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# Trienamine-Mediated Asymmetric [4+2]-Cycloaddition of α,β-Unsaturated Ester Surrogates Applying 4-Nitro-5-Styrylisoxazoles

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#### **1. GENERAL METHODS**

NMR spectra were acquired on a bruker AS 400 spectrometer, running at 400 MHz for <sup>1</sup>H and 100 MHz for <sup>13</sup>C, respectively. Chemical shifts ( $\delta$ ) are reported in ppm relative to residual solvent signals (CHCl<sub>3</sub>, 7.26 ppm for <sup>1</sup>H NMR, CDCl<sub>3</sub>, 77.0 ppm for <sup>13</sup>C NMR). The following abbreviations are used to indicate the multiplicity in NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; hept, heptet; m, multiplet; br, broad resonance; app., apparent. <sup>13</sup>C NMR spectra were acquired on a broad band decoupled mode. For characterization of diastereomeric mixtures, \*denotes minor diastereoisomer, <sup>+</sup>denotes overlap of signals from both diastereoisomers, while the major diastereomer is characterized without further denotations. The number of protons/carbons given in the parenthesis is the sum over both diastereomers. Mass spectra were recorded on a Bruker MicroTOF-Q High-Performance LC-MS system. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation, KMnO<sub>4</sub> or *p*-anisaldehyde dip. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (ee) of the products was either determined by: i) Ultraperformance Convergence Chromatography (UPC<sup>2</sup>) using Daicel Chiralpak IA-3, IB-3, IC-3 and ID-3 columns as chiral stationary phases; or by ii) chiral stationary phase HPLC on a Daicel Chiralpak IA-5, IB-5 column. Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography (FC) silica gel (SiO<sub>2</sub> 60, 230-400 mesh, Fluka) was used. Racemic samples were prepared using a mixture of enantiomers of 3 (20 mol%) in combination with DABCO (20 mol%), H<sub>2</sub>O (10 equiv.) in THF.

## **2. STARTING MATERIALS**

Dienals 1 were prepared from the corresponding alkenyl bromides according to the procedure reported by Fabrizi *et al.*<sup>1</sup> 4-Nitro-5-styrylisoxazoles  $2^2$  were prepared following literature procedures. For **1n** and **2c,h,i** the data are given below.



Dienal **1n** was obtained after FC on silica gel ( $CH_2Cl_2$ ) in 61% yield as a yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.60 (d, J = 7.8 Hz, 1H), 7.66 (d, J = 15.3 Hz, 1H), 6.12 (dd, J = 15.3, 7.8 Hz, 1H), 2.01 (s, 3H), 1.94 (s, 3H), 1.84 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 194.6, 151.6, 144.6,

127.0, 126.8, 22.9, 21.1, 14.2. **HRMS** (ESI+) *m/z* calcd. for C<sub>8</sub>H<sub>12</sub>O [M+H]<sup>+</sup>: 125.0961; found: 125.0961.



4-Nitro-5-styrylisoxazole **2c** was obtained in 53% yield as a pale yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.84 – 7.68 (m, 6H), 2.62 (s, 3H). <sup>13</sup>C NMR (100 MHz, **CDCl**<sub>3</sub>) δ 166.4, 156.2, 140.9, 137.6, 128.4 (2C), 126.1 (q, J = 3.8 Hz, 2C), 113.2,

11.8 (two of the signals in the aromatic/olefinic region denotes two overlapping carbons; signals for CF3carbons were not detected after prolonged scans). **HRMS** (ESI+) m/z calcd. for C<sub>13</sub>H<sub>9</sub>F<sub>3</sub>N<sub>2</sub>O<sub>3</sub> [M+H]<sup>+</sup>: 299.0638; found: 299.0641.



4-Nitro-5-styrylisoxazole 2h was obtained in 56% yield as a pale yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.75 – 7.67 (m, 3H), 7.65 – 7.57 (m, 2H), 2.61 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 166.0, 156.2, 139.4, 137.8, 136.0, 129.7 (2C), 123.7 (2C), 113.4, 11.8 (one of the signals in the aromatic/olefinic region denotes two

overlapping carbons). **HRMS** (ESI+) m/z calcd. for  $C_{12}H_8Br_2N_2O_3[M+H]^+$ : 386.8974; found: 386.8982.



4-Nitro-5-styrylisoxazole 2i was obtained in 57% yield as a yellow solid. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.14 (d, J = 16.5 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.65 (d, J = 16.5 Hz, 1H), 7.50 (d, J = 2.0 Hz, 1H), 7.35 (dd, J = 8.5, 2.0 Hz, 1H), 2.62 (s, 3H). <sup>13</sup>C NMR

(100 MHz, CDCl<sub>3</sub>)  $\delta$  166.4, 156.2, 137.2, 137.2, 135.9, 131.1, 130.2, 128.3, 127.8, 113.4, 11.8 (one of the signals in the aromatic/olefinic region denotes two overlapping carbons). HRMS (ESI+) m/z calcd. for C<sub>12</sub>H<sub>8</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>3</sub> [M+H]<sup>+</sup>: 298.9985; found: 298.9984.

<sup>&</sup>lt;sup>1</sup> (a) G. Battistuzzi, S. Cacchi and G. Fabrizi, Org. Lett., 2003, 5, 777. All spectroscopic data matched those previously reported: (b) Z.-J. Jia, Q. Zhou, Q.-Q. Zhou, P.-Q. Chen and Y.-C. Chen, Angew. Chem. Int. Ed., 2011, 50, 8638.

<sup>&</sup>lt;sup>2</sup> H. Kawai, K. Tachi, E. Tokunaga, M. Shiro and N. Shibata, *Angew. Chem. Int. Ed.*, 2011, **50**, 7803.

#### **3. PROCEDURES AND PRODUCTS**



#### General Procedure for the Trienamine-mediated [4+2]-Cycloaddition

A mixture of the dienal **1** (0.15 mmol, 1.5 equiv), olefin substrate **2** (0.1 mmol, 1 equiv), DABCO (0.02 mmol, 0.2 equiv),  $H_2O$  (10 equiv) and catalyst **3e** (0.02 mmol, 0.2 equiv) were dissolved in 0.4 mL of THF and brought to 40 °C and stirred until complete consumption of **2**, which usually was reached in 24-72 h (unless specific reaction time is given). Excess solvents were removed *in vacuo* and the crude mixture was purified by FC on silica gel to afford the corresponding cycloadduct **4**.



General Derivatization Procedure for Determination of the Enantioselectivities

To a solution of the aldehyde **4** (0.05 mmol, 1 equiv) in  $CH_2CI_2$  (0.2 mL) was added  $Ph_3P=COPh$  (0.1 mmol, 2 equiv). The reaction mixture was heated to 40 °C and stirring for 2-48 h (unless specific reaction time is given; monitored by TLC or <sup>1</sup>H NMR), after which it was allowed to cool to rt. The crude mixture of the Wittig reaction was directly purified by FC on silica gel to afford the pure enone products **5**.



Following the general procedure, cycloadduct **4a** was obtained after FC on silica gel (gradient: pentane/EtOAc 20:1 to 10:1) in 68% yield and 8.7:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = -10.0 \ (c \ 0.2, \ CH_2Cl_2)$ . <sup>1</sup>H NMR (**400** MHz, CDCl<sub>3</sub>):  $\delta$  9.57 (s, 1H), 7.24 – 7.03 (m, 5H), 5.51 (d,  $J = 3.3 \ Hz$ , 1H), 4.51 (dd,  $J = 11.7, 5.3 \ Hz$ , 1H), 3.44 – 3.27 (m, 2H), 2.68 (dd,  $J = 18.1, 7.1 \ Hz$ , 1H), 2.56 (dd,  $J = 18.1, 6.3 \ Hz$ , 1H), 2.38 (s, 3H), 2.35 – 2.20 (m, 2H), 1.75 (s, 3H). <sup>13</sup>C NMR (**100** MHz, CDCl<sub>3</sub>):  $\delta$  199.6, 175.1, 171.1, 155.3, 142.7, 134.7,

128.7 (2C), 127.0 (2C), 126.9, 122.7, 46.4, 41.5, 39.3, 39.0, 31.8, 23.1, 11. 6. **HRMS** (ESI+) m/z calcd. for  $C_{19}H_{20}N_2O_4$  [M+Na]<sup>+</sup>: 363.1315; found: 363.1317. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5a** was obtained after FC on silica gel (gradient: pentane/EtOAc 20:1 to 10:1) in 63% yield and 7:1 dr as a pale yellow oil.  $[\alpha]_D^{20}$  = +60.0 (*c* 0.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.90 (d, *J* = 7.3 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 2H), 7.25 – 7.05 (m, 5H), 6.78 – 6.73 (m, 2H), 5.56 (d, *J* = 3.0 Hz, 1H), 4.45 (dd, *J* = 11.4, 5.6 Hz, 1H), 3.48 (ddd, *J* = 11.3, 10.3,

5.9 Hz, 1H), 3.05 - 2.90 (m, 1H), 2.49 - 2.15 (m, 7H), 1.77 (s, 3H). <sup>13</sup>**C NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  189.7, 175. 6, 155.2, 145.7, 143.2, 137.6, 134.5, 132.8, 128.7 (2C), 128.5 (2C), 128.5 (2C), 127.0 (2C), 126.8, 126.6, 122.9, 42.1, 39.2, 38.7, 38.2, 36.0, 30.9, 23.2, 11.4. **HRMS** (ESI+) *m/z* calcd. for C<sub>27</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]<sup>+</sup>: 465.1785; found: 465.1786. **UPC**<sup>2</sup>: IC-3, CO<sub>2</sub>/*i*-PrOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer: t<sub>major</sub> = 4.7 min; t<sub>minor</sub> = 4.2 min (94% ee).



