Supplementary Material for Organic & Biomolecular Chemistry

SUPPLEMENTARY MATERIAL

for the

article

entitled

Total Syntheses of Enantiomerically Enriched *R*(+)- and *S*(–)- Deplancheine.

authored by

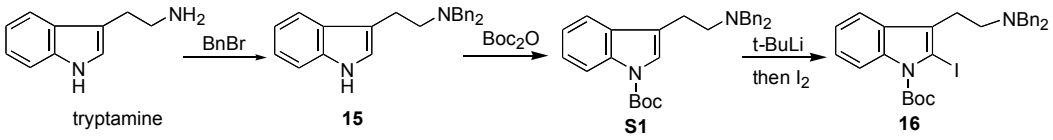
Nadiya Sydorenko, Craig A. Zificsak, Aleksey I. Gerasyuto, and Richard P. Hsung*

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

EXPERIMENTAL SECTION

Solvents were distilled prior to use. Reagents were used as purchased (*Aldrich*, *Acros*), except where noted. Chromatographic separations were performed using ICN SiliTech 32-63 D 60 Å SiO_2. ^1H and ^{13}C NMR spectra were obtained on Varian VI-300, VXR-300, and VI-500 spectrometers using $CDCl_3$ (except where noted) with TMS or residual solvent as standard. Melting points were determined using a Laboratory Devices MEL-TEMP and are uncorrected/calibrated. Infrared spectra were obtained using NaCl plates on a Midac M2000 FTIR. TLC analysis was performed using Whatman 254 nm polyester-backed silica plates (60 Å, 250 μm) and visualized using UV and vanillin or $KMnO_4$ stains. Low-resolution mass spectra were obtained using an Agilent 1100 series LC/MSD (APCI) and HP 6890 series GC/MS (EI). High-resolution mass spectral analyses were performed at University of Minnesota Department of Chemistry Mass Spectrometry Laboratory. Enantiomeric ratios were determined on an Agilent HPLC instrument equipped with a Chiralcel OD column. All spectral data obtained for new compounds are reported here.

N,N-Dibenzyl-*N*-Boc-2-Iodotryptamine 16.



Tryptamine **14** (3.02 g, 18.9 mmol) was added to a suspension of K_2CO_3 (10.7 g, 78.0 mmol) in absolute EtOH (90 mL), followed by BnBr (4.70 mL, 39.5 mmol). After stirring at rt for 24 h, the solution was concentrated, dissolved in CH_2Cl_2 (100 mL) and filtered through Celite. Excess of solvent was removed under reduced pressure to give *N,N*-dibenzyl-tryptamine **15** (6.10 g, 93%) as an orange oil.

15: R_f = 0.39 (EtOAc : hexane = 3 : 2); ^1H NMR (500 MHz, $CDCl_3$) δ 2.73 (dd, 2H, *J* = 8.5, 7.5 Hz), 2.89 (dd, 2H, *J* = 8.5, 7.5 Hz), 3.61 (s, 4H), 6.56 (d, 1H, *J* = 1.5 Hz), 6.99 (td, 1H, *J* = 7.5, 1.5 Hz), 7.06 (t, 2H, *J* = 7.5 Hz), 7.16 (t, 2H, *J* = 7.5 Hz), 7.18 – 7.21 (m, 1H), 7.26 (t, 4H, *J* = 7.5 Hz), 7.33 (d, 4H, *J* = 7.5 Hz), 7.38 (brs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.1, 54.0, 58.4, 111.2, 114.3, 118.3, 119.1, 121.6, 121.8, 126.9, 127.6, 128.3, 128.9, 136.2, 140.0; IR (thin film) cm^{-1} 3440brs, 3013s, 2944s, 1612s; mass spectrum (APCI): m/e (% relative intensity) 341 (5) $M+H^+$, 234 (10), 210 (100), 198 (15), 144 (60); HRMS: m/e calcd for $C_{24}H_{24}N_2Na$ 363.1837 (M^++Na), found 363.1845.

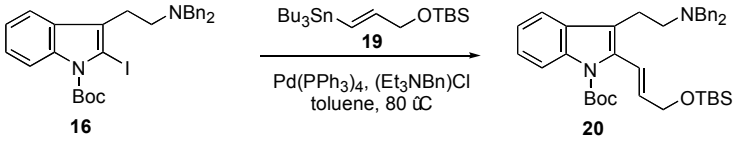
N,N-Dibenzyl-tryptamine **15** (6.10 g, 17.9 mmol) was dissolved in CH_2Cl_2 (50 mL). DMAP (230.0 mg, 2.00 mmol) and Boc_2O (6.50 mL, 28.0 mmol) were added and the resulting mixture was stirred at rt overnight. The mixture was then poured onto silica gel and washed with 20% EtOAc in hexanes. Concentration of the combined washes afforded *N,N*-dibenzyl-*N*-Boc-tryptamine **S1** (7.80 g, 99%), which was sufficiently pure for the next step. **S1**: R_f = 0.55 (EtOAc : hexane = 2 : 3); ^1H NMR (500 MHz, $CDCl_3$) δ 1.65 (s, 9H), 2.78 (dd, 1H, *J* = 9.5, 1.5 Hz), 2.79 (d, 1H, *J* = 8.5 Hz), 2.87 (d, 1H, *J* = 8.5 Hz), 2.89 (dd, 1H, *J* = 9.5, 1.5 Hz), 3.68 (s, 4H), 7.12 (td, 1H, *J* = 7.5, 1.0 Hz), 7.20 – 7.27 (m, 4H), 7.29 (t, 4H, *J* = 7.5 Hz), 7.37 (d, 4H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.1, 28.5, 53.3,

58.6, 83.4, 115.4, 119.1, 119.2, 122.4, 122.9, 124.3, 124.4, 127.1, 128.4, 129.0, 130.9, 139.9, 150.0; IR (thin film) cm^{-1} 3445brs, 3012s – 2860s, 1610s; mass spectrum (APCI): m/e (% relative intensity) 441 (5) $M+H^+$, 385 (10), 341 (15), 269 (18), 210 (100), 144 (30); HRMS: m/e calcd for $C_{29}H_{32}N_2O_2Na$ 463.2361 (M^++Na), found 463.2390.

N,N-Dibenzyl-*N*-Boc-tryptamine **S1** (7.80 g, 17.8 mmol) was azeotroped with benzene and then dissolved in THF (100 mL) before being cooled to –78 °C. To the cooled solution was added *t*-BuLi (25.0 mL, 1.7 *M* in pentane, 42.5 mmol) dropwise, and after stirring at -78 °C for 45 min, iodine (12.0 g, 47.0 mmol) was added as a solution in THF (50 mL). The resulting reaction mixture was stirred for 5 h at –78 °C before being gradually brought to rt. The reaction was quenched with 50 g of sodium thiosulfate and 50 mL of water. The layers were separated and washed with saturated aqueous sodium thiosulfate (3 x 50 mL) and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was dissolved in CH_2Cl_2 and filtered through silica gel, eluting first with 20% CH_2Cl_2 in EtOAc and then with 50% EtOAc in hexanes. Removal of solvent under reduced pressure afforded iodide **16** (6.20 g, 62%) as a yellow solid.

16: R_f = 0.60 (EtOAc : hexane = 2 : 3); mp = 66–69 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.69 (s, 9H), 2.65 – 2.68 (m, 2H), 2.91 – 2.94 (m, 2H), 3.73 (s, 4H), 7.06 (t, 1H, *J* = 7.5 Hz), 7.10 (d, 1H, *J* = 7.5 Hz), 7.16 (t, 1H, *J* = 7.5 Hz), 7.23 (t, 2H, *J* = 7.5 Hz), 7.29 (t, 4H, *J* = 7.5 Hz), 7.39 (d, 4H, *J* = 7.5 Hz), 8.02 (d, 1H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.0, 28.5, 52.3, 58.7, 85.1, 115.6, 118.4, 122.7, 124.3, 124.4, 127.1, 128.4, 129.0, 129.5, 129.9, 139.1, 139.9, 159.8; IR (thin film) cm^{-1} 3422brs, 3025w, 2973s, 2924s, 1733s, 1618m, 456s; mass spectrum (APCI): m/e (% relative intensity) 567 (5) $M+H^+$, 511 (30), 269 (25), 210 (100); HRMS: m/e calcd for $C_{29}H_{31}N_2O_2INa$ 589.1328 (M^++Na), found 589.1303.

Stille Coupling Product 20.

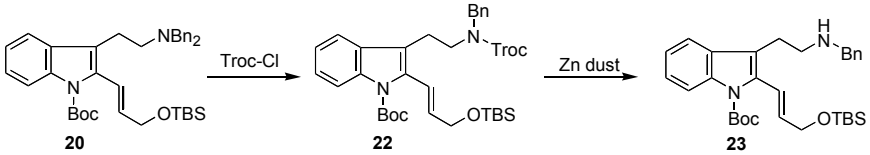


A mixture of iodide **16** (25.0 mg, 0.044 mmol), benzyltriethylammonium chloride (20.0 mg, 0.088 mmol), $Pd(PPh_3)_4$ (5.50 mg, 0.005 mmol), and *E*-vinylstannane **19** (25.0 mg, 0.054 mmol) in toluene (1 mL) was heated at 80 °C. After 6 h, an additional aliquot of **19** (16.0 mg, 0.034 mmol) was added and heating was continued for a total of 24 h. The solution was cooled, diluted with Et_2O and filtered through Celite. Concentration under reduced pressure and purification of the crude residue via basic alumina gel column chromatography afforded **20** (23.0 mg, 86%) as yellow oil.

20: R_f = 0.21 (EtOAc : hexane = 1 : 9); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 6H), 1.01 (s, 9H), 1.54 (s, 9H), 2.71 (dd, 2H, *J* = 11.5, 7.5 Hz), 2.94 (dd, 2H, *J* = 11.5, 7.5 Hz), 3.69 (s, 4H), 4.28 (dd, 2H, *J* = 4.5, 2.0 Hz), 5.68 (dt, 1H, *J* = 16.0, 4.5 Hz), 6.73 (d, 1H, *J* = 16.0 Hz), 7.05 – 7.13 (m, 2H), 7.19 - 7.25 (m, 3H), 7.31 (t, 4H, *J* = 7.5 Hz), 7.40 (d, 4H, *J* = 7.5 Hz), 8.05 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (125

MHz, $CDCl_3$) δ -4.9, 23.0, 23.2, 29.1, 29.8, 55.9, 57.7, 61.3, 80.0, 111.3, 112.6, 119.0, 119.9, 122.2, 122.8, 122.9, 127.3, 127.6, 128.4, 128.9, 130.4, 135.5, 136.7, 150.1; IR (thin film) cm^{-1} 3120m, 3027m, 2987s, 2964s, 1735s, 1610m, 908s; mass spectrum (APCI): m/e (% relative intensity) 611 (2) $M+H^+$, 511 (30), 414 (100), 224 (80), 172 (55); HRMS: m/e calcd for $C_{38}H_{51}N_2O_3Si$ 611.3669 (M^++H), found 611.3677.

Benzyl deprotection.

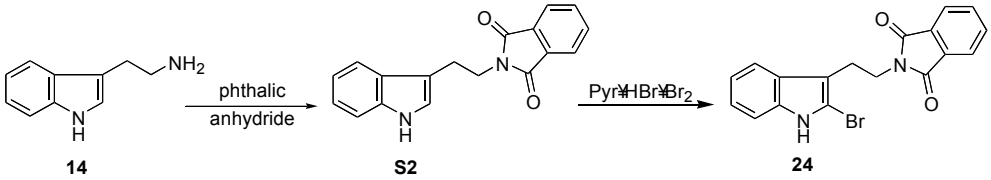


To a stirred solution of compound **20** (60.0 mg, 0.098 mmol) in 1 mL of anhy $CHCl_3$ was added 2,2,2-trichloroethyl carbonochloridate (42.0 μL, 0.29 mmol) and the reaction mixture was stirred at rt 24 h. Reaction progress was monitored by TLC. Upon completion, reaction mixture was filtered through basic alumina with diethyl ether and concentrated under reduced pressure. Purification of the crude residue via basic alumina column chromatography afforded **22** (45.0 mg, 67 %) as two rotameric isomers: *minor rotamer:* ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 6H), 0.88 (s, 9H), 1.57 (s, 9H), 2.96 (dd, 2H, *J* = 8.5, 8.0 Hz), 3.42 – 3.47 (m, 2H), 4.31 (dd, 2H, *J* = 3.0, 2.0 Hz), 4.48 (s, 2H), 4.78 (s, 2H), 5.85 (dt, 1H, *J* = 16.0, 5.0 Hz), 6.73 (d, 1H, *J* = 16.0 Hz), 7.09 – 7.25 (m, 7H), 7.45 (t, 1H, *J* = 8.0 Hz), 8.00 (d, 1H, *J* = 8.0 Hz); *major rotamer:* ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 6H), 0.88 (s, 9H), 1.57 (s, 9H), 3.01 (dd, 2H, *J* = 8.5, 8.0 Hz), 3.42 – 3.47 (m, 2H), 4.31 (dd, 2H, *J* = 3.0, 2.0 Hz), 4.49 (s, 2H), 4.81 (s, 2H), 5.79 (dt, 1H, *J* = 16.0, 5.0 Hz), 6.71 (d, 1H, *J* = 16.0 Hz), 7.09 – 7.25 (m, 7H), 7.45 (t, 1H, *J* = 8.0 Hz), 8.00 (d, 1H, *J* = 8.0 Hz).

To 45.0 mg (0.064 mmol) of **22** in 1 mL of THF was added with vigorous stirring 20 mg of zinc powder followed by addition of 0.40 mL 1 *M* KH_2PO_4, and the progress of the reaction was monitored by TLC analysis. After 2 h, 1 mL of THF, 20.0 mg of Zn powder, and 0.40 mL of 1 M KH_2PO_4 were added, and the reaction was continued for 12 h more. The product was extracted with EtOAc, washed with water and brine, dried over anhydrous Na_2SO_4, and filtered. The EtOAc was evaporated under reduced pressure. The crude product was purified via silica gel column chromatography to afford amine **23** (9.0 mg, 17 %) as yellow oil.

23: R_f = 0.22 (EtOAc : hexane = 3 : 2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.12 (s, 6H), 0.95 (s, 9H), 1.64 (s, 9H), 2.93 (dd, 2H, *J* = 13.0, 6.5 Hz), 2.98 (dd, 2H, *J* = 13.0, 6.5 Hz), 3.82 (s, 2H), 4.39 (dd, 2H, *J* = 5.0, 2.0 Hz), 6.01 (dt, 1H, *J* = 16.0, 5.0 Hz), 6.81 (d, 1H, *J* = 16.0 Hz), 7.19 – 7.38 (m, 7H), 7.51 (d, 1H, *J* = 8.0 Hz), 8.10 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.1, 22.9, 23.5, 29.4, 29.9, 56.1, 57.8, 59.9, 81.2, 107.1, 110.3, 112.1, 119.4, 119.8, 122.8, 123.3, 127.3, 127.5, 128.0, 128.5, 131.0, 136.4, 136.5, 150.6; IR (thin film) cm^{-1} 3113w, 2989s, 2975m, 1731s, 1608m; mass spectrum (APCI): m/e (% relative intensity) 521 (5) $M+H^+$, 421 (100), 248 (15), 115 (55); HRMS: m/e calcd for $C_{31}H_{44}N_2O_3SiNa$ 543.3019 (M^++Na), found 543.3036.

2-Bromo-*N*-Phthaloyltryptamine 24.

