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Electronic Supplementary Information for New Journal of Chemistry; Beng

Supporting Information for:

Copper-catalyzed alkenylation of novel *N*-iodoarylated allylic ketopiperazinonates with

unactivated alkenes

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Contents:

1. General Experimental Information and Procedures	S2
2. Scheme 1 results (CCR)	S3
3. Scheme 2 results (Alkenylation)	S30
4. References	S65

### 2. Experimental Section

All experiments involving air and moisture-sensitive reagents were carried out under an inert atmosphere of nitrogen and using freshly distilled solvents. Freshly purchased 1,4-dioxane was stored under 4 A<sup>o</sup> molecular sieves for several days prior to use. THF was distilled from sodium benzophenone ketyl. All amines, alkenes and enals were newly purchased and used without further purification. Column chromatography was performed on silica gel (230-400 mesh). Thin-layer chromatography (TLC) was performed using Silicycle SiliaplateTM glass backed plates (250 µm thickness, 60 Å porosity, F-254 indicator) and visualized using UV (254 nm) or CAM, *p*-anisaldehyde, or KMnO<sub>4</sub> stain. All reported temperatures were internal to a reaction vessel. Unless otherwise indicated, <sup>1</sup>H, <sup>13</sup>C, and DEPT-135 spectra were acquired using CDCl<sub>3</sub> as solvent, at room temperature. Chemical shifts are quoted in parts per million (ppm). HRMS-EI<sup>+</sup> data were obtained using either electronspray ionization (ESI) or electron impact (EI) techniques. High-resolution ESI was obtained on an LTQ-FT (ion trap; analyzed using MassLynx). Brine solutions are saturated solutions of aqueous sodium chloride.

#### General Procedure A: Reaction of 1,3-azadienes with 4

A 20 mL screw-cap vial was flame-dried, evacuated and flushed with nitrogen. A solution of the 1,3-azadiene (10.0 mL, 0.10 M in freshly distilled toluene) was added to the vial at room temperature followed by anhydride **4** (10 mmol, 1.0 equiv). The contents were placed in a pre-heated oil bath thermostatted 100 °C. After complete consumption of the enal (as judged by TLC and NMR), the mixture/suspension was cooled to room temperature and washed several times with petroleum ether, then concentrated under reduced pressure to afford the crude cycloadduct.

**Methyl esterification of cycloadducts:** To a stirring suspension of the acid (1 mmol), dissolved in DMF (10 mL), and  $K_2CO_3$  (3 equiv) was added methyl iodide (2 equiv) under a nitrogen atmosphere. The reaction mixture was stirred for 12 h (TLC monitoring). After complete conversion, it was diluted with water and extracted with EtOAc (2×50 mL). The combined organic extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* to give the desired ester, which was purified by flash chromatography on silica.

**General Procedure B (CuBr-catalyzed cross-coupling with alkenes)**: To the *N*-iodoaryl ketopiperazinonate (0.5 mmol) and alkene (2.0 mmol, 2.0 equiv), dissolved in 1,4-dioxane (2 mL), was added CuBr (0.05 mmol, 10 mol%) in an oven-dried vial equipped with a stir bar. A solution of potassium carbonate (138 mg, 2.0 mmol, 2.0 equiv) was next added. The suspension was heated to 100 °C. It was then monitored by TLC until complete consumption of the starting material (16 to 36 h). The reaction mixture was then filtered through a short plug of Celite with the aid of ethyl acetate. The filtrate was concentrated and the crude material was purified by flash chromatography on silica eluting with hexanes:EtOAc.