Following the general procedure, cycloadduct **4b** was obtained after FC on silica gel (gradient: pentane/EtOAc 20:1 to 10:1 to 4:1) in 76% yield and 4.2:1 dr as a pale yellow solid.  $[\alpha]_D^{20} = +13.2$  (*c* 1.5, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.66\* (s, 1H\*), 9.55 (s, 1H), 7.46 – 7.28<sup>+</sup> (m, 2H, 2H\*), 7.06 (d, *J* = 8.3 Hz, 2H), 6.98\* (d, *J* = 8.3 Hz, 2H\*), 5.51 (d, *J* = 2.9 Hz, 1H), 5.39\* (s, 1H\*), 4.46 (dd, *J* = 11.7, 5.2 Hz, 1H), 4.00\* (app. t, *J* = 11.2 Hz, 1H), 3.43 – 3.28<sup>+</sup> (m, 2H, 2H\*), 2.71 – 2.14<sup>+</sup> (m, 7H, 7H\*), 1.75 – 1.74<sup>+</sup> (m, 3H, 3H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  200.1\*, 199.3, 174.7\*, 174.6, 155.4, 155.1\*, 141.8, 140.9\*,

135.8\*, 135.6, 135.0\*, 134.4, 131.9 (2C), 131.8\* (2C\*), 128.8 (2C), 128.6\* (2C), 122.8, 122.5\*, 121.0\*, 120.7, 47.9, 46.3\*, 41.4<sup>+</sup> (1C, 1C\*), 39.1, 38.9\*, 38.5, 35.8\*, 31.7<sup>+</sup> (1C, 1C\*), 23.1, 23.1\*, 11.6<sup>+</sup> (1C, 1C\*). **HRMS** (ESI+) m/z calcd. for  $C_{19}H_{19}BrN_2O_4$  [M+Na]<sup>+</sup>: 441.0420, 443.0400; found: 441.0424, 443.0402. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5b** was obtained after FC on silica gel (gradient: pentane/EtOAc 20:1 to 10:1 to 4:1) in 86% yield and 3:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = +134.0 (c \ 0.5, CH_2Cl_2)$ . <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.95 – 7.84<sup>+</sup> (m, 2H, 2H<sup>\*</sup>), 7.56<sup>+</sup> (app. t, *J* = 7.3 Hz, 1H, 1H<sup>\*</sup>), 7.46<sup>+</sup> (app. t, *J* = 7.6 Hz, 2H, 2H<sup>\*</sup>), 7.34 (d, *J* = 8.4 Hz, 2H), 7.28<sup>\*</sup> (d, *J* = 8.4 Hz, 2H<sup>\*</sup>), 7.07 (d, *J* = 8.4 Hz, 2H), 6.97<sup>\*</sup> (d, *J* = 8.4 Hz, 2H), 6.85 – 6.72<sup>+</sup> (m, 2H, 2H<sup>\*</sup>), 5.56 (d, *J* = 3.2 Hz, 1H), 5.45<sup>\*</sup> (s, 1H<sup>\*</sup>), 4.40 (dd, *J* = 11.5, 5.6 Hz, 1H), 3.97<sup>\*</sup> (app. t, *J* = 11.2 Hz, 1H<sup>\*</sup>), 3.46 (ddd, *J* = 11.5, 10.6, 5.8 Hz, 1H), 3.40 – 3.29<sup>\*</sup> (m, 1H<sup>\*</sup>), 3.16 – 3.05<sup>\*</sup> (m, 1H<sup>\*</sup>), 3.05 –

2.94 (m, 1H), 2.51 – 2.10<sup>+</sup> (m, 7H, 7H<sup>\*</sup>), 1.77<sup>+</sup> (s, 3H, 3H<sup>\*</sup>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  189.7<sup>+</sup> (1C, 1C<sup>\*</sup>), 175.2<sup>\*</sup>, 175.1, 155.4, 155.3<sup>\*</sup>, 145.4, 145.2<sup>\*</sup>, 142.3<sup>+</sup> (1C, 1C<sup>\*</sup>), 137.5<sup>+</sup> (1C, 1C<sup>\*</sup>), 134.9<sup>\*</sup>, 134.2, 132.9<sup>+</sup> (1C, 1C<sup>\*</sup>), 131.9 (2C), 131.75<sup>\*</sup> (2C), 128.8<sup>+</sup> (2C, 2C<sup>\*</sup>), 128.7<sup>+</sup> (1C, 1C<sup>\*</sup>), 128.6<sup>+</sup> (2C, 2C<sup>\*</sup>), 128.5<sup>+</sup> (2C, 2C<sup>\*</sup>), 127.6<sup>\*</sup>, 126.6, 123.0, 122.9<sup>\*</sup>, 120.9<sup>\*</sup>, 120.6, 42.0<sup>+</sup> (1C, 1C<sup>\*</sup>), 39.1<sup>+</sup> (1C, 1C<sup>\*</sup>), 38.3<sup>+</sup> (1C, 1C<sup>\*</sup>), 38.2<sup>+</sup> (1C, 1C<sup>\*</sup>), 35.9<sup>+</sup> (1C, 1C<sup>\*</sup>), 23.2, 23.1<sup>\*</sup>, 11.5<sup>\*</sup>, 11.4. HRMS (ESI+) *m/z* calcd. for C<sub>27</sub>H<sub>25</sub>N<sub>2</sub>O<sub>4</sub>Br [M+Na]<sup>+</sup>: 543.0890, 545.0869; found: 543.0899, 545.0886. UPC<sup>2</sup>: IC-3, CO<sub>2</sub>/MeOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer: t<sub>maior</sub> = 5.5 min; t<sub>minor</sub> = 4.8 min (94% ee).



3H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 200.0\*, 199.2, 174.4<sup>+</sup> (1C, 1C\*), 155.5, 155.1\*, 146.9, 145.9\*, 135.6<sup>+</sup> (1C, 1C\*), 134.9\*, 134.3, 129.2<sup>+</sup> (q, *J* = 33.2 Hz, 1C, 1C\*), 127.4 (2C), 127.3\* (2C), 125.8<sup>+</sup> (q, *J* = 3.7 Hz, 2C, 2C\*),

122.9, 122.6<sup>\*</sup>, 47.9<sup>\*</sup>, 46.3, 41.2<sup>+</sup> (1C, 1C<sup>\*</sup>), 39.0, 38.9, 38.7<sup>\*</sup>, 35.7<sup>\*</sup>, 31.6<sup>+</sup> (1C, 1C<sup>\*</sup>), 23.1<sup>+</sup> (1C, 1C<sup>\*</sup>), 11.5, 11.5<sup>\*</sup> (signals for CF3-carbons were not detected after prolonged scans). **HRMS** (ESI+) m/z calcd. for C<sub>20</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub>F<sub>3</sub> [M+Na]<sup>+</sup>: 431.1189; found: 431.1195. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5c** was obtained after FC on silica gel (pentane/EtOAc 20:1 to 10:1) in 80% yield and 5:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = +125.0 (c \ 0.4, CHCl_3)$ . <sup>1</sup>H NMR (400 MHz, CDCl\_3)  $\delta$  7.90<sup>+</sup> (d, J = 7.3 Hz, 2H, 2H\*), 7.56<sup>+</sup> (t, J = 7.3 Hz, 1H, 1H\*), 7.52 – 7.37<sup>+</sup> (m, 4H, 4H\*), 7.31 (d, J = 8.1 Hz, 2H), 7.22\* (d, J = 8.1 Hz, 2H\*), 6.86 – 6.69<sup>+</sup> (m, 2H, 2H\*), 5.58 (d, J = 3.1 Hz, 1H), 5.47\* (br, 1H\*), 4.46 (dd, J = 11.5, 5.6 Hz, 1H), 4.02\* (app. t, J = 10.7 Hz, 1H\*), 3.57 (ddd, J = 11.0, 10.7, 5.8 Hz, 1H), 3.51 – 3.38\* (m, 1H), 3.17 – 3.08\* (m, 1H\*), 3.08 – 2.94 (m, 1H), 2.50 – 2.14<sup>+</sup> (m, 7H, 7H\*), 1.78<sup>+</sup> (s, 3H, 3H\*). <sup>13</sup>C NMR (100

**MHz, CDCl<sub>3</sub>**)  $\delta$  189.6, 174.9, 155.4, 147.4, 145.2, 137.5, 134.8, 134.1, 132.9, 129.1 (q, *J* = 33.4 Hz), 128.6 (2C), 128.5 (2C), 127.4 (2C), 126.6, 125.8 (q, *J* = 3.7 Hz, 2C), 124.0 (q, *J* = 271.1 Hz), 123.1, 41.8, 39.0, 38.6, 38.2, 35.9, 23.1, 11.4 (only the major diastereomer is characterized). **HRMS** (ESI+) *m/z* calcd. for C<sub>28</sub>H<sub>25</sub>N<sub>2</sub>O<sub>4</sub>F<sub>3</sub> [M+Na]<sup>+</sup>: 533.1659; found: 533.1664. **UPC**<sup>2</sup>: IC-3, CO<sub>2</sub>/*i*-PrOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)] 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer: t<sub>major</sub> = 5.2 min; t<sub>minor</sub> = 3.8 min (93% ee).



