

## Supporting Information for

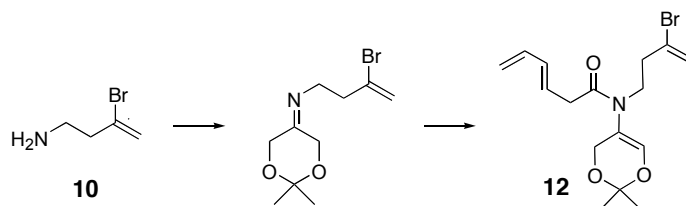
### Total Syntheses of (±)-β-Erythroidine and (±)-8-oxo-β-Erythroidine by an Intramolecular Diels-Alder Cycloaddition of a 2-Amidoacrolein

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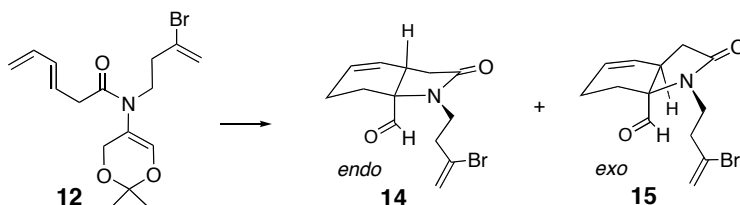
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**General Methods.** Unless otherwise noted, all reactions were carried out under a nitrogen atmosphere using flame-dried glassware. All moisture sensitive reagents were added via a dry syringe or cannula where possible. Anhydrous acetonitrile (CH<sub>3</sub>CN), benzene, tetrahydrofuran (THF), dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>), diethyl ether (Et<sub>2</sub>O), toluene, triethylamine (Et<sub>3</sub>N), and dimethylformamide (DMF) were obtained from a solvent dispensing system. All other solvents and reagents were used as obtained from commercial sources without further purification. <sup>1</sup>H and <sup>13</sup>C NMR spectra were obtained on Bruker 300 or 400 MHz spectrometers. Infrared spectra were obtained using a Perkin-Elmer 1600 FTIR. Chromatographic purification was performed using Sorbent Technologies silica gel 60 (230-400 mesh). Melting points were obtained on a Thomas Hoover melting point apparatus.



**Amidodioxin (12).** To a solution of 2,2-dimethyl-1,3-dioxan-5-one (9) (4.23 g, 32.5 mmol) in anhydrous benzene (110 mL) was added anhydrous  $\text{Na}_2\text{SO}_4$  (25.0 g) followed by dropwise addition of a solution of 3-bromo-3-buten-1-amine<sup>1</sup> (6.57 g, 36.7 mmol) in anhydrous benzene (10 mL) at rt. After stirring at rt for 7 hrs, the reaction mixture was filtered and concentrated to provide the imine (8.50 g, 100%) which was directly used in the next step.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 5.61 (m, 1H), 5.43 (d,  $J = 1.8$  Hz, 1H), 4.37 (s, 2H), 4.18 (s, 2H), 3.40 (t,  $J = 6.9$  Hz, 2H), 2.73 (t,  $J = 6.9$  Hz, 2H), 1.38 (s, 6H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 170.0, 131.5, 118.4, 100.1, 64.7, 60.0, 48.0, 42.3, 23.7. To the freshly prepared imine (8.50 g, 32.4 mmol) in anhydrous THF (108 mL) at  $-25$  °C was added (*E*)-3,5-hexadienoyl chloride<sup>2</sup> (4.28 g, 32.8 mmol) dropwise. The mixture was stirred at the same temperature for 10 ~ 15 min and then  $\text{PhNEt}_2$  (distilled from  $\text{CaH}_2$ , 6.71 mL, 42.2 mmol) was added dropwise. The reaction mixture was allowed to warm to rt slowly and stirred overnight. The mixture was then diluted with EtOAc and washed with sat.  $\text{NaHCO}_3$ ,  $\text{H}_2\text{O}$  and brine. The organics were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated. Purification by silica-gel chromatography (hexane/EtOAc, 4/1) provided the amidodioxin 12 as a light-brown oil (8.05 g, 70%).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.51 (t,  $J = 1.1$  Hz, 1 H), 6.32 (ddd,  $J = 16.9, 10.3, 10.1$  Hz, 1 H), 6.11 (dd,  $J = 15.3, 10.3$  Hz, 1H), 5.81 (dt,  $J = 15.3, 7.0$  Hz, 1H), 5.64 (br s, 1H),

5.46 (d,  $J = 1.7$  Hz, 1H), 5.14 (d,  $J = 16.9$  Hz, 1H), 5.04 (d,  $J = 10.1$  Hz, 1H), 4.15 (d,  $J = 1.1$  Hz, 2H), 3.59 (br s, 2H), 3.18 (d,  $J = 7.0$  Hz, 2H), 2.70 (t,  $J = 7.0$  Hz, 2H), 1.52 (s, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 171.7, 142.4, 136.3, 133.7, 130.7, 127.2, 118.7, 116.5, 115.0, 99.4, 59.6, 46.3, 39.9, 37.2, 24.2; IR (neat) 2992, 2940, 1662  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{16}\text{H}_{22}^{79}\text{BrNO}_3\text{Na}^+$  378.0675, found 378.0669; calcd for  $\text{C}_{16}\text{H}_{22}^{81}\text{BrNO}_3\text{Na}^+$  378.0655, found 378.0650.