Prepared from 1,3-azadiene **3a** (3.33 g, 10.0 mmol) and anhydride **4** (1.291 g, 10.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). T = 100 °C, time = 16 h. Yield = 3.57 g, 75%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform*d*)  $\delta$  7.67 (d, *J* = 8.2 Hz, 2H), 7.38 – 7.22 (m, 6H), 6.94 (d, *J* = 8.1 Hz, 2H), 6.43 (dd, *J* = 16.0, 8.2 Hz, 1H), 6.31 (d, *J* = 15.9 Hz, 1H), 4.56 (dd, *J* = 8.5, 2.4 Hz, 1H), 3.82 (s, 3H), 3.63 – 3.57 (m, 3H), 2.60 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.79, 166.76, 140.59, 138.50, 135.81, 133.86, 129.74, 128.77, 128.40, 126.82, 126.77, 92.95, 65.80, 64.78, 54.74, 52.09, 42.65. **HRMS-EI**<sup>+</sup> (*m*/*z*): calc'd for C<sub>21</sub>H<sub>21</sub>IN<sub>2</sub>O<sub>3</sub> 476.0597; found 476.0591. FTIR (KBr): 2932.4213, 1721.5204, 1666.3806, 1606.9472, 1511.0233, 1448.5693, 1414.7191, 1384.979, 1357.4641, 1298.7878, 1247.5543, 1179.3944, 1135.9684, 1031.8974, 995.8644, 968.9312, 919.9415, 831.0313, 750.2581, 694.7613.





**2b**, 70%

Prepared from 1,3-azadiene **3b** (694 mg, 2.0 mmol) and anhydride **4** (258 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). T = 100 °C, time = 16 h. Yield = 687 mg, 70%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform*d*) δ 7.71 – 7.58 (m, 2H), 7.31 – 7.21 (m, 3H), 7.11 – 7.05 (m, 2H), 7.03 – 6.88 (m, 2H), 6.31 (s, 1H), 4.48 – 4.42 (br s, 1H), 3.74 (s, 3H), 3.69 – 3.58 (m, 2H), 3.56 (d, *J* = 4.2 Hz, 1H), 2.35 (s, 6H), 1.85 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 170.93, 167.37, 140.38, 138.38, 138.27, 136.62, 134.28, 130.53, 129.16, 129.03, 128.96, 128.92, 128.33, 128.28, 127.17, 92.54, 69.20, 65.87, 55.64, 52.25, 42.48, 15.13. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>22</sub>H<sub>23</sub>IN<sub>2</sub>O<sub>3</sub> 490.0753; found 490.0761.





Prepared from 1,3-azadiene **3c** (1815 mg, 5.0 mmol) and anhydride **4** (646 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). T = 100 °C, time = 16 h. Yield = 1949 mg, 77%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform*d*)  $\delta$  7.67 (d, 2H), 7.27 (d, 2H), 6.84 (d, 2H), 6.73 (d, 2H), 6.29 – 6.14 (m, 2H), 4.37 (dd, *J* = 7.0, 2.6 Hz, 1H), 3.64 (overlapping singlets, 6H), 3.66 – 3.59 (m, 3H), 2.53 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.8, 166.7, 159.8, 140.6, 138.4, 133.3, 129.8, 128.5, 128.0, 124.5, 114.1, 92.9, 65.9, 64.9, 55.4, 54.8, 52.1, 42.7. **HRMS-EI**<sup>+</sup> (*m*/*z*): calc'd for C<sub>22</sub>H<sub>23</sub>IN<sub>2</sub>O<sub>4</sub> 506.0703; found 506.0709.





Prepared from 1,3-azadiene **3d** (0.5 mmol) and anhydride **4** (65 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). T = 100 °C, time = 16 h. Yield = 153.1 mg, 84%, 95:5 dr. **HRMS-EI**<sup>+</sup> (m/z): calc'd for C<sub>22</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub> 364.1787; found 364.1783.





Prepared from 1,3-azadiene **3e** (0.5 mmol) and anhydride **4** (65 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). T = 100 °C, time = 16 h. Yield = 209.6 mg, 79%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.46 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.22 (m, 6H), 7.13 (d, *J* = 8.1 Hz, 2H), 6.43 (dd, *J* = 15.9, 8.2 Hz, 1H), 6.31 (d, *J* = 15.9 Hz, 1H), 4.63 – 4.53 (m, 1H), 3.83 (s, 3H), 3.75 – 3.57 (m, 3H), 2.60 (s, 3H), 1.10 – 1.03 (m, 21H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.8, 166.7, 140.7, 138.5, 135.9, 133.8, 133.7, 133.0, 128.7, 128.3, 127.5, 126.9, 126.7, 106.4, 91.4, 65.9, 64.8, 54.8, 52.0, 42.6, 18.7, 11.3. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>32</sub>H<sub>42</sub>N<sub>2</sub>O<sub>3</sub>Si 530.2965; found 530.2973.





