SUPPORTING INFORMATION

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# A Copper-Catalyzed Ficini [2 + 2] Cycloaddition of Ynamides.

authored by

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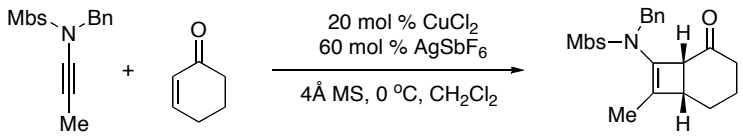
## GENERAL EXPERIMENTAL INFORMATION

All reactions were performed in flame-dried glassware under a nitrogen atmosphere. Solvents were distilled prior to use. Reagents were used as purchased (Aldrich, Acros), except where noted. Chromatographic separations were performed using Bodman 60 Å $SiO_2$. $^1H$ and $^{13}C$ NMR spectra were obtained on Varian VI-300, VI-400, and VI-500 spectrometers using $CDCl_3$ (except where noted) with TMS or residual $CHCl_3$ in the solvent as standard. Melting points were determined using a Laboratory Devices MEL-TEMP and are uncorrected/calibrated. Infrared spectra were obtained using NaCl plates on a Bruker Equinox 55/S FT–IR Spectrophotometer, and relative intensities are expressed qualitatively as s (strong), m (medium), and w (weak). TLC analysis was performed using Aldrich 254 nm polyester-backed plates (60 Å, 250 μm) and visualized using UV and a suitable chemical stain. Low-resolution mass spectra were obtained using an Agilent-1100-HPLC/MSD and can be either APCI or ESI, or an IonSpec HiRes-MALDI FT-Mass Spectrometer. High-resolution mass spectral analyses were performed at University of Wisconsin Mass Spectrometry Laboratories. All spectral data obtained for new compounds are reported. X-Ray analyses were performed at the X-Ray facility in University of Minnesota.

**General Procedure for Copper-Catalyzed Ficini [2 + 2] Cycloadditions of Ynamides.**




**12** **13**

To a stirring suspension of $CuCl_2$ (4.00 mg, 0.03 mmol) and 4Å MS (50.0 mg) in $CH_2Cl_2$ (0.5 mL) was added $AgSbF_6$ (31.0 mg, 0.090 mmol) in the dark at room temperature. After stirring for 1 h at RT, a solution of ynamide **12** (47.3 mg, 0.15 mmol) and 2-cyclohexen-1-one (17.3 mg, 0.18 mmol) in $CH_2Cl_2$ (0.4 mL) was added to the catalyst mixture at 0 °C over 1 h via a syringe pump. After stirring for an additional 30 min at the same temperature post addition, phosphate buffer (pH = 6.8, 1 mL) was added to the mixture and the resulting mixture was extracted with EtOAc. The organic layers were washed with sat aq NaCl and dried over $MgSO_4$. Filtration and concentration of the mixture *in vacuo* afforded the crude product that was purified by flash silica gel column chromatography [gradient eluent: EtOAc in hexanes] to afford product **13** (47.0 mg, 0.114 mmol, 76%).

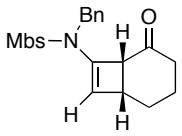
**13:** $R_f$ = 0.15 [25% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.23-1.32 (m, 2 H), 1.39-1.48 (m, 2 H), 1.66-1.67 (m, 3 H), 1.76-1.85 (m, 2 H), 2.74 (br, 1 H), 3.18-3.20 (m, 1 H), 3.88 (s, 3 H), 4.55, 4.61 (ABq, 2 H, $J_{AB}$ = 14.8 Hz), 6.98-7.00 (m, 2 H), 7.23-7.32 (m, 5 H), 7.78-7.80 (m, 2 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.6, 17.2, 23.9, 38.7, 40.6, 51.4, 54.1, 55.9, 114.5, 127.1, 127.8, 128.0, 128.7, 129.8, 131.4, 136.6, 144.1, 163.4, 210.7;

IR (film) cm$^{-1}$ 2929(w), 1686(s), 1593(s), 1577(m) 1495(s), 1456(w), 1442(w), 1403(w), 1371(w), 1345(s), 1328(m), 1310(m), 1261(s);

mass spectrum (APCI): m/z (% relative intensity) 412.2 (100) $[M + H]^+$.




