Copper(II) Carboxylate Promoted Intramolecular Carboamination of Alkenes for the Synthesis of Polycyclic Lactams

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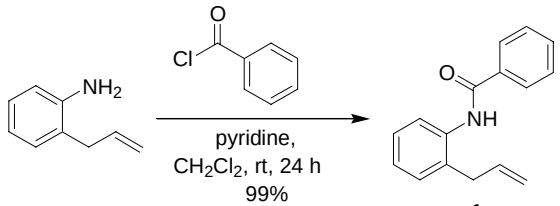
Supporting Information 1

Table of Contents

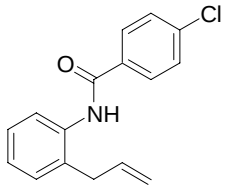
General Experimental Information: All reagents were used out of the bottle as purchased from the supplier without further purification unless otherwise noted. Copper(II) ethylhexanoate, DMF, and tert-butyl benzene were purchased from the supplier and used out of the bottle. ^{1}H NMR spectra were recorded in $CDCl_3$ (using 7.26 ppm for reference of residual $CHCl_3$) at 300, 400 or 500 MHz unless otherwise noted. ^{13}C NMR spectra were recorded in $CDCl_3$ (using 77.0 ppm as internal reference) at 75 or 125.7 MHz unless otherwise noted. IR spectra were taken neat using a Nicolet-Impact 420 FTIR. Wave numbers in cm^{-1} are reported for characteristic peaks. High resolution mass spectra were obtained at SUNY Buffalo's mass spec. facility on a ThermoFinnigan MAT XL spectrometer purchased by a National Science Foundation grant to the center (NSF CHE0091977). Melting points are reported as uncorrected.

Representative synthesis of amide substrates derived from 2-allyl aniline
Each substrate was made by treating *o*-allylaniline with the corresponding acid chloride.



1a

***N*-(2-allyl-phenyl)-benzamide (1a)**
o-Allyl aniline (0.55 g, 4.09 mmol, 1 equiv) was dissolved in dry CH_2Cl_2 (20.5 mL) and the solution was treated with pyridine (1.00 mL, 12.3 mmol, 3 equiv) followed by benzoyl chloride (0.623 mL, 4.90 mmol, 1.2 equiv). The reaction mixture was stirred at room temperature overnight, then diluted with H_2O (30 mL) and extracted with Et_2O (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Chromatography of the resulting crude oil on SiO_2 (0-30% Et_2O/hexanes gradient) afforded 1.1 g (99.5%) of the known *N*-(2-allyl-phenyl)-benzamide as a brown solid.[1]

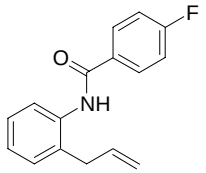


1b

***N*-(2-allyl-phenyl)-4-chloro-benzamide (1b)**
Compound **1b** was obtained as a white solid from benzoylation of *o*-allyl aniline with 4-chlorobenzoyl chloride in 99% yield.

Data for **1b**: mp 126 – 128 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.95 (d, J = 8.1 Hz, 1H), 7.77 (d, J = 8.7 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.32-7.14 (m, 3H), 6.08-6.01 (m, 1H), 5.30 (d, J = 10.4 Hz, 1H), 5.17 (d, J = 17.2 Hz, 1H), 3.44 (d, J = 5.7 Hz,

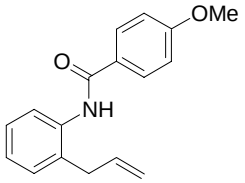
2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5, 161.7, 138.0, 136.2, 136.0, 133.2, 130.3, 130.2, 128.9, 128.4, 127.5, 125.5, 123.7, 116.8, 37.0; IR (neat, thin film) υ 3276, 2998, 2885, 1653, 1585, 1530, 1489, 1452, 1311, 1091, 1015 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}O_1N_1Cl_1Na_1$ $[M+Na]^+$ 294.0662, found 294.0661.



1c

***N*-(2-allyl-phenyl)-4-fluoro-benzamide (1c)**

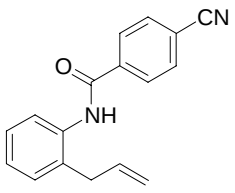
Compound **1c** was obtained as a pale yellow solid from benzoylation of *o*-allyl aniline with 4-fluorobenzoyl chloride in 40% yield. mp 83 – 85 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 8.0 Hz, 2H), 7.85-7.83 (m, 2H), 7.33-7.30 (m, 1H), 7.60-7.22 (m, 1H), 7.21-7.13 (m, 3H), 6.07-6.00 (m, 1H), 5.23 (d, J = 10.5 Hz, 1H), 5.11 (d, J = 17 Hz, 1H), 3.45 (d, J = 6.0 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 165.9, 163.9, 136.4, 136.2, 130.4, 129.5, 129.4, 127.7, 125.5, 123.7, 116.9, 115.9, 115.8, 37.1; IR (neat, thin film) υ 3377, 3007, 2936, 2252, 2198, 1690, 1653, 1587, 1312, 1009, 812 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{14}ONF$ $[M]^+$ 255.1054, found 255.1062.



1d

***N*-(2-allyl-phenyl)-4-methoxy-benzamide (1d)**

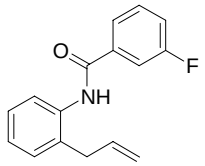
Compound **1d** was obtained as a yellow solid from benzoylation of *o*-allyl aniline with 4-methoxy benzoyl chloride in 98% yield. mp 129 – 131 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 1H), 7.90 (s, 1H), 7.82 (d, J = 8.8 Hz, 2H), 7.34-7.30 (m, 1H), 7.22 (d, J = 6.0 Hz, 1H), 7.16-7.13 (m, 1H), 7.00-6.97 (m, 2H), 6.10-6.01 (m, 1H), 5.25 (d, J = 10.2 Hz, 1H), 5.12 (d, J = 17.1 Hz, 1H), 3.88 (s, 3H), 3.46 (d, J = 6.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 163.0, 137.0, 133.3, 130.8, 130.6, 129.4, 128.1, 127.7, 125.6, 124.1, 117.3, 114.6, 114.5, 56.0, 37.5; IR (neat, thin film) υ 3284, 2987, 2888, 1653, 1509, 1302, 1253, 1178, 1024, 913, 842 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}O_2NNa$ $[M+Na]^+$ 290.1152, found 290.1152.



1e

***N*-(2-allyl-phenyl)-4-cyano-benzamide (1e)**

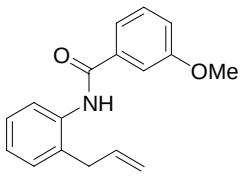
Compound **1e** was obtained as a light brown solid from benzoylation of *o*-allyl aniline with 4-cyano benzoyl chloride in 58% yield. mp 113 – 115 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.90-7.70 (m, 3H), 7.68 (d, J = 8.0 Hz, 2H), 7.29-7.26 (m, 1H), 7.22-7.17 (m, 2H), 6.02-5.95 (m, 1H), 5.25 (d, J = 9 Hz, 1H), 5.06 (d, J = 17.5 Hz, 1H), 3.42 (d, J = 6 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.0, 138.6, 136.3, 135.6, 132.6, 131.1, 130.5, 127.8, 127.6, 126.2, 124.2, 118.0, 117.0, 115.3, 36.9; IR (neat, thin film) υ 3365, 3018, 2948, 1693, 1611, 1499, 1326, 1091, 991 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{14}ON_2$ $[M]^+$ 262.1101, found 262.1108.



3

***N*-(2-allyl-phenyl)-3-fluoro-benzamide (3)**

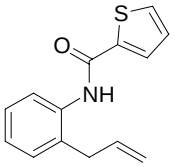
Compound **3** was obtained as a white solid from benzoylation of *o*-allyl aniline with 3-fluoro benzoyl chloride in 57% yield. mp 110 – 112 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.90 (d, J = 8 Hz, 1H), 7.60-7.56 (m, 2H), 7.43-7.40 (m, 1H), 7.30-7.27 (m, 1H), 7.24-7.20 (m, 2H), 7.17-7.14 (m, 2H), 6.04-5.98 (m, 1H), 5.21 (d, J = 10.5 Hz, 1H), 5.10 (d, J = 17.5 Hz, 1H), 3.43 (d, 6 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.8, 161.9, 137.2, 137.1, 136.3, 135.9, 130.7, 130.5, 130.4, 127.6, 125.8, 124.0, 122.5, 122.4, 118.9, 118.7, 116.9, 114.7, 114.5, 37.0; IR (neat, thin film) υ 3268, 3071, 2919, 2842, 2490, 1643, 1583, 1525, 1475, 1450, 1306, 1268, 1199, 993 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}ONFNa$ $[M+Na]^+$ 278.0952, found 278.0954.



6

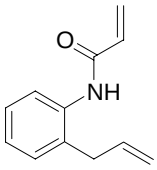
***N*-(2-allyl-phenyl)-3-methoxy-benzamide (6)**

Compound **6** was obtained as a yellow solid from benzoylation of *o*-allyl aniline with 3-methoxy benzoyl chloride in 37% yield. mp 138 – 140 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 6 Hz, 1H), 7.97 (s, 1H), 7.44 (s, 1H), 7.40-7.29 (m, 3H), 7.24-7.20 (m, 1H), 7.17-7.09 (m, 2H), 6.09-6.03 (m, 1H), 5.24 (d, J = 10 Hz, 1H), 5.12 (d, J = 17 Hz, 1H), 3.86 (s, 3H), 3.46 (d, J = 6 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 165.5, 160.0, 136.4, 136.2, 130.3, 129.7, 127.5, 125.5, 123.8, 118.8, 118.0, 116.9, 112.5, 55.4, 36.9; IR (neat, thin film) υ 3296, 3267, 3069, 2959, 2837, 2569, 2531, 1784, 1649, 1583, 1489, 1452, 1302, 1226, 1152, 1040, 997 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{17}O_2N$ $[M]^+$ 267.1254, found 267.1267.