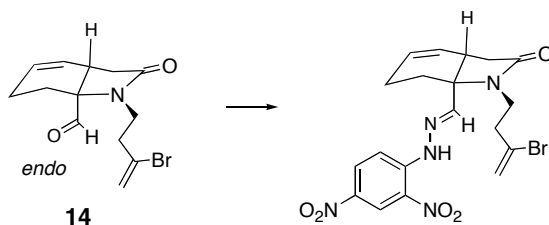


***Endo* cycloadduct 14 and *exo* cycloadduct 15** The amidodioxin **12** (7.00 g, 19.6 mmol) was dissolved in toluene (660 mL) and then a catalytic amount of BHT (~ 50 mg) and  $\text{PhNEt}_2$  (distilled, 31 mL) were added. The solution was heated at reflux for 5 hrs and then concentrated. Purification by silica-gel chromatography (hexane/EtOAc, 3/1 to 1/1) provided the *endo* cycloadduct **14** as a yellow oil (700 mg, 12%) and *exo* cycloadduct-**15** as a yellow oil (3.85 g, 66%) in the order of elution from chromatography.

Data for *endo* cycloadduct **14**:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.52 (s, 1H), 5.89 (dddd,  $J = 9.6, 2.0, 2.0, 2.0$  Hz, 1H), 5.71 (ddd,  $J = 9.6, 6.8, 3.2$  Hz, 1H), 5.60 (dt,  $J = 1.6, 0.8$  Hz, 1H), 5.43 (d,  $J = 1.6$  Hz, 1 H), 3.54 (ddd,  $J = 14.0, 7.6, 5.2$  Hz, 1H), 3.09 (ddd,  $J = 14.0, 7.6, 7.6$  Hz,

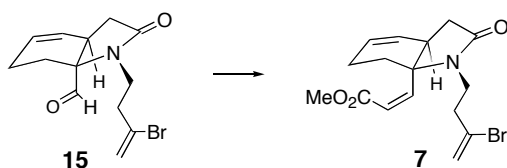
1H), 3.01 (m, 1H), 2.67 (ddd,  $J = 14.0, 6.8, 6.8$  Hz, 1H), 2.60-2.42 (m, 5H), 2.30 (m, 1H), 1.76 (ddd,  $J = 14.0, 8.0, 8.0$  Hz, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  195.8, 175.6, 130.6, 130.2, 123.3, 118.8, 70.1, 41.0, 40.5, 39.3, 33.1, 26.3, 23.4; IR (neat) 2934, 1724, 1698  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{13}\text{H}_{16}^{79}\text{BrNO}_2\text{Na}^+$  320.0257, found 320.0247; calcd for  $\text{C}_{13}\text{H}_{16}^{81}\text{BrNO}_2\text{Na}^+$  322.0237, found 322.0219.

Data for *exo* cycloadduct **15**:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.53 (s, 1H), 5.85 (m, 1H), 5.67 (dt,  $J = 2.0, 0.8$  Hz, 1H), 5.54 (dddd,  $J = 10.0, 3.6, 2.0, 2.0$  Hz, 1H), 5.46 (d,  $J = 2.0$  Hz, 1H), 3.51 (ddd,  $J = 15.2, 9.6, 6.0$  Hz, 1H), 3.27 (ddd,  $J = 15.2, 9.6, 6.4$  Hz, 1H), 2.87 (m, 1H), 2.80-2.61 (m, 3H), 2.20-2.08 (m, 3H), 2.02 (m, 1H), 1.90 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.2, 175.3, 130.2, 127.2, 126.1, 119.0, 70.5, 40.3, 39.8, 36.3, 32.7, 22.5, 19.6; IR (neat) 2926, 1732, 1684  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{13}\text{H}_{16}^{79}\text{BrNO}_2\text{Na}^+$  320.0257, found 320.0248; calcd for  $\text{C}_{13}\text{H}_{16}^{81}\text{BrNO}_2\text{Na}^+$  322.0237, found 322.0231.



**2,4-Dinitrophenylhydrazone derivative of *endo* cycloadduct 14 for X-ray analysis:** 2,4-Dinitrophenylhydrazine (contains ~30% water, 2.14 g, 7.56 mmol) in conc.  $\text{H}_2\text{SO}_4$  (7.5 mL) was added carefully to a mixture of water (10 mL) and EtOH (35 mL), providing a DNP solution (~0.13 M). To a solution of *endo*