**11**

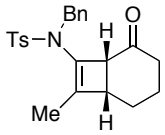
**11** was isolated in ≤5% yield from ynamide **10** following the general procedure.

**11:** $R_f$ = 0.13 [25% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.40-1.50 (m, 3 H), 1.69-1.74 (m, 1 H), 1.93-1.97 (m, 2 H), 3.03 (br, 1 H), 3.39 (d, 1 H, $J$ = 4.0 Hz), 3.88 (s, 3 H), 4.67 (d, 1 H, $J$ = 16.0 Hz), 4.94 (d, 1 H, $J$ = 16.0 Hz), 5.51 (m, 1 H), 6.96-6.98 (m, 2 H), 7.27-7.36 (m, 5 H), 7.76-7.79 (m, 2 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 17.8, 26.1, 37.4, 40.5, 50.8, 54.7, 55.9, 114.3, 121.4, 127.68, 127.72, 128.8, 129.8, 131.0, 134.2, 137.2, 163.5, 210.8;

mass spectrum (APCI): m/z (% relative intensity) 398.2 (100) $[M + H]^+$.




**14**

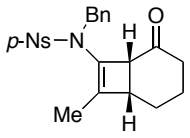
**14** (36.2 mg, 0.092 mmol) was isolated in 61% yield following the general procedure.

**14:** $R_f$ = 0.26 [25% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.23-1.32 (m, 2 H), 1.39-1.48 (m, 2 H), 1.66-1.67 (m, 3 H), 1.78-1.82 (m, 2 H), 2.45 (s, 3 H), 2.74 (br, 1 H), 3.18 (dq, 1 H, $J$ = 2.0, 4.4 Hz), 4.55, 4.62 (ABq, 2 H, $J_{AB}$ = 15.2 Hz), 7.25-7.33 (m, 7 H), 7.72-7.75 (m, 2 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.6, 17.2, 21.8, 23.9, 38.7, 40.6, 51.4, 54.0, 126.9, 127.7, 127.8, 128.0, 128.7, 129.9, 136.6, 136.8, 144.1, 144.2, 210.7;

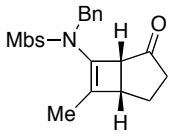
IR (film) $cm^{-1}$ 3014(w), 2986(w), 1687(w), 1455(w), 1347(w), 1276(s), 1261(s);
mass spectrum (APCI): m/z (% relative intensity) 396.2 (100) $[M + H]^+$.



**15**

**15** (40.9 mg, 0.096 mmol) was isolated in 64% yield following the general procedure.

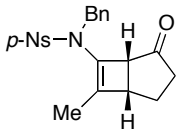
**15:** $R_f$ = 0.12 [15% EtOAc in hexanes];
$^1$H NMR (500 MHz, $CDCl_3$) δ 1.25-1.32 (m, 1 H), 1.47-1.55 (m, 2 H), 1.65 (m, 3 H), 1.79-1.97 (m, 3 H), 2.78 (br, 1 H), 3.20 (br, 1 H), 4.58, 4.66 (ABq, 2 H, $J_{AB}$ = 15.0 Hz), 7.25-7.34 (m, 5 H), 8.03-8.05 (m, 2 H), 8.36-8.38 (m, 2 H);
$^{13}$C NMR (125 MHz, $CDCl_3$) δ 12.6, 17.4, 24.0, 38.9, 41.1, 52.0, 53.6, 124, 6, 126.0, 128.2, 128.3, 128.9, 129.0, 135.7, 145.7, 146.2, 150.5, 210.2;
IR (film) $cm^{-1}$ 3014(w), 2986(w), 1688(w), 1528(w), 1456(w), 1348(w), 1276(s), 1261(s);
mass spectrum (APCI): m/z (% relative intensity) 427.1 (61) $[M + H]^+$, 409.1 (100).