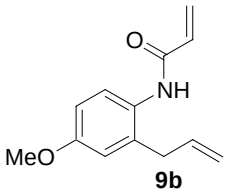
34c

Thiophene-2-carboxylic acid (2-allyl-phenyl)-amide (34c)
Compound **34c** was obtained as a white solid from benzoylation of *o*-allyl aniline in 58% yield. mp 107 – 109 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 1H), 7.87 (s, 1H), 7.56-7.54 (m, 2H), 7.34-7.29 (m, 2H), 7.21-7.12 (m, 2H), 6.11-6.03 (m, 1H), 5.28 (d, J = 10.2 Hz, 1H), 5.19 (d, J = 17.4 Hz, 1H), 3.47 (d, J = 5.4 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 159.8, 139.3, 136.1, 135.8, 130.5, 130.2, 130.1, 128.3, 127.7, 127.4, 125.3, 123.6, 116.9, 36.9; IR (neat, thin film) υ 3282, 3076, 2977, 2914, 2846, 1829, 1635, 1603, 1585, 1509, 1418, 1355, 1301, 1268, 1184, 1103, 1038, 996, 916 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{13}ONNaS$ $[M+Na]^+$ 266.0610, found 266.0600



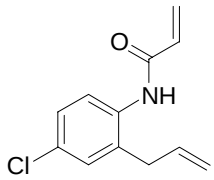
9a

***N*-(2-allyl-phenyl)-acrylamide (9a)**
The known compound **9a** was obtained as a white solid from acylation of *o*-allyl aniline with acryloyl chloride in 42% yield.[2] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 6.8 Hz, 1H), 7.38 (s, 1H), 7.31-7.27 (m, 1H), 7.21-7.18 (m, 1H), 7.16-7.14 (m, 1H), 6.40 (d, J = 16.8 Hz, 1H), 6.20 (dd, J = 10.4, 17.2 Hz, 1H), 6.01-5.95 (m, 1H), 5.76 (d, J = 10 Hz, 1H), 5.20 (d, J = 10 Hz, 1H), 5.12 (d, J = 17.2 Hz, 1H), 3.41 (d, J = 5.6 Hz, 2H).



9b

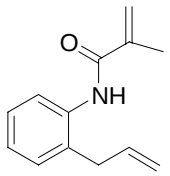
***N*-(2-allyl-4-methoxy-phenyl)-acrylamide (9b)**
The known compound **9b** was obtained as an off white solid from acylation of *p*-methoxy-*o*-allyl aniline with acryloyl chloride in 64% yield.[2] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 9 Hz, 1H), 7.28 (s, 1H), 6.79 (d, J = 8.5 Hz, 1H), 6.77 (s, 1H), 6.36 (d, J = 17.5 Hz, 1H), 6.21 (dd, J = 10, 17 Hz, 1H), 5.97-5.91 (m, 1H), 5.72 (d, J = 10 Hz, 1H), 5.16 (d, J = 9.5 Hz, 1H), 5.08 (d, J = 17 Hz, 1H), 3.78 (s, 3H), 3.34 (d, J = 6 Hz, 2H).



9c

***N*-(2-allyl-4-chloro-phenyl)-acrylamide (9c)**

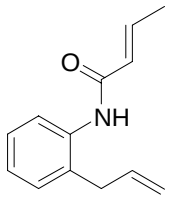
The known compound **9c** was obtained as a white solid from acylation of *p*-chloro-*o*-allyl aniline *p*-methoxy-*o*-allyl aniline with acryloyl chloride in 61% yield.[2] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, 7 Hz, 1H), 7.31 (s, 1H), 7.28-7.25 (m, 1H), 7.18 (s, 1H), 6.38 (d, J = 17 Hz, 1H), 6.19 (dd, J = 10, 16.5 Hz, 1H), 5.98-5.92 (m, 1H), 5.77 (d, J = 10 Hz, 1H), 5.24 (d, J = 10 Hz, 1H), 5.14 (d, J = 17.5 Hz, 1H), 3.38 (d, J = 6 Hz, 2H).



12

***N*-(2-allyl-phenyl)-2-methyl-acrylamide (12)**

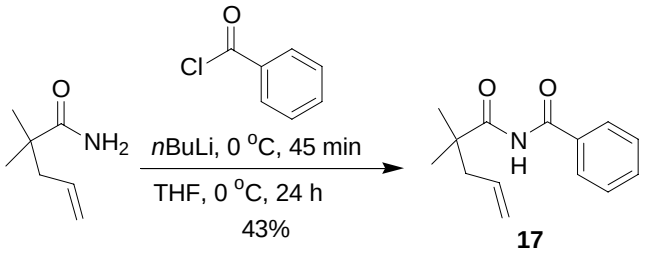
Compound **12** was obtained as a white solid from acylation of *o*-allyl aniline with methacryloyl chloride in 47% yield. mp 76 - 78 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 7.5 Hz, 1H), 7.67 (s, 1H), 7.31 (t, J = 9 Hz, 1H), 7.21 (d, J = 6.5 Hz, 1H), 7.13 (t, J = 8.5 Hz, 1H), 6.05-5.98 (m, 1H), 5.80 (s, 1H), 5.46 (s, 1H), 5.23 (d, J = 11.5 Hz, 1H), 5.10 (d, J = 19 Hz, 1H), 3.43 (d, J = 5.5 Hz, 2H), 2.07 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.4, 140.9, 136.2, 136.1, 130.3, 129.6, 127.6, 125.1, 123.2, 119.9, 116.8, 37.0, 18.8; IR (neat, thin film) υ 3270, 3073, 3002, 2978, 2929, 2823, 1849, 1660, 1621, 1600, 1515, 1500, 1443, 1305, 1241, 1010, 923 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{15}ON$ $[M]^+$ 201.1148, found 201.1144.



14

But-2-enoic acid (2-allyl-phenyl)-amide (14)

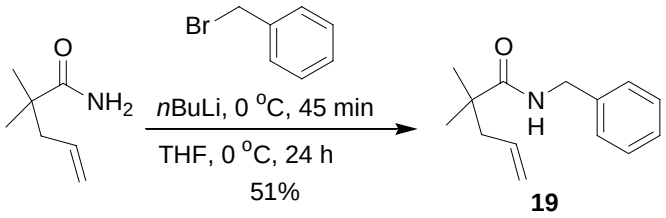
The known compound **14** was obtained as a yellow solid from acylation of *o*-allyl aniline with but-2-enoyl chloride in 40% yield.[2] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.29 (t, J = 8.5 Hz, 1H), 7.25-7.18 (m, 2H), 7.13-7.10 (m, 1H), 6.97-6.91 (m, 1H), 6.00-5.96 (m, 1H), 5.92-5.88 (d, J = 16.5 Hz, 1H), 5.20 (d, J = 10 Hz, 1H), 5.12 (d, J = 17.5 Hz, 1H), 3.40 (d, J = 6 Hz, 2H), 1.91 (d, J = 6.5 Hz, 3H).



***N*-(2,2-dimethyl-pent-4-enoyl)-benzamide (17)**

In a 25 mL round bottom flask equipped with magnetic stir bar under [Ar], 2,2-dimethyl-pent-4-enoic acid amide (0.12 g, 0.943 mmol, 1 equiv) was treated with 1.6 M *n*butyl lithium in hexanes (0.59 mL, 0.943 mmol, 1 equiv) in THF (2 mL) at 0 °C. After 45 minutes, benzoyl chloride (0.12 mL, 1.04 mmol, 1.1 equiv) was added. The reaction mixture was stirred overnight, quenched with sat. aq. NH_4Cl (25 mL) and extracted with Et_2O (3 x 25 mL). The combined organic layers were dried with Na_2SO_4, and concentrated *in vacuo*. Chromatography of the resulting crude oil on SiO_2 (20-50% Et_2O/hexanes gradient) afforded 0.093 g (43%) of N-(2,2-dimethyl-pent-4-enoyl)-benzamide as a white solid.

Data for **17**: mp 91 – 93 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.75 (d, J = 7 Hz, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.50-7.47 (m, 2H), 5.89-5.83 (m, 1H), 5.19-5.15 (m, 2H), 2.38 (d, J = 7.5 Hz, 2H), 1.31 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 175.6, 166.8, 134.1, 133.9, 133.3, 130.7, 129.3, 129.0, 128.2, 119.8, 45.1, 44.5, 25.4; IR (neat, thin film) υ 3190, 3031, 2992, 2847, 2460, 2532, 1750, 1685, 1474, 1190, 1033 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{17}O_2N$ $[M]^+$ 231.1254, found 231.1255.