Following the general procedure, cycloadduct **4d** was obtained after FC on silica gel (gradient: pentane/EtOAc 10:1 to 2:1) in 60% yield and 3.6:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = +22.0$  (*c* 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (**400** MHz, CDCl<sub>3</sub>):  $\delta$  9.67\* (s, 1H\*), 9.55 (s, 1H), 8.09 (d, *J* = 8.6 Hz, 2H), 8.05\* (d, *J* = 8.6 Hz, 2H\*), 7.37 (d, *J* = 8.6 Hz, 2H), 7.30\* (d, *J* = 8.6 Hz, 2H\*), 5.54 (d, *J* = 3.5 Hz, 1H), 5.42\* (br, 1H\*), 4.53 (dd, *J* = 11.7, 5.3 Hz, 1H), 4.13 – 4.03\* (m, 1H), 3.61 – 3.49<sup>+</sup> (m, 1H, 1H\*), 3.43 – 3.32<sup>+</sup> (m, 1H, 1H\*), 2.65 (dd, *J* = 18.3, 7.2 Hz, 1H), 2.57 (dd, *J* = 18.3, 6.3 Hz, 1H), 2.53 – 2.19<sup>+</sup> (m, 5H, 7H\*), 1.80 – 1.73<sup>+</sup> (m, 3H, 2H)

3H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  199.8\*, 199.0, 174.0\*, 174.0, 155.6, 155.2\*, 150.4, 149.4\*, 147.0\*, 146.9, 134.6<sup>+</sup> (1C, 1C\*), 134.0<sup>+</sup> (1C, 1C\*), 128.0 (2C), 128.0\* (2C\*), 124.1 (2C), 124.0\* (2C\*), 123.0, 122.7\*, 47.8\*, 46.2, 41.2<sup>+</sup> (1C, 1C\*), 39.0, 38.8, 38.6\*, 35.7\*, 31.6<sup>+</sup> (1C, 1C\*), 23.0, 23.0\*, 11.5<sup>+</sup> (1C, 1C\*). HRMS (ESI+) m/z calcd. for C<sub>19</sub>H<sub>19</sub>N<sub>3</sub>O<sub>6</sub> [M+Na]<sup>+</sup>: 408.1166; found: 408.1166. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5d** was obtained after FC on silica gel (gradient: pentane/EtOAc 10:1 to 4:1) in 90% yield and 4:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = +69.0 \ (c \ 1.0, CHCl_3)$ . <sup>1</sup>H NMR (400 MHz, CDCl\_3)  $\delta$  8.10 (d,  $J = 8.8 \ Hz, 2H$ ), 8.04\* (d,  $J = 8.7 \ Hz, 2H^*$ ), 7.90<sup>+</sup> (d,  $J = 7.1 \ Hz, 2H, 2H^*$ ), 7.62 – 7.52<sup>+</sup> (m, 1H, 1H\*), 7.46<sup>+</sup> (t,  $J = 7.6 \ Hz, 2H, 2H^*$ ), 7.37 (d,  $J = 8.8 \ Hz, 2H$ ), 7.29\* (d,  $J = 8.7 \ Hz, 2H^*$ ), 6.87 – 6.67<sup>+</sup> (m, 2H, 2H\*), 5.60 (d,  $J = 3.0 \ Hz, 1H$ ), 5.48\* (s, 1H\*), 4.46 (dd,  $J = 11.6, 5.6 \ Hz, 1H$ ), 4.09 – 3.97\* (m, 1H\*), 3.63 (ddd,  $J = 11.1, 10.7, 5.8 \ Hz, 1H$ ), 3.58 – 3.49\* (m, 1H\*), 3.18 – 3.10\* (m, 1H\*), 3.10 – 2.96 (m, 1H), 2.50 – 2.16<sup>+</sup> (m, 7H, 7H\*), 1.79<sup>+</sup> (s,

3H, 3H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 189.5, 174.4, 155.6, 150.9, 149.5, 146.9, 145.0, 137.4, 133.8, 132.9, 128.6 (2C), 128.4 (2C), 128.0 (2C), 126.6, 124.1 (2C), 123.2, 41.8, 38.8, 38.7, 38.3, 35.8, 23.1, 11.4 (only

major diastereomer is characterized). **HRMS** (ESI+) m/z calcd. for  $C_{27}H_{25}N_3O_6$  [M+Na]<sup>+</sup>: 510.1636; found: 510.1639. **UPC**<sup>2</sup>: IC-3, CO<sub>2</sub>/ACN gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer:  $t_{major} = 5.4$  min;  $t_{minor} = 5.0$  min (92% ee).



Following the general procedure, cycloadduct **4e** was obtained after FC on silica gel (gradient: pentane/EtOAc 20:1 to 10:1 to 4:1) in 71% yield and >11:1 dr as a pale yellow oil.  $[\alpha]_D^{20}$  = +9.0 (*c* 1.0, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.57 (s, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 5.50 (d, *J* = 3.4 Hz, 1H), 4.48 (dd, *J* = 11.7, 5.3 Hz, 1H), 3.40 – 3.28 (m, 2H), 2.67 (dd, *J* = 18.1, 7.1 Hz, 1H), 2.55 (dd, *J* = 18.1, 6.4 Hz, 1H), 2.39 (s, 3H), 2.36 – 2.18 (m, 5H), 1.74 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  199.6, 175.2, 155.3, 139.7, 136.4, 134.8, 129.4 (2C), 126.8 (2C), 122.7, 46.5, 41.6, 39.4, 38.6, 31.8,

23.1, 21.0, 11.6 (one of the signals in the aromatic/olefinic region denotes two overlapping carbons). **HRMS** (ESI+) m/z calcd. for  $C_{20}H_{22}N_2O_4$  [M+Na]<sup>+</sup>: 377.1472; found: 377.1477. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5e** was obtained after FC on silica gel (pentane/EtOAc 20:1 to 10:1) in 73% yield and >10:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = +109.6 (c \ 0.5, CHCl_3)$ . <sup>1</sup>H NMR (400 MHz, CDCl\_3)  $\delta$  7.92 – 7.87 (m, 2H), 7.59 – 7.51 (m, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 8.1 Hz, 2H), 6.79 – 6.72 (m, 2H), 5.55 (d, *J* = 3.1 Hz, 1H), 4.42 (dd, *J* = 11.4, 5.6 Hz, 1H), 3.50 – 3.38 (m, 1H), 3.04 – 2.93 (m, 1H), 2.48 – 2.16 (m, 4H), 2.28 (s, 3H), 2.25 (s, 3H), 1.77 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl\_3)  $\delta$  189.8, 175.7, 155.2, 145.7, 140.2, 137.6, 136.3, 134.5, 132.8, 129.4 (2C), 128.5 (2C), 128.5 (2C), 126.8 (2C), 126.6

122.9, 42.2, 39.3, 38.2 (2C), 36.0, 23.2, 21.0, 11.4 (one of the signals in the aromatic/olefinic region denotes two overlapping carbons). **HRMS** (ESI+) m/z calcd. for  $C_{28}H_{28}N_2O_4$  [M+Na]<sup>+</sup>: 479.1941; found: 479.1950. **UPC**<sup>2</sup>: IC-3, CO<sub>2</sub>/*i*-PrOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer:  $t_{major} = 5.2 \text{ min}; t_{minor} = 4.2 \text{ min} (94\% \text{ ee}).$ 



Following the general procedure, cycloadduct **4f** was obtained after FC on silica gel (pentane/EtOAc 10:1 to 4:1) in 70% yield and 13:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = -6.6$  (*c* 0.9, CHCl<sub>3</sub>). <sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)**:  $\delta$  9.57 (s, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.01 – 6.91 (m, 3H), 5.50 (d, *J* = 3.4 Hz, 1H), 4.50 (dd, *J* = 11.7, 5.2 Hz, 1H), 3.40 – 3.28 (m, 2H), 2.67 (dd, *J* = 18.1, 7.1 Hz, 1H), 2.56 (dd, *J* = 18.1, 6.3 Hz, 1H), 2.46 – 2.19 (m, 2H), 2.39 (s, 3H), 2.25 (s, 3H), 1.74 (s, 3H). <sup>13</sup>**C NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  199.6, 175.2, 155.2, 142.7, 138.2,