cycloadduct **14** (58 mg, 0.19 mmol) in EtOH (1.2 mL) at rt was added the above prepared DNP solution (~0.13 M, 1.80 mL, 0.23 mmol) dropwise and stirred at rt for 15 – 20 min. Then it was diluted with H<sub>2</sub>O and extracted with CH<sub>2</sub>Cl<sub>2</sub>. Combined organics were washed with H<sub>2</sub>O, brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to provide the pure hydrazone derivative (70 mg, 93%) as a yellow solid. mp: 140 – 142 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 11.1 (s, 1H), 9.11 (d, *J* = 4.0 Hz, 1H), 8.35 (dd, *J* = 10.0, 4.0 Hz, 1H), 7.85 (d, *J* = 10.0 Hz, 1H), 7.44 (s, 1H), 5.84 (m, 1H), 5.74 (m, 1H), 5.64 (br s, 1H), 5.46 (d, *J* = 1.6 Hz, 1H), 3.66 (dddd, *J* = 6.8, 5.6, 5.6, 5.6 Hz, 1H), 3.16 (ddd, *J* = 14.4, 7.2, 7.2 Hz, 1H), 3.03 (m, 1H), 2.78-2.68 (m, 2H), 2.60 (dd, *J* = 12.4 8.0 Hz, 1H), 2.57 (m, 1H), 2.53 (dd, *J* = 16.0, 7.6 Hz, 1H), 2.38 (m, 1H), 2.35 (dd, *J* = 16.0, 14.0 Hz, 1H), 2.01 (m, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 176.0, 146.9, 144.7, 138.4, 130.8, 130.3, 129.7, 129.4, 123.9, 123.3, 119.0, 116.3, 66.0, 42.8, 41.0, 39.7, 33.1, 29.7, 24.0. IR (neat) 3298, 2937, 1693, 1615, 1588, 1519, 1333 cm<sup>-1</sup>.



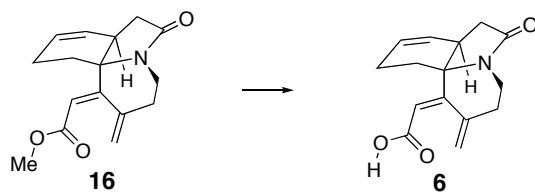
**Z-Enolate (7).** To a solution of (CF<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>P(O)CH<sub>2</sub>CO<sub>2</sub>Me (4.09 mL, 19.3 mmol) and 18-crown-6 (17.0 g, 64.3 mmol) in anhydrous THF (100 mL) at -78 °C was added KHMDS (0.5 M in toluene, 38.5 mL, 19.3 mmol) dropwise. After stirring for 20 min at the same temperature, a solution of aldehyde **15** (3.83 g, 12.8 mmol) in anhydrous THF (140 mL) was added dropwise via cannula. The

reaction was allowed to warm to 0 °C over 3 hrs and quenched with sat. NH<sub>4</sub>Cl (250 mL). The resulting solution was extracted with EtOAc (350 mL) and the organic layer was washed with H<sub>2</sub>O, brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. Purification by silica-gel chromatography (hexane/EtOAc, 1/1) provided *Z*-enolate **7** (4.32 g, 95%) as a yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.15 (d, *J* = 12.8 Hz, 1 H), 5.94 (d, *J* = 12.8 Hz, 1 H), 5.80 (dddd, *J* = 10.0, 3.9, 3.9, 1.9 Hz, 1H), 5.66 (dt, *J* = 1.8, 1.1 Hz, 1H), 5.58 (dddd, *J* = 10.0, 3.9, 2.0, 2.0 Hz, 1H), 5.44 (d, *J* = 1.8 Hz, 1H), 3.71 (s, 3H), 3.36 (ddd, *J* = 15.4, 9.9, 5.6 Hz, 1H), 3.26 (ddd, *J* = 15.4, 9.8, 5.5 Hz, 1H), 3.20 (m, 1H), 2.88 (dddd, *J* = 14.2, 9.8, 5.6, 0.9 Hz, 1H), 2.66 (dddd, *J* = 14.2, 9.8, 5.6, 0.9 Hz, 1H), 2.65 (dd, *J* = 16.7, 9.3 Hz, 1H), 2.30 (dt, *J* = 13.9, 6.1 Hz, 1H), 2.10 (dd, *J* = 16.5, 6.3 Hz, 1H), 2.07-2.02 (m, 2H), 1.73 (dt, *J* = 13.9, 6.1 Hz, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 175.2, 165.5, 148.9, 130.8, 127.9, 125.9, 122.7, 118.7, 65.3, 51.9, 40.1, 40.0, 39.2, 37.1, 28.5, 21.0; IR (neat) 2927, 1726, 1690 cm<sup>-1</sup>; HRMS (MNa<sup>+</sup>) calcd for C<sub>16</sub>H<sub>20</sub><sup>79</sup>BrNO<sub>3</sub>Na<sup>+</sup> 376.0519, found 376.0491; calcd for C<sub>16</sub>H<sub>20</sub><sup>81</sup>BrNO<sub>3</sub>Na<sup>+</sup> 378.0498, found 378.0464.



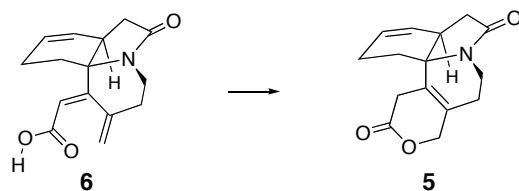
***E*-Dienolate (16).** To a solution of *Z*-enolate **7** (3.78 g, 10.7 mmol) in anhydrous CH<sub>3</sub>CN (890 mL) were added Pd(OAc)<sub>2</sub> (241 mg, 1.07 mmol), PPh<sub>3</sub> (562 mg, 2.14 mmol) and anhydrous K<sub>2</sub>CO<sub>3</sub> (2.96 g, 21.4 mmol). The solution was bubbled through N<sub>2</sub> for 15 min and