2,2-Dimethyl-pent-4-enoic acid benzylamide (19)

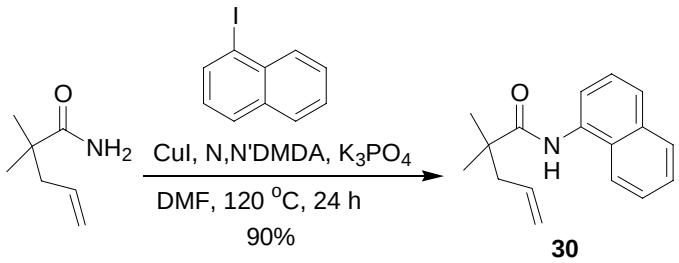
In a 25 mL round bottom flask equipped with magnetic stir bar under [Ar], 2,2-dimethyl-pent-4-enoic acid amide (0.26 g, 2.0 mmol, 1 equiv) was treated with 1.6 M *n*butyl lithium in hexanes(1.5 mL, 2.4 mmol, 1.2 equiv) in THF (4 mL) at 0 °C. After 45 minutes, benzyl bromide (0.29 mL, 2.4 mmol, 1.2 equiv) was added. The reaction mixture was stirred overnight, quenched with sat. aq. NH_4Cl (30 mL) and extracted with Et_2O (3 x 35 mL). The combined organic layers were dried with Na_2SO_4, and concentrated *in vacuo*. Chromatography of the resulting crude oil on SiO_2 (20-50% Et_2O/hexanes gradient) afforded 0.21 g (51%) of 2,2-dimethyl-pent-4-enoic acid benzylamide as a white solid.

Data **19**: mp 54 – 56 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 5.88 (s, 1H), 5.80-5.71 (m, 1H), 5.08-5.04 (m, 2H), 4.44 (d, J = 5.4 Hz, 2H), 2.30 (d, J = 7.5 Hz, 2H), 1.20 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 177.6, 139.1, 134.9, 129.2, 128.2, 127.9,

118.6, 45.7, 44.1, 42.5, 25.7; IR (neat, thin film) υ 3341, 3066, 3031, 2968, 2927, 1946, 1835, 1670, 1532, 1496, 1454, 1390, 1247, 1182, 1080, 1029, 998, 916 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{20}ON$ $[M]^+$ 218.1539, found 218.1535.

Representative Synthesis of Alkyl Aryl Amides

The following substrates were synthesized via a known coupling reaction between the amide and the corresponding aryl iodide.[3]

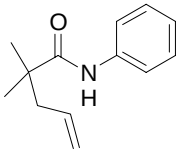


30

2,2-Dimethyl-pent-4-enoic acid naphthalene-1-ylamide (30)

In a 25 mL round bottom flask equipped with magnetic stir bar the amide (50.0 mg, 0.393 mmol, 1.2 equiv), copper(I) idodide (3.0 mg, 0.0164 mmol, 0.05 equiv), and potassium phosphate tribasic (139 mg, 0.655 mmol, 2 equiv) in DMF was charged with, *N*, *N'* dimethylenediammine (3.0 mg, 0.0328 mmol, 0.1 equiv) and the aryl iodide (83.0 mg, 0.328 mmol, 1 equiv). The reaction mixture was heated to 120 °C for 24 hours. Upon cooling to room temperature, the reaction mixture was diluted with Et_2O, filtered through a pad of SiO_2 gel, and concentrated *in vacuo*. Chromatography of the resulting crude oil on SiO_2 (0-20% Et_2O/hexanes gradient) afforded 0.074 g (90%) of 2,2-dimethyl-pent-4-enoic acid naphthalene-1-ylamide as a light brown solid.

Data for **30**: mp 104 – 106 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.5 Hz, 1H), 7.88 (d, J = 7 Hz, 1H), 7.78 (d, J = 8 Hz, 1H), 7.74 (s, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.53-7.47 (m, 3H), 5.95-5.90 (m, 1H), 5.20-5.16 (m, 2H), 2.48 (d, J = 7.5 Hz, 2H), 1.43 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.4, 134.7, 134.6, 132.9, 129.4, 127.9, 126.8, 126.4, 126.3, 126.2, 121.5, 120.9, 119.1, 116.2, 45.9, 43.7, 25.9; IR (neat, thin film) υ 3301, 3051, 2972, 2925, 2361, 1651, 1597, 1500, 1408, 1392, 1269, 1247, 1015, 918, 795, 772 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{20}ON$ $[M]^+$ 254.1539, found 254.1543.

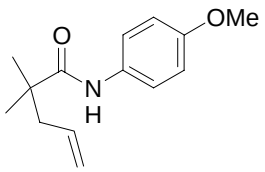


22

2,2-Dimethyl-pent-4-enoic acid phenylamide (22)

The known compound **22** was obtained as a white solid from arylation of 2,2-dimethyl-pent-4-enoic acid amide with iodobenzene in 89% yield. The ^{1}H NMR spectra matched the reported characterization.[4] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 8.5 Hz, 2H),

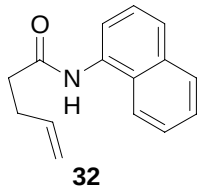
7.47 (s, 1H), 7.31-7.27 (m, 2H), 7.10 (t, J = 7.5 Hz, 1H), 5.82-5.78 (m, 1H), 5.14-5.10 (m, 2H), 2.36 (d, J = 7.5 Hz, 2H), 1.28 (s, 6H).



25

2,2-Dimethyl-pent-4-enoic acid (4-methoxy-phenyl)-amide (25)

Compound **25** was obtained as a white solid from arylation of 2,2-dimethyl-pent-4-enoic acid amide with *p*-methoxy iodobenzene in 79% yield. mp 61 – 63 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 6.5 Hz, 2H), 7.23 (s, 1H), 6.85 (d, J = 9.5 Hz, 2H), 5.84-5.78 (m, 1H), 5.15-5.11 (m, 2H), 3.79 (s, 3H), 2.36 (d, J = 7.5 Hz, 2H), 1.29 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.4, 156.3, 134.2, 130.9, 122.2, 118.1, 113.8, 55.3, 45.1, 42.5, 25.1; IR (neat, thin film) υ 3335, 3075, 2972, 2835, 2060, 1651, 1598, 1510, 1467, 1410, 1397, 1367, 1301, 1243, 1179, 1036, 997, 915 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{20}O_2N$ $[M]^+$ 234.1489, found 234.1484.

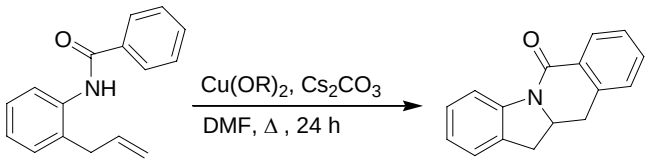


32

Pent-4-enoic acid naphthalene-1-ylamide (32)

The known compound **32** was obtained as an off white solid from arylation of pent-4-enoic acid amide with iodonaphthalene in 89% yield. The ^{1}H NMR spectra matched the previously reported characterization.[5] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89-7.82 (m, 3H), 7.69 (d, J = 6 Hz, 1H), 7.60 (s, 1H), 7.51-7.44 (m, 3H), 5.98-5.91 (m, 1H), 5.20 (d, J = 12.9 Hz, 1H), 5.11 (d, J = 7.2, 1H), 2.61-2.57 (m, 4H).

Carboamination reaction optimization for *o*-allyl aryl amides:



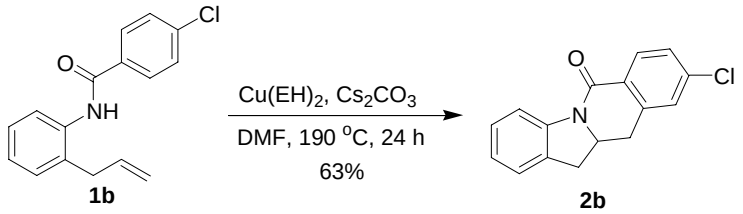
1a **2a**

Entry	copper salt	temperature	yield
1	$Cu(OAc)_2$	170 °C	16%
2	$Cu(OAc)_2$	190 °C	39%
3	$Cu(ND)_2$	190 °C	59%
4	$Cu(EH)_2$	190 °C	61%

$Cu(ND)_2$ = copper(II) neodecanoate, $Cu(EH)_2$ = copper(II) ethylhexanoate

N-(2-allyl-phenyl)-benzamide (50.0 mg, 0.211 mmol, 1 equiv) in a glass pressure tube equipped with a magnetic stir bar was treated with Cs_2CO_3 (68.0 mg, 0.211 mmol, 1 equiv), $Cu(OR)_2$ (3 equiv), and DMF (2.11 mL). The tube was capped and the reaction mixture was stirred at the indicated temperature for 24 h. The reaction mixture was allowed to cool to room temperature, and diluted with Et_2O (60 mL). This mixture was then washed with sat. aq. $EDTANa_2$ (30 mL x 3) and 2M NaOH (30 mL x 3). The organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography on SiO_2 (0 – 40% EtOAc in hexanes gradient) to give the carboamination product as a brown solid in the indicated yield.

Representative carboamination procedure for *o*-allyl aryl amides:



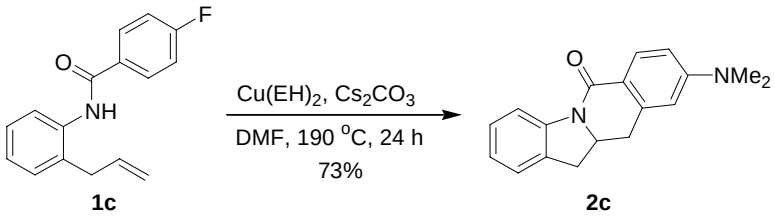
1b **2b**

$Cu(EH)_2$ = Copper (II) Ethylhexanoate

9-Chloro-11a, 12-dihydro-11*H*-indolo[1,2-*b*]isoquinolin-6-one (2b)

N-(2-allyl-phenyl)-4-chloro-benzamide (50.0 mg, 0.184 mmol, 1 equiv) in a glass pressure tube equipped with a magnetic stir bar was treated with Cs_2CO_3 (60.0 mg, 0.184 mmol, 1 equiv) and Cu(II) ethylhexanoate (EH) (188.0 mg, 0.552 mmol, 3 equiv) in 1.84 mL of the given solvent. The tube was capped and the reaction mixture was stirred at 190 °C for 24 h. The reaction mixture was allowed to cool to room temperature, and diluted with Et_2O (60 mL). This mixture was then washed with sat. aq. $EDTANa_2$ (30 mL x 3) and 2M NaOH (30 mL x 3). The organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography on SiO_2 (0 – 40% EtOAc in hexanes gradient) to give the carboamination product in 63% yield (31.5 mg, 0.116 mmol) as a brown solid.

