7.29 (m, 5H), 7.12 (d, $J = 8.7$ Hz, 2H), 6.66 (d, $J = 8.7$ Hz, 2H), 5.05-5.01 (m, 1H), 4.70-4.66 (m, 1H), 4.20 (dd, $J = 9.0$, 7.2 Hz, 1H), 3.67 (m, 3H); $[\alpha]^\text{D} +154.9$ (c 1.36, CHCl$_3$).

Ynamide 10. colorless acicular crystal. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.33 (d, $J = 7.8$ Hz, 2H), 7.11 (d, $J = 7.8$ Hz, 2H), 4.47-4.43 (m, 2H), 3.99-3.53 (m, 2H), 2.34 (s, 3H).

Ynamide 11. colorless acicular crystal. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.45-7.43 (m, 2H), 7.31-7.30 (m, 3H), 4.50-4.47 (m, 2H), 4.02-3.99 (m, 2H).
**Ynamide 12.** colorless acicular crystal. $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 8.03 (s, 1H), 7.92-7.89 (m, 3H), 7.51-7.56 (m, 2H), 7.48-7.45 (m, 1H), 3.50-4.46 (m, 2H), 4.06-4.02 (m, 2H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 155.9, 132.7, 132.2, 130.5, 128.3, 127.9, 127.7, 126.7, 126.9, 119.3, 81.1, 70.5, 63.8, 46.7; HRMS: m/z (ESI) measured 238.0869 (calcd [M+H]$^+$ = 238.0868).

**Ynamide 13.** colorless powder. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.43-4.40 (m, 2H), 3.93-3.90 (m, 2H), 0.18 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 155.8, 91.3, 73.7, 62.9, 46.8, 0.016; HRMS: m/z (ESI) measured 184.0795 (calcd [M+H]$^+$ = 184.0793).

**Z-Enamide 14.** yellow powder. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.19 (d, $J$ = 8.3 Hz, 2H), 7.36 (d, $J$ = 8.3 Hz, 2H), 6.82 (d, $J$ = 9.6 Hz, 1H), 5.97 (d, $J$ = 9.6 Hz, 1H), 4.34-4.31 (m, 2H), 3.39-3.35 (m, 2H).

**E-Enamide 14.** yellow powder. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.15 (d, $J$ = 8.5 Hz, 2H), 7.56 (d, $J$ = 14.5 Hz, 1H), 7.43 (d, $J$ = 8.5 Hz, 2H), 5.74 (d, $J$ = 14.5 Hz, 1H), 4.58-4.54 (m, 2H), 3.92-3.88 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 155.1, 146.1, 142.9, 127.8, 125.7, 124.3, 108.7, 62.4, 42.4; HRMS: m/z (ESI) measured 235.0713 (calcd [M+H]$^+$ = 235.0718).
(Z)-Enamide 15. yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.57 (m, 1H), 7.61 (td, $J = 7.8, 2.0$ Hz, 1H), 7.21 (d, $J = 7.8$ Hz, 1H), 7.10 (ddd, $J = 7.8, 5.0, 1.0$ Hz, 1H), 6.77 (d, $J = 10.4$ Hz, 1H), 5.86 (d, $J = 10.4$ Hz, 1H), 4.36-4.32 (m, 2H), 3.87-3.83 (m, 2H): $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 157.1, 154.3, 148.7, 136.0, 126.1, 124.5, 121.1, 110.1, 62.7, 45.5; HRMS: m/z (ESI) measured 191.0823 (calcd [M+H]$^+$ = 191.0820).

(E)-Enamide 15. yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.49 (d, $J = 4.4$ Hz, 1H), 7.81 (d, $J = 14.3$ Hz, 1H), 7.60 (td, $J = 7.7, 2.2$ Hz, 1H), 7.29 (d, $J = 7.7$ Hz, 1H), 7.07 (m, 1H), 5.90 (d, $J = 14.3$ Hz, 1H), 4.54-4.51 (m, 2H), 3.90-3.87 (m, 2H): $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$156.1, 155.9, 150.3, 137.4, 128.6, 122.1, 120.7, 112.0, 63.2, 43.4; HRMS: m/z (ESI) measured 191.0820 (calcd [M+H]$^+$ = 191.0820).

Reference: