Novel Synthesis of Heterocycles Having a Functionalized Carbon Center via Nickel-Mediated Carboxylation: Total Synthesis of Erythrocaline

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Supporting Information

General Information. ^{1}H NMR and ^{13}C NMR were recorded on a JEOL EX-270 (270 MHz for ^{1}H, 67.5 MHz for ^{13}C), or JEOL AL-400 (400 MHz for ^{1}H, 100 MHz, for ^{13}C) instrument in $CDCl_3$ with tetramethylsilane as an internal standard otherwise mentioned. Data are reported as follows: chemical shift in ppm (*d*), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal), coupling constant (Hz), integration. Infrared spectra (IR) were obtained on a Perkin Elmer 1605 FTIR spectrometer. Mass spectra were obtained on either a JEOL JMS-FABmate (EI), a JEOL JMS-HX110 (FAB), or a JEOL JMS-700TZ (ESI). Silica gel column chromatography was performed by Merck Silica Gel 60 (70-230 or 230-400 mesh ATM). For analytical or preparative TLC, Merck Silica Gel 60 PF_{254} was used.
All solvents and reagents were purified when necessary using standard procedures. $Ni(cod)_2$ was prepared by a literature procedure[1] and handled under an argon atmosphere. All reactions were carried out under argon. Me_2Zn was purchased from Kanto Chemical Co. Inc. Alkynyl zinc reagent was prepared from lithium TNS acetylide and $ZnCl_2$ in the usual method.

Typical Procedure for the synthesis of α,β-unsaturated ester (2a) To a stirred suspension of $Ni(cod)_2$ (110 mg, 0.40 mmol) and DBU (0.12 mL, 0.80 mmol) in degassed THF (5.8 mL) was slowly added **1a** (89 mg, 0.36 mmol) at 0 °C for 1 h and

the solution was stirred at the same temperature for 2 h. To this solution was added Me_2Zn (1.0 M hexane solution_1.1 mL, 1.1 mmol) at 0 °C and the solution was stirred at 0 °C until the spot of **1a** disappeared on TLC. To this solution was added 10% HCl and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The crude product was treated with CH_2N_2 and it was purified by column chromatography (hexane/ethyl acetate, 10/1) on silica gel to give a crude α,β-unsaturated ester **2a** (94 mg, 81%)

Typical Procedure for Synthesis of Heterocycles Using Michael Addition. To a solution of **2a** (53.4 mg, 0.167 mmol) in THF (1.0 ml) was added TBAF (1.0 M THFsolution, 0.4 mL, 0.4 mmol) at 0 _ and the solution was stirred at 0 °C for 100 min. To this solution was added aqueous sat. NH_4Cl solution and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 3/1) to give isobenzofurane **3a** (28 mg, 81%).

Substrate for Synthesis of Heterocycles

tert-Butyl-(2-ethynyl-benzyloxy)-dimethylsilane (1a). IR (neat) 3301, 2955, 2100, 1078 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *d* 0.15 (s, 6 H), 1.00 (s, 9 H), 3.31 (s, 1 H), 4.94 (s, 2 H), 7.21 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.39 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.47 (d, *J* = 8.0 Hz, 1 H), 7.59 (d, *J* = 8.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$)_δ -5.22, 18.47, 26.02, 63.10, 81.03, 82.00, 118.73, 125.69, 126.33, 128.89, 1 32.20, 143.72; LR MS (ESI) *m/z* 246 (M^+), 231, 189, 115, 75; HR MS (EI) calcd for $C_{15}H_{22}OSi$ 246.1440, found 246.1456.