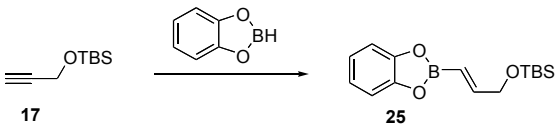


Tryptamine **14** (6.00 g, 36.7 mmol) and phthalic anhydride (6.00 g, 40.5 mmol) were heated in toluene at reflux with azeotropic removal of water using a Dean–Stark trap for 16 h. Concentration of the crude reaction gave the crude phthaloyltryptamine **S2** (10.0 g, 98%) as a clear oil, which can be used in the bromination step crude. **S2:** R_f = 0.08 (EtOAc : hexanes = 1 : 3); mp = 173.5–174 °C (Lit. mp = 165 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.18 (t, 2H, *J* = 7.6 Hz), 4.03 (t, 2H, *J* = 7.6 Hz), 7.13 (dd, 1H, *J* = 6.6, 1.2 Hz), 7.14 (dt, 1H, *J* = 7.4, 1.2 Hz), 7.21 (dt, 1H, *J* = 7.4, 1.2 Hz), 7.37 (td, 1H, *J* = 7.4, 1.2 Hz), 7.72 (dd, 2H, *J* = 5.0, 3.0 Hz), 7.76 (dd, 1H, *J* = 7.4, 1.2 Hz), 7.86 (dd, 2H, *J* = 5.0, 3.0 Hz), 8.04 (brs, 1H).

The crude phthaloyltryptamine **S2** (10.0 g, 36.0 mmol) was dissolved in the mixture THF : $CHCl_3$ (1 : 1, 100 mL), cooled to -10 ^{o}C in an ice-acetone bath, and treated with pyridinium bromide perbromide (13.2 g, 41.3 mmol). When the reaction was complete as indicated by TLC analysis (1–3 h), the reaction was warmed up to rt and washed with sat aq $Na_2S_2O_3$ (2 X 100 mL) and the aqueous washes were extracted with EtOAc (100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to give bromide **24** (12.6 g, 95%) as an oil. For subsequent coupling reactions, the intermediate can be purified on silica gel.

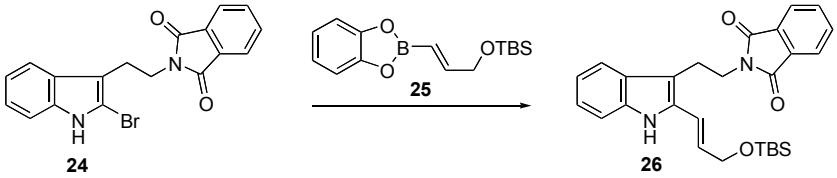
24: R_f = 0.27 (EtOAc : hexane = 2 : 3), mp = 180.5–181 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.10 (t, 2H, *J* = 7.5 Hz), 3.95 (t, 2H, *J* = 7.5 Hz), 7.08 (td, 1H, *J* = 7.5, 1.0 Hz), 7.14 (td, 1H, *J* = 7.5, 1.0 Hz), 7.26 (d, 1H, *J* = 7.5 Hz), 7.62 (d, 1H, *J* = 7.5 Hz), 7.69 (dd, 2H, *J* = 5.5, 3.0 Hz), 7.81 (dd, 2H, *J* = 5.5, 3.0 Hz), 8.00 (brs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.3, 37.7, 109.8, 110.7, 115.3, 115.4, 115.7, 118.3, 120.5, 122.7, 123.4, 131.4, 134.0, 168.0; IR (thin film) cm^{-1} 3427brs, 3079m, 2950s, 1652s, 1558s, 741s, 668s; mass spectrum (APCI): m/e (% relative intensity) 289 (100) M^+-Br, 271 (60), 262 (5), 142 (35); HRMS: m/e calcd for $C_{18}H_{13}N_2O_2BrNa$ 391.0058, 393.0038 (M^++Na), found 391.0024, 393.0013.

Vinyl Catechol Borane 25.[1]



Catechol borane (2.30 mL, 21.6 mmol) was added dropwise to neat silyl ether **17** (3.40 g, 20.0 mmol). After stirring for 5 d, the mixture was diluted with pentane (6 mL) and filtered. Kugelrohr distillation afforded boronate **25** (3.50 g, 60%) as a clear oil.

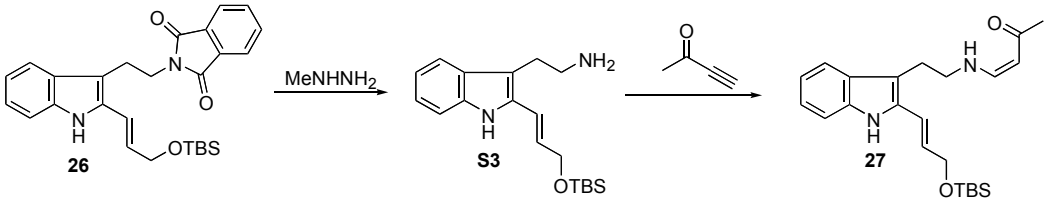
Suzuki-Miyaura Coupling Product 26.



Bromide **24** (124.0 mg, 0.34 mmol), LiCl (43.0 mg, 1.00 mmol), and $Pd(PPh_3)_4$ (20.0 mg, 0.017 mmol) were placed in a flask and purged with nitrogen. The mixture was dissolved in toluene (6 mL) and to this solution were added boronate **25** (174.0 mg, 0.6 mmol) as a solution in toluene (2 mL) and 2 *N* aq NaOH (0.75 mL). The solution was heated to reflux for 5 h, and an additional 175 mg of boronate **25** was added at this time. After an additional 5 h at reflux, the reaction was filtered through Celite eluted with EtOAc. Concentration of the crude mixture under reduced pressure and purification of the crude residue via silica gel column chromatography afforded allyl ether **26** (100.0 mg, 65%).

26: R_f = 0.34 (CH_2Cl_2 : MeOH = 10 : 1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.14 (s, 6H), 0.96 (s, 9H), 3.14 (dd, 2H, *J* = 8.0, 7.2 Hz), 3.91 (dd, 2H, *J* = 8.0, 7.2 Hz), 4.32 (dd, 2H, *J* = 4.5, 1.2 Hz), 6.03 (dt, 1H, *J* = 16.2, 5.2 Hz), 6.75 (d, 1H, *J* = 16.2 Hz), 7.09 (td, 1H, *J* = 7.2, 1.2 Hz), 7.17 (td, 1H, *J* = 7.2, 1.2 Hz), 7.30 (d, 1H, *J* = 7.2 Hz), 7.62 – 7.73 (m, 3H), 7.80 - 7.85 (m, 2H), 7.99 (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.3, 21.9, 23.3, 28.1, 49.7, 59.6, 107.8, 112.8, 119.0, 119.7, 121.9, 122.3, 127.3, 127.4, 127.5, 131.1, 132.0, 134.5, 136.7, 169.2; IR (thin film) cm^{-1} 3341 brm, 3011m, 2987s, 2965m, 1732s, 1608s; mass spectrum (APCI): m/e (% relative intensity) 461 (5) M^++ H, 271 (60), 313 (100), 290 (35), 115 (80); HRMS: m/e calcd for $C_{27}H_{32}N_2O_3SiNa$ 483.2080 (M^++Na), found 483.2066.

Vinylogous Amide 27.



