Supplementary Information for:

Interfacing Whole Cell Biocatalysis with a Biocompatible Pictet-Spengler Reaction for One-Pot Syntheses of Tetrahydroisoquinolines and Tryptolines

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**General Methods**

Unless otherwise noted, all chemicals and solvents were used as received from commercial sources. Water (DI-water) used in biological procedures or as reaction solvent was deionized using a Barnstead E-pure Series 1090 water purification system (Thermo Fisher Scientific, USA.) Optima™ water (HPLC-grade water) was used to prepare HPLC samples (Fisher Chemical). A Sorvall Biofuge Stratos Centrifuge (Thermo Fisher Scientific, USA) was used to centrifuge samples in 15 mL or 50 mL polypropylene screw-cap centrifuge tubes. Liquid cultures were shaken in an I24 Incubator (New Brunswick Scientific, USA). Sterilization was carried out in a Sterilmatic Autoclave (Market Forge Industries, USA). Solvent evaporation were carried out with a USA Lab RE-200A rotary evaporator with a recirculating chiller (Propylene Glycol Power Pack H35G) set at 22 °F or on a Schlenk line equipped with a liquid nitrogen finger and an HFS VP2200 Vacuum Pump.

**High-Performance Liquid Chromatography**

HPLC with in-line UV detection and mass spectroscopy was carried out on an Agilent 1260 Infinity II equipped with an Agilent Poroshell 120 EC-C18 Threaded Column and paired with an Agilent InfinityLab LC/MSD iQ Mass Spectrometer in ESI® mode. All samples were diluted to 10-50 µg/mL in 1 mL HPLC-grade water with 0.1% formic acid for analysis. K. pasteuris samples were additionally filtered through 0.22 µm Luer lock syringe filters while G. oxydans samples were filtered through Celite®. An injection volume of 1.00 µL was used. Samples were eluted with an acetonitrile/water gradient at 0.400 mL/min over 10 min. Tryptamines were eluted with 3-60% v/v acetonitrile in water with 0.1% formic acid, while m-tyramines were eluted with 3-40% v/v acetonitrile in water with 0.1% formic acid. Column temperature was not controlled. UV absorbance was monitored at 280 nm with 4 nm bandwidth and written to the UV trace. Mass spectra were recorded from 50 to 250 m/z at one scan per second in Total Ion Count mode. Agilent OpenLab Data Analysis software was used to process the raw data, integrate TIC and UV spectra, and to extract mass spectra from the TIC. Microsoft Excel was used to construct calibration curves and perform calculations.

A calibration curve relating the HPLC-UV area fraction and mole fraction of m-tyramine and its butyraldehyde annulation products (4) was generated from twenty standards with varying proportions of the two analytes. Stock solutions (500 mg/mL) of m-tyramine·HCl and its butyraldehyde annulation products 4 (synthesized in-house according to Pesnot et al.) were prepared by dissolving 5.0 mg analyte in 10.0 mL LC-grade water. The stock solutions were combined in various proportions and diluted to 50 µg/mL net analyte concentration in LC-grade water. The standards were analyzed with HPLC-UV and used to generate the calibration curve. Both linear fits had slope ~1 and intercept ~0, suggesting that substrate and products had comparable molar absorption. Thus, the HPLC-UV area ratio was taken directly as the mole ratio. Mole ratio product was reported as conversion. Product distributions were taken as the area ratio of the corresponding HPLC-UV peaks. For pairs of regioisomeric products, the major-to-minor product ratio was designated the regioisomeric ratio (r.r.) and included alongside conversion.
**Figure S1.** Calibration curve for annulation of *m*-tyramine to its butyraldehyde annulation products. Area fraction is the ratio of the combined HPLC-UV area of the two regioisomeric annulation products to the total area of the *m*-tyramine and the products. Likewise, mole fraction represents the known molar ratio of the products to the products plus *m*-tyramine. A linear fit across the whole range failed to capture its slight curvature, so the data was broken into two segments of eleven and ten points that were fit independently. These curves were used to derive conversion (mole fraction product) from the HPLC-UV trace for annulations of *m*-tyramine with butyraldehyde.