***tert*-Butyl-[2-(2-ethynyl-phenyl)-ethoxy]-dimethyl-silane (1b).** IR (neat) 3303, 2105, 1094 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 6 H), 0.89 (s, 9 H), 3.05 (t, *J* = 7.6 Hz, 2 H), 3.25 (s, 1 H), 3.87 (t, *J* = 7.6 Hz, 2 H), 7.13-7.30 (m, 3 H), 7.47(d, *J* =

7.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.31, 18.39, 25.99, 38.17, 63.31, 80.53, 82.30, 121.75, 126.05, 128.56, 130.00, 132.73, 141.48; LR MS (EI) *m/z* 260 (M^+), 245, 203, 129, 115, 75; HR MS (EI) calcd for $C_{16}H_{24}OSi$ 260.1596, found 260.1602.

Benzyl-(2-ethynyl-benzyl)-carbamic acid tert-butyl ester (1c). IR (neat) 3291, 2976, 1694, 1165, 760 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9/2 H), 1.48 (s, 9/2 H), 3.20 (s, 1 H), 4.36 (s, 2/2 H), 4.47 (s, 2/2 H), 4.56 (s, 2/2 H), 4.76 (s, 2/2 H), 7.19-7.48 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.41, 47.66 (Bn-C), 48.05 (Bn-C), 49.93, 80.03, 81.31, 81.90 (alkyne-C), 82.15 (alkyne-C), 126.23, 126.67 (Ar-CH), 126.84 (Ar-CH), 127.07, 127.34 (Ar-CH), 127.50 (Ar-CH), 128.29, 129.01, 132.76, 137.86 (Ar-C), 138.10 (Ar-C), 140.35 (Ar-C), 155.91 (Ar-C); LR MS (EI) *m/z* 265 (M^+-^{t}Bu-H), 248, 220, 115; HR MS (EI) calcd for $C_{17}H_{14}O_2N$ (-Bu) 264.1024, found 264.1022.

Benzyl-[2-(2-ethynyl-phenyl)-ethyl]-carbamic acid tert-butyl ester (1d). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9 H), 2.99 (br, 17/15 H),), 3.07 (br, 13/15 H), 3.21 (s, 1 H), 3.41 (br, 2 H), 4.32 (s, 13/15 H), 4.43 (br, 17/15 H), 7.12-7.48 (m, 8 H), 3.07 (d, *J* = 7.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.45, 28.45, 33.21, 47.17, 50.40, 79.75, 80.64, 82.09, 121.67, 126.19, 127.02, 127.15, 127.76, 128.33, 128.92, 129.46, 132.84, 138.35, 138.65; LR MS (EI) *m/z* 335 (M^+), 262, 234, 220, 91, 57; HR MS (EI) calcd for $C_{22}H_{25}NO_2$ 335.1885, found 335.1885.

Synthesis of Heterocycles

3-[2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-phenyl]-but-2-enoic acid methyl ester (2a). IR (neat) 2952, 1721, 1641, 1169, 838 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 6 H), 0.92 (s, 9 H), 2.46 (s, 3 H), 3.74 (s, 3 H), 4.65 (s, 2 H), 5.80 (s, 1 H), 7.07 (d, *J* = 7.2 Hz, 1 H), 7.24 (dd, *J* = 7.6, 7.0 Hz, 1 H), 7.31 (dd, *J* = 7.2, 7.0 Hz, 1 H), 7.50 (d, *J* = 7.2, 7.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.27, 18.38, 21.07,

25.94, 51.03, 62.65, 118.99, 126.84, 126.92, 127.61, 127.75, 136.99, 142.11, 157.20, 166.70; LR MS (EI) *m/z* 315 (M^+-Me), 289, 263, 59; HR MS (EI) calcd for $C_{14}H_{19}O_3Si$ (M-Me) 263.1103, found 263.1115.

(1-Methyl-1,3-dihydro-isobenzofuran-1-yl)-acetic acid methyl ester (3a). IR (neat) 1738, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.62 (s, 3 H), 2.77 (d, *J* = 14.4 Hz, 1 H), 2.82 (d, *J* = 14.4 Hz, 1 H), 3.60 (s, 3 H), 5.08 (d, *J* = 12.4 Hz, 1 H), 5.11 (d, *J* = 12.4 Hz, 1 H), 7.14-7.29 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.12, 45.80, 51.51, 71.62, 85.91, 120.90, 120.95, 127.28, 127.64, 138.55, 144.30, 170.48; LR MS (EI) *m/z* 206 (M^+), 191, 133, 91, 77; HR MS (EI) calcd for $C_{12}H_{14}O_3$ 206.0939, found 206.0943; Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.83; H, 6.95.