**16**

**16** (34.6 mg, 0.087 mmol) was isolated in 58% yield following the general procedure.

**16:** $R_f$ = 0.13 [25% EtOAc in hexanes];
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.66-1.71 (m, 2 H), 1.727-1.734 (m, 3 H), 1.76-1.83 (m, 1 H), 1.89-1.99 (m, 1 H), 2.89-2.91 (m, 1 H), 2.95-2.97 (m, 1 H), 3.89 (s, 3 H), 4.44, 4.50 (ABq, 2 H, $J_{AB}$ = 15.2 Hz), 6.98-7.02 (m, 2 H), 7.22-7.32 (m, 5 H), 7.76-7.79 (m, 2 H);
$^{13}$C NMR (100 MHz, $CDCl_3$) δ 13.1, 20.0, 34.2, 40.3, 51.3, 54.4, 55.9, 114.6, 127.9, 128.0, 128.7, 129.5, 129.7, 131.2, 126.3, 144.1, 163.5, 215.9;
IR (film) $cm^{-1}$ 3014(w), 2986(w), 1459(w), 1276(s), 1261(s);
mass spectrum (APCI): m/z (% relative intensity) 398.2 (100) $[M + H]^+$.




**17**

**17** (21.0 mg, 0.051 mmol) was isolated in 34% yield following the general procedure.

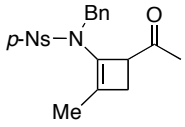
**17:** $R_f$ = 0.27 [25% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.70-1.76 (m, 5 H), 1.84-1.91 (m, 1 H), 1.99-2.09 (m, 1 H), 2.94-2.96 (m, 1 H), 2.99-3.01 (m, 1 H), 4.51 (s, 2 H), 7.21-7.23 (m, 2 H), 7.27-7.36 (m, 3 H), 8.00-8.04 (m, 2 H), 8.36-8.39 (m, 2 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 13.1, 19.9, 34.3, 40.6, 51.9, 54.4, 124.3, 124.6, 128.1, 128.3, 128.8, 128.9, 135.3, 145.5, 146.1, 150.5, 215.4;

IR (film) cm$^{-1}$ 3014(w), 2986(w), 1524(w), 1458(w), 1350(w), 1276(s), 1261(s);

mass spectrum (APCI): m/z (% relative intensity) 413.1 (100) $[M + H]^+$.




**18**

**18** (31.8 mg, 0.080 mmol) was isolated in 53% yield following the general procedure.

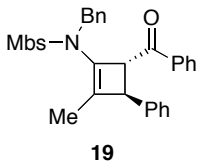
**18:** $R_f$ = 0.12 [15% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.43-1.50 (m, 3 H), 1.99 (s, 3 H), 2.13-2.17 (m, 1 H), 2.25-2.29 (m, 1 H), 3.73-3.75 (m, 1 H), 4.54, 4.67 (ABq, 2 H, $J_{AB}$ = 14.8 Hz), 7.28-7.35 (m, 5 H), 7.99-8.02 (m, 2 H), 8.33-8.36 (m, 2 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 14.7, 28.5, 31.3, 52.6, 54.2, 124.5, 128.26, 128.34, 128.8, 128.9, 129.0, 135.9, 138.1, 145.6, 150.3, 207.7;

IR (film) cm$^{-1}$ 3014(w), 2986(w), 1700(w), 1529(w), 1475(w), 1458(w), 1350(w), 1276(s), 1261(s);

mass spectrum (APCI): m/z (% relative intensity) 401.1 (100) $[M + H]^+$.