134.7, 128.6, 127.9, 127.7, 123.8, 122.7, 46.4, 41.4, 39.4, 38.9, 31.8, 23.1, 21.4, 11.6 (one of the signals in the aromatic/olefinic region denotes two overlapping carbons). **HRMS** (ESI+) m/z calcd. for C<sub>20</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]<sup>+</sup>: 377.1472; found: 377.1477. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5f** was obtained after FC on silica gel (pentane/EtOAc 20:1 to 10:1) in 89% yield and >10:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = 80.7$  (*c* 0.8, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.91 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.01 (s, 1H), 6.99 - 6.92 (m, 2H), 6.81 - 6.72 (m, 2H), 5.55 (d, *J* = 3.1 Hz, 1H), 4.44 (dd, *J* = 11.4, 5.6 Hz, 1H), 3.50 - 3.38 (m, 1H), 3.06 - 2.93 (m, 1H), 2.47 - 2.17 (m, 10H), 1.77 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  189.7, 175.7, 155.2, 145.7, 143.2, 138.2, 137.6,

134.5, 132.8, 128.6, 128.5 (2C), 128.5 (2C), 127.9, 127.6, 126.5, 123.8, 122.9, 42.1, 39.2, 38.6, 38.2, 36.0, 23.2, 21.4, 11.4 (one of the signals in the aromatic/olefinic region denotes two overlapping carbons). **HRMS** (ESI+) m/z calcd. for  $C_{28}H_{28}N_2O_4$  [M+Na]<sup>+</sup>: 479.1941; found: 479.1944. **UPC**<sup>2</sup>: IC-3, CO<sub>2</sub>/*i*-PrOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer:  $t_{major} = 5.0 \text{ min}$ ;  $t_{minor} = 4.5 \text{ min}$  (92% ee).



Following the general procedure (reaction time: 4 d), cycloadduct **4g** was obtained after FC on silica gel (pentane/EtOAc 15:1 to 10:1) in 74% yield and 8.5:1 dr as a orange oil.  $[\alpha]_D^{20} = -1.5$  (*c* 0.8, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (**400** MHz, CDCl<sub>3</sub>):  $\delta$  9.68\* (s, 1H\*), 9.58 (s, 1H), 7.13 - 6.92<sup>+</sup> (m, 4H, 4H\*), 5.53 (d, J = 3.8 Hz, 1H), 5.40\* (br, 1H\*), 4.58 (dd, J = 12.1, 5.2 Hz, 1H), 4.12 (t, J = 11.0 Hz, 1H\*), 3.78 - 3.60<sup>+</sup> (m, 1H, 1H\*), 3.46 - 3.34<sup>+</sup> (m, 1H, 1H\*), 2.66 (dd, J = 18.0, 7.0 Hz, 1H), 2.57 (dd, J = 18.1, 6.5 Hz, 1H), 2.47 - 2.09<sup>+</sup> (m, 8H,10H\*) 2H\*). <sup>13</sup>C NARP (100 MHz, CDCl):  $\delta$  200 2\* 100 5 175 2\* 175 2 155 0\* 141 1<sup>+</sup>

1.80 – 1.70<sup>+</sup> (m, 3H, 3H<sup>\*</sup>). <sup>13</sup>**C NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  200.3<sup>\*</sup>, 199.5, 175.3<sup>\*</sup>, 175.3, 155.3, 155.0<sup>\*</sup>, 141.1<sup>+</sup> (1C, 1C<sup>\*</sup>), 135.6, 135.6<sup>\*</sup>, 135.4<sup>\*</sup>, 135.0, 131.0<sup>+</sup> (1C, 1C<sup>\*</sup>), 130.6, 130.1<sup>\*</sup>, 127.9<sup>\*</sup>, 127.4<sup>\*</sup>, 126.6, 126.5, 124.8<sup>+</sup> (1C, 1C<sup>\*</sup>), 122.7, 122.5<sup>\*</sup>, 48.0<sup>\*</sup>, 46.4, 41.1<sup>+</sup> (1C, 1C<sup>\*</sup>), 39.1<sup>+</sup> (1C, 1C<sup>\*</sup>), 36.0<sup>\*</sup>, 33.3, 32.2<sup>+</sup> (1C, 1C<sup>\*</sup>), 23.1<sup>+</sup> (1C, 1C<sup>\*</sup>), 19.4, 19.3<sup>\*</sup>, 11.6, 11.5<sup>\*</sup>. **HRMS** (ESI+) *m/z* calcd. for C<sub>20</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]<sup>+</sup>: 377.1472; found: 377.1475. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5g** was obtained after FC on silica gel (pentane/EtOAc 10:1) in 85% yield and 6.4:1 dr (Determined by <sup>1</sup>H NMR spectroscopy of the isolated product) as a yellow oil.  $[\alpha]_D^{20} = 116.9 (c \ 0.7, CH_2Cl_2)$ . <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.97 – 7.83<sup>+</sup> (m, 2H, 2H\*), 7.56<sup>+</sup> (t, J = 7.4 Hz, 1H, 1H\*), 7.46<sup>+</sup> (t, J = 7.5 Hz, 2H, 2H\*), 7.11 – 6.95<sup>+</sup> (m, 4H, 4H\*), 6.87 – 6.78<sup>+</sup> (m, 2H,2H\*), 5.57 (d, J = 3.3 Hz, 1H), 5.46 (br, 1H\*), 4.54 (dd, J = 12.0, 5.6 Hz, 1H), 4.12 – 4.03 (m, 1H\*), 3.74 (ddd, J = 21.6, 13.5, 8.0 Hz, 1H, 1H\*), 3.18 – 3.00<sup>+</sup> (m,

1H, 1H\*),  $2.51 - 2.07^{+}$  (m, 10H,10H\*),  $1.81 - 1.72^{+}$  (m, 3H, 3H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  189.7, 175.8, 155.3, 145.7, 141.6, 137.6, 135.8, 134.9, 132.8, 130.6, 128.5, 128.4, 126.6, 126.5, 126.4 (2C), 124.6, 122.8, 41.8, 39.0, 38.7, 36.0, 33.1, 23.2, 19.5, 11.4 (only major diastereomer is characterized). HRMS (ESI+) m/z calcd. for C<sub>28</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]<sup>+</sup>: 479.1941; found: 479.1947. HPLC: IB-5, hexane/*i*-PrOH 90:10, 1.0 mL·min<sup>-1</sup>; major diastereomer: t<sub>major</sub> = 8.0 min; t<sub>minor</sub> = 12.4 min (96% ee).



Following the general procedure, cycloadduct **4h** was obtained after FC on silica gel (pentane/EtOAc 10:1 to 4:1) in 78% yield and 5.5:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = +9.6$  (*c* 1.5, CHCl<sub>3</sub>). <sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)**:  $\delta$  9.66\* (s, 1H\*), 9.55 (s, 1H), 7.47 – 7.43<sup>+</sup> (m, 1H, 1H\*), 7.29 – 7.27 (m, 2H), 7.21 – 7.19\* (m, 2H\*), 5.51 (d, *J* = 3.5 Hz, 1H), 5.39\* (s, 1H\*), 4.43 (dd, *J* = 11.6, 5.3 Hz, 1H), 4.03 – 3.93\* (m, 1H\*), 3.40 – 3.29<sup>+</sup> (m, 2H, 2H\*), 2.61 (dd, *J* = 18.3, 7.1 Hz, 1H), 2.54 (dd, *J* = 18.3, 6.4 Hz, 1H), 2.45 (s, 3H), 2.42\* (s, 3H\*), 2.48 – 2.14<sup>+</sup> (m, 2H, 4H\*), 1.78 – 1.72<sup>+</sup> (m, 3H, 3H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ 

199.8\*, 199.1, 174.0<sup>+</sup> (1C, 1C\*), 155.6, 155.2\*, 146.8, 145.8\*, 135.6<sup>+</sup> (1C, 1C\*), 134.6\*, 134.0, 133.0\*, 132.8, 129.0 (2C), 128.9\* (2C\*), 123.2 (2C), 123.1\* (2C\*), 122.9, 122.5\*, 47.8\*, 46.2, 41.0<sup>+</sup> (1C, 1C\*), 38.9, 38.7\*, 38.6, 35.6\*, 31.6<sup>+</sup> (1C, 1C\*), 23.0<sup>+</sup> (1C, 1C\*), 11.6, 11.5\*. **HRMS** (ESI+) m/z calcd. for C<sub>19</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>Br<sub>2</sub> [M+Na]<sup>+</sup>: 520.9506; found: 520.9501. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5h** was obtained after FC on silica gel (pentane/EtOAc 20:1 to 10:1) in 77% yield and 5.5:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = 57.2$  (*c* 0.9, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.93 – 7.86<sup>+</sup> (m, 2H, 2H<sup>\*</sup>), 7.56<sup>+</sup> (app. t, *J* = 7.4 Hz, 1H, 1H<sup>\*</sup>), 7.50 – 7.41<sup>+</sup> (m, 3H, 3H<sup>\*</sup>), 7.28 (d, *J* = 1.5 Hz, 2H), 7.19<sup>\*</sup> (d, *J* = 1.6 Hz, 2H<sup>\*</sup>), 6.84 – 6.68<sup>+</sup> (m, 2H, 2H<sup>\*</sup>), 5.56 (d, *J* = 3.1 Hz, 1H), 5.45<sup>\*</sup> (br, 1H<sup>\*</sup>), 4.36 (dd, *J* = 11.4, 5.6 Hz, 1H), 3.98 – 3.88<sup>\*</sup> (m, 1H<sup>\*</sup>), 3.49 – 3.37 (m, 1H), 3.37 – 3.25<sup>\*</sup> (m, 1H<sup>\*</sup>), 3.17 – 3.06<sup>\*</sup> (m, 1H<sup>\*</sup>), 3.07 – 2.96 (m, 1H), 2.47 – 2.11<sup>+</sup> (m, 7H, 7H<sup>\*</sup>), 1.77<sup>+</sup> (s, 3H, 3H<sup>\*</sup>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  189.6,