heated under reflux for 16 hrs. The reaction mixture was filtered and concentrated. Purification of the residue by silica-gel chromatography (hexane/EtOAc, 1/1) provided **16** (2.66 g, 90%) as a colorless solid. mp: 112-113 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.87-5.79 (m, 2H), 5.65 (s, 1H), 5.22 (s, 1H), 5.03 (s, 1H), 4.21 (ddd,  $J$  = 13.2, 6.2, 2.0 Hz, 1H), 3.67 (s, 3H), 2.93 (dddd,  $J$  = 12.6, 12.6, 4.8, 1.2 Hz, 1H), 2.77 (m, 1H), 2.66 (m, 1H), 2.45-2.35 (m, 2H), 2.20 (ddd,  $J$  = 16.0, 10.4, 1.2 Hz, 1H), 2.11-2.04 (m, 2H), 1.84 (m, 1H), 1.39 (m, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  171.4, 166.9, 154.1, 140.3, 127.9, 126.8, 116.6, 114.9, 64.6, 51.4, 37.6, 37.5, 37.2, 34.0, 26.3, 21.3; IR (neat) 2940, 1732, 1694, 1416, 1347, 1273, 1176  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{16}\text{H}_{19}\text{NO}_3\text{Na}^+$  296.1257, found 296.1256.



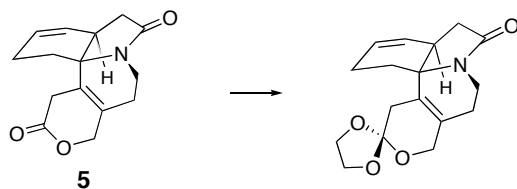
***E*-Dienoic acid (6).** To a solution of ester **16** (1.56 g, 5.71 mmol) in THF (14 mL) at rt was added LiOH (1M in  $\text{H}_2\text{O}$ , 14.3 mL, 14.3 mmol) and stirred at rt for 3 hrs. The reaction mixture was concentrated to remove most of the THF and diluted with water. The resulting colorless solid was collected via filtration and rinsed with a small amount of water and  $\text{Et}_2\text{O}$  to provide the pure acid **6** (1.10 g) as a colorless solid. The filtrate was further extracted with  $\text{CH}_2\text{Cl}_2$  (3x) to provide additional batch of acid (300 mg). Total yield: 95%. mp: 162-163 °C.  $^1\text{H}$  NMR (400 MHz,  $d_6$ -DMSO)  $\delta$  12.37 (br s, 1H), 5.82-5.78 (m, 2H), 5.55 (s, 1H), 5.17 (t,  $J$  = 1.8 Hz, 1H), 4.96 (s, 1H),

3.96 (ddd,  $J = 13.2, 6.4, 1.6$  Hz, 1H), 2.83 (ddd,  $J = 12.4, 12.4, 3.2$  Hz, 1H), 2.76 (dd,  $J = 9.4, 9.4$  Hz, 1H), 2.53 (dd,  $J = 8.8, 7.7$  Hz, 1H), 2.41 (ddd,  $J = 13.2, 3.8, 1.0$  Hz, 1H), 2.16 (m, 1H), 2.09-2.00 (m, 2H), 1.91 (dd,  $J = 12.8, 3.6, 3.6$  Hz, 1H), 1.72 (m, 1H), 1.39 (ddd,  $J = 12.8, 11.2, 4.8$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{d}_6\text{-DMSO}$ ):  $\delta$  170.7, 167.7, 151.2, 140.6, 127.7, 127.1, 116.1, 63.8, 36.9, 36.7, 36.6, 33.8, 26.1, 21.0; IR (neat) 2918, 1727, 1646  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{15}\text{H}_{17}\text{NO}_3\text{Na}^+$  282.1101, found 282.1098.

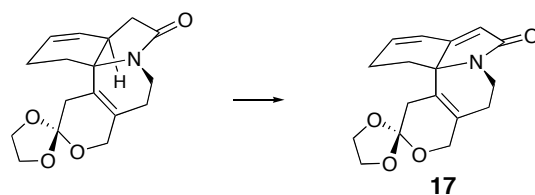


**Tetracyclic lactone (5).** A solution of acid **6** (1.26 g, 4.86 mmol) and BHT (~ 15 mg) in toluene (440 mL) was heated under reflux for 6 hrs. The reaction was then cooled to rt and concentrated. Purification by silica-gel chromatography (hexane/EtOAc, 1/4, then EtOAc only) afforded the lactone **5** (1.12 g, 89%) as a colorless solid. mp: 105-107 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.88 (br d,  $J = 9.2$  Hz, 1 H), 5.81 (br d,  $J = 9.2$  Hz, 1 H), 4.74 (d,  $J = 16.0$  Hz, 1H), 4.58 (d,  $J = 16.0$  Hz, 1H), 4.23 (dd, 13.6, 7.2 Hz, 1H), 3.16 (d,  $J = 19.2$  Hz, 1H), 3.04 (d,  $J = 19.2$  Hz, 1H), 3.00 (m, 1H), 2.68-2.61 (m, 2H), 2.30-2.17 (m, 3H), 2.05 (br d,  $J = 7.6$  Hz, 1H), 2.00 (br d,  $J = 7.6$  Hz, 1H), 1.92 (br d,  $J = 15.6$  Hz, 1H), 1.72 (m, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  171.9, 169.2, 130.4, 128.3, 127.3, 124.8, 70.0, 60.4, 38.1, 35.8, 32.9, 30.2, 29.8, 24.4, 22.1; IR (neat) 2923, 1738, 1685  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{15}\text{H}_{17}\text{NO}_3\text{Na}^+$  282.1101, found 282.1095.