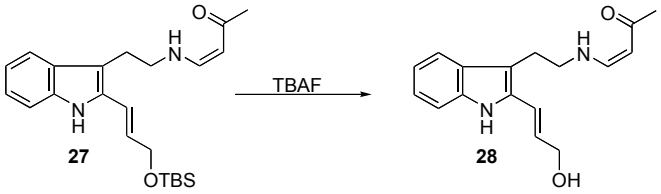
Allyl ether **26** (207.0 mg, 0.45 mmol) was dissolved in EtOH (5 mL) and 1,1-dimethylhydrazine (0.60 mL, 11.3 mmol) was added. After 3 h of stirring at rt, the reaction mixture was concentrated under reduced pressure and the crude residue was purified by silica gel column chromatography (EtOAc : MeOH = 9 : 1) to afford the amine **S3** (74.0 mg, 50%). **S3**: R_f = 0.25 (CH_2Cl_2 : MeOH = 7 : 1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.12 (s, 6H), 0.90 (s, 9H), 3.15 – 3.21 (m, 4H), 4.39 (d, 2H, *J* = 5.5 Hz), 5.30 (brs, 2H, NH), 6.12 (dt, 1H, *J* = 16.0, 5.5 Hz), 6.79 (d, 1H, *J* = 16.0 Hz), 7.01 (t, 1H, *J* = 7.5 Hz), 7.10 (t, 1H, *J* = 7.5 Hz), 7.28 (d, 1H, *J* = 7.5 Hz), 7.57 (d, 1H, *J* = 8.0 Hz), 8.49 (brs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ -4.8, 14.3, 29.6, 40.7, 64.4, 109.3, 111.1, 115.2, 118.9, 119.0, 120.1, 123.3, 128.4, 128.6, 133.4, 136.6; IR (thin film) cm^{-1} 3342brs, 3009m, 2983s, 2870m, 1611s, 913s; mass spectrum (APCI):

m/e (% relative intensity) 331 (5) M+H$^+$, 159 (20), 149 (100), 121 (45); HRMS: m/e calcd for $C_{19}H_{30}N_2OSiNa$ 353.2025 (M$^+$+Na), found 353.2023.

The amine **S3** (74.0 mg, 0.22 mmol) was dissolved in anhydrous CH_2Cl_2 (2 mL) and treated with 3-butyn-2-one (0.025 mL, 0.32 mmol). After 90 min at rt, the solution was concentrated under reduced pressure and the crude residue was purified over silica gel (20% EtOAc in hexanes) to give vinylogous amide **27** (44.0 mg, 50%).

27: R_f = 0.37 (EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.13 (s, 6H), 0.96 (s, 9H), 2.03 (s, 3H), 3.01 (t, 2H, *J* = 7.0 Hz), 3.40 (q, 2H, *J* = 7.0 Hz), 4.39 (ddd, 2H, *J* = 14.0, 5.0, 2.0 Hz), 4.89 (d, 1H, *J* = 7.5 Hz), 6.05 (dt, 1H, *J* = 16.0, 5.0 Hz), 6.44 (dd, 1H, *J* = 12.5, 7.5 Hz), 6.65 (d, 1H, *J* = 16.0 Hz), 7.09 (td, 1H, *J* = 7.5, 1.0 Hz), 7.19 (td, 1H, *J* = 7.5, 1.0 Hz), 7.30 (d, 1H, *J* = 8.0 Hz), 7.49 (d, 1H, *J* = 8.0 Hz), 8.06 (brs, 1H, NH), 9.87 (brs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ -4.9, 25.1, 26.2, 26.8, 29.2, 49.9, 63.9, 94.0, 110.8, 113.7, 113.8, 118.3, 118.7, 120.0, 123.2, 128.0, 129.7, 134.3, 152.5, 190.7; IR (thin film) cm^{-1} 3339brs, 3018m, 2988s, 1724s, 1612s; mass spectrum (APCI): m/e (% relative intensity) 399 (2) M+H$^+$, 397 (5), 276 (65), 182 (100), 170 (40), 156 (35), 144 (30); HRMS: m/e calcd for $C_{23}H_{34}N_2O_2SiNa$ 421.2287 (M$^+$+Na), found 421.2278.

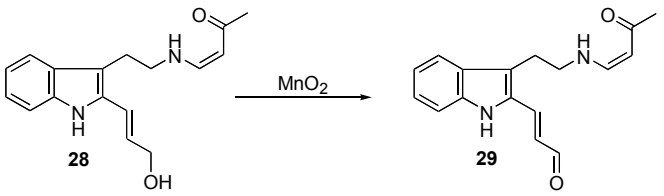
Alcohol 28.



To a solution of vinylogous amide **27** (40.0 mg, 0.10 mmol) in CH_2Cl_2 (2 mL) was added TBAF (0.15 mL, 1 *M* in THF, 0.15 mmol). The resulting mixture was stirred at rt for 24 h. The mixture was filtered through Celite, concentrated and purified silica gel column chromatography to give alcohol **28** (20.0 mg, 70%).

28: R_f = 0.30 (CH_2Cl_2 : MeOH = 7 : 1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.01 (s, 3H), 3.04 (t, 2H, *J* = 6.0 Hz), 3.44 (q, 2H, *J* = 6.0 Hz), 3.98 (brs, 1H, OH), 4.28 (dd, 2H, *J* = 5.0, 1.5 Hz), 4.80 (d, 1H, *J* = 7.5 Hz), 6.16 (dt, 1H, *J* = 16.0, 5.0 Hz), 6.28 (dd, 1H, *J* = 13.5, 7.5 Hz), 6.71 (d, 1H, *J* = 16.0 Hz), 7.09 (td, 1H, *J* = 7.5, 1.0 Hz), 7.18 (td, 1H, *J* = 7.5, 1.0 Hz), 7.31 (d, 1H, *J* = 8.0 Hz), 7.47 (d, 1H, *J* = 8.0 Hz), 8.48 (brs, 1H, NH), 9.73 (brs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.1, 28.9, 49.9, 63.1, 93.3, 110.8, 111.0, 118.0, 119.0, 119.5, 122.3, 127.4, 128.0, 133.7, 136.4, 153.3, 197.5; IR (thin film) cm^{-1} 3540brs, 3114s, 3065m, 2953s, 2883s, 1721s, 1653s; mass spectrum (APCI): m/e (% relative intensity) 285 (3) M+H$^+$, 267 (100), 227 (10), 215 (15), 159 (80); HRMS: m/e calcd for $C_{17}H_{20}N_2O_2Na$ 307.1422 (M$^+$+Na), found 307.1401.

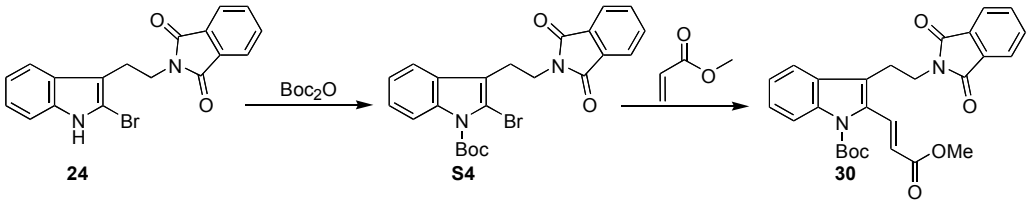
Aldehyde 29.



A solution of alcohol **28** (10.0 mg, 0.035 mmol) in acetone (1 mL) was stirred with MnO_2 (63.0 mg, 0.72 mmol, 20 equiv) at rt for 24 h. Filtration through Celite and removal of the solvent under reduced pressure afforded the pure aldehyde **29** (9.00 mg, 90%).

29: R_f = 0.33 (CH_2Cl_2 : MeOH = 10 : 1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.97 (s, 3H), 3.13 (t, 2H, *J* = 6.0 Hz), 3.49 (q, 2H, *J* = 6.0 Hz), 4.89 (d, 1H, *J* = 7.5 Hz), 6.35 (dd, 1H, *J* = 13.0, 7.6 Hz), 6.46 (dd, 1H, *J* = 15.6, 13.0 Hz), 7.13 (td, 1H, *J* = 7.5, 1.2 Hz), 7.25 – 7.34 (m, 2H), 7.39 (d, 1H, *J* = 15.6 Hz), 7.57 (d, 1H, *J* = 8.0 Hz), 9.17 (brs, 1H, NH), 9.57 (d, 1H, *J* = 7.6 Hz), 9.85 (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.9, 28.9, 50.4, 94.4, 111.1, 111.9, 118.8, 119.7, 122.1, 128.1, 134.0, 135.2, 136.5, 143.8, 153.5, 191.3, 197.8; IR (thin film) cm^{-1} 3333brm, 3081m, 2982s, 2887s, 1731s, 1685s, 1650s; mass spectrum (APCI): m/e (% relative intensity) 283 (5) M+H$^+$, 213 (30), 227 (10), 158 (100); HRMS: m/e calcd for $C_{17}H_{18}N_2O_2Na$ 305.1266 (M$^+$+Na), found 305.1293.