3-{2-[2-(*tert*-Butyl-dimethyl-silanyloxy)-ethyl]-phenyl}-but-2-enoic acid methyl ester (2b). IR (neat) 2952, 1721, 1640, 1169, 1094, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ -0.01 (s, 6 H), 0.86 (s, 9 H), 2.47 (d, *J* = 1.2 Hz, 3 H), 2.81 (t, *J* = 7.2 Hz, 2 H), 3.74 (s, 3 H), 3.75 (t, *J* = 7.2 Hz, 2 H), 5.78 (q, 1 H), 7.04-7.26 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.33, 18.42, 21.71, 25.97, 51.06, 64.27, 119.23, 126.11, 127.12, 127.51, 130.19, 134.65, 143.99, 158.14, 166.71; LR MS (EI) *m/z* 319 (M^+-Me), 303, 277, 115, 59; HR MS (EI) calcd for $C_{19}H_{30}O_3Si$ (M-Me) 334.1729, found 319.1733; Anal. Calcd for $C_{12}H_{14}O_3$: C, 68.22; H, 9.04. Found: C, 68.12; H, 8.90.

(1-Methyl-isochroman-1-yl)-acetic acid methyl ester (3b). IR (neat) 2949, 1737, 1099 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 3 H), 2.77 (d, *J* = 14.0 Hz, 1 H), 2.77-2.89 (m, 2 H), 2.93 (d, *J* = 14.0 Hz, 1 H),3.63 (s, 3 H),3.90-4.04 (m, 2 H), 7.05-7.20 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.78, 29.24, 46.49, 51.53, 59.87, 75.19, 125.05, 126.19, 126.32, 128.84, 133.18, 140.86, 170.47; LR MS (EI) *m/z* 220 (M^+), 205, 147, 91, 77; HR MS (EI) calcd for $C_{13}H_{16}O_3$ 220.1084, found 220.1099; Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.70; H, 7.42.

3-{2-[(Benzyl-*tert*-butoxycarbonyl-amino)-methyl]-phenyl}-but-2-enoic acid methyl ester (2c). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9 H), 2.35 (s, 3 H), 3.70 (s, 3 H), 4.34-4.46 (m, 4 H), 5.69 (s, 1 H), 7.05-7.32 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.71, 29.05, 47.37, 50.02, 51.67, 80.77, 119.84, 127.62, 127.81, 127.88, 128.43, 128.54, 129.05, 143.30, 138.24, 143.89, 156.47, 157.65, 167.03; LR MS (EI) *m/z* 395 (M^+), 339, 294, 91; HR MS (EI) calcd for $C_{24}H_{29}O_4N$ 395.2096, found 395.2097.

(2-Benzyl-1-methyl-2,3-dihydro-1*H*-isoindol-1-yl)-acetic acid methyl ester (3c). IR (neat) 2949, 1732, 1209, 1170 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52 (s, 3 H), 2.80 (d, *J* = 13.5 Hz, 1 H), 2.86 (d, *J* = 13.5 Hz, 1 H), 3.55 (s, 3 H), 3.74 (d, *J* = 12.9 Hz, 1 H), 3.84 (d, *J* = 13.0 Hz, 1 H), 3.88 (d, *J* = 13.0 Hz, 1 H), 3.99 (d, *J* = 12.9 Hz, 1 H), 7.13-7.44 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.25, 42.52, 51.28, 52.22, 55.44, 67.22, 122.22, 122.82, 126.51, 126.82, 126.89, 128.20, 128.41, 138.28, 139.61, 146.42, 171.47; LR MS (EI) *m/z* 295 (M^+), 280, 222, 204, 91; HR MS (EI) calcd for $C_{19}H_{21}NO_2$ 295.1572, found 295.1574.