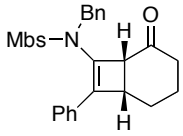



**19**

**19** (47.9 mg, 0.092 mmol) was isolated in 61% yield following the general procedure.

**19:** $R_f$ = 0.31 [25% EtOAc in hexanes];

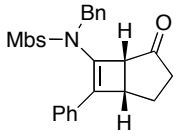
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.22-1.23 (m, 3 H), 3.46 (br, 1 H), 3.80 (s, 3 H), 4.37-4.39 (m, 1 H), 4.65, 4.69 (ABq, 2 H, $J_{AB}$ = 14.8 Hz), 6.86-6.90 (m, 2 H), 7.03-7.05 (m, 2 H), 7.27-7.36 (m, 8 H), 7.43-7.45 (m, 2 H), 7.48-7.52 (m, 1 H), 7.66-7.69 (m, 2 H), 7.80-7.84 (m, 2 H);
$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.5, 49.6, 52.6, 55.8, 60.1, 114.4, 127.5, 127.6, 127.9, 128.59, 128.64, 128.70, 128.73, 129.0, 129.9, 131.2, 131.7, 133.3, 136.6, 137.0, 139.6, 139.9, 163.2, 197.8;
IR (film) cm$^{-1}$ 3014(w), 2986(w), 1671(w), 1595(w), 1458(w), 1276(s), 1261(s);
mass spectrum (APCI): m/z (% relative intensity) 524.2 (100) $[M + H]^+$.



**20**

**20** (52.6 mg, 0.111 mmol) was isolated in 74% yield following the general procedure.

**20:** $R_f$ = 0.16 [25% EtOAc in hexanes];
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.44-1.53 (m, 1 H), 1.55-1.66 (m, 2 H), 1.94-2.12 (m, 2 H), 2.17-2.23 (m, 1 H), 3.29 (m, 2 H), 3.88 (s, 3 H), 4.42, 4.53 (ABq, 2 H, $J_{AB}$ = 14.4 Hz), 6.98-7.02 (m, 4 H), 7.14-7.18 (m, 3 H), 7.30-7.39 (m, 5 H), 7.88-7.91 (m, 2 H);
$^{13}$C NMR (100 MHz, $CDCl_3$) δ 17.6, 25.0, 37.5, 40.7, 51.2, 55.6, 55.9, 114.6, 127.1, 127.5, 128.0, 128.6, 128.7, 129.0, 129.1, 130.4, 131.0, 132.3, 135.6, 144.7, 163.6, 210.8;
IR (film) cm$^{-1}$ 3014(w), 2986(w), 1694(w), 1594(w), 1496(w), 1458(w), 1276(s), 1261(s);
mass spectrum (APCI): m/z (% relative intensity) 474.2 (100) $[M + H]^+$.

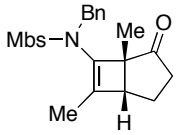


**21**

**21** (35.2 mg, 0.077 mmol) was isolated in 54% yield following the general procedure.

**21:** $R_f$ = 0.14 [25% EtOAc in hexanes];
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.83-1.91 (m, 2 H), 1.99-2.04 (m, 1 H), 2.08-2.17 (m, 1 H), 3.01-3.02 (m, 1 H), 3.39-3.41 (m, 1 H), 3.89 (s, 3 H), 4.33, 4.61 (ABq, 2 H, $J_{AB}$ = 14.4 Hz), 6.99-7.03 (m, 2 H), 7.06-7.09 (m, 2 H), 7.17-7.20 (m, 3 H), 7.29-7.38 (m, 3 H), 7.43-7.46 (m, 2 H), 7.83-7.87 (m, 2 H);
$^{13}$C NMR (100 MHz, $CDCl_3$) δ 21.5, 34.6, 38.2, 51.3, 54.8, 55.9, 114.7, 127.5, 128.0, 128.57, 128.62, 128.7, 129.1, 130.1, 130.9, 132.1, 135.6, 145.5, 163.7, 215.2, one carbon missing due to overlap;
IR (film) cm$^{-1}$ 3014(w), 2986(w), 1733(w), 1595(w), 1496(w), 1457(w), 1351(w), 1276(s), 1261(s);

mass spectrum (APCI): m/z (% relative intensity) 460.1 (100) $[M + H]^+$.