***N*-Boc-2-Bromo-*N*-Phthaloyltryptamine 30**.

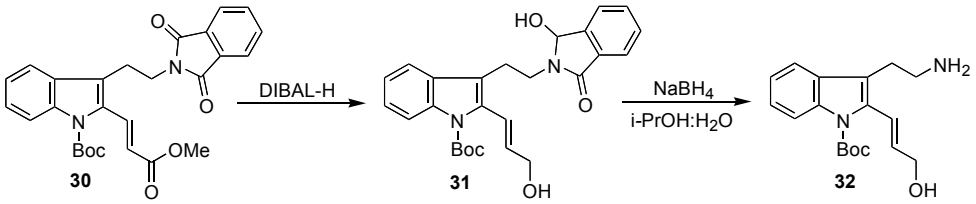


Boc_2O (15.0 mL, 65.3 mmol) was added to a solution of bromide **24** (1.35 g, 36.7 mmol) and DMAP (50.0 mg, 0.40 mmol) in CH_2Cl_2 (150 mL). The reaction mixture was stirred at rt until TLC indicated complete consumption of the starting **24**. The reaction mixture was concentrated under reduced pressure to give the Boc-protected bromide **S4** as a white solid. Purification was accomplished via adding 100 mL of MeOH, heating the mixture at 60 °C with sonication for 1 h, cooling, filtering and washing with cold MeOH (100 mL) and pentane (2 x 50 mL). This partial recrystallization process gave 15.2 g (88%) of the Boc-protected bromide **S4** as white solid. **S4**: R_f = 0.37 (EtOAc : hexanes = 1 : 3); mp = 118–120 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.69 (s, 9H), 3.13 (t, 2H, *J* = 7.5 Hz), 3.94 (t, 2H, *J* = 7.5 Hz), 7.22 (dt, 1H, *J* = 7.5, 1.0 Hz), 7.27 (dt, 1H, *J* = 7.5, 1.0 Hz), 7.62 (dd, 1H, *J* = 7.5, 1.0 Hz), 7.71 (dd, 2H, *J* = 5.5, 3.5 Hz), 7.84 (dd, 2H, *J* = 5.5, 3.5 Hz), 8.06 (d, 1H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.5, 28.1, 36.4, 84.8, 109.7, 115.2, 117.9, 119.4, 122.9, 123.1, 124.4, 128.5, 132.0, 133.8, 136.4, 148.9, 168.0; IR (thin film) cm^{-1} 2980m, 2937w, 2362w, 1772m, 1736s, 1713s, 1367s, 1158m, 710m; mass spectrum (APCI): m/e (% relative intensity) 469 (2) M+H$^+$, 371 (98), 369 (100), 289 (96); HRMS: m/e calcd for $C_{23}H_{21}N_2O_4BrNa$ 493.0562 (M$^+$+Na), found 493.0613.

The Boc-protected bromide **S4** (15.1 g, 32 mmol) and $Pd(PPh_3)_4$ (1.80 g, 1.6 mmol, 5 mol%) were placed in a 500 mL RB-flask and purged with N_2. Toluene (100 mL) was added then followed by methyl acrylate (14.5 mL, 160 mmol), dicyclohexylmethylamine (7.60 mL, 35.5 mmol) and additional toluene (60 mL). The reaction mixture was heated in an 85 °C oil bath for 48 h, before being filtered through silica gel. After removal of the solvent under reduced pressure, the crude residue was purified via adding 150 mL of MeOH, heating the mixture at 60 °C with sonication for 1 h cooling, filtering and washing with cold MeOH (100 mL) and pentane (2 x 50 mL). This partial recrystallization process gave 12.4 g (82%) of ester **30** as an off-white solid.

30: R_f = 0.25 (EtOAc : hexanes = 1 : 3); mp = 194–196 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.67 (s, 9H), 3.17 (t, 2H, *J* = 8.0 Hz), 3.86 (s, 3H), 3.94 (t, 2H, *J* = 8.0 Hz), 6.38 (d, 1H, *J* = 16.0 Hz), 7.28 (t, 1H, *J* = 7.5 Hz), 7.36 (t, 1H, *J* = 7.5 Hz), 7.73 (dd, 2H, *J* = 5.5, 3.5 Hz), 7.76 (d, 1H, *J* = 8.0 Hz), 7.86 (dd, 2H, *J* = 5.0, 3.5 Hz), 8.02 (d, 1H, *J* = 16.0 Hz), 8.16 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.2, 28.1, 37.6, 51.8, 84.7, 115.6, 119.3, 119.7, 119.9, 123.2, 123.3, 126.0, 129.4, 132.0, 132.2, 134.0, 136.1, 136.5, 150.0, 167.0, 168.1; IR (thin film) cm^{-1} 2924m, 2358m, 1770m, 1711s, 1635m, 1457m, 1364s, 1163s, 720m; mass spectrum (APCI): m/e (% relative intensity) 475 (4) M+H$^+$, 375 (100); HRMS: m/e calcd for $C_{27}H_{26}N_2O_6$ 475.1869 (M+H$^+$), found 475.1888.

Amino Alcohol 32.



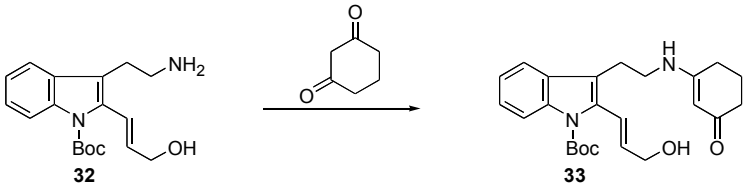
To a solution of ester **30** (1.00 g, 2.11 mmol) in 20 mL of CH_2Cl_2 at –78 °C was added DIBAL-H (1 *M* in hexane, 7.60 mL, 7.60 mmol) by dropwise and the resulting mixture was stirred at –78 °C for 1 h before MeOH (2 mL) was added. The mixture was poured into 30 mL of sat aq potassium sodium tartrate, and CH_2Cl_2 (20 mL) and H_2O (20 mL) were added. Layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to give the crude hydroxyaminal intermediate **31** as yellow foam, which was used in the next step without further purification.

31: R_f = 0.44 (EtOAc); ^{1}H NMR (500 MHz, CDCl3) δ 1.57 (s, 9H), 3.11 – 3.18 (m, 2H), 3.12 (brs, 1H), 3.57 - 3.74 (m, 2H), 4.16 – 4.25 (m, 2H), 5.66 (d, 1H, *J* = 9.0 Hz), 6.04 (dt, 1H, *J* = 16.0, 6.5 Hz), 6.53 (d, 1H, *J* = 16.0 Hz), 7.20 – 7.26 (m, 2H), 7.36 (t, 1H, *J* = 7.0 Hz), 7.46 – 7.52 (m, 2 H), 7.58 (d, 1 H, *J* = 7.0 Hz), 7.63 (d, 1H, *J* = 7.0 Hz), 8.02 (d, 1H, *J* = 8.0 Hz).

To a solution of the crude **31** in *i*-PrOH/H_2O (6 : 1, 20 mL) was added $NaBH_4$ (241.0 mg, 6.33 mmol) in portions. The reaction was stirred at rt for 18 h before AcOH (1.8 mL) was added. Following evolution of gas, the mixture was heated at 80 °C for 10 h. The reaction was then cooled and the contents were partitioned between 10% aq NH_4OH (30 mL) and CH_2Cl_2 (30 mL). Separation of the

layers was followed with the extraction of aqueous phase with CH_2Cl_2 (3 x 20 mL) and drying of the combined organic layers (Na_2SO_4). Concentration under reduced pressure gave a crude oil [51% overall crude yield from **30**] that consisted of both amino-alcohol **32** and phthalide. R_f = 0.14 (EtOAc). It was difficult to obtain meaningful characterizations for **32**, and thus, the crude **32** was used for the next step, and its full characterizations can be reflected in the concise synthesis of vinylogous amide **33**.