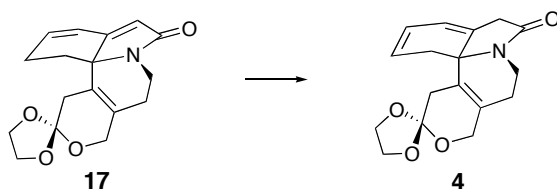


**Orthoester.** To a solution of lactone **5** (1.01 g, 4.08 mmol) in anhydrous THF (32 mL) at rt was added distilled ethylene glycol (2.29 mL, 40.9 mmol),  $\text{CH}(\text{OMe})_3$  (1.41 mL, 12.3 mmol) and conc.  $\text{H}_2\text{SO}_4$  (120 mg,  $\sim 1.23$  mmol) sequentially. Then, the resulting mixture was stirred at rt for 30 hrs. Several drops of  $\text{Et}_3\text{N}$  were added and the mixture was concentrated. To the residue was added sat.  $\text{NaHCO}_3$  and extracted with  $\text{CH}_2\text{Cl}_2$  (3x). The combined organics were dried ( $\text{K}_2\text{CO}_3$ ) and concentrated. The residue was further dried under high vacuum and then triturated with  $\text{Et}_2\text{O}$  to provide the pure orthoester (1.15 g, 95%) as a colorless solid. mp: 151-152 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.82 (ddd,  $J = 10.0, 3.6, 3.6, 1.3$  Hz, 1H), 5.73 (ddd,  $J = 10.0, 4.0, 2.0, 2.0$  Hz, 1H), 4.16 (ddd,  $J = 13.2, 7.6, 0.8$  Hz, 1H), 4.14-3.98 (m, 6H), 3.01 (dddd,  $J = 13.6, 11.2, 5.2, 1.2$  Hz, 1H), 2.69-2.59 (m, 2H), 2.50 (br d,  $J = 16.4$  Hz, 1H), 2.40 (dddd,  $J = 16.4, 4.8, 2.8, 2.4$  Hz, 1H), 2.21-2.01 (m, 5H), 1.78-1.69 (m, 2H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  172.7, 129.4, 128.5, 127.3, 124.9, 118.3, 66.6, 64.3, 64.2, 61.1, 38.1, 35.5, 33.3, 30.8, 29.8, 23.7, 22.2; IR (neat) 2907, 1687  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{17}\text{H}_{21}\text{NO}_4\text{Na}^+$  320.1363, found 326.1361.



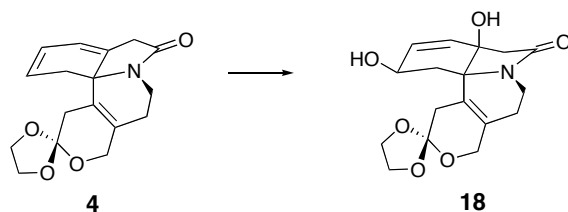
**Conjugated diene (17).** *n*-BuLi (2.5 M in hexane, 3.29 mL, 8.22 mmol) was added dropwise to a solution of diisopropylamine (1.16 mL, 8.22 mmol) in anhydrous THF (24 mL) at -78 °C. After stirring for 30 min at -78 °C, a solution of orthoester (1.04 g, 3.42 mmol) in anhydrous THF (44 mL) was added dropwise via cannula. The mixture was stirred for additional 40 min at -78 °C, then PhSeSePh (2.35 g, 7.53 mmol) was added in one portion. Then the reaction mixture was allowed to warm to -20 °C within 2 hrs and then quenched with sat. NH<sub>4</sub>Cl (88 mL) and H<sub>2</sub>O (18 mL). The mixture was extracted with EtOAc (2x) and the combined organics were dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. Purification by silica-gel chromatography (hexane/EtOAc, 4/1 with 1% NEt<sub>3</sub>, then hexane/EtOAc, 1/4 with 1% NEt<sub>3</sub>) afforded the selenide (1.56 g, 95%) as a light-brown foamy solid. <sup>1</sup>H NMR of the crude product showed the formation of a single diastereomer. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.68-7.65 (m, 2H), 7.28-7.22 (m, 3H), 5.85-5.81 (m, 1H), 5.74-5.70 (m, 1H), 4.17-4.09 (m, 3H), 4.06-3.95 (m, 4H), 3.62 (d, *J* = 7.2 Hz, 1H), 3.00 (ddd, *J* = 12.4, 12.4, 5.2 Hz, 1H), 2.69 (m, 1H), 2.42 (br d, *J* = 16.4 Hz, 1H), 2.28 (dddd, *J* = 16.4, 4.8, 2.8, 2.4 Hz, 1H), 2.15-1.96 (m, 4H), 1.72-1.63 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 171.0, 135.0, 129.0, 128.7, 128.5, 128.2, 128.0, 127.0, 124.9, 118.2, 66.5, 64.22, 64.21, 60.4, 48.5, 43.4, 33.9, 30.7, 30.5, 23.6, 22.2. The selenide (1.56 g, 3.40 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (34 mL) at 0 °C and pyridine (0.64 mL, 7.3 mmol) was added followed