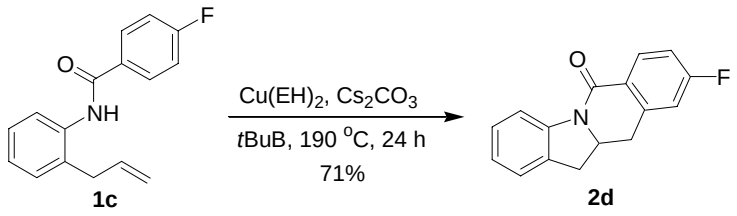
Data for **2b**: mp 191 – 193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.50-7.41 (m, 2H), 7.32-7.26 (m, 3H), 7.09 (t, J = 7 Hz, 1H), 4.51-4.44 (m, 1H), 3.40 (dd, J = 8.5, 15.5 Hz, 1H), 3.25-3.02 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.7, 143.1, 137.8, 132.5, 130.8, 128.9, 128.4, 128.0, 127.8, 125.1, 124.7, 124.5, 117.1, 58.9, 36.3, 35.8; IR (neat, thin film) υ 3013, 2919, 2887, 1603, 1554, 1432, 1290, 1247, 1187, 1099, 1034, 999 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{12}ONClNa$ $[M+Na]^+$ 292.0493, found 292.04933.



1c **2c**

9-Dimethylamino-11a, 12-dihydro-11*H*-indolo[1,2-*b*]isoquinolin-6-one (2c)

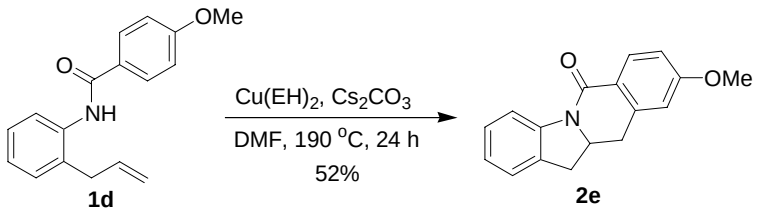
Compound **2c** was obtained in 73% yield as a brown solid. mp 221 – 223 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8 Hz, 1H), 8.05 (d, J = 8.8 Hz, 1H), 7.26-7.21 (m, 2H), 7.01 (t, J = 7.2 Hz, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.44 (s, 1H), 4.43-4.37 (m, 1H), 3.34 (dd, J = 10.5, 19.5 Hz, 1H), 3.13-2.95 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 153.2, 143.6, 139.6, 130.5, 128.3, 124.9, 123.6, 118.5, 116.7, 111.2, 109.7, 59.0, 40.6, 36.6, 36.4; IR (neat, thin film) υ 3027, 2932, 2882, 2360, 1710, 1606, 1519, 1478, 1404, 1364, 1315, 1234, 1129, 1096 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{19}ON_2$ $[M]^+$ 279.1492, found 279.1491.



1c **2d**

9-Fluoro-11a, 12-dihydro-11*H*-indolo[1,2-*b*]isoquinolin-6-one (2d)

Compound **2d** was obtained in 71% yield as a light brown solid. mp 185 – 187 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, J = 8 Hz, 1H), 8.22 (t, J = 8.5 Hz, 1H), 7.30-7.27 (m, 2H), 7.11-7.07 (m, 2H), 6.97 (d, J = 9 Hz, 1H), 4.51-4.43 (m, 1H), 3.40 (dd, J = 8.5, 15.5, 1H), 3.24-3.05 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 163.7, 161.8, 142.9, 140.6, 131.7, 131.6, 128.4, 127.2, 125.1, 124.6, 117.1, 114.9 (m, 1C), 58.8, 36.2, 35.8; IR (neat, thin film) υ 3027, 3062, 2993, 2941, 2712, 2363, 1597, 1479, 1407, 1368, 1315, 1238, 1086, 907, 865 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{13}ONF$ $[M]^+$ 254.0976, found 254.09756.

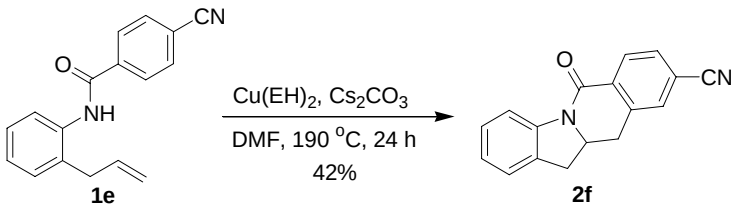


1d **2e**

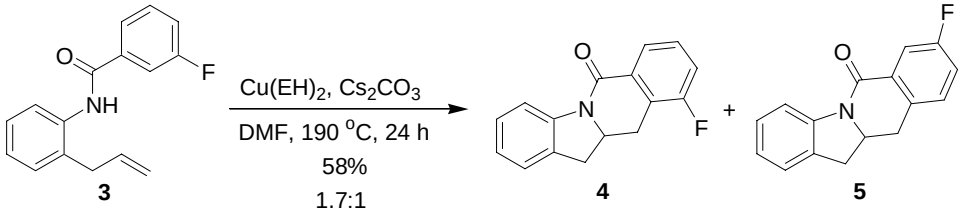
9-Methoxy-11a, 12-dihydro-11*H*-indolo[1,2-*b*]isoquinolin-6-one (2e)

Compound **2e** was obtained in 56% yield as a light yellow solid. mp 169 – 171 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (d, J = 8.1 Hz, 1H), 8.15 (d, J = 5.1 Hz, 1H), 7.28 (t, J = 7.5 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 6.93 (dd, J = 2.5, 8.5 Hz, 1H), 6.76 (s, 1H), 4.49-4.43 (m, 1H), 3.87 (s, 1H), 3.38 (dd, J = 8.5, 15.5 Hz, 1H), 3.20-3.05 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 143.2, 139.9, 131.0, 130.5, 128.4, 125.0, 124.2, 123.7, 116.9, 113.9, 113.3, 113.0, 58.9, 55.9, 36.3; IR (neat, thin film) υ 3093, 2986, 2866, 1687, 1599,

1447, 1295, 1006, 919 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{12}O_3N_2$ $[M]^+$ 265.6109, found 265.6131.



9-Cyano-11a, 12-dihydro-11*H*-indolo[1,2-*b*]isoquinolin-6-one (2f)
Compound **2f** was obtained in 42% yield as a brown solid. mp 188 – 190 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, J = 7.8 Hz, 1H), 8.32 (d, J = 8.1 Hz, 1H), 7.60 (s, 1H), 7.34-7.26 (m, 3H), 7.13 (t, J = 7.2 Hz, 1H), 4.54-4.48 (m, 1H), 3.45 (dd, J = 10.5, 19.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 142.5, 138.6, 134.5, 131.7, 131.5, 130.5, 129.7, 128.6, 125.2, 118.6, 117.3, 115.8, 59.7, 36.2, 35.3; IR (neat, thin film) υ 3093, 2975, 2918, 2488, 2227, 1600, 1565, 1482, 1435, 1402, 1374, 1159, 1090 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{12}ON_2$ $[M]^+$ 260.0944, found 260.09525.



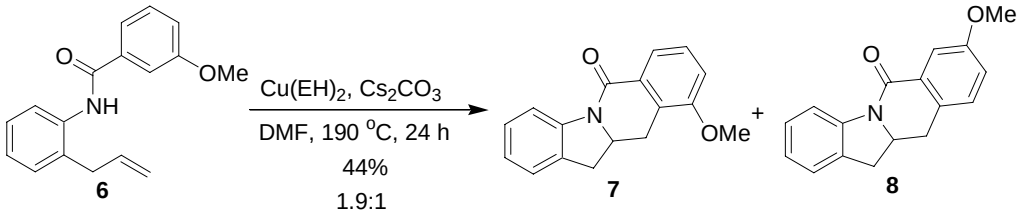
10-Fluoro-11a, 12-dihydro-11*H*-indolo[1,2-*b*]isoquinolin-6-one (4) and 8-fluoro-11a, 12-dihydro-11*H*-indolo[1,2-*b*]isoquinolin-6-one (5)

Regioisomers **4** and **5** were obtained as a 1.7:1 ratio in 58% combined yield as white solids. **4** and **5** were separated via flash chromatography (**4** eluted first followed by **5** in 0 – 30% EtOAc in hexanes gradient).