Prepared from 1,3-azadiene **3f** (0.5 mmol) and anhydride **4** (65 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). T = 100 °C, time = 16 h. Yield = 154.1 mg, 81%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.37 – 7.21 (m, 6H), 6.92 – 6.69 (m, 3H), 6.44 (dd, *J* = 15.9, 8.2 Hz, 1H), 6.33 (d, *J* = 15.9 Hz, 1H), 4.59 (dd, *J* = 8.3, 2.7 Hz, 1H), 3.83 (s, 3H), 3.67 – 3.57 (m, 6H), 2.59 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.8, 166.7, 160.2, 141.9, 136.0, 133.6, 129.9, 128.7, 128.2, 127.2, 126.7, 119.9, 113.5, 65.9, 64.9, 55.3, 54.9, 52.0, 42.6. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>22</sub>H<sub>24</sub>N<sub>2</sub>O<sub>4</sub> 380.1736; found 380.1741.







Prepared from 1,3-azadiene **3g** (0.5 mmol) and anhydride **4** (65 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). T = 100 °C, time = 16 h. Yield = 148.5 mg, 71%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.69 – 7.38 (m, 7H), 6.51 – 6.37 (m, 1H), 6.30 (d, *J* = 15.9 Hz, 1H), 5.86 (d, *J* = 11.4 Hz, 1H), 4.60 (dd, *J* = 8.4, 2.6 Hz, 1H), 3.73 – 3.58 (m, 6H), 2.59 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.9, 166.8, 140.8, 136.0, 134.7, 133.6, 129.3, 128.7, 127.8, 126.7, 112.6, 65.9, 64.9, 56.5, 54.8, 42.6. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>20</sub>H<sub>21</sub>F<sub>3</sub>N<sub>2</sub>O<sub>3</sub> 418.1504; found 418.1508.





Prepared from 1,3-azadiene **3h** (1.0 mmol) and anhydride **4** (129.2 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). T = 100 °C, time = 2 h. Yield = 272.4 mg, 85%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.36 (d, *J* = 7.0 Hz, 2H), 7.28 (dt, *J* = 14.9, 7.6 Hz, 3H), 7.21 (d, *J* = 7.4 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 6.28 (dd, *J* = 16.0, 7.3 Hz, 1H), 4.69 (dd, *J* = 7.7, 2.8 Hz, 1H), 3.73 (s, 3H), 3.62 – 3.49 (m, 3H), 2.44 (s, 3H), 1.40 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  171.3, 168.0, 136.2, 131.4, 130.9, 130.2, 129.9, 129.2, 128.7, 128.1, 128.0, 126.6, 126.0, 67.1, 58.2, 58.1, 55.6, 51.7, 41.7, 28.4. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>19</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub> 330.1943; found 330.1946.



Me

I CMe₃

1.07 1.04

6

mm

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6.38

hund

8

0.6

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10

9

Normalized Intensity

O

ЭМе

Ph

1.10

m

7

Chemical Shift (ppm)

3.05 3.02 ЦЦ

3

9.00 U

0





Prepared from 1,3-azadiene **3i** (1.0 mmol) and anhydride **4** (129.2 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). T = 100 °C, time = 2 h. Yield = 317.2 mg, 88%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.30 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 6.43 (d, *J* = 16.0 Hz, 1H), 6.13 (dd, *J* = 16.0, 7.5 Hz, 1H), 4.66 (dd, *J* = 7.5, 2.6 Hz, 1H), 3.87 – 3.64 (m, 6H), 3.61 – 3.54 (m, 3H), 2.44 (s, 3H), 1.39 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  171.4, 168.0, 159.5, 130.8, 130.3, 128.9, 128.6, 127.7, 127.1, 114.1, 67.2, 58.3, 58.0, 55.5, 55.3, 51.6, 41.7, 29.7. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>20</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub> 360.2049; found 360.2045.