by addition of H<sub>2</sub>O<sub>2</sub> (50 wt%, 0.56 mL, 9.72 mmol). The mixture was stirred at 0 °C for 12 hrs, diluted with CH<sub>2</sub>Cl<sub>2</sub>, washed with sat. NaHCO<sub>3</sub>, dried (K<sub>2</sub>CO<sub>3</sub>) and concentrated. Purification by silica-gel chromatography (ethyl acetate/hexane, 1/19) afforded the conjugated diene **17** (889 mg, 86%) as a colorless solid. mp: 170-172 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 6.64 (dt, *J* = 10.0, 0.8 Hz, 1H), 6.13 (ddd, *J* = 10.0, 4.0, 4.0 Hz, 1H), 5.81 (s, 1H), 4.21 (ddd, *J* = 13.4, 7.8, 2.0 Hz, 1H), 4.15-3.97 (m, 6H), 3.18 (ddd, *J* = 13.5, 10.1, 6.0 Hz, 1H), 2.63 (dddd, *J* = 16.9, 5.0, 2.5, 2.5 Hz, 1H), 2.54 (br d, *J* = 16.9 Hz, 1H), 2.48-2.42 (m, 3H), 2.23 (m, 1H), 1.88-1.75 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 170.6, 157.5, 135.5, 127.8, 126.4, 123.3, 118.8, 118.0, 66.3, 64.2, 64.1, 63.5, 34.2, 34.0, 33.2, 24.9, 24.2; IR (neat) 2904, 1682 cm<sup>-1</sup>; HRMS (MNa<sup>+</sup>) calcd for C<sub>17</sub>H<sub>19</sub>NO<sub>4</sub>Na<sup>+</sup> 324.1206, found 324.1180.



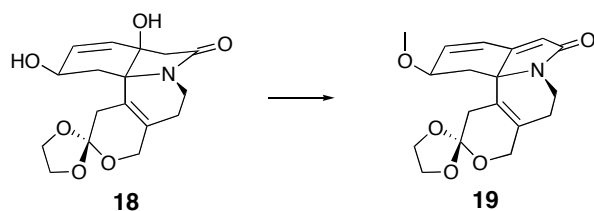
**Deconjugated diene (4).** KHMDS (0.5 M in toluene, 8.39 mL, 4.20 mmol) was added to anhydrous DME (21 mL) at -78 °C followed by addition of distilled HMPA (4.38 mL, 25.2 mmol) and then stirred for 15 min. Conjugated diene **17** (632 mg, 2.10 mmol) was added in one portion at -78 °C. The reaction was allowed to slowly warm up to -30 ~ -25 °C in 3 hrs. Then the mixture was re-cooled to -78 °C, HOAc (0.68 mL) was added followed by addition of sat. NH<sub>4</sub>Cl (46 mL). The mixture was allowed to warm to rt and extracted with

EtOAc (3x). The combined organics were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated. Purification by silica-gel chromatography (ethyl acetate/benzene, 4/1) afforded the deconjugated diene **4** (532 mg, 84%) as a colorless solid. mp: 172-174 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.99 (m, 1H), 5.93 (m, 1H), 5.80 (m, 1H), 4.18 (ddd,  $J = 13.6, 7.2, 0.5$  Hz, 1H), 4.12-3.96 (m, 6H), 3.12 (d,  $J = 19.6$  Hz, 1H), 3.04 (m, 1H), 3.00 (d,  $J = 19.6$  Hz, 1H), 2.71 (dddd,  $J = 17.2, 5.2, 2.4, 2.4$  Hz, 1H), 2.69-2.64 (m, 2H), 2.57 (br d,  $J = 17.2$  Hz, 1H), 2.29 (m, 1H), 1.65 (dd,  $J = 16.8, 3.8$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  174.2, 130.8, 129.8, 124.7, 124.6, 124.2, 120.4, 118.4, 66.3, 64.2, 64.1, 61.6, 35.8, 35.5, 34.8, 31.2, 23.1; IR (neat) 2902, 1702  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{17}\text{H}_{19}\text{NO}_4\text{Na}^+$  324.1206, found 324.1206.



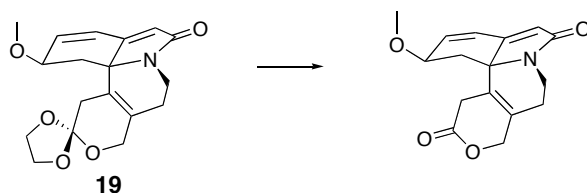
**Diol (18).** A solution of deconjugated diene **4** (140 mg, 0.46 mmol) and rose bengal (14 mg, 0.014 mmol) in MeOH (56 mL) was bubbled through  $\text{O}_2$  at 0 °C under a GE 275 watt sun lamp irradiation for 1.5 ~ 2 hrs. Then the solution was concentrated to provide the crude endoperoxide which was directly used in the next step. mp: 165-166 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.72 (dd,  $J = 8.4, 5.6$  Hz, 1H), 6.64 (dd,  $J = 8.4, 1.2$  Hz, 1H), 4.82 (m, 1H), 4.18 (dd,  $J = 13.6, 7.2$  Hz, 1H), 4.14 (m, 1H), 4.06-3.98 (m, 5H), 3.05 (ddd,  $J = 13.6, 12.0, 5.2$  Hz, 1H), 2.63 (d,  $J = 17.0$  Hz, 1H), 2.48-2.39 (m, 2H),