Data for **4**: mp 164 – 166 °C; ^{1}H NMR (500 MHz, C_3D_6) δ 8.29 (d, J = 8.5 Hz, 1H), 7.76 (dd, J = 3 Hz, 9.5 Hz, 1H), 7.48-7.45 (m, 1H), 7.33-7.30 (m, 2H), 7.23 (t, J = 8 Hz, 1H), 7.10 (t, J = 7 Hz, 1H), 4.55-4.49 (m, 1H), 3.58 (dd, J = 4, 16 Hz, 1H) 3.47 (dd, J = 8.5, 15.5 Hz, 1H), 3.10 (dd, J = 10, 15.5 Hz, 1H), 2.96 (dd, J = 8.0, 15.5 Hz, 1H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 161.1, 160.0, 158.0, 142.3, 132.3, 130.1, 128.3, 128.2, 127.9, 124.4 (m, 1C), 118.7, 118.6, 116.7, 58.0, 35.8, 27.7; IR (neat, thin film) υ 3004, 2961, 1660, 1579, 1483, 1419, 1324, 1248, 1237, 1190, 1001, 913 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{12}ONFNa$ $[M+Na]^+$ 276.0795, found 276.0791.

Data for **5**: mp 163 – 165 °C; ^{1}H NMR (500 MHz, C_3D_6) δ 8.30 (d, J = 8 Hz, 1H), 7.94 (d, J = 8 Hz, 1H), 7.47-7.44 (m, 1H), 7.30-7.22 (m, 3H), 7.07 (t, J = 7.5 Hz, 1H), 4.49-4.41 (m, 1H), 3.55 (dd, J = 4, 16 Hz, 1H), 3.43 (dd, J = 8.5, 15.5 Hz, 1H), 3.09 (dd, J = 10.5, 15.5 Hz, 1H), 2.88 (dd, J = 14, 15.5 Hz, 1H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.2, 161.2, 142.2, 132.9, 132.3, 130.2, 129.0, 128.9, 128.0, 124.6, 124.3, 119.1 (d, J =

22.1 Hz, 1C) , 116.7, 115.0 (d, J = 23.1 Hz, 1C), 58.6, 35.7, 34.6; IR (neat, thin film) υ 3065, 2924, 2849, 1614, 1593, 1471, 1370, 1282, 1169, 1064, 934, 842 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{13}ONF[M]^+$ 254.0976, found 254.0969.

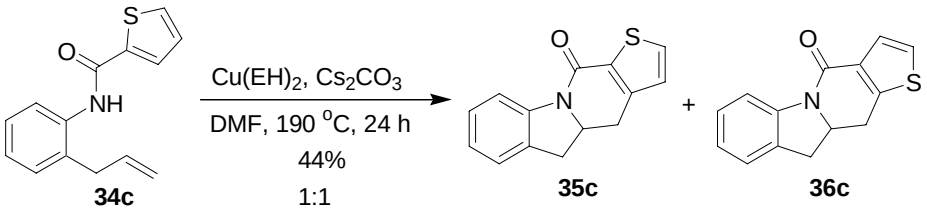


10-Methoxy-11a, 12-dihydro-11*H*-indolo[1,2-*b*]isoquinolin-6-one (7) and 8-methoxy-11a, 12-dihydro-11*H*-indolo[1,2-*b*]isoquinolin-6-one (8)

Regioisomers **7** and **8** were obtained as a 1.9:1 ratio in 44% combined yield as light yellow solids. **7** and **8** were separated via flash chromatography (**7** eluted first followed by **8** in 0 – 30% EtOAc in hexanes gradient).

Data for **7**: mp 138 – 140 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, J = 8 Hz, 1H), 7.84 (d, J = 7.5 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.30-7.27 (m, 2H), 7.10-7.04 (m, 2H), 4.40-4.37 (m, 1H), 3.89 (s, 3H), 3.61 (dd, J = 4.5, 16 Hz, 1H), 3.39 (dd, J = 8.5, 16 Hz, 1H), 3.07 (dd, J = 10.5, 15.5 Hz, 1H), 2.72 (dd, J = 14, 16 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.7, 156.2, 143.1, 131.9, 130.8, 128.3, 128.2, 126.7, 125.1, 124.4, 120.8, 117.1, 114.0, 58.6, 56.3, 36.5, 28.9; IR (neat, thin film) υ 2952, 2896, 2836, 1654, 1599, 1582, 1463, 1440, 1410, 1364, 1327, 1263, 1169, 1091, 980 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{15}O_2N$ $[M]^+$ 265.1097, found 265.1108.

Data for **8**: mp 144 – 146 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, J = 7.5 Hz, 1H), 7.76 (s, 1H), 7.32-7.28 (m, 2H), 7.21 (d, J = 8.5 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.07 (dd, J = 3, 8.5 Hz, 1H), 4.47-4.42 (m, 1H), 3.89 (s, 3H), 3.39 (dd, J = 8, 15.5 Hz, 1H), 3.21-3.02 (m, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 162.1, 159.1, 142.5, 131.3, 130.3, 129.5, 128.4, 127.9, 124.6, 124.0, 119.6, 116.6, 111.4, 58.7, 55.6, 35.7, 34.5; IR (neat, thin film) υ 3090, 2977, 2919, 2880, 1684, 1598, 1489, 1410, 1272, 1173, 1014, 914cm^{-1}; HRMS (EI) calcd for $C_{17}H_{15}O_2N$ $[M]^+$ 265.1097, found 265.1107.



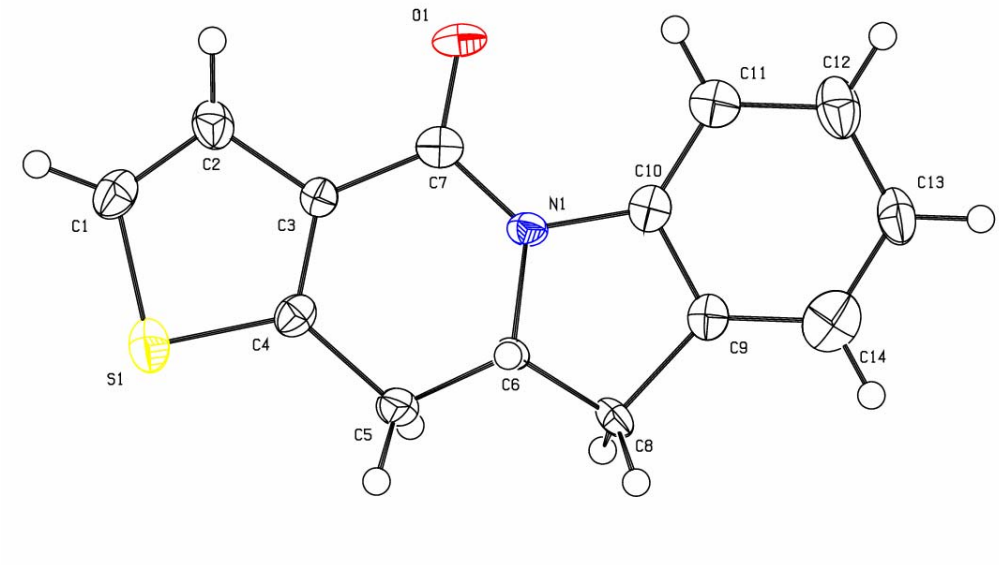
9a, 10-Dihydro-9*H*-3-thia-4a-aza-cyclopenta[*b*]fluoren-4-one (35c) and 9a, 10-dihydro-9*H*-1-thia-4a-aza-cyclopenta[*b*]fluoren-4-one (36c)

Regioisomers **35c** and **36c** were obtained as a 1:1 ratio in 44% combined yield as light brown solids. **35c** and **36c** were separated via flash chromatography (**35c** eluted first followed by **36c** in 0 – 30% EtOAc in hexanes gradient).

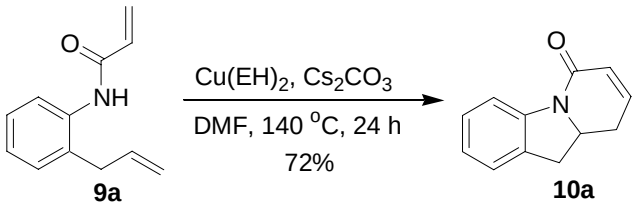
Data for **35c**: mp 177 – 179 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, J = 8 Hz, 1H), 7.54 (d, J = 5 Hz, 1H), 7.29-7.27 (m, 2H), 7.06 (t, J = 7 Hz, 1H), 6.99 (d, J = 5 Hz, 1H), 4.54-4.49 (m, 1H), 3.37 (dd, J = 8.5, 16 Hz, 1H), 2.90 (dd, J = 4.5, 16 Hz, 1H), 3.01 (dd, J = 11, 15.5 Hz, 1H), 2.92 (dd, J = 13.5, 15 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 143.1, 142.2, 133.6, 131.6, 130.1, 127.9, 126.5, 124.6, 123.6, 116.2, 60.4, 35.5, 31.5; IR (neat, thin film) υ 3021, 2986, 2882, 1711, 1590, 1502, 1454, 1387, 1143, 787 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{12}ONS$ $[M]^+$ 242.0634, found 242.0643.

Data for **36c**: mp 164 – 166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, J = 8 Hz, 1H), 7.54 (d, J = 5 Hz, 1H), 7.29-7.26 (m, 2H), 7.17 (d, J = 5 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 4.57-4.51 (m, 1H), 3.42-3.37 (m, 2H), 3.13-3.01 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 144.8, 142.9, 134.6, 130.3, 128.4, 126.7, 125.1, 124.3, 124.1, 116.7, 60.6, 35.9, 31.6; IR (neat, thin film) υ 2990, 2878, 2842, 1700, 1598, 1478, 1434, 1363, 1313, 1228, 1010, 836 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{12}ONS$ $[M]^+$ 242.0712, found 242.0707.