**22**

**22** (13.0 mg, 0.032 mmol) was isolated in 21% yield following the general procedure.

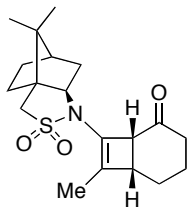
**22:** $R_f$ = 0.24 [25% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 0.82 (s, 3 H), 1.58-1.66 (m, 2 H), 1.74 (s, 3 H), 1.81-1.87 (m, 1 H), 2.05-2.15 (m, 1 H), 2.55-2.57 (m, 1 H), 2.88 (s, 3 H), 4.17 (d, 1 H, $J$ = 15.4 Hz), 4.71 (d, 1 H, $J$ = 15.4 Hz), 6.97-7.01 (m, 2 H), 7.22-7.35 (m, 5 H), 7.78-7.82 (m, 2 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.8, 13.6, 18.5, 34.8, 47.7, 51.1, 55.9, 59.0, 114.4, 127.7, 128.1, 128.6, 128.8, 129.9, 132.1, 136.5, 144.8, 163.4, 218.2;

IR (film) $cm^{-1}$ 3014(w), 2986(w), 1698(w), 1594(w), 1495(w), 1459(w), 1276(s), 1261(s);

mass spectrum (APCI): m/z (% relative intensity) 412.1 (100) $[M + H]^+$.




**23** [1 : 1]

**23** (35.1 mg, 0.101 mmol) was isolated in 67% yield following the general procedure.

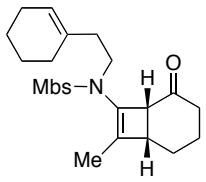
**23:** $R_f$ = 0.22 [25% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 0.92 (s, 3 H), 0.93 (s, 3 H), 1.14 (s, 3 H), 1.17 (s, 3 H), 1.20-1.76 (m, 10 H), 1.78-1.79 (m, 3 H), 1.79-1.80 (m, 3 H), 1.82-2.23 (m, 14 H), 2.54-2.60 (m, 1 H), 2.68-2.73 (m, 1 H), 3.00 (m, 1 H), 3.05 (m, 1 H), 3.15-3.23 (m, 4 H), 3.44-3.46 (m, 1 H), 3.58-3.62 (m, 2 H), 3.69 (dd, 1 H, $J$ = 4.0, 4.0 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.19, 12.24, 17.2, 17.7, 20.21, 20.23, 20.7, 20.8, 23.7, 24.3, 27.1, 27.2, 32.0, 32.1, 35.4, 35.7, 39.7, 39.8, 40.3, 40.4, 44.9, 45.1, 48.1, 50.1, 50.3, 50.6, 50.7, 54.7, 56.2, 63.9, 64.6, 123.6, 123.8, 143.3, 145.5, 211.79, 211.83, missing one carbon due to overlap;

IR (film) $cm^{-1}$ 3014(w), 2986(w), 1692(w), 1456(w), 1304(w), 1276(s), 1261(s);

mass spectrum (APCI): m/z (% relative intensity) 350.1 (100) $[M + H]^+$.