Prepared from 1,3-azadiene **3j** (1.0 mmol) and anhydride **4** (129.2 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). T = 100 °C, time = 4 h. Yield = 306.1 mg, 78%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.41 – 7.15 (m, 10H), 6.27 (d, *J* = 9.4 Hz, 1H), 4.47 (h, *J* = 9.3, 8.1 Hz, 1H), 4.36 (d, *J* = 9.4 Hz, 1H), 3.63 – 3.53 (m, 6H), 2.49 (s, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.6, 166.6, 142.3, 141.5, 138.8, 129.9, 129.7, 128.6, 128.4, 128.1, 127.9, 127.8, 66.6, 54.2, 53.4, 51.6, 45.7, 42.2, 20.6, 19.1. **HRMS-EI**<sup>+</sup> (*m*/*z*): calc'd for C<sub>24</sub>H<sub>28</sub>N<sub>2</sub>O<sub>3</sub> 392.2100; found 392.2104.







Prepared from 1,3-azadiene **3k** (1.0 mmol) and anhydride **4** (129.2 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). T = 100 °C, time = 2 h. Yield = 235.9 mg, 77%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.36 (br s, 1H), 6.41 – 6.22 (m, 4H), 4.57 (h, *J* = 7.0 Hz, 1H), 4.34 (dd, *J* = 7.3, 2.3 Hz, 1H), 3.73 (s, 3H), 3.60 (d, *J* = 17.4 Hz, 1H), 3.58 – 3.45 (m, 2H), 2.48 (s, 3H), 1.12 (dd, *J* = 11.9, 6.9 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  171.0, 166.9, 151.8, 142.4, 128.9, 120.1, 111.5, 108.8, 66.5, 56.9, 54.5, 51.8, 46.4, 42.1, 20.5, 19.8. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>16</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub> 306.1580; found 306.1576.







Prepared from 1,3-azadiene **31** (1.0 mmol) and anhydride **4** (129.2 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (20:80). T = 100 °C, time = 2 h. Yield = 283 mg, 70%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  6.99 - 6.82 (m, 3H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.30 (dd, *J* = 16.0, 7.7 Hz, 1H), 4.58 (q, *J* = 7.1 Hz, 1H), 4.38 (d, *J* = 7.6 Hz, 1H), 3.86 - 3.73 (m, 9H), 2.48 (s, 3H), 2.31 (s, 3H), 1.13 (m, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.9, 169.1, 166.9, 151.3, 139.6, 131.2, 130.8, 123.0, 119.3, 110.3, 66.6, 57.2, 56.0, 54.5, 51.8, 46.5, 42.1, 20.7, 20.6, 19.8. **HRMS-EI**<sup>+</sup> (*m*/*z*): calc'd for C<sub>21</sub>H<sub>28</sub>N<sub>2</sub>O<sub>6</sub> 404.1947; found 404.1954.







Prepared from 1,3-azadiene **3m** (1.0 mmol) and anhydride **4** (129.2 mg, 1.0 equiv) using General Procedure A. Purification: Flash chromatography on silica eluting with hexane/EtOAc (20:80). T = 100 °C, time = 5 h. Yield = 238.5 mg, 66%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  8.12 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 6.64 – 6.47 (m, 2H), 4.54 (tt, *J* = 18.9, 9.6 Hz, 1H), 4.39 (t, *J* = 4.2 Hz, 1H), 3.70 - 3.61 (m, 6H), 2.43 (s, 3H), 1.08 (d,d, *J* = 7.0 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.5, 166.8, 142.6, 135.7, 129.7, 127.2, 124.1, 66.1, 56.9, 54.4, 51.8, 46.4, 42.1, 20.5, 19.7. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>19</sub>H<sub>23</sub>N<sub>3</sub>O<sub>5</sub> 361.1638; found 361.1642.