3-{2-[2-(Benzyl-*tert*-butoxycarbonyl-amino)-ethyl]-phenyl}-but-2-enoic acid methyl ester (2d). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9 H), 2.41 (s, 3 H), 2.75 (br, 2 H), 3.26 (s, 8/7 H), 3.36 (s, 6/7 H), 3.75 (s, 3 H), 4.30 (s, 6/7 H), 4.39 (s, 8/7 H), 5.74 (s, 1 H), 7.01-7.31 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.62, 28.41, 31.51, 48.20, 50.03, 51.01, 79.70, 119.12, 126.17, 127.07, 127.19, 127.77, 128.34, 129.85, 134.94, 138.12, 143.71, 155.37, 157.85, 166.49.

(2-Benzyl-1-methyl-1,2,3,4-tetrahydro-isoquinolin-1-yl)-acetic acid methyl ester (3d). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56 (s, 3 H), 2.56-2.66 (m, 2 H), 2.74-2.84 (m, 2 H), 2.96 (d, *J* = 14.0 Hz, 1 H), 3.03 (d, *J* = 14.0 Hz, 1 H), 3.50 (s, 1 H), 3.56 (d, *J* =

14.0 Hz, 1 H), 4.08(d, *J* = 14.0 Hz, 1 H) 7.04-7.56 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 23.82, 29.91, 42.81, 45.29, 51.17, 53.33, 60.30, 125.61, 125.70, 126.44, 126 .60, 128.11, 128.63, 135.45, 140.42, 141.97, 171.20.

3-{2-[(Benzyl-*tert*-butoxycarbonyl-amino)-methyl]-phenyl}-5-(trimethyl-silanyl)-pent-2-en-4-ynoic acid methyl ester (2e). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.15 (s, 9 H), 1.43 (s, 9 H), 3.78 (s, 3 H), 4.45 (br, 4 H), 6.05 (s, 1 H), 7.20-7.37 (m, 10 H).

[2-Benzyl-1-(trimethyl-silanylethynyl)-2,3-dihydro-1*H*-isoindol-1-yl]-acetic acid methyl ester (3e). ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.16 (s, 9 H), 3.13 (s, 2 H), 3.56 (s, 3 H), 3.63 (d, *J* = 13.2 Hz, 1 H), 3.68 (d, *J* = 13.2 Hz, 1 H), 3.90 (d, *J* = 13.2 Hz, 1 H), 4.18 (d, *J* = 13.2 Hz, 1 H).

Total Synthesis of Erythrocaline

Trimethyl-[6-(2-nitro-vinyl)-benzo[1,3]dioxol-5-ylethynyl]-silane (10). A solution of **9** (246 mg, 1.0 mmol), NH_4OAc (64 mg, 0.83 mmol) and CH_3NO_2 (0.27 ml, 5.0 mmol) in AcOH (2.5 ml) was heated at 100 °C for 7 h. Solvent was removed and the residue was purified by recrystalization from ether to give colorless crystals of **10** (1.23 g, 85 %). IR (film) 3104, 2955, 2149, 1610, 1330, 1253, 1034 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.28 (s, 9 H), 6.05 (s, 2 H), 6.94 (s, 1 H), 6.96 (s, 1 H), 7.57 (d, *J* = 13.6 Hz, 1 H), 8.46 (d, *J* = 13.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.21, 101.35, 101.40, 101.90, 105.95, 112.34, 120.84, 126.62, 136.50, 136.92, 148.63, 150.50; LR MS (EI) *m/z* 289 (M^+), 243, 73; HR MS (EI) calcd for $C_{14}H_{15}NO_4Si$ 289.0770, found 289.0788; Anal. Calcd for $C_{14}H_{15}NO_4Si$: C, 58.11; H, 5.22; N, 4.84. Found: C, 58.06; H, 5.32; N, 4.82.