**24**

**24** (16.1 mg, 0.038 mmol) was isolated in 25% yield following the general procedure.

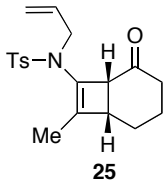
**24:** $R_f$ = 0.10 [20% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.53-1.70 (m, 8 H), 1.73-1.74 (m, 3 H), 1.90-1.99 (m, 6 H), 2.11-2.18 (m, 2 H), 2.90 (br, 1 H), 3.32 (br, 1 H), 3.38-3.45 (m, 1 H), 3.50-3.57 (m, 1 H), 3.86 (s, 3 H), 5.42 (m, 1 H), 6.92-6.97 (m, 2 H), 7.68-7.72 (m, 2 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.7, 17.5, 22.5, 23.1, 24.1, 25.5, 28.4, 38.2, 38.7, 40.6, 46.5, 53.9, 55.8, 114.3, 124.0, 127.2, 129.7, 131.9, 134.2, 143.3, 163.2, 210.3;

IR (film) $cm^{-1}$ 3014(w), 2986(w), 1691(w), 1595(w), 1497(w), 1459(w), 1334(w), 1276(s), 1261(s);

mass spectrum (APCI): m/z (% relative intensity) 430.2 (100) $[M + H]^+$.




**25**

**25** (38.9 mg, 0.113 mmol) was isolated in 75% yield following the general procedure.

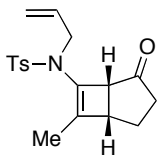
**25:** $R_f$ = 0.23 [25% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.48-1.68 (m, 3 H), 1.71-1.72 (m, 3 H), 1.85-1.96 (m, 2 H), 2.09-2.15 (m, 1 H), 2.41 (s, 3 H), 2.86 (br, 1 H), 3.26-3.27 (m, 1 H), 3.98 (ddt, 1 H, $J$ = 1.6, 6.0, 16.0 Hz), 4.08 (ddt, 1 H, $J$ = 1.6, 5.2, 16.0 Hz), 5.11-5.24 (m, 2 H), 5.70-5.80 (m, 1 H), 7.26-7.28 (m, 2 H), 7.64-7.67 (m, 2 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.6, 17.4, 21.8, 24.0, 38.7, 40.6, 50.4, 54.0, 117.8, 127.1, 127.7, 129.8, 133.8, 136.9, 143.2, 144.0, 210.5;

IR (film) $cm^{-1}$ 3014(w), 2986(w), 1687(w), 1596(w), 1441(w), 1349(w), 1276(s), 1261(s);

mass spectrum (APCI): m/z (% relative intensity) 346.1 (100) $[M + H]^+$.




**26**

**26** (32.3 mg, 0.098 mmol) was isolated in 65% yield following the general procedure.

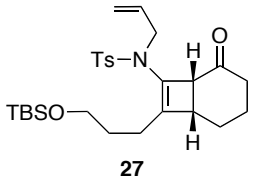
**26:** $R_f$ = 0.26 [25% EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.76-1.90 (m, 5 H), 1.98-2.05 (m, 1 H), 2.43 (s, 3 H), 2.52-2.62 (m, 1 H), 2.99-3.02 (m, 2 H), 3.91-3.93 (m, 2 H), 5.11-5.22 (m, 2 H), 5.66-5.76 (m, 1 H), 7.28-7.32 (m, 2 H), 7.65-7.68 (m, 2 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 13.1, 20.2, 21.8, 34.7, 40.4, 50.2, 54.4, 117.9, 127.6, 129.3, 129.9, 133.5, 136.7, 143.0, 144.1, 215.7;

IR (film) cm$^{-1}$ 3014(w), 2986(w), 1720(w), 1460(w), 1351(w), 1276(s), 1261(s);

mass spectrum (APCI): m/z (% relative intensity) 332.1 (100) $[M + H]^+$.