174.5, 155.6, 147.3, 145.0, 137.5, 134.6, 133.8, 132.9, 132.7, 129.0 (2C), 128.6 (2C), 128.4 (2C), 126.6, 123.2 (2C), 123.1, 41.7, 38.9, 38.3, 38.2, 35.8, 23.1, 11.4 (only major diastereomer is characterized). **HRMS** (ESI+) m/z calcd. for  $C_{27}H_{24}N_2O_4Br_2$  [M+Na]<sup>+</sup>: 622.9975; found: 622.9984. **UPC**<sup>2</sup>: IC-3, CO<sub>2</sub>/ACN gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer:  $t_{major} = 5.5 min; t_{minor} = 5.0 min (93\% ee).$ 



Following the general procedure, cycloadduct **4i** was obtained after FC on silica gel (pentane/EtOAc 20:1 to 10:1 to 4:1) in 69% yield and 5.0:1 dr as a white solid.  $[\alpha]_D^{20} = -10.0$  (*c* 0.8, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.66\* (s, 1H\*), 9.55 (s, 1H), 7.65 – 7.60\* (m, 1H\*), 7.46 – 7.35\* (m, 1H\*), 7.32 (d, J = 2.1 Hz, 1H), 7.18 – 7.05<sup>+</sup> (m, 1H, 1H\*), 7.05 – 6.97 (m, 1H), 5.52 (d, 1H), 5.39\* (br, 1H\*), 4.57 (dd, J = 12.1, 5.1 Hz, 1H), 4.09\* (br, 2H\*), 3.96 (td, J = 11.3, 5.7 Hz, 1H), 3.46 – 3.32<sup>+</sup> (m, 1H, 1H\*), 2.67 (dd, J = 18.3, 7.1 Hz, 1H), 2.57 (dd, J = 18.3, 6.3 Hz, 1H), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 3H, 1H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 2H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 2H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 1.79 – 1.71<sup>+</sup> (m, 2H\*), 2.50 – 2.00<sup>+</sup> (m, 5H, 7H\*), 2.5

3H\*). <sup>13</sup>**C NMR (100 MHz, CDCl<sub>3</sub>)**: 13C NMR (101 MHz, CDCl3)  $\delta$  200.0\*, 199.2, 174.4\*, 174.3, 155.4, 155.2\*, 138.8<sup>+</sup>(1C, 1C\*), 134.9\*, 134.9\*, 134.4, 134.3, 133.0, 132.9\*, 131.0<sup>+</sup>(1C, 1C\*), 130.1\*, 129.7, 127.9\*, 127.7, 127.6<sup>+</sup>(1C, 1C\*), 122.9, 122.6\*, 47.7\*, 46.2, 43.0\*, 40.3, 39.7\*, 38.1, 36.0\*, 34.2, 31.9<sup>+</sup>(1C, 1C\*), 23.0, 22.9\*, 11.6\*, 11.5. **HRMS** (ESI+) *m/z* calcd. for C<sub>19</sub>H<sub>18</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]<sup>+</sup>: 431.0536; found: 431.0541. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5i** was obtained after FC on silica gel (pentane/EtOAc 10:1) in 74% yield and 6.9:1 dr as a pale yellow oil.  $[\alpha]_D^{20}$  = 78.6 (*c* 0.6, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.95 – 7.83<sup>+</sup> (m, 2H, 2H<sup>\*</sup>), 7.67 – 7.51<sup>+</sup> (m, 1H, 1H<sup>\*</sup>), 7.50 – 7.38<sup>+</sup> (m, 2H, 2H<sup>\*</sup>), 7.33 (d, J = 2.1 Hz, 1H), 7.25<sup>\*</sup> (d, J = 2.1 Hz, 1H<sup>\*</sup>), 7.19<sup>\*</sup> (d, J = 8.4 Hz, 1H<sup>\*</sup>), 7.09<sup>+</sup> (dd, J = 8.4, 2.1 Hz, 1H, 1H<sup>\*</sup>), 6.99 (d, J = 8.4 Hz, 1H), 6.87 – 6.68<sup>+</sup> (m, 2H, 2H<sup>\*</sup>), 5.57 (d, J = 3.2 Hz, 1H), 5.46<sup>\*</sup> (bs, 1H<sup>\*</sup>), 4.52 (dd, J = 11.9, 5.4 Hz, 1H), 4.04<sup>+</sup> (app. td, J = 11.2, 5.7 Hz, 1H, 1H<sup>\*</sup>), 3.20 – 3.00<sup>+</sup> (m, 1H, 1H<sup>\*</sup>), 2.47 – 1.99<sup>+</sup> (m, 7H, 8H<sup>\*</sup>), 1.82 – 1.72<sup>+</sup> (m, 3H, 3H<sup>\*</sup>).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  189.6<sup>+</sup>(1C,1C<sup>\*</sup>), 174.8<sup>+</sup>(1C,1C<sup>\*</sup>), 155.4<sup>+</sup>(1C,1C<sup>\*</sup>), 145.2<sup>+</sup>(1C,1C<sup>\*</sup>), 139.4<sup>+</sup>(1C,1C<sup>\*</sup>), 137.5<sup>+</sup>(1C,1C<sup>\*</sup>), 134.8<sup>+</sup>(1C,1C<sup>\*</sup>), 134.5<sup>+</sup>(1C,1C<sup>\*</sup>), 134.3<sup>+</sup>(1C,1C<sup>\*</sup>), 132.9<sup>+</sup>(1C,1C<sup>\*</sup>), 132.9<sup>+</sup>(1C,1C<sup>\*</sup>), 129.8<sup>+</sup>(1C,1C<sup>\*</sup>), 128.6<sup>\*</sup>(2C<sup>\*</sup>), 128.5(2C), 128.4<sup>+</sup>(2C,2C<sup>\*</sup>), 127.7, 127.6<sup>\*</sup>, 126.6<sup>+</sup>(1C,1C<sup>\*</sup>), 123.0, 122.9<sup>\*</sup>, 41.0<sup>+</sup>(1C,1C<sup>\*</sup>), 38.7<sup>+</sup>(1C,1C<sup>\*</sup>), 38.0, 37.6<sup>\*</sup>, 35.8<sup>+</sup>(1C,1C<sup>\*</sup>), 34.0<sup>+</sup>(1C,1C<sup>\*</sup>), 23.1<sup>+</sup>(1C,1C<sup>\*</sup>), 11.6<sup>\*</sup>, 11.4. HRMS (ESI+) *m/z* calcd. for C<sub>27</sub>H<sub>24</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]<sup>+</sup>: 533.1005; found: 533.1011. UPC<sup>2</sup>: IC-3, CO<sub>2</sub>/*i*-PrOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer: t<sub>major</sub> = 5.6 min; t<sub>minor</sub> = 4.9 min (93% ee).



Following the general procedure (reaction time: 1 week), cycloadduct **4j** was obtained after FC on silica gel (gradient: pentane/EtOAc 10:1 to 4:1) in 83% yield and 1.9:1 dr as a dark yellow oil.  $[\alpha]_D^{20} = +105.3$  ( $c \ 0.7, \ CH_2Cl_2$ ). <sup>1</sup>H NMR (**400 MHz, CDCl\_3**):  $\delta$  9.40\* (s, 1H\*), 9.34 (s, 1H), 7.38 – 7.27<sup>+</sup>, 7.24<sup>+</sup> (m, 5H, 5H\*), 7.12 – 6.99<sup>+</sup> (m, 2H, 2H\*), 6.15 – 6.11 (m, 1H), 6.10 – 6.05\* (m, 1H\*), 4.71 (dd, J = 12.5, 4.8 Hz, 1H), 4.42 – 4.28 (app. m, 1H\*), 4.18 – 4.05 (m, 1H), 3.87\* (br, 1H\*), 3.52 – 3.31<sup>+</sup> (m, 1H, 1H\*), 3.08 (dd, J = 19.4, 9.4 Hz, 1H), 2.72 – 2.34<sup>+</sup> (m, 6H, 7H\*). <sup>13</sup>C NMR (100 MHz, CDCl\_3):

δ 199.3\*, 198.7, 174.6\*, 174.1, 155.4, 155.2\*, 141.5, 140.7\*, 140.5<sup>+</sup>(1C,1C\*), 139.3, 139.3\*, 131.9(2C), 131.8\*(2C\*), 128.8(2C), 128.8(2C), 128.7\*(2C), 128.6\*(2C), 127.9, 127.6\*, 126.8\*, 126.6, 126.3<sup>+</sup>(1C,1C\*), 124.9<sup>+</sup>(1C,1C\*), 121.1\*, 120.8, 46.2\*, 44.9, 42.0<sup>+</sup>(1C,1C\*), 37.6, 37.1\*, 35.9, 34.0\*, 32.5<sup>+</sup>(1C,1C\*), 11.6<sup>+</sup>(1C,1C\*). **HRMS** (ESI+) *m/z* calcd. for C<sub>24</sub>H<sub>21</sub>BrN<sub>2</sub>O<sub>4</sub> [M+Na]<sup>+</sup>: 503.0577, 505.0556; found: 503.0588, 505.0560. The enantioselectivity was determined after derivatization.