### Alkenylation



1a1, 86%

Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (15:85). Yield = 194.4 mg, 86%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.45 – 7.31 (m, 4H), 7.31 – 7.18 (m, 4H), 7.22 – 7.13 (m, 2H), 7.17 – 7.08 (m, 2H), 7.12 – 7.03 (m, 2H), 6.94 (s, 2H), 6.34 (dd, *J* = 15.9, 8.3 Hz, 1H), 6.22 (d, *J* = 15.9 Hz, 1H), 4.51 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.71 (s, 3H), 3.62 (d, *J* = 17.5 Hz, 1H), 3.58 – 3.48 (m, 2H), 2.48 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.94, 166.90, 140.12, 137.25, 136.70, 136.06, 133.70, 129.48, 128.83, 128.79, 128.34, 127.97, 127.94, 127.90, 127.41, 127.24, 126.82, 126.70, 65.96, 64.89, 54.92, 52.11, 42.68. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>29</sub>H<sub>28</sub>N<sub>2</sub>O<sub>3</sub> 452.2100; found 452.1007. FTIR (KBr): 2932.5571, 1721.483, 1665.4081, 1607.2449, 1511.11, 1431.8598, 1414.7076, 1344.99, 1298.4941, 1245.6515, 1179.4413, 1135.306, 1031.8607, 996.7789, 921.8434, 832.167, 701.6744.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (15:85). Yield = 196 mg, 84%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.53 – 7.35 (m, 2H), 7.29 – 7.19 (m, 11H), 7.02 (dd, *J* = 4.7, 2.8 Hz, 2H), 6.41 (ddd, *J* = 15.9, 12.6, 8.3 Hz, 1H), 6.35 – 6.23 (m, 1H), 4.55 (ddd, *J* = 24.7, 8.3, 2.5 Hz, 1H), 3.69 (s, 3H), 3.66 – 3.55 (m, 1H), 3.55 – 3.43 (m, 2H), 2.57 (s, 3H), 2.31 (s, 3H). <sup>13</sup>C NMR (101 MHz,

CDCl<sub>3</sub>) δ 170.95, 166.89, 139.85, 138.55, 137.79, 136.91, 136.04, 134.45, 133.68, 129.51, 129.40, 128.76, 128.30, 127.91, 127.26, 127.22, 126.92, 126.80, 126.59, 65.97, 64.88, 54.88, 52.10, 42.66, 21.39. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>30</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub> 466.2256; found 466.2261.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yield = 206 mg, 81%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.30 – 7.17 (m, 11H), 7.16 – 7.07 (m, 2H), 6.99 (d, *J* = 1.4 Hz, 2H), 6.42 (dd, *J* = 15.9, 8.3 Hz, 1H), 6.30 (d, *J* = 15.9 Hz, 1H), 4.58 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.80 (s, 3H), 3.68 – 3.56 (m, 3H), 2.57 (s, 3H), 1.29 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.95, 166.90, 151.05, 139.85, 136.94, 136.03, 134.46, 133.67, 129.27, 128.76, 128.29, 127.89, 127.28, 127.23, 127.15,

126.79, 126.40, 125.73, 67.20, 65.98, 64.88, 54.87, 52.09, 42.66, 34.74, 31.39. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>33</sub>H<sub>36</sub>N<sub>2</sub>O<sub>3</sub> 508.2726; found 508.2721.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (20:80). Yield = 205 mg, 85%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.50 – 7.42 (m, 2H), 7.37 – 7.17 (m, 9H), 7.16 – 7.08 (m, 3H), 6.87 – 6.74 (m, 1H), 6.48 – 6.35 (m, 1H), 6.35 (d, *J* = 15.8 Hz, 1H), 4.54 (d, *J* = 15.8, 2.0 Hz, 1H), 3.78 – 3.60 (m, 6H), 3.60 – 3.48 (m, 3H), 2.57 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.94, 166.88, 159.99, 140.12, 138.68, 136.59, 136.03, 133.69, 129.76, 129.36, 128.77, 128.32, 128.23, 127.95, 127.43, 127.20, 126.80, 119.40, 113.59, 111.84, 65.97, 64.87, 55.37, 54.89, 52.10, 42.66. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>30</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub> 482.2206; found 482.2202.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (20:80). Yield = 231 mg, 88%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.67 – 7.30 (m, 9H), 7.27 – 7.17 (m, 2H), 6.95 – 6.81 (m, 4H), 6.47 – 6.23 (m, 2H), 4.55 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.77 (s, 3H), 3.65 – 3.54 (m, 3H), 2.35 (s, 3H), 1.30 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.94, 166.89, 155.39, 139.81, 138.54, 136.93, 136.04, 133.88, 133.67, 132.42, 129.77, 129.02, 128.80, 128.76, 128.30, 127.90, 127.22, 126.79, 126.74, 124.39,