An X-ray crystal structure was obtained for structural confirmation of 9a, 10-dihydro-9*H*-1-thia-4a-aza-cyclopenta[*b*]fluoren-4-one **36c**. Structural assignment for the regioisomer, 9a, 10-dihydro-9H-3-thia-4a-aza-cyclopenta[b]fluoren-4-one (**35c**), was determined by the NMR data and process of elimination.

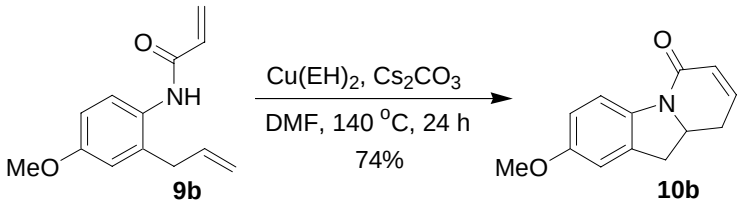


Representative carboamination procedure for *o*-allyl-vinyl amides

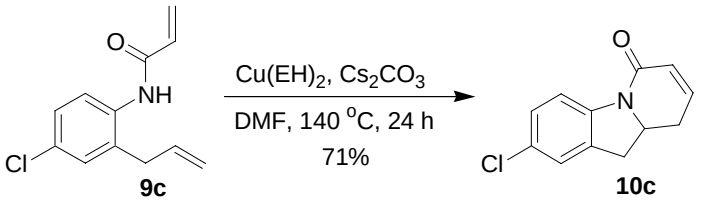


9a, 10-Dihydro-9*H*-pyrido[1,2-*a*]indol-6-one (10a)
N-(2-allyl-phenyl)-acrylamide (50.0 mg, 0.267 mmol, 1 equiv) in a glass pressure tube equipped with a magnetic stir bar was treated with Cs_2CO_3 (87.0 mg, 0.267 mmol, 1 equiv) and Cu(II) ethylhexanoate (EH) (273.0 mg, 0.801 mmol, 3 equiv) in 2.67 mL of the given solvent. The tube was capped and the reaction mixture was stirred at the indicated temperature for 24 h. The reaction mixture was allowed to cool to r.t., and diluted with Et_2O (60 mL). This mixture was then washed with sat. aq. $EDTANa_2$ (30 mL x 3) and 2M NaOH (30 mL x 3). The organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography on SiO_2 (0 – 40% EtOAc in hexanes gradient) to give the carboamination product in 72% yield (36.0 mg, 0.192 mmol) as a white solid.

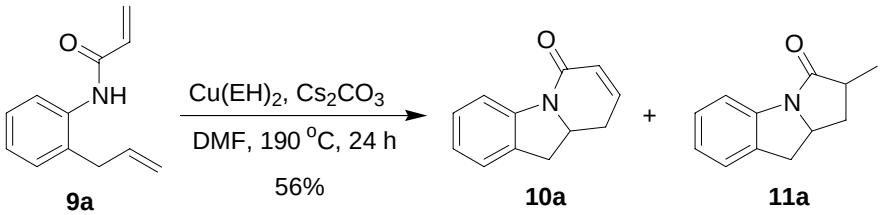
Data for **10a**: mp 87 – 89 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 7.5 Hz, 1H), 7.26-7.20 (m, 2H), 7.07 (t, J = 7.2 Hz, 1H), 6.07 (s, 1H), 5.42 (s, 1H), 4.63-4.57 (m, 1H), 3.26-3.14 (m, 2H), 2.92 (dd, 10.8, 15.6 Hz, 1H), 2.78-2.70 (m, 1H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.3, 143.7, 139.6, 134.0, 127.9, 125.3, 124.7, 117.0, 115.1, 60.1, 36.2, 34.1; IR (neat, thin film) υ 2918, 1656, 1604, 1483, 1464, 1405, 1305, 1222, 1159, 1112, 927 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{11}ON$ $[M]^+$ 185.0835, found 185.0841.



2-Methoxy-9a, 10-dihydro-9*H*-pyrido[1,2-*a*]indol-6-one (10b)
Compound **19b** was obtained in 74% yield as a white solid. mp 77 – 79 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 8.5 Hz, 1H), 6.79-6.76 (m, 2H), 6.04 (s, 1H), 5.39 (s, 1H), 4.61-4.57 (m, 1H), 3.79 (s, 3H), 3.19-3.13 (m, 2H), 2.88 (dd, 10.5, 15.5 Hz, 1H), 2.76-2.72 (m, 1H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.9, 157.3, 143.6, 135.7, 133.2, 116.5, 115.6, 112.2, 112.0, 60.4, 55.7, 36.5, 33.9; IR (neat, thin film) υ 2998, 2799, 1670, 1505, 1444, 1328, 1176, 990 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{13}O_2NNa$ $[M+Na]^+$ 238.0838, found 238.0838.

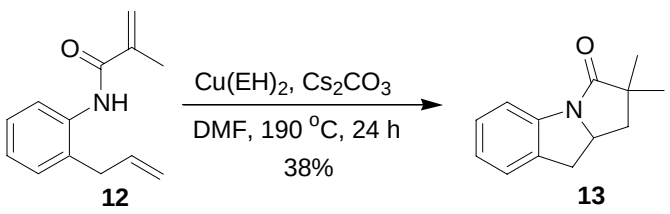


2-Chloro-9a, 10-dihydro-9*H*-pyrido[1,2-*a*]indol-6-one (10c)
Compound **19c** was obtained in 71% yield as a white solid. mp 111 – 113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8 Hz, 1H), 7.23 – 7.19 (m, 2H), 6.08 (s, 1H), 5.45 (s, 1H), 4.64-4.58 (m, 1H), 3.25-3.16 (m, 2H), 2.92 (dd, J = 13, 15.2 Hz, 1H), 2.77-2.71 (m, 1H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.3, 157.1, 143.0, 138.2, 135.8, 129.7, 127.9, 125.6, 117.5, 115.8, 60.1, 36.1, 34.0; IR (neat, thin film) υ 2968, 2900, 2845, 1868, 1694, 1655, 1601, 1439, 1395, 1291, 1222, 1066, 907, 817 cm^{-1}; HRMS (EI) calcd for $C_{12}H_{11}ONCl$ $[M]^+$ 220.0524, found 220.0525.



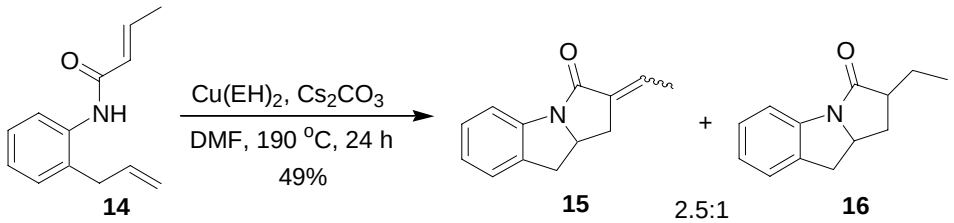
9a, 10-Dihydro-9*H*-pyrido[1,2-*a*]indol-6-one (10a) and 2-methyl-1,2,8,8a-tetrahydro-3a-aza-cyclopenta[*a*]inden-3-one (11a)
N-(2-allyl-phenyl)-acrylamide (50.0 mg, 0.267 mmol, 1 equiv) in a glass pressure tube equipped with a magnetic stir bar was treated with Cs_2CO_3 (87.0 mg, 0.267 mmol, 1 equiv) and Cu(II) ethylhexanoate (EH) (273.0 mg, 0.801 mmol, 3 equiv) in DMF (2.67 mL). The tube was capped and the reaction mixture was stirred at 190 °C for 24 h. The reaction mixture was allowed to cool to r.t., and diluted with Et_2O (60 mL). This mixture was then washed with sat. aq. $EDTANa_2$ (30 mL x 3) and 2M NaOH (30 mL x 3). The organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography on SiO_2 (0 – 40% EtOAc in hexanes gradient) to give **19a** and **20a** in 56% overall yield as a 1.2:1 mixture, respectively.

2-Methyl-1,2,8,8a-tetrahydro-3a-aza-cyclopenta[*a*]inden-3-one (11a)
Compound **11a** matched the reported characterization.[6] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J = 5.7 Hz, 1H), 7.24 – 7.17 (m, 2H), 7.02 (t, J = 7.6 Hz, 1H), 4.54-4.49 (m, 1H), 3.18 (dd, J = 8.8, 16 Hz, 1H), 2.96-2.83 (m, 2H), 2.67 (dt, J = 6.4, 12.4 Hz, 1H), 1.68-1.56 (m, 1H) 1.25 (d, J = 5.4 Hz, 3H).



2,2-Dimethyl-1,2,8,8a-tetrahydro-3a-aza-cyclopenta[*a*]inden-3-one (13)
Compound **22** was obtained in 38% yield as an off white solid. mp 82 – 84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 7.8 Hz, 1H), 7.26 – 7.17 (m, 2H), 7.03 (t, J = 7.5 Hz,

1H), 4.63-4.57 (m, 1H), 3.18 (dd, 8.4, 15.6 Hz, 1H), 2.84 (dd, J = 8, 15.9 Hz, 1H), 2.30 (dd, J = 6, 12.3 Hz, 1H), 1.85 (dd, J = 10.2, 11.7 Hz, 1H), 1.32 (s, 3H), 1.25 (s, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ 177.1, 140.0, 134.8, 128.2, 125.7, 124.5, 115.4, 59.2, 47.2, 45.1, 36.4, 30.2, 25.3, 24.3; IR (neat, thin film) υ 3049, 2962, 2927, 2867, 2360, 2341, 1604, 1463, 1402, 1364, 1301, 1288, 1104, 1016, 993, 889 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{16}ON$ $[M]^+$ 202.1226, found 202.1224.