Following the derivatization procedure (reaction time: 4 d), enone **5j** was obtained after FC on silica gel (gradient: pentane/EtOAc 9:1) in 77% yield and 1.9:1 dr as a yellow oil.  $[\alpha]_D^{20}$  = +162.5 (*c* 0.6, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.87 - 7.80<sup>+</sup> (m, 2H, 2H\*), 7.60 - 7.27<sup>+</sup> (m, 10H, 10H\*), 7.12 - 6.96<sup>+</sup> (m, 2H, 2H\*), 6.76 - 6.44<sup>+</sup> (m, 2H, 2H\*), 6.13 - 6.06<sup>+</sup> (m, 1H, 1H\*), 4.61 (dd, J = 12.6, 5.2 Hz, 1H), 4.27\* (app. t, J = 10.9 Hz, 1H\*), 3.85 - 3.67<sup>+</sup> (m, 1H, 1H\*), 3.55 (td, J = 11.6, 5.8 Hz, 1H), 3.44 - 3.30\* (m, 1H\*), 2.74 - 2.16<sup>+</sup> (m, 7H, 7H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  189.3<sup>+</sup>(1C,1C\*), 175.0\*, 174.6, 155.5\*, 155.4, 145.1, 144.0\*,

142.2, 140.7\*, 140.5\*, 140.2, 139.6, 139.5\*, 137.4\*, 137.3, 132.9\*, 132.8, 131.9(2C), 131.8\*(2C\*), 128.8(4C), 128.7\*(2C\*), 128.6\*(2C\*), 128.5\*(2C\*), 128.5(2C), 128.4\*(2C\*), 128.3(2C), 127.8\*, 127.7, 127.4, 127.3\*, 126.6\*(2C\*), 126.5(2C), 125.6<sup>+</sup>(1C,1C\*), 125.1<sup>+</sup>(1C,1C\*), 121.1\*, 120.6, 42.7<sup>+</sup>(1C,1C\*), 41.0<sup>+</sup>(1C,1C\*), 36.9<sup>+</sup>(1C,1C\*), 35.9, 35.4\*, 34.2, 33.9\*, 11.5\*, 11.2.**HRMS** (ESI+) m/z calcd. for C<sub>32</sub>H<sub>27</sub>BrN<sub>2</sub>O<sub>4</sub> [M+Na]<sup>+</sup>: 605.1046, 607.1026; found: 605.1050, 607.1040. **UPC**<sup>2</sup>: IC-3, CO<sub>2</sub>/ACN 85:15, 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer: t<sub>major</sub> = 5.1 min; t<sub>minor</sub> = 4.6 min (95% ee).



Following the general procedure, at an elevated temperature of 50 °C, cycloadduct **4k** was obtained after FC on silica gel (gradient: pentane/EtOAc 9:1 to 5:1) in 74% yield and 8.1:1 dr as a yellow solid.  $[\alpha]_D^{20} = -1.3$  (*c* 0.7, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, **CDCl<sub>3</sub>**):  $\delta$  9.72\* (s, 1H\*), 9.60 (s, 1H), 7.47 – 7.28<sup>+</sup> (m, 7H, 7H\*), 7.13 (d, J = 8.4 Hz, 2H), 7.05\* (d, J = 8.4 Hz, 2H\*), 6.16 (d, J = 4.8 Hz, 1H), 6.04\* (br, 1H\*), 4.61 (dd, J = 11.6, 5.4 Hz, 1H), 4.22 – 4.12\* (m, 1H\*), 3.63 – 3.45<sup>+</sup> (m, 2H, 2H\*), 2.92 – 2.55<sup>+</sup> (m, 4H, 4H\*), 2.42<sup>+</sup> (d, 3H, 3H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  199.6\*, 198.9, 174.4\*,

174.3, 155.5, 155.2\*, 141.5, 140.7\*, 140.0, 137.4\*, 136.9, 135.5\*, 132.0(2C), 131.9\*(2C\*), 131.1<sup>+</sup>(1C, 1C\*), 128.8(2C), 128.7\*(2C\*), 128.5<sup>+</sup>(2C, 2C\*), 127.8<sup>+</sup>(1C, 1C\*), 125.3<sup>+</sup>(2C, 2C\*), 125.2, 124.8\*, 121.2\*, 120.9, 47.8\*, 46.1, 43.9\*, 41.2, 38.8<sup>+</sup>(1C, 1C\*), 36.5, 36.23\*, 32.0<sup>+</sup>(1C, 1C\*), 11.6<sup>+</sup>(1C, 1C\*). **HRMS** (ESI+) *m/z* calcd. for  $C_{24}H_{21}BrN_2O_4$  [M+Na]<sup>+</sup>: 503.0577, 505.0556; found: 503.0582, 505.0571. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5k** was obtained after FC on silica gel (gradient: pentane/EtOAc 9:1) in 85% yield and 11.0:1 dr as a yellow oil.  $[\alpha]_D^{20}$  = +62.2 (*c* 0.6, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.94 – 7.82<sup>+</sup> (m, 2H, 2H\*), 7.62 – 7.52<sup>+</sup> (m, 1H, 1H\*), 7.51 – 7.28<sup>+</sup> (m, 9H, 9H\*), 7.14 (d, J = 8.4 Hz, 2H), 7.04\* (d, J = 8.4 Hz, 1H\*), 6.93 – 6.72<sup>+</sup> (m, 2H, 2H\*), 6.21 (d, J = 4.4 Hz, 1H), 6.11\* (bs, 1H\*), 4.54 (dd, J = 11.4, 5.7 Hz, 1H), 4.19 – 4.05\* (m, 1H\*), 3.68 – 3.43<sup>+</sup> (m, 1H, 1H\*), 3.40 – 3.19<sup>+</sup> (m, 1H, 1H\*), 2.94 – 2.78<sup>+</sup> (m, 1H, 1H\*), 2.71 – 2.28<sup>+</sup> (m, 6H, 6H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  189.51, 174.72, 155.45, 144.82,

141.99, 140.21, 137.45, 136.79, 132.93, 131.98(2C), 128.83, 128.59(2C), 128.52(4C), 128.46(2C), 127.76, 126.86, 125.44, 125.34(2C), 120.84, 77.32, 77.20, 77.00, 76.68, 41.89, 38.57, 38.45, 36.40, 35.87, 11.41 (only major diastereomer is characterized). **HRMS** (ESI+) m/z calcd. for  $C_{32}H_{27}BrN_2O_4$  [M+H]<sup>+</sup>: 583.1227, 585.1206; found: 583.1228, 585.1217. **UPC**<sup>2</sup>: IC-3, CO<sub>2</sub>/ACN gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer:  $t_{major} = 6.2 min; t_{minor} = 5.8 min (89\% ee).$ 



Following the general procedure (reaction time: 4 d), at an elevated temperature of 50 °C, cycloadduct **4I** was obtained after FC on silica gel (gradient: pentane/EtOAc 9:1 to 5:1) in 75% yield and 5.7:1 dr as a orange solid.  $[\alpha]_D^{20} = -5.9$  (*c* 0.6, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR **(400 MHz, CDCl<sub>3</sub>)**:  $\delta$  9.69\* (s, 1H\*), 9.51 (s, 1H), 7.37 – 7.27<sup>+</sup> (m, 2H, 2H\*), 7.03 (d, J = 8.4 Hz, 2H), 6.96\* (d, J = 8.4 Hz, 1H\*), 5.71\* (s, 1H\*), 5.57 (s, 1H), 4.52 (dd, J = 12.4, 4.8 Hz, 1H), 4.25\* (app. t, J = 11.1 Hz, 1H\*), 3.35 – 3.18<sup>+</sup> (m, 2H, 2H\*), 3.03 (dd, J = 19.2, 9.1 Hz, 1H), 2.65 – 2.04<sup>+</sup> (m, 7H, 8H\*), 1.75<sup>+</sup> (s, 3H, 3H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ 

199.9\*, 199.0, 174.8\*, 174.3, 155.3, 155.2\*, 141.8, 140.9\*, 134.3, 133.1\*, 131.8(2C), 131.7\*(2C\*), 128.8(2C), 128.6\*(2C\*), 123.7<sup>+</sup>(1C, 1C\*), 122.4<sup>+</sup>(1C, 1C\*), 121.0\*, 120.6, 44.8\*, 44.3, 41.8<sup>+</sup>(1C, 1C\*), 39.0\*, 37.7, 35.2<sup>+</sup>(1C, 1C\*), 35.1, 33.8\*, 21.8, 21.5\*, 11.6<sup>+</sup>(1C, 1C\*). **HRMS** (ESI+) m/z calcd. for C<sub>19</sub>H<sub>19</sub>BrN<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 419.0601, 421.0580; found: 419.0606, 421.0586. The enantioselectivity was determined after derivatization.