2.41 (d,  $J = 17.0$  Hz, 1H), 2.31 (br d,  $J = 17.2$  Hz, 1H), 2.01 (br d,  $J = 17.2$  Hz, 1H), 1.80 (dd,  $J = 14.4, 2.8$  Hz, 1H), 1.61 (m, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  175.5, 133.4, 130.0, 129.9, 127.1, 117.6, 81.1, 70.3, 66.2, 64.6, 63.9, 63.8, 36.4, 35.9, 35.5, 32.4, 22.6; IR (neat) 2904, 1703  $\text{cm}^{-1}$ . HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{17}\text{H}_{19}\text{NO}_6\text{Na}^+$  356.1105, found 356.1103. The residue was dissolved in MeOH (5 mL) and thiourea (52 mg, 0.68 mmol) was added and stirred overnight at rt. The reaction mixture was concentrated and purification by silica-gel chromatography (ethyl acetate only, to EtOAc/MeOH, 10/1) afforded the diol **18** (112 mg, 73% for two steps) as a colorless solid. mp: 145-147  $^{\circ}\text{C}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.32 (d,  $J = 9.6$  Hz, 1 H), 6.00 (dd,  $J = 9.6, 2.8$  Hz, 1H), 4.35 (m, 1H), 4.11-3.93 (m, 7H), 3.69 (br s, 1H), 3.63 (br s, 1H), 3.15 (m, 1H), 2.50-2.41 (m, 4H), 2.32-2.27 (m, 3H), 1.86 (m, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  177.1, 136.1, 130.1, 129.3, 129.2, 117.7, 72.3, 68.4, 66.4, 65.2, 64.3, 64.0, 41.5, 37.5, 37.0, 34.2, 22.4; IR (neat) 3417, 2904, 1682  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{17}\text{H}_{21}\text{NO}_6\text{Na}^+$  358.1261, found 358.1256.



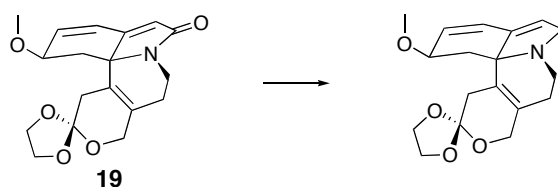
**Lactam (19).** To a solution of diol **18** (110 mg, 0.33 mmol) in anhydrous THF (10 mL) were added anhydrous DMSO (1 mL), KOH (ground powder, 220 mg, 3.92 mmol),  $\text{Et}_4\text{NBr}$  (208 mg, 0.99 mmol) and MeI (0.69 mL, 11 mmol). The resulting mixture was stirred

vigorously at rt overnight. Then, the mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> and filtered. The filtrate was concentrated and the residue was purified by silica-gel chromatography (ethyl acetate) to afford the methyl ether **19** (96 mg, 88%) as a colorless solid. mp: 152-154 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 6.71 (dd, *J* = 10.4, 2.0 Hz, 1H), 6.18 (d, *J* = 10.4 Hz, 1H), 5.94 (s, 1H), 4.24 (ddd, *J* = 12.8, 7.6, 2.0 Hz, 1H), 4.19-3.97 (m, 7H), 3.41 (s, 3H), 3.23 (ddd, *J* = 13.6, 10.0, 6.0 Hz, 1H), 2.87 (dd, *J* = 11.6, 5.6 Hz, 1H), 2.46 (dddd, *J* = 16.8, 4.8, 2.4, 2.4 Hz, 1H), 2.37 (br d, *J* = 16.8 Hz, 1H), 2.27 (m, 1H), 1.91 (m, 1H), 1.68-1.63 (m, 2H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 170.1, 156.5, 135.4, 127.4, 126.9, 124.1, 120.2, 117.8, 73.8, 66.2, 65.9, 64.2, 64.1, 56.4, 41.8, 33.9, 33.5, 24.2; IR (neat) 2927, 1683 cm<sup>-1</sup>; HRMS (MNa<sup>+</sup>) calcd for C<sub>18</sub>H<sub>21</sub>NO<sub>5</sub>Na<sup>+</sup> 354.1312, found 354.1312.



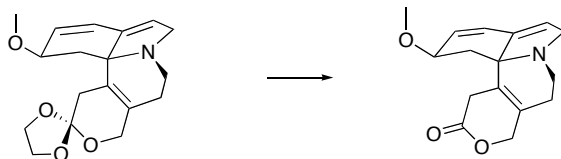
**8-Oxo-β-erythroidine.** To a solution of **19** (10.0 mg, 0.030 mmol) in THF (0.25 mL) was added 1 N HCl (30 μL, 0.030 mmol) and stirred at 0 °C for 20 min. The reaction mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> and washed with sat. NaHCO<sub>3</sub>, brine, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated to provide pure 8-oxo-β-erythroidine (8.3 mg, 96%). NMR data is consistent to the literature report.<sup>3</sup> <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.78 (dd, *J* = 10.0, 2.4 Hz, 1H), 6.27 (d, *J* = 10.0 Hz, 1 H), 5.97 (s, 1H); 4.74 (br d, *J* = 15.6 Hz, 1H), 4.59 (br d, *J* = 15.6 Hz, 1H), 4.36 (ddd, *J* = 13.8, 7.5, 1.0 Hz, 1H), 4.09 (m, 1H), 3.43 (s, 3H),