[2-(6-Ethynyl-benzo[1,3]dioxol-5-yl)-ethyl]-carbamic acid *tert*-butyl ester (1f). To a suspension of $LiAlH_4$ (885 mg, 23.3 mmol) in ether (25 ml) was added **10** (2.25 g) in ether (25 ml) at –78_ and the solution was stirred at room temperature for 3 h. Water (0.9 ml), 15% aqueous NaOH solution (0.9 ml) and water (2.7 ml) were added to this solution at –78 °C and the solution was stirred at room temperature for 14 h. An undissolved material was filtered off and the filtrate was concentrated. The residue was dissolved in MeOH (26 ml) and to this solution was added NEt_3 (1.6 ml, 11.66 mmol) and $(Boc)_2O$ (2.7 ml, 11.66 mmol). The solution was stirred at room temperature for 14 h. After solvent was removed, the residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 10/1) to give colorless oil of **1f** (1.37 g, 61%). IR (neat) 3290, 2977, 2101, 1700, 1366, 1252, 1038 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.43 (s, 9 H), 2.92 (t, J = 6.8 Hz, 2 H), 3.37 (td, J = 6.8, 6.4 Hz, 2 H), 4.57 (s, 1 H), 5.96 (s, 2 H), 6.91 (s, 1 H), 7.26 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 28.43, 34.60, 41.08, 79.11, 79.53, 82.10, 101.32, 109.55, 112.14, 114.39, 13 6.72, 145.78, 148.29, 155.71; LR MS (EI) *m/z* 289 (M^+), 233, 216, 188, 172, 159, 57; HR MS (EI) calcd for $C_{16}H_{19}NO_4$ 289.1314, found 289.1315; Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.23; H, 6.61; N, 4.74.

_3-[6-(2-*tert*-Butoxycarbonylamino-ethyl)-benzo[1,3]dioxol-5-yl]-5-(trimethyl-silanyl)-pent-2-en-4-ynoic acid methyl ester (2f). According to the typical procedure for the synthesis of α,β-unsaturated ester, α,β-unsaturated acid was synthesized from $Ni(cod)_2$ (109 mg, 0.4 mmol), DBU (0.18 mL, 1.2 mmol), **1f** (0.36 mmol) and alkynyl zinc reagent **5** (2.2 mL, 1.1 mmol) in THF (5.8 mL). The crude product was converted into ester **2f**, which was purified by column chromatography on silica gel (hexane/ethyl acetate, 5/1) to give **2f** (111.2 mg, 69%).

(5-Ethynyl-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*]isoquinolin-5-yl)-acetic acid

methyl ester (3f). A solution of CH_2Cl_2 (8.4 ml) of **2f** (933 mg, 3.1 mmol) and CF_3CO_2H (1.6 mL, 21 mmol, 10 equiv.) was stirred at room temperature for 3 h. After solvent was removed, the residue was dissolved in ethyl acetate. The organic layer was washed with sat. $NaHCO_3$ solution and brine, and dried over Na_2SO_4 and concentrated. The residue was dissolved in MeOH (20 ml) and the solution was refluxed for 18 h. Solvent was removed and the residue was dissolved in THF (8 ml). To this solution was added TBAF (THF solution, 1.0 M, 2.3 mL, 1.1equiv.) and the solution was stirred at room temperature for 1 h. Water was added and the aqueous layer was extracted with ethyl acetate and the organic layer was washed with sat.. $NaHCO_3$ solution and brine, and dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (ethyl acetate) to give **3f** (438 mg, 76%). IR (film) 3286, 2952, 1734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 1 H), 2.62 (ddd, *J* = 16.0, 4.0, 3.2 Hz, 1 H), 2.84 (ddd, *J* = 16.0, 10.4, 5.6 Hz, 1 H), 2.89 (d, *J* = 16.0 Hz, 1 H), 3.12 (ddd, *J* = 12.0, 5.6, 3.2 Hz, 1 H), 3.13 (d, *J* = 16.0 Hz, 1 H), 3.22 (ddd, *J* = 12.0, 10.4, 4.0 Hz, 1 H), 3.70 (s, 3 H), 5.90 (d, *J* = 1.2 Hz, 1 H), 5.92 (d, *J* = 1.2 Hz, 1 H), 6.54 (s, 1 H) 6.79 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.71, 39.57, 46.68, 51.77, 53.40, 71.61, 87.00, 100.89, 105.96, 108.84, 128.33, 130.29, 146.08, 146.55, 170.76; LR MS (EI) *m/z* 273 (M^+), 200, 185; HR MS (EI) calcd for $C_{15}H_{15}NO_4$ 273.1001, found 273.1009.