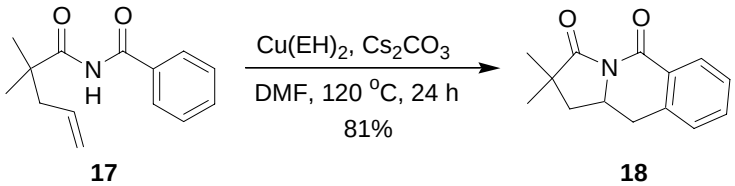
2-Ethylidene-1,2,8,8a-tetrahydro-3a-aza-cyclopenta[*a*]inden-3-one (15) and 2-ethyl-1,2,8,8a-tetrahydro-3a-aza-cyclopenta[*a*]inden-3-one (16)

Compounds **15** and **16** were obtained as a 2.5:1 ratio in 49% combined yield as white solids. **15** and **16** were separated via flash chromatography (**15** eluted first followed by **16** in 0 – 30% EtOAc in hexanes gradient).

Data for **15** (obtained as a mixture of *E* and *Z* isomers) matched the reported characterization[2]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, J = 8 Hz, 1H), 7.26-7.20 (m, 2H), 7.05 (t, J = 7 Hz, 1H), 6.63-6.59 (m, 1H), 4.63-4.56 (m, 1H), 3.22 (dd, J = 7.5, 15.5 Hz, 1H), 3.14 (dd, J = 7, 15.5 Hz, 1H), 2.90 (dd, J = 11, 15.5 Hz, 1H), 2.60-2.55 (m, 1H), 1.83 (d, J = 7 Hz, 3H).

Data for **16**: mp 110 – 112 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, J = 7.5 Hz, 1H), 7.25-7.18 (m, 2H), 7.02 (t, J = 7 Hz, 1H), 4.55-4.49 (m, 1H), 3.19 (dd, J = 8.5, 15.5 Hz, 1H), 2.86 (dd, J = 10.5, 16 Hz, 1H), 2.80-2.78 (m, 1H), 2.62 (dd, J = 6.5, 12 Hz, 1H), 2.02-1.98 (m, 1H), 1.65-1.61 (m, 1H), 1.45-1.42 (m, 1H), 0.99 (t, 3H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 165.9, 127.7, 127.6, 125.2, 140.0, 123.9, 114.7, 60.3, 48.6, 35.9, 35.8, 23.2, 11.7; IR (neat, thin film) υ 2960, 2362, 1602, 1484, 1463, 1404, 1301, 1166 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{15}ON$ $[M]^+$ 201.1148, found 201.1147.

Representative carboamination procedure for alkyl amides

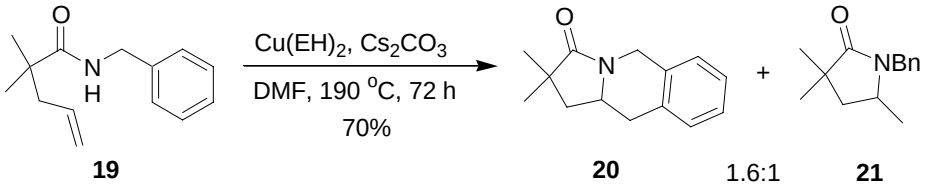


2,2-Dimethyl-1,2,10,10a-tetrahydro-pyrrolo[1,2-*b*]isoquinoline-3,5-dione (18)

N-(2,2-dimethyl-pent-4-enoyl)-benzamide (30.0 mg, 0.130 mmol, 1 equiv) in a glass pressure tube equipped with a magnetic stir bar was treated with Cs_2CO_3 (42.0 mg, 0.130 mmol, 1 equiv) and Cu(II) ethylhexanoate (EH) (142.0 mg, 0.390 mmol, 3 equiv) in 1.3

mL of the given solvent. The tube was capped and the reaction mixture was stirred at the indicated temperature for 24 h. The reaction mixture was allowed to cool to r.t., and diluted with Et_2O (60 mL). This mixture was then washed with sat. aq. $EDTANa_2$ (30 mL x 3) and 2M NaOH (30 mL x 3). The organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography on SiO_2 (0 – 40% EtOAc in hexanes gradient) to give **18** in 81% yield (24.0 mg, 0.105 mmol) as a white solid.

Data for **18**: mp 206 – 208 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 7.5 Hz, 1H), 7.51 (t, J = 6.5 Hz, 1H), 7.41 (t, J = 8 Hz, 1H), 7.23 (d, J = 7.5 Hz, 1H), 4.28-4.22 (m, 1H), 3.07 (dd, J = 3.5, 15 Hz, 1H), 2.94 (dd, J = 8.5, 22.5 Hz, 1H), 2.21 (dd, J = 6, 12.5 Hz, 1H), 1.76 (dd, J = 10.5, 12.5 Hz, 1H), 1.31 (s, 3H), 1.23 (s, 3H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 179.2, 162.7, 137.9, 133.3, 129.6, 129.4, 127.7, 127.4, 53.3, 41.5, 41.1, 35.8, 24.6, 24.2; IR (neat, thin film) υ 3024, 2960, 2860, 1771, 1663, 1600, 1488, 1398, 1310, 1107, 990 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{15}O_2N$ $[M]^+$ 229.1097, found 229.1102.

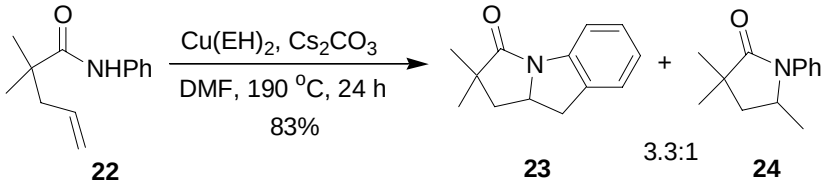


2,2-Dimethyl-1,5,10,10a-tetrahydro-2*H*-pyrrolo[1,2-*b*]isoquinolin-3-one (20) and 1-benzyl-3,3,5-trimethyl-pyrrolidin-2-one (21)

Compounds **20** and **21** were obtained as a 1.6:1 ratio in 70% combined yield as colorless oils. **20** and **21** were separated via flash chromatography (**20** eluted first followed by **21** in 0 – 30% EtOAc in hexanes gradient).

Data for **20**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23-7.12 (m, 4H), 4.86 (d, J = 17.4 Hz, 1H), 4.31 (d, J = 17.4, 1H), 3.75-3.67 (m, 1H), 3.00 (dd, J = 3.6, 15.3 Hz, 1H), 2.66 (dd, J = 11.1, 14.7 Hz, 1H), 2.27 (dd, J = 6.9, 12.6 Hz, 1H), 1.68 (dd, J = 7.5, 13.5 Hz, 1H), 1.25 (s, 3H), 1.20 (s, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ 179.5, 133.9, 132.4, 129.4, 127.4, 127.3, 127.1, 51.2, 43.4, 42.7, 41.4, 38.1, 26.2, 25.8; IR (neat, thin film) υ 2962, 2928, 2867, 1583, 1497, 1455, 1424, 1364, 1319, 1283, 1218, 1160, 1009 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{18}ON$ $[M]^+$ 216.1383, found 216.1386.

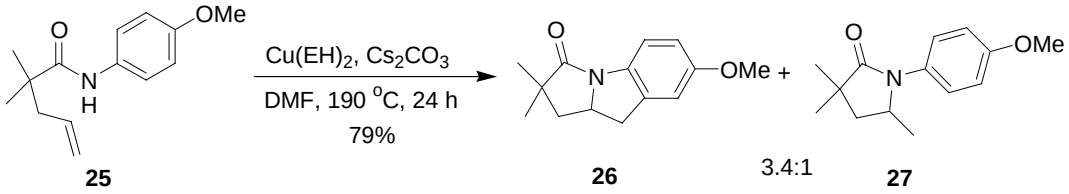
Data for **21**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.31 (m, 3H), 7.29-7.26 (m, 2H), 7.23 (d, J = 7.5 Hz, 1H), 5.03 (d, J = 15 Hz, 1H), 3.96 (d, J = 15 Hz, 1H), 3.43-3.39 (m, 1H), 2.01 (dd, J = 7, 12.5 Hz, 1H), 1.46 (dd, J = 8, 12.5 Hz, 1H), 1.26 (s, 3H), 1.18 (d, J = 6 Hz, 3H), 1.14 (s, 3H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 179.8, 137.0, 128.6, 127.9, 127.3, 49.1, 43.8, 43.1, 40.4, 25.6, 24.7, 19.9; IR (neat, thin film) υ 3063, 3030, 2965, 2929, 2868, 1605, 1496, 1467, 1455, 1415, 1363, 1268, 1212, 1080, 1029 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{20}ON$ $[M]^+$ 218.1539, found 218.1541.



2,2-Dimethyl-1,2,8,8a-tetrahydro-3a-aza-cyclopenta[*a*]inden-3-one (23) and 3,3,5-trimethyl-1-phenyl-pyrrolidin-2-one (24)
Compounds **23** and **24** were obtained as a 3.3:1 ratio in 83% combined yield as colorless oils. **23** and **24** were separated via flash chromatography (**24** eluted first followed by **23** in 0 – 30% EtOAc in hexanes gradient).