78.92, 65.96, 65.83, 64.87, 64.81, 54.88, 54.78, 52.12, 52.09, 42.69, 42.65, 28.99. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>33</sub>H<sub>36</sub>N<sub>2</sub>O<sub>4</sub> 524.2675; found 524.2675.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (10:90). Yield = 204 mg, 80%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.33 (m, 3H), 7.35 – 7.09 (m, 12H), 6.42 (dd, *J* = 15.9, 8.3 Hz, 1H), 6.36 – 6.24 (dd, dd, *J* = 15.9, 8.3 Hz, 1H), 4.58 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.80 (s, 3H), 3.81 – 3.66 (m, 3H), 2.57 (s, 3H), 2.26 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 170.92, 169.58, 166.98, 140.10, 136.57, 136.01, 135.05, 133.73, 128.77, 128.44, 128.33, 128.15, 127.96, 127.60, 127.40, 127.14,

126.80, 121.93, 65.94, 64.89, 54.86, 52.11, 42.66, 21.27. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>31</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub> 510.2155; found 510.2162.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yield = 185 mg, 76%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.50 – 7.40 (m, 2H), 7.40 – 7.33 (m, 2H), 7.21 – 7.09 (m, 9H), 6.95 – 6.80 (m, 2H), 6.42 (dd, *J* = 15.9, 8.3 Hz, 1H), 6.29 (d, *J* = 15.9 Hz, 1H), 4.59 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.80 (s, 3H), 3.69 (d, *J* = 17.6 Hz, 1H), 3.65 – 3.56 (m, 2H), 2.57 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.94, 166.88, 140.28, 136.33, 136.01, 135.75, 133.70, 133.40, 128.95, 128.77, 128.53, 128.33, 128.12, 128.00, 127.82, 127.49, 127.43, 127.17, 126.79, 65.97, 64.86, 54.88, 52.11, 42.67. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>29</sub>H<sub>27</sub>ClN<sub>2</sub>O<sub>3</sub> 486.1710; found 486.1717.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (5:95). Yield = 161 mg, 71%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  8.52 (d, *J* = 5.0 Hz, 1H), 7.66 – 7.51 (m, 5H), 7.24 – 7.16 (m, 9H), 6.40 (dd, *J* = 15.9, 8.3 Hz, 1H), 6.26 (d, *J* = 15.9 Hz, 1H), 4.56 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.78 (s, 3H), 3.75 – 3.61 (m, 2H), 3.58 (d, *J* = 2.5 Hz, 1H), 2.54 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.79, 167.25, 154.61, 148.25, 140.86, 138.05, 135.88, 135.64, 133.91, 133.20, 128.76, 128.36, 128.26, 128.01, 126.85, 126.80, 122.82, 122.60, 65.78, 64.88, 54.85, 52.19, 42.63. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for

C<sub>28</sub>H<sub>27</sub>N<sub>3</sub>O<sub>3</sub> 453.2052; found 453.2059. FTIR (KBr): 2965.2971, 2872.3128, 1716.4748, 1650.8904, 1612.9884, 1585.9456, 1513.1051, 1455.3449, 1359.3702, 1304.1365, 1251.3997, 1177.4761, 1135.5369, 1033.8548, 996.7497, 896.0777, 833.6912, 804.9269.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (5:95). Yield = 173 mg, 73%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  8.52 (d, *J* = 8.4 Hz, 1H), 7.41 (dd, *J* = 8.8, 2.3 Hz, 2H), 7.33 – 7.18 (m, 8H), 6.73 (d, *J* = 15.9 Hz, 1H), 6.40 (dd, *J* = 15.9, 8.3 Hz, 1H), 6.28 (d, *J* = 15.9 Hz, 1H), 4.57 (dd, *J* = 8.3, 2.6 Hz, 1H), 3.79 (s, 3H), 3.63 – 3.54 (m, 3H), 2.56 (s, 3H), 2.47 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.93, 166.85, 150.93, 149.72, 140.38, 136.04, 135.97, 133.71, 130.84, 130.45, 128.76, 128.33, 128.04, 127.22, 127.12, 126.77, 119.00, 65.97, 64.84, 54.87, 52.10, 42.66, 15.54. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>27</sub>H<sub>27</sub>N<sub>3</sub>O<sub>3</sub>S 473.1773; found 473.1778.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yield = 215.5 mg, 80%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.56 – 7.29 (m, 11H), 7.18 – 7.06 (m, 4H), 6.33 (s, 1H), 4.54 – 4.48 (m, 1H), 3.62 – 3.53 (m, 6H), 2.41 (s, 3H), 1.85 (s, 3H), 1.21 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  171.05, 167.48, 155.36, 139.55, 138.27, 136.66, 134.57, 132.43, 130.40, 129.03, 128.97, 128.93, 128.34, 128.29, 127.21, 127.19, 127.05, 126.96, 126.73, 124.39, 78.92, 69.33, 66.02, 55.79, 52.22, 42.48, 28.97, 28.93, 15.14. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>34</sub>H<sub>38</sub>N<sub>2</sub>O<sub>4</sub> 538.2832; found 538.2837.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yield = 230 mg, 83%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.34 – 7.27 (m, 2H), 7.28 – 7.17 (m, 4H), 7.15 – 7.06 (m, 2H), 6.83 – 6.74 (m, 4H), 6.69 (dd, J = 8.9, 2.3 Hz, 2H), 6.31 – 6.16 (m, 2H), 4.46 – 4.33 (m, 1H), 3.72 – 3.62 (overlapping singlets, 6H), 3.61 – 3.50 (m, 3H), 2.54 (s, 3H), 1.30 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  171.00, 166.88, 159.74, 155.35, 139.82, 138.49, 136.86, 133.11, 132.42, 129.79, 129.33,