**Nuclear Magnetic Resonance**

NMR spectra were acquired with a JEOL ECA-500 spectrometer operating at 500 MHz for proton spectra (¹H NMR) and 125 MHz for carbon-13 (¹³C NMR). NMR solvents CDCl₃, DMSO-D₆, and CD₃OD were acquired from Cambridge Isotope Laboratories. Chemical shifts are expressed as parts per million (ppm) and referenced to the residual solvent signal. ¹H NMR: CDCl₃, δ 7.26 ppm; DMSO-D₆, δ 2.50 ppm; and CD₃OD, 3.31 ppm. ¹³C NMR: CDCl₃, δ 77.16 ppm; DMSO-D₆, δ 39.50 ppm; and CD₃OD, 49.00 ppm. NMR spectra were processed and annotated with Mnova software from Mestrelab.

**Media, Strains, Culture Conditions**

YDP media was prepared as described by Stewart et al.² from 20 g/L peptone, 10 g/L yeast extract, and 20 g/L dextrose. pH was adjusted to 5.6 with 1 M HCl. The solution was autoclaved at 121 °C for 20 minutes.

Methanol media was prepared as described by Stewart et al.³ from 2.6 g/L monobasic potassium phosphate, 0.3 g/L dibasic potassium phosphate, 1.5 g/L ammonium sulfate, 0.3 g/L magnesium sulfate heptahydrate, 1 mg/L ferrous sulfate heptahydrate, 7 µg/L cupric sulfate pentahydrate, 10 µg/L manganese sulfate monohydrate, 120 µg/L zinc sulfate heptahydrate, 10 µg/L boric acid, and 1 g/L yeast extract in de-ionized water. pH was adjusted to 5.6 with 1 M HCl and 1 M NaOH. The solution was autoclaved at 121 °C for 40 minutes. After the solution had cooled, 10 g/L methanol was added.

Glycerol media was prepared as described by Stewart et al. (2020)⁴ from 1.4 g/L monobasic potassium phosphate, 10 g/L yeast extract, and 25 g/L glycerol in de-ionized
water. pH was adjusted to 5.0 with 1M HCl and 1M NaOH. The solution was autoclaved at 121 °C for 40 minutes.

Freeze-dried Komagataella pastoris ATCC® 28485TM was cultured in YDP media under air with ample headspace at 30 °C to mid-exponential phase (~48 hours). The K. pastoris cultures were diluted 1:1 with 20% glucose then left to rest for 15 minutes. The diluted cell cultures were then divided in 1 mL aliquots in cryogenic tubes, placed in an insulated Styrofoam cooler and frozen at -80 °C. Frozen K. pastoris were cultured in methanol media to induce alcohol oxidase expression. Freeze-dried Gluconobacter oxydans ATCC® 621 were cultured in glycerol media to induce alcohol dehydrogenase expression.

**K. pastoris Tandem System**

*K. pastoris* was cultured from frozen stock in ~125 mL methanol media with ~875 mL air headspace in a shaker incubator at 28 °C and 180 rpm. After 72 hours, 10 mL cell cultures were pelleted at 500 × g for 10 min, re-suspended in 10 mL KPi buffer, pelleted again, and resuspended once more in 10 mL KPi buffer. The 10 mL cell suspensions were transferred to 125 mL screw-cap flasks. The amine substrate was added, followed by the alcohol. The flasks were capped and incubated in a shaker incubator at 28 °C and 180 rpm. After 48 h, reactions were sampled for HPLC analysis. HPLC samples were prepared by filtering ~10 uL reaction media through 0.22 µm Luer lock syringe filters and then diluting the filtrate 100-fold into HPLC-grade water.

Optimization reactions used *m*-tyramine and *n*-butanol substrates at varied stoichiometries and a range of KPi buffer concentrations and pH ([Table 1](#)). The time-course reaction ([Figure S2](#)) used *m*-tyramine (300 µmol) and 1-butanol (600 µmol) in 10 mL pH 6.3, 200 mM KPi. Alcohol scope reactions used *m*-tyramine·HCl (300 µmol) and methanol, ethanol, 1-propanol, 1-butanol, 1-hexanol, isobutyl alcohol, or isoamyl alcohol (600 µmol) in 10 mL pH 6.3 200 mM KPi ([Table 2](#)). Tryptamine scope reactions used tryptamine·HCl, serotonin·HCl, or 5-methoxytryptamine·HCl (300 µmol) and 1-butanol (600 µmol) in 10 mL pH 6.7 250 mM KPi ([Table 6](#)).