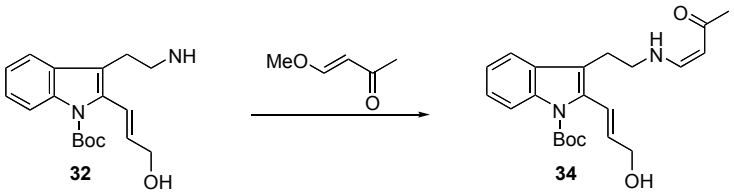
Vinylogous Amide 33.



The crude amino-alcohol **32** (200.0 mg, 0.65 mmol) was dissolved in toluene (10 mL) and 1,3-cyclohexanedione (112.0 mg, 1.00 mmol) was added. After being heated at reflux for 1 h, TLC indicated complete consumption of the starting material. Removal of the solvent and purification by silica gel column chromatography (CH_2Cl_2 loading, hexanes washing, then EtOAc followed by acetone) gave the vinylogous amide **33** (187.0 mg, 69 %) as a red solid.

33: R_f = 0.34 (acetone): mp = 68 –70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.70 (s, 9H), 2.01 (t, 2H, J = 6.2 Hz), 2.32 - 2.41 (m, 4H), 3.09 - 3.14 (m, 2H), 3.34 - 3.41 (m, 2H), 4.43 (d, 2H, J = 5.1 Hz), 5.24 (brs, 1H), 5.39 (s, 1H), 6.11 (td, 1H, J = 16.2, 5.1 Hz), 6.87 (d, 1H, J = 16.2 Hz), 7.28 (t, 1H, J = 6.9 Hz), 7.35 (t, 1H, J = 7.9 Hz), 7.51 (d, 1H, J = 7.4 Hz), 8.19 (d, 1H, J = 8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 22.9, 28.2, 29.7, 36.0, 43.1, 62.5, 84.0, 96.9, 115.6, 115.7, 118.0, 121.6, 122.7, 124.5, 129.5, 134.8, 135.3, 135.6, 150.3, 164.9, 198.1; IR (thin film) cm^{-1} 3584brm, 3263m, 3076m, 2939m, 1728s, 1538s, 1456m, 1368m, 2926s, 1141s; mass spectrum (APCI): m/e (% relative intensity) 411 (47) M+H$^+$, 393 (25), 337 (100), 293 (45); HRMS: m/e calcd for $C_{24}H_{31}N_2O_4$ 411.2284 (M+H$^+$), found 411.2280.

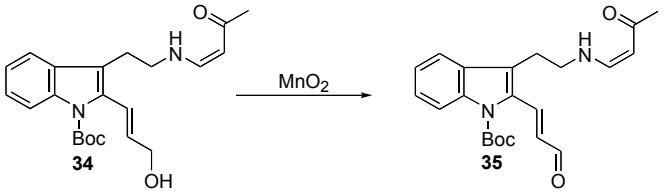
Vinylogous Amide 34.



Crude amino alcohol **32** (500.0 mg, 1.58 mmol) was dissolved in CH_2Cl_2 (5 mL). Triethylamine (0.35 mL, 2.50 mmol) was added followed by addition of 4-methoxy-3-buten-2-one (0.20 mL, 1.80 mmol), and the reaction mixture was allowed to stir at rt for 20 h. Purification of the concentrated mixture by silica gel column chromatographyafforded vinylogous amide **34** as a yellow oil (200.0 mg, 33%).

34: R_f = 0.21 (EtOAc : hexane = 4 : 1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.61 (s, 9H), 1.95 (s, 3H), 2. 96 (t, 2H, *J* = 6.5 Hz), 3.34 (q, 2H, *J* = 6.5 Hz), 3.98 (brs, 1H, OH), 4.23 (dd, 2H, *J* = 5.5, 1.5 Hz), 4.77 (d, 1H, *J* = 7.5 Hz), 5.89 (dt, 1H, *J* = 16.0, 5.5 Hz), 6.20 (dd, 1H, *J* = 13.5, 7.5 Hz), 6.58 (d, 1H, *J* = 16.0 Hz), 7.15 (t, 1H, *J* = 7.5 Hz), 7.21 (t, 1H, *J* = 7.5 Hz), 7.34 (d, 1H, *J* = 7.5 Hz), 8.04 (d, 1H, *J* = 7.5 Hz), 9.82 (brs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.8, 28.3, 28.9, 49.4, 63.2, 84.1, 93.7, 115.6, 115.7, 118.2, 122.2, 122.8, 124.7, 129.4, 133.0, 135.8, 135.9, 150.4, 153.3, 197.7; IR (thin film) cm^{-1} 3440brs, 3109s, 2970s, 2863s, 1725s, 1622s; mass spectrum (APCI): m/e (% relative intensity) 385 (1) M+H$^+$, 367 (10), 311 (45), 267 (100), 182 (80), 170 (30); HRMS: m/e calcd for $C_{22}H_{28}N_2O_4Na$ 407.1947 (M$^+$+Na), found 407.1921.

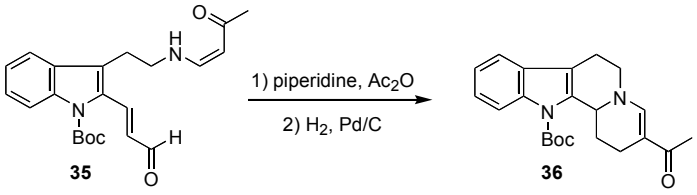
Aldehyde 35.



A solution of alcohol **34** (200.0 mg, 0.52 mmol) in acetone (3 mL) was stirred with MnO_2 (1.02 g, 10.4 mmol, 20 equiv) at rt for 6 h. Filtration through Celite and removal of the solvent under reduced pressure afforded the pure aldehyde **35** (133.0 mg, 67 %) as a yellow oil.

35: R_f = 0.33 (EtOAc : hexane = 4 : 1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.67 (s, 9H), 2.01 (s, 3H), 3.07 (t, 2H, *J* = 6.5 Hz), 3.45 (q, 2H, *J* = 6.5 Hz), 4.92 (d, 1H, *J* = 12.0 Hz), 6.33 (dd, 1H, *J* = 16.0, 7.5 Hz), 6.42 (dd, 1H, *J* = 12.0, 7.5 Hz), 7.28 (td, 1H, *J* = 7.5, 1.0 Hz), 7.40 (td, 1H, *J* = 7.5, 1.0 Hz), 7.53 (d, 1H, *J* = 7.5 Hz), 7.88 (d, 1H, *J* = 16.0 Hz), 8.11 (d, 1H, *J* = 7.5 Hz), 9.68 (d, 1H, *J* = 7.5 Hz), 9.83 (brs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.4, 28.4, 29.2, 48.9, 85.4, 94.7, 116.0, 119.7, 121.7, 123.6, 126.8, 129.3, 130.2, 132.4, 137.0, 143.6, 150.4, 152.1, 193.7, 197.8; IR (thin film) cm^{-1} 3452brs, 3024s, 2970s, 2844m, 1731s, 1683s, 1652s; mass spectrum (APCI): m/e (% relative intensity) 383 (5) M+H$^+$, 283 (75), 263 (30), 198 (100), 180 (40), 170 (50); HRMS: m/e calcd for $C_{22}H_{26}N_2O_4Na$ 405.1790 (M$^+$+Na), found 405.1802.

(±) 3-Acetyl-12-(*t*-Butoxycarbonyl)-1,2,6,7,12,12b-Hexahydro-Indolo[2,3-a]quinolizine 36.