128.95, 128.75, 128.03, 128.01, 127.97, 127.91, 127.81, 127.17, 126.78, 126.75, 124.88, 124.38, 114.16, 114.12, 66.12, 65.01, 55.43, 54.89, 52.05, 42.64, 28.96. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>34</sub>H<sub>38</sub>N<sub>2</sub>O<sub>5</sub> 554.2781; found 554.2788.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yield = 216.4 mg, 91%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.40 (d, *J* = 15.5 Hz, 1H), 7.24 (d, *J* = 1.9 Hz, 1H), 7.30 – 7.21 (m, 5H), 7.25 – 7.16 (m, 1H), 7.14 – 7.06 (m, 2H), 6.39 (dd, *J* = 15.8, 8.3 Hz, 1H), 6.25 (d, *J* = 15.9 Hz, 1H), 6.14 (d, *J* = 15.5 Hz, 1H), 5.70 (s, 1H), 4.54 (dd, *J* = 8.3, 2.4 Hz, 1H), 3.77 (s, 3H), 3.72 – 3.53 (m, 6H), 2.55 (s, 3H), 1.34 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.82, 166.95, 165.09, 141.58, 138.94, 135.88, 134.46, 133.83, 128.76, 128.68, 128.36, 127.92, 126.93, 126.77, 122.85, 67.18, 65.78,

64.79, 54.81, 52.09, 51.49, 42.63, 28.96, 28.91. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>28</sub>H<sub>32</sub>N<sub>3</sub>O<sub>4</sub> 475.2471; found 475.2478.





1a13, 76%

Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (15:85). Yield = 170.4 mg, 76%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.67 – 7.59 (d, 2H), 7.41 – 7.28 (m, 6H), 6.85 (d, 2H), 6.56 (d, *J* = 15.8 Hz, 1H), 6.39 (ddd, *J* = 15.8, 8.4, 3.7 Hz, 1H), 6.33 – 6.13 (m, 1H), 4.65 (dd, *J* = 6.4, 1.4 Hz, 1H), 4.53 (ddd, *J* = 15.8, 8.4, 2.5 Hz, 1H), 3.68 (s, 3H), 3.63 – 3.42 (m, 4H), 2.55 (s, 3H), 2.04 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.90, 166.84, 166.77, 140.62, 138.54, 135.56, 133.88, 133.71, 133.34, 129.77, 128.80, 128.75, 128.43, 127.91, 127.53, 126.86, 126.79, 126.77, 124.02, 65.83, 64.81, 54.78, 52.13, 42.69, 21.11. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>26</sub>H<sub>28</sub>N<sub>2</sub>O<sub>5</sub> 448.1998; found 448.1992.





Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yield = 136.3 mg, 63%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.35 – 7.26 (m, 7H), 7.20 – 7.12 (m, 2H), 6.39 (ddd, *J* = 15.8, 8.4, 5.4 Hz, 1H), 6.31 – 6.11 (m, 1H), 6.21 – 6.11 (m, 1H), 4.53 (td, *J* = 9.7, 9.0, 2.5 Hz, 1H), 3.78 (s, 3H), 3.63 – 3.52 (m, 3H), 2.55 (s, 3H), 1.05 (s, 9H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.95, 166.84, 142.72, 139.26, 138.54, 137.47, 136.06, 133.88, 133.59, 129.76, 128.79, 128.73, 128.43, 128.25, 127.74, 127.26, 126.88, 126.85, 126.79, 126.77, 123.92, 66.00, 65.85, 64.91, 64.81, 54.87, 54.77, 52.12, 52.06, 42.68, 42.64, 33.49, 29.81, 29.63. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>27</sub>H<sub>32</sub>N<sub>2</sub>O<sub>3</sub> 432.2413; found 432.2418.





1a15, 74% (combined yield)

Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yield = 172.5 mg, 74%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.25 (m, 14H), 6.96 (dd, *J* = 8.3, 3.6 Hz, 1H), 6.46 – 6.21 (m, 3H), 4.43 (ddd, *J* = 11.0, 6.9, 2.8 Hz, 1H), 3.73 – 3.64 (m, 8H), 2.56 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 170.94, 166.93, 166.86, 166.78, 139.62, 139.60, 138.93, 138.55, 136.88, 136.09, 136.04, 133.89, 133.64, 133.59, 131.43, 130.41, 130.10, 129.77, 129.64, 128.82, 128.80, 128.75, 128.69, 128.62, 128.48, 128.43, 128.27, 127.79, 127.74, 127.40, 127.35, 127.26, 127.21, 127.06, 127.03, 126.86, 126.80, 126.78, 126.32, 126.23, 66.04, 65.98, 65.85, 64.94, 64.88, 64.82, 54.89, 54.86, 54.78,

52.07, 42.69, 42.65, 39.42, 39.00. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>30</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub> 466.2256; found 466.2263.





1a16, 77% (combined yield)

Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Yield = 191.2 mg, 77%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.14 (m, 13H), 6.83 – 6.69 (m, 2H), 6.36 – 6.09 (m, 4H), 4.54 (dt, *J* = 8.4, 2.9 Hz, 1H), 3.76 – 3.68 (m, 6H), 3.68 – 3.56 (m, 3H), 3.58 – 3.43 (m, 2H), 2.55 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 170.94, 166.92, 166.85, 139.91, 138.86, 138.55, 136.94, 136.10, 133.62, 133.57, 130.79, 130.08, 129.69, 129.61, 128.74, 128.26, 127.77, 127.69, 127.37, 127.34, 127.22,

127.00, 126.77, 126.65, 114.02, 66.04, 65.98, 64.93, 64.88, 55.39, 54.87, 52.07, 42.64, 38.98, 38.51. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>31</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub> 496.2362; found 496.2369.





1a17, 81% (combined yield)

Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (15:85). Yield = 213.3 mg, 81%, 95:5 dr. <sup>1</sup>H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.25 (m, 6H), 7.10 – 7.02 (m, 2H), 6.71 – 6.56 (m, 4H), 6.46 – 6.20 (m, 4H), 4.45 (dt, *J* = 8.4, 2.5 Hz, 1H), 3.80 – 3.67 (m, 12H), 3.63 – 3.53 (m, 2H), 3.49 – 3.40 (m, 2H), 2.55 (s, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 170.94, 166.93, 166.86, 149.08, 149.03, 148.55, 147.56, 139.80, 139.59, 138.91, 136.88, 136.08, 136.03, 133.61, 133.55, 132.63, 130.97, 130.32, 130.21, 129.67, 128.75, 128.28, 127.79, 127.72, 127.39, 127.23, 127.03, 127.00, 126.76, 120.58,

119.27, 111.94, 111.35, 111.17, 108.56, 66.03, 65.98, 64.93, 64.87, 56.05, 56.02, 55.94, 55.90, 54.87, 52.07, 42.64, 39.01, 38.99. **HRMS-EI**<sup>+</sup> (*m/z*): calc'd for C<sub>31</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub> 496.2362; found 496.2369.





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