3.22 (ddd,  $J = 13.8, 10.8, 6.0$  Hz, 1H), 3.13-3.10 (m, 2H), 2.82 (dd,  $J = 12.0, 5.6$  Hz, 1H), 2.40 (m, 1H), 2.00 (br dd,  $J = 16.0, 5.6$  Hz, 1H), 1.72 (dd,  $J = 12.0, 10.2$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.1, 168.5, 155.8, 135.9, 127.7, 127.4, 124.3, 120.6, 73.6, 70.0, 65.2, 56.6, 41.7, 33.8, 31.7, 24.8; IR (neat) 2931, 1739, 1682, 1456, 1390, 1380, 1361, 1245, 1188, 1120, 1097, 1053, 918, 886, 857, 730  $\text{cm}^{-1}$ ; HRMS ( $\text{MNa}^+$ ) calcd for  $\text{C}_{16}\text{H}_{17}\text{NO}_4\text{Na}^+$  310.1050, found 310.1032.



**Amine.** To a solution of lactam **19** (40 mg, 0.12 mmol) in anhydrous THF (4 mL) at 0 °C was added  $\text{AlH}_3 \cdot \text{EtNMe}_2$  complex (0.5 M in toluene, 0.31 mL, 0.16 mmol). After stirring for 20 min at 0 °C, the reaction was quenched by careful addition of THF/ $\text{H}_2\text{O}$  (1/1, 5.6 mL). After stirring for a while, brine and couple of drops of  $\text{NEt}_3$  were added and the resulting solution was extracted with EtOAc (3x). The combined organics were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated. Purification by silica-gel chromatography ( $\text{CH}_2\text{Cl}_2$  + 1%  $\text{NEt}_3$ ) afforded the amine as a colorless semi-solid (32 mg, 80%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  6.40 (dd,  $J = 10.2, 2.1$  Hz, 1H), 5.82 (br d,  $J = 10.2$  Hz, 1 H), 5.72 (br s, 1H); 4.20 (m, 1H), 4.14-4.08 (m, 4H), 4.00-3.98 (m, 2H), 3.70 (d,  $J = 14.1$  Hz, 1H), 3.47 (dd,  $J = 14.1, 3$  Hz, 1H), 3.37 (s, 3H), 3.27 (ddd,  $J = 14.4, 11.7, 5.7$  Hz, 1H), 3.07 (dd,  $J = 14.4, 6.9$  Hz, 1H), 2.63 (dd,  $J = 12.0, 6.3$  Hz, 1H), 2.35-2.32 (m, 2H), 2.20 (m, 1H), 1.76 (dd,  $J = 12.0, 10.5$  Hz, 1H), 1.54 (dd,  $J = 16.8, 5.1$

Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  140.5, 130.7, 127.4, 125.2, 124.1, 123.6, 118.6, 75.5, 66.7, 65.8, 64.1, 55.9, 54.1, 40.8, 39.9, 32.4, 19.1; IR (neat)  $2925\text{ cm}^{-1}$ ; HRMS ( $\text{MH}^+$ ) calcd for  $\text{C}_{18}\text{H}_{24}\text{NO}_4^+$  318.1700, found 318.1704.



**$\beta$ -Erythroidine.** To a solution of the amine from last step (16.0 mg, 0.048 mmol) in THF (0.25 mL) was added 1 N HCl (48  $\mu\text{L}$ , 0.048 mmol) and stirred at 0  $^\circ\text{C}$  for 20 min. The reaction mixture was diluted with  $\text{CH}_2\text{Cl}_2$  and washed with sat.  $\text{NaHCO}_3$ , brine, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to provide the pure  $\beta$ -erythroidine (12.3 mg, 95%). NMR data is consistent with the literature report.<sup>3,4</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.45 (dd,  $J = 10.0, 2.0\text{ Hz}$ , 1 H), 5.91 (d,  $J = 10.0\text{ Hz}$ , 1 H), 5.72 (s, 1H), 4.73 (br d,  $J = 15.2\text{ Hz}$ , 1H), 4.57 (br d,  $J = 15.2\text{ Hz}$ , 1H), 4.11 (m, 1H), 3.65 (br d,  $J = 14.4\text{ Hz}$ , 1H), 3.52 (dd,  $J = 14.4, 2.8\text{ Hz}$ , 1H), 3.38 (s, 3H), 3.25 (m, 1H), 3.15 (dd,  $J = 8.0, 6.8\text{ Hz}$ , 1H), 3.10 (br d,  $J = 19.2\text{ Hz}$ , 1H), 2.97 (br d,  $J = 19.2\text{ Hz}$ , 1H), 2.56 (dd,  $J = 12.0, 6.4\text{ Hz}$ , 1H), 2.35 (m, 1H), 1.81 (dd,  $J = 12.0, 11.2\text{ Hz}$ , 1H), 1.69 (br d,  $J = 14.8\text{ Hz}$ , 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  170.2, 139.3, 131.0, 128.8, 125.3, 124.4, 124.2, 75.1, 70.4, 65.6, 56.0, 53.9, 40.5, 39.6, 31.8, 19.6; IR (neat) 2926, 1736, 1458, 1396, 1240, 1099, 1052  $\text{cm}^{-1}$ ; HRMS ( $\text{MH}^+$ ) calcd for  $\text{C}_{16}\text{H}_{20}\text{NO}_3^+$  274.1438, found 274.1436.



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