(6-Allyl-5-ethynyl-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*]isoquinolin-5-yl)-acetic acid methyl este (3f). To a suspension of **3f** (100 mg, 0.366 mmol) and K_2CO_3 (253 mg, 1.83 mmol, 5 equiv.) in CH_3CN (1.2 mL) was added ally bromide (0.12 mL, 1.46 mmol, 4 equiv.) and the solution was stirred at room temperature for 60 h. Water was added and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated to give **11** (116.4 mg).

Acetic acid 1-(6-allyl-5-ethynyl-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*]isoquinolin-5-ylmethyl)-allyl ester (13). A solution of **11** (116.4 mg) in THF was added $LiAlH_4$ (36 mg, 0.95 mmol, 3equiv.) at –78 °C and the solution was stirred at 0 °C for 2 h. To this suspension was added $Na_2SO_4 \cdot 10H_2O$ and the suspension was stirred at room temperature overnight. An undissolved material was filtered off and the filtrate was concentrated to give alcohol (102.7 mg). To the solution of oxalyl chloride (0.1 ml, 1.1 mmol, 3equiv.) in CH_2Cl_2 (1.5 mL) was added DMSO (0.16 mL, 2.2 mmol, 6 equiv.) at –78 °C and the solution was stirred for 2 min. A solution of **12** (102.7 mg) in CH_2Cl_2 (1.5 mL) was stirred at –78 °C for 30 min. To this solution was added NEt_3 (0.6 mL). After the solution was stirred at 0 °C for 30 min, water was added. The aqueous layer was made basic by K_2CO_3 and extracted with ethyl acetate. The organic layer was washed with brine dried over Na_2SO_4 and concentrated. The crude aldehyde was dissolved in THF (2 mL) and to this solution was added vinyl magnesium bromide (THF solution, 1.0 M, 1.1 mL, 1.1 mmol) at –78 °C. After the solution was stirred for 2 h at the same temperature, water was added. The aqueous layer was extracted with ethyl acetate and the organic layer was washed with brine dried over Na_2SO_4 and concentrated. The residue **12** (102 mg) was dissolved in pyridine (1 mL). To this solution was added Ac_2O (0.5 mL, 5.3 mmol) and DMAP (5 mg) and the solution was stirred at room temperature for 14 h. Water was added and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 4/1) to give colorless oil of **13** (90.2 mg, 70% from **3f**). **less polar**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.01 (s, 3 H), 2.29 (dd, *J* = 15.4, 5.4 Hz, 1 H), 2.46 (s, 1 H), 2.46-2.51 (m, 2 H), 2.65 (dd, *J* = 15.4, 5.4 Hz, 1 H), 2.77-2.97 (m, 3 H), 3.64 (d, *J* = 14.0 Hz, 1 H), 4.83 (d, *J* = 10.4 Hz, 1 H), 4.92 (d, *J* = 16.8 Hz, 1 H), 5.16 (d, *J* = 10.4 Hz, 1 H), 5.23-5.27 (m, 2 H), 5.39 (ddd, *J* = 17.2, 10.4, 6.2 Hz, 1 H), 5.82-5.96 (m, 1 H), 5.91 (d, *J* = 11.6 Hz, 2 H), 6.49 (s, 1 H), 6.82 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.51, 29.81, 43.96,