Data for **23**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 8 Hz, 1H), 7.23-7.18 (m, 2H), 7.02 (t, J = 7.5 Hz, 1H), 4.63-4.57 (m, 1H), 3.18 (dd, J = 8, 15.5 Hz, 1H), 2.85 (dd, J = 10.5, 16 Hz, 1H), 2.30 (dd, J = 5.5, 12 Hz, 1H), 1.85 (dd, J = 10, 12 Hz, 1H), 1.32 (s, 3H), 1.25 (s, 3H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 176.6, 157.1, 139.5, 134.3, 127.7, 125.2, 124.0, 114.9, 58.7, 46.7, 44.5, 35.9, 24.7, 23.8; IR (neat, thin film) υ 2998, 2945, 2868, 1711, 1630, 1548, 1444, 1412, 1380, 1199, 1076, 998 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{16}ON$ $[M]^+$ 202.1226, found 202.1227.

Data for **24** matched the reported characterization[7]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.37 (m, 2H), 7.33-7.31 (m, 2H), 7.20 (t, J = 7 Hz, 1H), 4.23-4.18 (m, 1H), 2.20 (dd, J = 7, 12.5 Hz, 1H), 1.61 (dd, J = 8.5, 13 Hz, 1H), 1.30 (s, 3H), 1.21 (s, 3H), 1.19 (s, 3H).

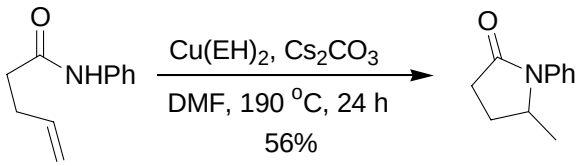


6-Methoxy-2,2-dimethyl-1,2,8,8a-tetrahydro-3a-aza-cyclopenta[*a*]inden-3-one (26) and 1-(4-methoxy-phenyl)-3,3,5-trimethyl-pyrrolidin-2-one (27)
Compounds **26** and **27** were obtained as a 3.4:1 ratio in 79% combined yield as colorless oils. **26** and **27** were separated via flash chromatography (**27** eluted first followed by **26** in 0 – 30% EtOAc in hexanes gradient).

Data for **26**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J = 8.5 Hz, 1H), 6.76-6.74 (m, 2H), 4.67-4.60 (m, 1H), 3.77 (s, 3H), 3.14 (dd, J = 7.8, 14.7 Hz, 1H), 2.83 (dd, J = 10.5, 16.5 Hz, 1H), 2.31-2.27 (m, 1H), 1.84 (dd, J = 5.5, 13.5 Hz, 1H), 1.30 (s, 3H), 1.24 (s, 3H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 176.1, 156.7, 135.9, 133.2, 115.2, 112.0, 111.9, 59.1, 55.7, 46.6, 44.4, 36.2, 24.8, 23.9; IR (neat, thin film) υ 2962, 2903, 2853, 2363, 2521, 1690, 1595, 1495, 1465, 1402, 1249, 1137, 1099, 1032 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{18}O_2N$ $[M]^+$ 232.1332, found 232.1338.

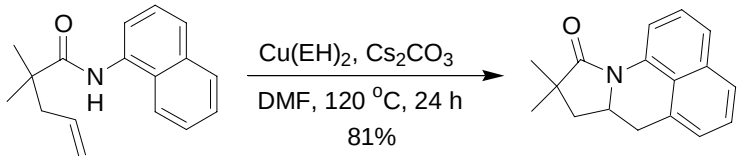
Data for **27**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, J = 9 Hz, 2H), 6.92 (d, J = 9 Hz, 2H), 4.12-4.07 (m, 1H), 3.80 (s, 3H), 2.21 (dd, J = 8, 12.5 Hz, 1H), 1.59 (dd, J = 8, 13.5 Hz,

1H), 1.28 (s, 3H), 1.20 (s, 3H), 1.15 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 179.1, 157.5, 130.6, 126.1, 114.1, 55.4, 51.9, 43.1, 40.9, 25.8, 24.8, 20.7; IR (neat, thin film) υ 2965, 2909, 1692, 1520, 1465, 1393, 1293, 1248, 1181, 1133, 1033, 833 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{17}O_2N$ $[M]^+$ 233.1410, found 233.1405.



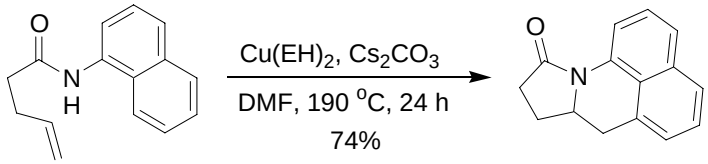
28 **29**

5-Methyl-1-phenyl-pyrrolidin-2-one (29)
Compound **29** was obtained in 56% yield and matched the reported characterization[8]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.36 (m, 4H), 7.21 (t, J = 6.5 Hz, 1H), 4.33-4.28 (m, 1H), 2.67-2.63 (m, 1H), 2.58-2.54 (m, 1H), 2.41-2.37 (m, 1H), 1.79-1.73 (m, 1H), 1.22 (d, J = 6.5 Hz, 3H).



30 **31**

9,9-Dimethyl-7, 7a, 8,9-tetrahydro-benzo[*de*]pyrrolo[1,2-*a*]quinolin-10-one (31)
Compound **31** was obtained in 81% yield as a white solid. mp 150 – 152 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, J = 9 Hz, 1H), 7.72 (d, J = 10.5 Hz, 1H), 7.59 (d, J = 9.5, 1H), 7.47 (t, J = 8.5 Hz, 1H), 7.41 (t, J = 9 Hz, 1H), 7.21 (d, J = 8 Hz, 1H), 4.13-4.07 (m, 1H), 3.35 (dd, J = 3.6, 15.6 Hz, 1H), 3.04 (dd, J = 14, 14.4 Hz, 1H), 2.35 (dd, J = 6.4, 12.4 Hz, 1H), 1.79 (dd, J = 9.2, 15.5 Hz, 1H), 1.35 (s, 3H), 1.29 (s, 3H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 178.6, 134.0, 133.7, 126.6, 126.4, 125.7, 123.7, 123.5, 122.7, 114.4, 52.9, 41.6, 41.5, 37.9, 25.4, 25.1; IR (neat, thin film) υ 3052, 2962, 2928, 2869, 1596, 1507, 1465, 1429, 1407, 1384, 1350, 1292, 1262, 1246, 1100, 947 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{18}ON$ $[M]^+$ 252.1383, found 252.1374.

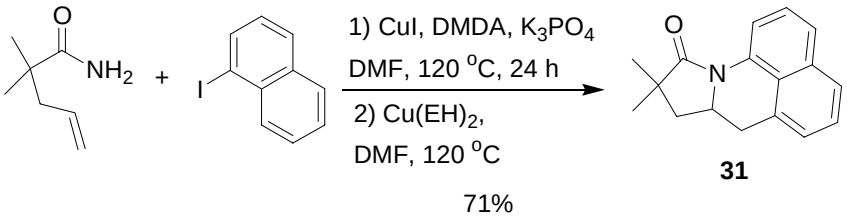


32 **33**

7,7a,8,9-Tetrahydro-benzo[*de*]pyrrolo[1,2-*a*]quinolin-10-one (33)
Compound **33** was obtained in 74% yield as a light brown solid. mp 144 – 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 9.5 Hz, 1H), 7.71 (d, J = 10 Hz, 1H), 7.61 (d, J = 10 Hz, 1H), 7.50 (t, J = 8.5 Hz, 1H), 7.42 (t, J = 10 Hz, 1H), 7.21 (d, J = 8.5 Hz, 1H), 4.20-4.14 (m, 1H), 3.35 (dd, J = 3.2, 15.6 Hz, 1H), 3.11 (dd, J = 13.6, 14 Hz, 1H), 2.75-

2.65 (m, 2H), 2.54-2.47 (m, 1H), 1.96-1.91 (m, 1H);^{13}C NMR (125.7 MHz, $CDCl_3$) δ 173.7, 157.1, 133.8, 133.7, 130.5, 126.6, 126.3, 125.7, 123.9, 123.8, 123.7, 122.8, 114.8, 56.5, 38.1, 31.8, 25.2; IR (neat, thin film) υ 3092, 2890, 1640, 1515, 1440, 1339, 1120, 1097, 993 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{14}ON$ $[M]^+$ 224.1070, found 224.1062.

Representative procedure for one-pot arylation/carboamination reaction



DMDA = N, N'-dimethylenediamine

9,9-Dimethyl-7, 7a, 8,9-tetrahydro-benzo[*de*]pyrrolo[1,2-*a*]quinolin-10-one (31)
In a 25 mL round bottom flask equipped with magnetic stir bar the amide (50.0 mg, 0.393 mmol, 1.2 equiv), copper(I) idodide (3.0 mg, 0.0164 mmol, 0.05 equiv), and potassium phosphate tribasic (139 mg, 0.655 mmol, 2 equiv) in DMF was charged with, *N*, *N'* dimethylenediammine (3.0 mg, 0.0328 mmol, 0.1 equiv) and the aryl iodide (83.0 mg, 0.328 mmol, 1 equiv). The reaction mixture was heated to 120 °C for 24 hours. Upon cooling to room temperature (rt), $Cu(EH)_2$ (335.0 mg, 0.983 mmol, 3 equiv) was added. The reaction mixture was reheated to 120 °C for 24 h, cooled to room temperature, and diluted with Et_2O (60 mL). This mixture was then washed with sat. aq. $EDTANa_2$ (30 mL x 3) and 2M NaOH (30 mL x 3). The organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography on SiO_2 (0-20% Et_2O in hexanes gradient) afforded 0.058 g (71%) of 9,9-dimethyl-7, 7a, 8,9-tetrahydro-benzo[de]pyrrolo[1,2-a]quinolin-10-one (**31**) as a light brown solid.

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