Following the derivatization procedure (reaction time: 3 d), enone **5I** was obtained after FC on silica gel (gradient: pentane/EtOAc 20:1 to 10:1) in 82% yield (major disomer) and 6.8:1 dr as a white solid.  $[\alpha]_D^{20} = +99.5$  (*c* 0.5, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.95 – 7.87 (m, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 6.73 (d, J = 15.4 Hz, 1H), 6.67 – 6.57 (m, 1H), 5.61 (s, 1H), 4.42 (dd, J = 12.5, 5.2 Hz, 1H), 3.43 (td, J = 11.4, 6.0 Hz, 1H), 2.88 (bs, 1H), 2.63 – 2.36 (m, 3H), 2.26 – 2.10 (m, 4H), 1.86 (s, 3H). (only major diastereomer is characterized) <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ 

189.3, 174.8, 155.3, 145.4, 142.5, 137.4, 134.2, 132.9, 131.8(2C), 131.3, 128.8(2C), 128.6(2C), 128.4(2C), 125.7, 122.4, 120.5, 77.3, 77.0, 76.7, 43.3, 42.5, 37.1, 35.3, 33.4, 22.2, 11.3. (only major diastereomer is characterized) **HRMS** (ESI+) m/z calcd. for  $C_{27}H_{25}BrN_2O_4$  [M+H]<sup>+</sup>: 521.1070, 523.1050; found: 521.1076, 523.1056. **UPC**<sup>2</sup>: IA-3, CO<sub>2</sub>/*i*-PrOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer:  $t_{major} = 4.4$  min;  $t_{minor} = 4.3$  min (93% ee).



Following the general procedure, at an elevated temperature of 60 °C, cycloadduct **4m** was obtained after FC on silica gel (gradient: pentane/EtOAc 9:1 to 5:1) in 80% yield and 4.1:1 dr as a orange solid.  $[\alpha]_D^{20} = -1.3$  (*c* 0.75, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  9.67\* (s, 1H\*), 9.58 (s, 1H), 7.40 – 7.28<sup>+</sup> (m, 2H, 2H\*), 7.03 (d, J = 8.4 Hz, 2H), 6.90\* (d, J = 8.3 Hz, 1H\*), 5.55 (d, J = 5.6 Hz, 1H), 5.30\* (bs, 1H\*), 4.51 (dd, J = 12.7, 5.0 Hz, 1H), 4.15\* (bs, 1H\*), 3.72\* (bs, 1H\*), 3.34 – 3.23 (m, 1H), 2.91 (dd, J = 12.6, 9.8 Hz, 1H), 2.71 (dd, J = 18.2, 7.1 Hz, 1H), 2.58 (dd, J = 18.2, 6.3 Hz, 1H), 2.51 – 1.92<sup>+</sup> (m, 6H,

9H\*),  $1.89 - 0.87^{+}$  (m, 6H, 6H\*). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  200.1\*, 199.4, 175.3\*, 174.6, 155.4<sup>+</sup>(1C,1C\*), 144.0\*, 141.0, 140.0, 138.6\*, 131.7(2C), 131.5\*(2C\*), 130.9\*, 129.7, 129.6<sup>+</sup>(1C,1C\*), 121.1(2C), 120.8\*, 120.7, 118.86\*(2C\*), 47.85\*, 46.42, 45.57(2C), 43.84\*(2C\*), 41.66<sup>+</sup>(1C,1C\*), 36.35\*, 34.93, 32.58, 31.83, 30.01\*, 29.2\*, 27.1<sup>+</sup>(1C,1C\*), 26.5\*, 25.8, 11.6\*, 11.5. HRMS (ESI+) *m/z* calcd. for C<sub>22</sub>H<sub>23</sub>BrN<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 459.0914, 461.0893; found: 459.0915, 461.0897. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5m** was obtained after FC on silica gel (gradient: pentane/EtOAc 10:1) in 84% yield and 7.5:1 dr (determined by <sup>1</sup>H NMR spectroscopy of the isolated product) as a pale yellow solid.  $[\alpha]_D^{20}$  = +97.4 (*c* 0.7, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.95 – 7.89<sup>+</sup> (m, 2H, 2H<sup>+</sup>), 7.59 – 7.53<sup>+</sup> (m, 1H, 1H<sup>+</sup>), 7.50 – 7.43<sup>+</sup> (m, 2H, 2H<sup>+</sup>), 7.35 – 7.27<sup>+</sup> (m, 2H, 2H<sup>+</sup>), 7.05 (d, J = 8.4 Hz, 2H), 6.91<sup>+</sup> (d, J = 8.3 Hz, 1H<sup>+</sup>), 6.87 – 6.74<sup>+</sup> (m, 2H, 2H<sup>+</sup>), 5.59 (d, J = 5.5 Hz, 1H), 5.37<sup>+</sup> (bs, 1H<sup>+</sup>), 4.46 (dd, J = 12.7, 5.3 Hz, 1H), 4.13<sup>+</sup> (bs, 1H<sup>+</sup>), 3.80 – 3.60<sup>+</sup> (m, 2H<sup>+</sup>), 3.10 – 2.90 (m, 2H), 2.48 – 1.96<sup>+</sup> (m, 8H, 8H<sup>+</sup>), 1.88 –

0.77<sup>+</sup> (m, 6H, 6H<sup>\*</sup>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  189.9<sup>\*</sup>, 189.7, 175.1<sup>+</sup>(1C,1C<sup>\*</sup>), 155.3<sup>+</sup>(1C,1C<sup>\*</sup>), 145.6, 144.0<sup>\*</sup>, 141.5<sup>+</sup>(1C,1C<sup>\*</sup>), 140.9<sup>+</sup>(1C,1C<sup>\*</sup>), 137.6<sup>+</sup>(1C,1C<sup>\*</sup>), 132.8<sup>+</sup>(2C,2C<sup>\*</sup>), 131.6(2C), 131.5<sup>\*</sup>(2C<sup>\*</sup>), 131.4, 131.1<sup>\*</sup>, 129.6<sup>\*</sup>, 128.6(2C), 128.5<sup>\*</sup>(2C<sup>\*</sup>), 128.5(2C), 128.3<sup>\*</sup>(2C<sup>\*</sup>), 127.8<sup>\*</sup>(2C<sup>\*</sup>), 126.6(2C), 121.2<sup>+</sup>(1C,1C<sup>\*</sup>), 120.7<sup>\*</sup>, 120.6, 45.7<sup>\*</sup>, 45.5, 45.1, 44.0<sup>\*</sup>, 42.5<sup>+</sup>(1C,1C<sup>\*</sup>), 38.5, 37.6<sup>\*</sup>, 36.4<sup>\*</sup>, 35.8, 35.1<sup>+</sup>(1C,1C<sup>\*</sup>), 32.6<sup>+</sup>(1C,1C<sup>\*</sup>), 27.2, 26.6<sup>\*</sup>, 25.9<sup>+</sup>(1C,1C<sup>\*</sup>), 11.6<sup>\*</sup>, 11.4. HRMS (ESI+) *m/z* calcd. for C<sub>30</sub>H<sub>29</sub>BrN<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 561.1383, 563.1363; found: 561.1384, 563.1369. HPLC: IA-5, hexane/*i*-PrOH 90:10, 1.0 mL·min<sup>-1</sup>; major diastereomer: t<sub>major</sub> = 26.2 min; t<sub>minor</sub> = 32.2 min (86% ee).



Following the general procedure, cycloadduct **4n** was obtained after FC on silica gel (pentane/EtOAc 30:1) in 82% yield and >20:1 dr as a pale yellow oil.  $[\alpha]_D^{20} = -34.2$  (c 1.2, CHCl3). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  9.52 (s, 1H), 7.22 – 7.05 (m, 5H), 4.54 (dd, J = 12.6, 4.7 Hz, 1H), 3.44 – 3.31 (m, 1H), 3.28 – 3.16 (m, 1H), 3.07 (dd, J = 19.0, 9.2 Hz, 1H), 2.52 (dd, J = 19.1, 2.0 Hz, 1H), 2.42 – 2.21 (m, 5H), 1.70 (s, 3H), 1.67 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  199.6, 174.9, 155.2, 142.8, 128.7 (2C), 127.5, 127.0 (2C), 126.8),

126.3, 44.7, 42.1, 41.7, 39.0, 36.7, 18.9, 17.8, 11.5 (one of the signals in the aromatic/olefinic region denotes two overlapping carbons). **HRMS** (ESI+) m/z calcd. for  $C_{20}H_{22}N_2O_4$  [M+H]<sup>+</sup>: 355.1652; found: 355.1651. The enantioselectivity was determined after derivatization.