44.79, 53.91, 60.11, 71.47, 73.34, 84.44, 100.86, 107.28, 108.07, 114.93, 116.75, 129.81, 130.72, 136.40, 136.47, 146.11, 146.35, 169.61. **more polar**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57 (s, 3 H), 2.35-2.57 (m, 3 H), 2.46 (s, 1 H), 2.53 (dd, *J* = 11.2, 11.2 Hz, 1 H), 2.82-2.92 (m, 2 H), 2.98 (d, *J* = 11.2 Hz, 1 H), 3.51 (d, *J* = 14.8 Hz, 1 H), 5.04 (d, *J* = 10.0 Hz, 1 H), 5.08 (d, *J* = 15.6 Hz, 1 H), 5.17 (d, *J* = 10.0 Hz, 1 H), 5.32 (d, *J* = 16.8 Hz, 1 H), 5.65 (d, *J* = 6.4 Hz, 1 H), 5.73 (ddd, *J* = 16.8, 10.0, 5.6 Hz, 1 H), 5.80-5.91 (m, 1 H), 5.88 (s, 1 H), 5.91 (s, 1 H), 6.47 (s, 1 H) 6.91 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.46, 29.80, 44.51, 44.74, 54.03, 59.66, 70.00, 73.00, 84.84, 100.80, 107.91, 108.24, 114.92, 116.61, 129.08, 130.62, 136.14, 137.08, 145.74, 146.03, 169.35.

Ring Closure Metathesis of 13. To a solution of **13** (8.2 mg, 0.023 mmol) in ether (1 ml) was added HCl solution in ether (1.0 M, 0.05 mL, 0.05 mmol, 3equiv.) and the solvent was removed under reduced pressure. A solution of the residue and **16** (2 mg, 0.002mmol, 10 mol %) was dissolved in CH_2Cl_2 (0.5 mL). The solution was stirred at room temperarure under argon for 16 h. The CH_2Cl_2 solution was washed with aqueous K_2CO_3 solution, and brine, dried over Na_2SO_4 and concentrated. The residue was purified by preparative chromatography on silica gel (ethyl acetate/ MeOH, 5/1) to give **14a** (4.5 mg, 50%) and **14b** (4.5 mg, 50%).

Erythrocarine 6b

A solution of **14a** (4.5 mg, 0.015 mmol) and K_2CO_3 (3.4 mg, 0.025 mmol) in MeOH (0.5 ml) was stirred at 0 °C for 1 h. Water was added and the organic layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by preparative chromatography on silica gel (ethyl acetate/ MeOH, 5/1) to give erythrocarine **6b** (3.7 mg, 93%).

In a similar manner, **14b** (4.5 mg) was treated with K_2CO_3 in MeOH for 4 h to give **15b** (2.0 mg, 53%). **Erythrocaline (6b)**:^{1}H NMR (400 MHz, $CDCl_3$) δ 1.70 (s, 3 H),

2.39 (br, 1 H), 2.55 (d, *J* = 14.4 Hz, 1 H), 2.79-2.91 (m, 3 H), 3.41 (d, *J* = 14.4 Hz, 1 H), 3.62 (m, 1 H), 3.86 (br, 1 H), 5.38 (t, *J* = 5.6 Hz, 1 H), 5.87 (s, 1 H), 5.88 (s, 1 H), 5.92 (s, 1 H), 5.99-6.05 (m, 1 H), 6.61 (s, 1 H), 6.77 (d, *J* = 10.0 Hz, 1 H), 6.88 (s, 1 H). **Epierythrocaline (15b)**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.50(d, *J* = 10.0 Hz, 1 H), 3.74 (d, *J* = 15.0 Hz, 1 H), 5.43 (br, 1 H), 5.77 (s, 1 H), 5.82 (dd, *J* = 10.0, 2.4 Hz, 1 H), 5.88 (s, 2 H), 6.58 (dd, *J* = 10.0, 2.4 Hz, 1 H), 6.60 (s, 1 H). 6.78 (s, 1 H).

References

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