**27**

**27** (28.3 mg, 0.056 mmol) was isolated in 56% yield following the general procedure.

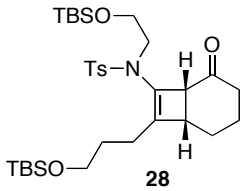
**27:** $R_f$ = 0.40 (2:1 hexanes/EtOAc);

$^1$H NMR (500 MHz, $CDCl_3$) δ 0.00 (s, 6H), 0.84 (s, 9H), 1.46-1.59 (m, 3H), 1.60-1.70 (m, 2H), 1.84-1.92 (m, 2H), 1.98-2.05 (m, 1H), 2.09 (d, 1H, $J$ = 18.5 Hz), 2.30 (ddd, 1H, $J$ = 16.0, 10.0, 6.5 Hz), 2.37 (s, 3H), 2.91 (s, 1H), 3.22 (s, 1H), 3.51-3.57 (m, 2H), 3.92 (dd, 1H, $J$ = 15.5, 6.5 Hz), 4.03 (dd, 1H, $J$ = 16.0, 5.5 Hz), 5.07 (d, 1H, $J$ = 10.5 Hz), 5.16 (d, 1H, $J$ = 17.0 Hz), 5.69 (ddt, 1H, $J$ = 17.0, 10.5, 6.0 Hz), 7.22 (d, 2H, $J$ = 8.0 Hz), 7.61 (d, 2H, $J$ = 8.0 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ -5.0, 17.6, 18.6, 21.8, 23.6, 24.4, 26.2, 29.8, 37.4, 40.7, 50.6, 53.8, 63.1, 118.0, 126.8, 127.7, 129.8, 133.7, 137.0, 143.9, 147.3, 210.5;

IR (film) cm$^{-1}$ 2934(m), 2858(m), 1697(m), 1598(w), 1352(m), 1164(s);

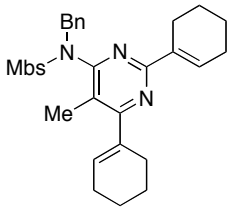
mass spectrum (APCI): m/e (% relative intensity) 504 (100) $[M + H]^+$.




**28**

**28** (66.9 mg, 0.108 mmol) was isolated in 43% yield following the general procedure.

**28:** $R_f$ = 0.20 [20 % EtOAc in hexanes];
$^1$H NMR (500 MHz, $CDCl_3$) δ 0.05 (m, 12 H), 0.90 (m, 18 H), 1.55-1.75 (m, 5 H), 1.86-1.95 (m, 2 H), 2.00-2.15 (m, 2 H), 2.30-2.40 (m, 1 H), 2.41 (s, 3 H), 2.95-3.00 ( br, 1 H), 3.40 (s, 1 H), 3.50-3.55 (m 1 H), 3.55-3.65 (m, 3 H), 3.65- 3.75 (m, 2 H), 7.25 (m, 2 H), 7.65 (m , 2 H);
$^{13}$C NMR (125 MHz, $CDCl_3$) δ -5.17, -5.14, -4.99, -4.98, 17.74, 18.51, 18.61, 21.84, 23.95, 24.71, 26.13, 26.24, 29.89, 37.30, 40.62, 50.21, 53.09, 62.81, 63.31, 127.26, 127.77,129.77, 137.162, 143.93, 144.72, 210.37;
IR (film) cm$^{-1}$ 2952(m), 2929(m), 2857(m), 1694(m), 1354(w), 1254(m), 1164(s), 1094(s);
mass spectrum (APCI): m/e (% relative intensity) 622.3 (100) $[M + H]^+$.



III

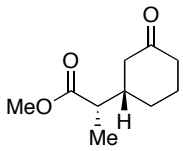
Pyrimidine **iii** (15.0 mg, 0.028 mmol) was isolated following the general procedure used for cyclobutene synthesis from ynamide **12** (44.3 mg, 0.15 mmol) and cyclohexene-1-carbonitrile (20.0 μL, 0.18 mmol) in 31% yield [nitrile as limiting reagent].