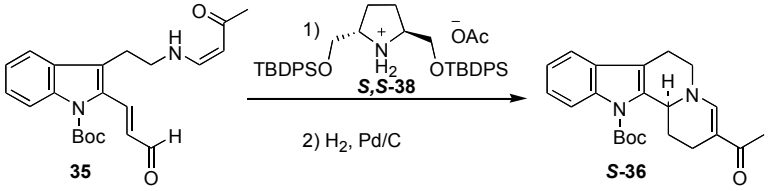


To a solution of aldehyde **35** (133.0 mg, 0.35 mmol) in EtOAc (5 mL) were added Na_2SO_4 (510.0 mg) and piperidinium acetate (82.0 mg, 0.56 mmol). The mixture was sealed under nitrogen and heated in an 85°C oil bath for 6 h. After cooling the mixture, Pd/C (25 mol%) was added and the

mixture was stirred under 1 atm of H_2 for 24 h. Filtration through Celite, removal of solvent under reduced pressure, and purification of the crude residue via silica gel column chromatography [eluent EtOAc : hexanes = 2 : 3] afforded the cycloadduct **36** (61.0 mg, 48%).

36: R_f = 0.16 (EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31 (ddd, 1H, *J* = 24.0, 13.0, 5.5 Hz), 1.59 (s, 9H), 2.05 (s, 3H), 2.24 – 2.30 (m, 1H), 2.53 (dd, 1H, *J* = 13.0, 5.5, 4.5, 2.5 Hz), 2.67 (dd, 1H, *J* = 16.5, 2.5 Hz), 2.73 (ddd, 1H, *J* = 15.5, 2.5, 2.0 Hz), 2.78 (ddd, 1H, *J* = 10.0, 5.5, 2.5 Hz), 3.57 (ddd, 1H, *J* = 13.0, 5.5, 1.5 Hz), 3.63 (dd, 1H, *J* = 13.0, 3.5 Hz), 4.76 (dd, 1H, *J* = 10.0, 1.5 Hz), 7.19 (td, 1H, *J* = 7.5, 1.0 Hz), 7.25 (td, 1H, *J* = 7.5, 1.0 Hz), 7.36 (d, 1H, *J* = 7.5 Hz), 7.37 (s, 1H), 8.08 (d, 1H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 22.8, 24.2, 28.4, 29.5, 51.0, 54.3, 86.4, 115.9, 116.5, 118.2, 123.2, 124.9, 128.6, 134.5, 137.0, 148.2, 150.1, 179.5, 193.7; IR (thin film) cm^{-1} 2974m, 2924m, 1728s, 1660m, 1588s, 1456m, 1402m; mass spectrum (APCI): m/e (% relative intensity) 367 (1) $M+H^+$, 311 (100) M^+-Boc, 267 (45), 261 (10), 170 (20), 144 (15); HRMS: m/e calcd for $C_{22}H_{26}N_2O_3Na$ 389.1841 (M^++Na), found 389.1830.

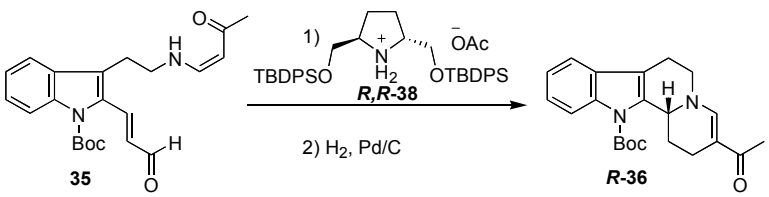
(*S*) – (–) - 3-Acetyl-12-(*t*-Butoxycarbonyl)-1,2,6,7,12,12b-Hexahydro-Indolo[2,3-a]quinolizine 36.



According to the general procedure (described for the synthesis of racemic **36**), the cycloaddition reaction of amide **35** (20.7 mg, 0.06 mmol) through treatment with amine salt ***S,S*-38** (21.3 mg, 0.03 mmol, prepared *in situ* from equimolar amounts of the corresponding free amine and acetic acid) in EtOAc (2 mL) with subsequent hydrogenation over Pd/C (25 mol%) afforded enantiomerically enriched cycloadduct ***S*-36** (12.2 mg, 69 %) as yellow oil upon purification on silica gel column [eluent EtOAc : hexanes = 2 : 3].

***S*-36**: $[\alpha]_D^{20}$ = –70.0 ° [c = 0.40, $CHCl_3$]; CSP-HPLC (Chiralcel OD column, IPA/hexane [10 : 90], 0.75 mL/min) τ = 20.2 min (80%, *S*), τ = 24.3 min (20%, *R*); 60% *ee*.

(*R*) – (+) - 3-Acetyl-12-(*t*-Butoxycarbonyl)-1,2,6,7,12,12b-Hexahydro-Indolo[2,3-a]quinolizine 36.

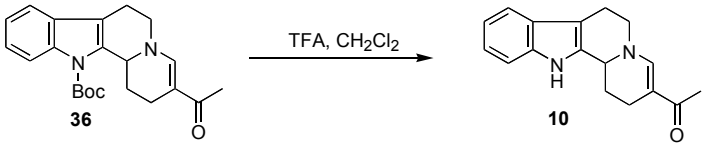


According to the general procedure (described for the synthesis of racemic **36**), the cycloaddition reaction of amide **35** (27.0 mg, 0.07 mmol) through treatment with amine salt ***R,R*-38** (18.8 mg, 0.028 mmol, prepared *in situ* from equimolar amounts of the corresponding free amine and acetic acid) in

EtOAc (2 mL) with subsequent hydrogenation over Pd/C (25 mol%) afforded enantiomerically enriched cycloadduct ***R*-36** (6.0 mg, 23 %) as yellow oil upon purification on silica gel column [eluent: EtOAc : hexanes = 2 : 3].

***R*-36**: $[\alpha]_D^{20}$ = +44.8° [c = 0.50, $CHCl_3$]; CSP-HPLC (Chiralcel OD column, IPA/hexane [10 : 90], 0.75 mL/min) τ = 20.2 min (31 %, *S*), τ = 24.3 min (69 %, *R*); 38% *ee*.

(±) 3-Acetyl-1,2,6,7,12,12b-Hexahydro-indolo[2,3-a]quinolizine 10.



A solution of racemic cycloadduct **36** (40.0 mg, 0.10 mmol) in CH_2Cl_2 : TFA (1 : 1, 2mL) was stirred at rt for 20 h. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and 10% aq NH_4OH (5 mL). The layers were separated and aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Crude product was purified via silica gel column chromatography [eluent EtOAc : hexanes = 4 : 1] to give desired (±) **10** (24.0 mg, 90%) as a yellow oil. The ^{1}H NMR spectral data of **10** was in accordance with those reported in literature.[2]

10: R_f = 0.12 (EtOAc : hexanes = 4 : 1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.75 (ddd, 1H, *J* = 24.0, 12.5, 5.0 Hz), 2.22 (s, 3H), 2.34 (ddd, 1H, *J* = 17.0, 16.5, 5.0 Hz), 2.45 – 2.50 (m, 1H), 2.76 (ddd, 1H, *J* = 16.5, 5.0, 2.5 Hz), 2.85 (dddd, 1H, *J* = 16.5, 4.0, 2.5, 1.0 Hz), 2.94 – 3.01 (m, 1H), 3.68 (ddd, 2H, *J* = 24.0, 12.5, 5.0 Hz), 4.54 (br d, 1H, *J* = 11.0 Hz), 7.14 (td, 1H, *J* = 7.5, 1.0 Hz), 7.21 (td, 1H, *J* = 7.5, 1.0 Hz), 7.37 (d, 1H, *J* = 8.0 Hz), 7.45 (s, 1H), 7.51 (d, 1H, *J* = 8.0 Hz), 8.17 (brs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.0, 22.2, 24.1, 28.6, 51.7, 52.4, 81.4, 108.4, 111.3, 118.4, 120.1, 122.4, 127.0, 132.9, 139.5, 148.5, 193.8; IR (neat) cm^{-1} 3228m, 2960m, 1574s, 1440m, 1402m; mass spectrum (APCI): m/e (% relative intensity) 267 (100) M+H$^+$, 263 (10), 238 (5), 223 (5), 196 (5), 170 (70), 144 (35); HRMS: m/e calcd for $C_{17}H_{19}N_2O$ 267.1497 (M$^+$+H), found 267.1526.