Following the derivatization procedure, enone **5n** was obtained after FC on silica gel (pentane/EtOAc 20:1) in 55% yield and >20:1 dr as a pale yellow oil.  $[\alpha]_D^{20}$  = +90.8 (c 0.3, CHCl3). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.91 (d, J = 7.1 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.22 – 7.08 (m, 5H), 6.71 (d, J = 15.3 Hz, 1H), 6.65 – 6.56 (m, 1H), 4.45 (dd, J = 12.7, 5.2 Hz, 1H), 3.56 – 3.46 (m, 1H), 2.92 – 2.84 (m, 1H), 2.61 – 2.16 (m, 4H), 2.12 (s, 3H), 1.80 (s, 3H), 1.69 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  189.5, 175.4, 155.2, 146.1, 143.5, 137.5, 132.8, 128.7 (2C), 128.5

(2C), 128.4 (2C), 127.4, 126.9 (2C), 126.7, 126.5, 125.4, 45.1, 42.6, 41.9, 38.3, 33.8, 19.0, 18.2, 11.2 one of the signals in the aromatic/olefinic region denotes two overlapping carbons). **HRMS** (ESI+) m/z calcd. for C28H28N2O4 [M+H]+: 457.2122; found: 457.2115. **UPC**<sup>2</sup>: IA-3, CO<sub>2</sub>/MeOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer:  $t_{major} = 4.1 \text{ min}$ ;  $t_{minor} = 3.5 \text{ min}$  (92% ee).

#### Procedure for the transformations



To a solution of cycloadduct **4n** (1.5 mmol, 1 eq.) in MeOH (13 mL) was added NaBH<sub>4</sub> (2.25 mmol, 1.5 eq.) at 0 °C. After stirring for 5 min the reaction was allowed to reach rt and stirred for further 10 min. The reaction was quenched with a saturated solution of NH<sub>4</sub>Cl, extracted three times with  $CH_2Cl_2$  and the combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub>. Excess solvents were removed *in vacuo*, and the crude mixture was purified by FC on silica gel (pentane/EtOAc 5:1) to afford the product **6** in 62% yield, >20:1 dr as a white solid.



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.23 – 7.02 (m, 5H), 4.46 (dd, J = 12.5, 4.7 Hz, 1H), 3.54 – 3.44 (m, 1H), 3.34 – 3.26 (m, 1H), 3.24 – 3.16 (m, 1H), 2.62 – 2.54 (m, 1H), 2.44 – 2.32 (m, 4H), 2.21 (dd, J = 17.1, 11.9 Hz, 1H), 2.00 – 1.86 (m, 1H), 1.79 – 1.62 (m, 7H) (signal for the OH was not detected). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 176.1, 155.2, 143.6, 128.7 (2C), 128.1, 127.0 (2C), 126.7, 126.0, 61.8, 43.2, 41.8, 40.8, 38.9, 34.1, 18.9, 18.3, 11.7

(one of the signals in the aromatic/olefinic region denotes two overlapping carbons).  $[\alpha]_D^{20} = -6.5$  (*c* 0.12, CHCl<sub>3</sub>). **HRMS** (ESI+) *m/z* calcd. for C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>4</sub> [M+Na]<sup>+</sup>: 379.1628; found: 379.1629. **UPC<sup>2</sup>**: IB-3, CO<sub>2</sub>/*i*-PrOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer: t<sub>major</sub> = 3.1 min; t<sub>minor</sub> = 3.2 min (93% ee).



A solution of cycloadduct **6** (0.1 mmol, 1 eq.) in THF (0.07 mL) was treated with a aq. solution of NaOH (1N, 0.5 mmol, 5 eq.). The solution was refluxed at 100 °C for 2 d and then allowed to reach rt. Excess solvents (both THF and H<sub>2</sub>O) were removed *in vacuo*, and added another 1mL H<sub>2</sub>O. The aq. solution was cooled to 0 °C and was added conc. HCl dropwise until pH ~ 2-3, then extracted three times with Et<sub>2</sub>O, dried over Na<sub>2</sub>SO<sub>4</sub>.

Excess solvents were removed *in vacuo*. The crude mixture was redissolved in 1mL CH<sub>2</sub>Cl<sub>2</sub>, stirred at 40  $^{\circ}$ C with MS (4 Å) for overnight. Excess solvents were removed *in vacuo* and the crude mixture was purified by FC on silica gel (pentane/EtOAc 5:1) to afford the product **8** in 62% yield and >20:1 dr as a pale yellow oil.



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.31 – 7.26 (m, 2H), 7.24 – 7.16 (m, 3H), 4.28 – 4.15 (m, 2H), 3.75 – 3.69 (m, 1H), 2.81 (t, J = 5.2 Hz, 1H), 2.57 (d, J = 18.2 Hz, 1H), 2.37 – 2.30 (m, 1H), 2.19 (d, J = 17.4 Hz, 1H), 2.00 – 1.94 (m, 2H), 1.76 (s, 3H), 1.66 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 172.9, 143.5, 129.2, 128.4 (2C), 127.4 (2C), 126.4, 125.3, 66.7, 47.0, 38.0, 33.4, 33.2, 26.6, 19.6, 15.7. [α]<sup>20</sup><sub>D</sub> = -76.9 (c 0.065, CHCl<sub>3</sub>). HRMS (ESI+) m/z calcd. for C<sub>17</sub>H<sub>20</sub>O<sub>2</sub> [M+Na]<sup>+</sup>:

279.1356; found: 279.1359. **UPC<sup>2</sup>**: IA-3, CO<sub>2</sub>/MeOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min), 60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer:  $t_{major} = 3.1$  min;  $t_{minor} = 3.0$  min (93% ee).



A solution of cycloadduct **6** (0.1 mmol, 1 eq.) in THF (0.07 mL) was treated with a aq. solution of NaOH (1N, 0.5 mmol, 5 eq.). The solution was refluxed at 100 °C for 2 d and then allowed to reach rt. Excess solvents (both THF and H<sub>2</sub>O) were removed *in vacuo*, and added another 1ml H<sub>2</sub>O. The aq. solution was cooled to 0 °C and was added conc. HCl dropwise until pH ~ 2-3, then extracted three times with Et<sub>2</sub>O, dried over Na<sub>2</sub>SO<sub>4</sub>.

Excess solvents were removed *in vacuo* (Note: at rt). Dissolved the crude in 10 mL CH<sub>2</sub>Cl<sub>2</sub> and 1 mL MeOH, then 0.5ml TMS-diazomethane (2.0M in hexane) was added. The reaction was stirred under the rt for 20 min, several drops of conc. acetic acid was added to quench the excess TMS-diazomethane. Excess solvents

were removed *in vacuo* and the crude mixture was purified by FC on silica gel (pentane/EtOAc 10:1 to 2:1) to afford the product **9** in 80% yield and >20:1 dr as a pale yellow oil.



<sup>1</sup>H NMR (400 MHz, CDCl3) δ 7.30 – 7.24 (m, 2H), 7.21 – 7.14 (m, 3H), 3.59 – 3.53 (m, 2H), 3.44 (s, 3H), 3.20 – 3.06 (m, 2H), 2.49 – 2.41 (m, 1H), 2.27 (dd, J = 18.0, 5.2 Hz, 1H), 2.11 – 1.95 (m, 2H), 1.78 – 1.57 (m, 8H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 172.9, 143.5, 129.2, 128.4(2C), 127.4(2C), 126.4, 125.3, 66.7, 50.8, 47.0, 38.1, 33.5, 33.3, 26.6, 19.5, 15.6.  $[\alpha]_D^{20}$  = +50.4 (c 0.75, CH<sub>2</sub>Cl<sub>2</sub>). HRMS (ESI+) m/z calcd. for C18H24O3 [M+Na]+: 311.1618; found: 311.1619. UPC<sup>2</sup>: IC-3, CO<sub>2</sub>/i-PrOH gradient [99:1 (1 min); 99:1 to 60:40 (over 4 min),

60:40 (3 min)], 3.0 mL·min<sup>-1</sup>, 40 °C, 120 bar; major diastereomer:  $t_{major} = 4.2$  min;  $t_{minor} = 3.9$  min (93% ee).

# 4. X-RAY STRUCTURE



A solution of cycloadduct **6** (0.06 mmol, 1 eq.) in  $CH_2Cl_2$  (2 mL) was added 2-bromobenzoyl chloride (0.09 mmol, 1.5 eq.) and *N*,*N*-4-dimethylaminopyridine (0.09 mmol, 1.5 eq.). After stirring at rt for overnight, the crude mixture was purified by FC on silica gel (pentane/EtOAc 20:1) to afford the product **10** in 74% yield as a white solid.



Crystal data for [**10**]:  $C_{27}H_{27}BrN_2O_5$ , M = 539.41, monoclinic, space group P 2<sub>1</sub> (no. 6), a = 5.8905(7) Å, b = 23.7962(3) Å, c = 9.09712(12) Å,  $\theta = 102.961(13)^\circ$ , Flack parameter = 0.001, V = 1242.67(3) Å<sup>3</sup>, T = 100 K, Z = 2,  $d_c = 1.442$  g cm<sup>-3</sup>,  $\mu$ (Mo K $\alpha$ ,  $\lambda = 0.71073$  Å) = 1.695 mm<sup>-1</sup>, 40829 reflections collected, 8771 unique [ $R_{int} = 0.0275$ ], which were used in all calculations. Refinement on F<sup>2</sup>, final R(F) = 0.0518, R<sub>w</sub>(F2) = 0.1355. CCDC number 1026165.