**iii:** $R_f$ = 0.31 (6:1 hexanes/EtOAc);
$^1$H NMR (500 MHz, $CDCl_3$) δ 1.61 – 1.77 (m, 9H), 2.16 (brs, 1H), 2.17 (s, 3H), 2.23 (brs, 2H), 2.30 (brs, 4H), 3.89 (s, 3H), 4.61 (brs, 2H), 5.80 (s, 1H), 6.96 (d, 2H, $J$ = 8.0 Hz), 7.03 (s, 1H), 7.16 (s, 5H), 7.68 (d, 2H, $J$ = 8.0 Hz);
$^{13}$C NMR (125 MHz, $CDCl_3$) δ 15.4, 22.1, 22.4, 22.8, 22.9, 25.2, 25.5, 26.2, 27.6, 53.8, 55.9, 114.0, 126.0, 128.0, 128.5, 129.4, 130.0, 130.9, 131.4, 132.8, 135.6, 136.0, 136.7, 159.6, 162.2, 163.4, 170.4;
IR (film) cm$^{-1}$ 2927m, 2856w, 1645m, 1595m, 1555m, 1349s, 1158s;
mass spectrum (APCI): m/e (% relative intensity) 530 (100) $[M+H]^+$.

**General Procedure for Hydrolysis of 13.**

To a reflux solution of cyclobutenamide **13** (20.6 mg, 0.05 mmol) in anhyd MeOH (1 mL) or combined solvents (1 mL, MeOH: $H_2O$ = 9:1) was added TMSCl (50.0 μL) dropwise over 2 h. The reaction was stirred at 60 $^o$C until the reaction was complete; the mixture was concentrated *in vacuo* to

give the crude product that was then purified by silica gel flash column chromatography [gradient eluent: EtOAc in hexanes] to give **30**-*syn* in 54% yield and **31** in 34% yield.




**30**-*syn*

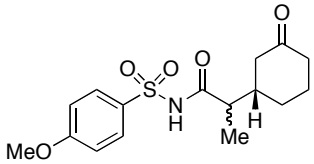
**30**-*syn*: $R_f$ = 0.36 [30 % EtOAc in hexanes];

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.15 (d, 3 H, $J$ = 6.8 Hz), 1.38-1.48 (m, 1 H), 1.59-1.70 (m, 1 H), 1.81-1.85 (m, 1 H), 2.00-2.13 (m, 3 H), 2.21-2.29 (m, 1 H), 2.35-2.46 (m, 3 H), 3.69 (s, 3 H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 13.9, 25.0, 29.2, 41.2, 41.4, 44.6, 44.9, 51.7, 175.6, 210.8;

IR (film) cm$^{-1}$ 2946(m), 2360(w), 2256(w), 1735(s), 1713(s), 1596(w), 1459(m), 1435(m);

mass spectrum (APCI): m/z (% relative intensity) 185.1 (100) $[M + H]^+$.




**31** [1 : 1]

**31:** $R_f$ = 0.15 [30 % EtOAc in hexanes];

$^1$H NMR (500 MHz, $CDCl_3$) δ 0.84 (d, 3 H, $J$ = 6.5 Hz), 0.92 (d, 3 H, $J$ = 6.5 Hz), 1.02 (dq, 1 H, $J$ = 4.0, 13.0 Hz), 1.16 (dq, 1 H, $J$ = 3.5, 13.0 Hz), 1.42-1.56 (m, 3 H), 1.72 (t, 1 H, $J$ = 13.0 Hz), 1.77-1.87 (m, 3 H), 1.91-1.99 (m, 3 H), 2.05-2.14 (m, 3 H), 2.27-2.30 (m, 2 H), 2.34-2.38 (m, 1 H), 3.01 (t, 2 H, $J$ = 7.0, 14.0 Hz), 3.867 (s, 3 H), 3.873 (s, 3 H), 5.04-5.15 (m, 4 H), 6.92-6.95 (m, 4 H), 7.30-7.38 (m, 10 H), 7.63-7.67 (m, 4 H);

IR (film) cm$^{-1}$ 2925(w), 2858(w), 2362(w), 2256(w), 1896(w), 1696(s), 1596(s), 1580(m), 1499(s), 1457(m), 1419(w);

mass spectrum (APCI): m/z (% relative intensity) 430.2 (100) $[M + H]^+$.