(*S*) – (–) - 3-Acetyl-1,2,6,7,12,12b-Hexahydro-indolo[2,3-a]quinolizine 10.

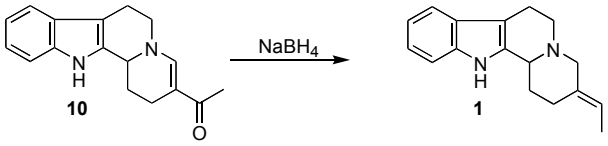
According to the general procedure (described for the synthesis of racemic **10**), the deprotection reaction of enantiomerically enriched ***S*-36** (16.8 mg, 0.043 mmol) in CH_2Cl_2 : TFA (1 : 1, 1 mL) afforded desired tetracycle ***S*-10** (7.60 mg, 66 %) as yellow oil upon purification on silica gel preparative TLC plate [eluent EtOAc : hexanes = 4 : 1]. ***S*-10**: $[\alpha]_D^{20}$ = –22.0 ° [c = 0.4, $CHCl_3$].

(*R*) – (+) -3-Acetyl-1,2,6,7,12,12b-Hexahydro-indolo[2,3-a]quinolizine 10.

According to the general procedure (described for the synthesis of racemic **10**), the deprotection reaction of enantiomerically enriched ***R*-36** (6.20 mg, 0.017 mmol) in CH_2Cl_2:TFA (1:1, 0.5 mL)

afforded desired tetracycle ***R*-10** (4.50 mg, 95%.) as yellow oil which was used in the next step without further purification. ***R*-10**: $[\alpha]_D^{20}$ = +18.0 ° [c = 0.1, $CHCl_3$].

(±)-(*E*)-3-ethylidene-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizine (1), (Deplancheine).[3,4,5]



Amide **10** (25.0 mg, 0.094 mmol) was dissolved in *t*-BuOH (2 mL) and $NaBH_4$ (37.8 mg, 0.10 mmol) was added then. Reaction mixture was refluxed with occasional addition of MeOH (0.5 mL) in portions for 6 h. When most of the starting material was consumed as indicated by TLC analysis (eluent EtOAc : hexanes = 4 : 1), the reaction mixture was cooled down to room temperature, water (1.5 mL) was added and excess of *t*-BuOH was removed in vacuo. The residue (containing *E*- and *Z*-deplancheine as 9:1 mixture) was purified by silica gel column chromatography, (eluent EtOAc : hexanes = 2 : 1) to yield (±)-*E*-deplancheine (**1**) (11.0 mg, 79 % based on recovered starting material) as yellowish gummy solid. For characterization purposes it was further purified via trituration in diethyl ether to yield (±)-E-deplancheine (**1**) (5.00 mg, 40 % based on recovered starting material) as white solid. The spectral data of **1** was in accordance with those reported in literature.[4,5]

(±)-1: R_f = 0.20 (EtOAc : hexanes = 4 : 1); mp = 137–140 °C (Lit.[3,4,5] mp = 140 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.55 – 1.61 (m, 1H), 1.64 (d, 3H, *J* = 7.0 Hz), 2.01 (br t, 1H, *J* = 10.0 Hz), 2.18 – 2.20 (m, 1H), 2.62 – 2.69 (m, 1H), 2.72 – 2.76 (m, 1H), 2.80 – 2.85 (m, 1H), 3.01 – 3.13 (m, 3H), 3.36 (d, 1H, *J* = 12.5 Hz), 3.42 – 3.45 (m, 1H), 5.45 (q, 1H, *J* = 7.0 Hz), 7.09 (td, 1H, *J* = 7.5, 1.0 Hz), 7.14 (td, 1H, *J* = 7.5, 1.0 Hz), 7.32 (d, 1H, *J* = 8.0 Hz), 7.48 (d, 1H, *J* = 8.0 Hz), 7.73 (brs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.9, 21.8, 26.1, 30.5, 53.1, 60.4, 63.6, 108.4, 110.9, 118.4, 119.6, 119.7, 121.6, 127.7, 134.1, 134.8, 136.4; IR (neat) cm^{-1} 3415s, 3123m, 2867s, 2790m, 1436m; mass spectrum (GC/MS, EI): m/e (% relative intensity) 252 (90) M^+, 251 (100), 237 (20), 223 (25), 169 (50), 156 (30); HRMS: m/e calcd for $C_{17}H_{21}N_2$ 253.1705 (M^++H), found 253.1678.

(*S*)–(–)-(*E*)-3-ethylidene-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizine (1), (Deplancheine).

According to the general procedure (described for the synthesis of racemic **1**), the reduction of tetracycle ***S*-10** (7.6 mg, 0.029 mmol) with $NaBH_4$ (11.0 mg, 0.3 mmol) in *t*-BuOH (1 mL) afforded enantiomerically enriched (–) deplancheine (***S*-1**) (1.6 mg, 78 % based on recovered starting material) as yellowish gummy solid upon purification on silica gel preparative TLC plate [eluent EtOAc : hexanes = 2 : 1].

***S*-(-)-1**: $[\alpha]_D^{20}$ = –26.0 ° [c = 0.2, $CHCl_3$]; 50 % ee (75 % *S*, 25 % *R*). Lit.[4] $[\alpha]_D^{20}$ = –52.0 ° [c = 1, $CHCl_3$].

(*R*)–(+)-(*E*)-3-ethylidene-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizine (1), (Deplancheine).

According to the general procedure (described for the synthesis of racemic **1**), the reduction of tetracycle ***R*-10** (4.50 mg, 0.017 mmol) with $NaBH_4$ (7.00 mg, 0.18 mmol) in *t*-BuOH (1 mL) afforded enantiomerically enriched (+) deplancheine (***R*-1**) (1.50 mg, 87 % based on recovered starting material) as yellowish gummy solid upon purification on silica gel preparative TLC plate [eluent EtOAc : hexanes = 2 : 1].

***R*-(+)-1**: $[\alpha]_D^{20}$ = +19.6 ° [c = 0.2, $CHCl_3$]; 43.5 % ee (31 % *S*, 69 % *R*). Lit.[4] $[\alpha]_D^{20}$ = +52.0 ° [c = 1, $CHCl_3$].

COMPARISON TABLES

Deplancheine, ^{13}C NMR.

δ, ppm (Allin)[5]	δ, ppm (observed)	Δ δ
12.7	12.9	0.2
21.6	21.8	0.2
25.9	26.1	0.2
30.3	30.5	0.2
52.9	53.1	0.2
60.2	60.4	0.2
63.5	63.6	0.1
108.4	108.4	0.0
110.7	110.9	0.2
118.2	118.4	0.2
119.4	119.6	0.2
119.4	119.7	0.3
121.3	121.6	0.3
127.4	127.7	0.3
134.0	134.1	0.1
134.6	134.8	0.2
136.0	136.4	0.4

Deplancheine, ^{1}H NMR.

δ, ppm (Allin)[5]	δ, ppm (observed)	Δ δ
1.52 – 1.60 (1H)	1.55 – 1.61 (1H)	
1.63 (3H)	1.64 (3H)	0.1
1.95 – 2.02 (1H)	2.01 (1H)	
2.15 – 2.20 (1H)	2.18 – 2.20 (1H)	
2.61 – 2.75 (2H)	2.62 – 2.69 (1H)	
	2.72 – 2.76 (1H)	
2.80 – 2.84 (1H)	2.80 – 2.85 (1H)	
2.98 – 3.11 (3H)	3.01 – 3.13 (3H)	
3.32 – 3.35 (1H)	3.36 (1H)	
3.38 – 3.41 (1H)	3.42 – 3.45 (1H)	
5.43 (1H)	5.45 (1H)	0.2
7.06 – 7.15 (2H)	7.09 (1H)	
	7.14 (1H)	
7.30 – 7.33 (1H)	7.32 (1H)	
7.46 – 7.48 (1H)	7.48 (1H)	
7.76 (1H)	7.73 (1H)	-0.3

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