![Figure S1](#)  Time-course conversion of *m*-tyramine to the annulation product in the optimized *K. pastoris* tandem system. Reaction conditions: KPi (200 mM, pH 6.3), *m*-tyramine (30 mM), 1-butanol (60 mM), 28 °C, 180 rpm. The reaction was sampled at each
timepoint and promptly returned to the incubator. Conversion was determined by HPLC-UV.

**G. oxydans Tandem System**

*G. oxydans* was cultured from freeze-dried pellet in ~125 mL glycerol media with ~875 mL air headspace in a shaker incubator at 28 °C and 180 rpm. After 48 hours, 10 mL cell cultures were pelleted at 6000 × g for 10 min, re-suspended in 10 mL KPi buffer, pellet again, and resuspended once more in 10 mL KPi buffer. The 10 mL cell suspensions were transferred to 125 mL screw-cap flasks. The amine substrate was added, followed by the alcohol. The flasks were capped and incubated in a shaker incubator at 28 °C and 180 rpm. After some time, reactions were sampled for HPLC analysis. HPLC samples were prepared by filtering ~10 uL reaction media through celite on a cotton plug and then diluting the filtrate 100-fold into HPLC-grade water. Celite was used instead of syringe filters because the latter swiftly clogged with *G. oxydans*.

Optimization reactions used *m*-tyramine and *n*-butanol substrates at varied stoichiometries and a range of KPi buffer concentrations and pH (Table 3). The time course reaction (Figure S3) used *m*-tyramine (300 µmol) and *n*-butanol (600 µmol) in 10 mL pH 6.7, 250 mM KPi. Alcohol scope reactions used *m*-tyramine (300 µmol) and ethanol, 1-propanol, 1-butanol, 1-pentanol, 1-hexanol, isobutyl alcohol, isoamyl alcohol, benzyl alcohol, 2-phenylethanol, 2-(4-hydroxyphenyl)ethanol, or 2-methoxyethanol (600 µmol) in 10 mL pH 6.7 250 mM KPi (Table 4). *m*-tyramine scope reactions used *m*-tyramine-HCl, dopamine-HCl, norfenefrine-HCl, or *m*-tyrosine-HCl (300 µmol) and 1-butanol (600 µmol) in 10 mL pH 6.7 250 mM KPi (Table 5). Tryptamine scope reactions used tryptamine-HCl, serotonin-HCl, or 5-methoxytryptamine-HCl (300 µmol) and 1-butanol (600 µmol) in 10 mL pH 6.7 250 mM KPi (Table 6).

![Figure S2](image-url) **Figure S2.** Time-course conversion of *m*-tyramine to the annulation product in the optimized *G. oxydans* tandem system. Reaction conditions: KPi (250 mM, pH 6.7), *m*-tyramine (30 mM), 1-butanol (60 mM), 28 °C, 180 rpm. The reaction was sampled at each timepoint and promptly returned to the incubator. Conversion was determined by HPLC-UV. Conversion plateaued at 84% after four hours. Sub-quantitative conversion was attributed to evaporative loss of butanol and butyraldehyde from the headspace at each sampling. The reaction was spiked with an additional 30 mM 1-butanol at 8 h and reached quantitative conversion overnight.
**G. oxydans oxidation of 2-phenylethanol**

G. *oxydans* was cultured from freeze-dried pellet in ~125 mL glycerol media with ~875 mL air headspace in a shaker incubator at 28 °C and 180 rpm. After 48 hours, 10 mL cell culture was pelleted at 6000 x g for 10 min, re-suspended in 10 mL 250 mM pH 6.7 KPi buffer, pelleted again, and resuspended once more in 10 mL KPi buffer. The 10 mL cell suspension was transferred to a 125 mL screw-cap flasks. 2-phenylethanol (10 mM, 12 µL) was added. The flask was capped and incubated in a shaker incubator at 28 °C and 180 rpm for 24 h. After 24 h, the reaction was extracted with 1 × 2 mL CDCl₃. ¹HNMR was performed on the extract to gauge the relative abundance of 2-phenylethanol and phenylacetaldehyde (Figure S4). ¹HNMR revealed 2.7:1 alcohol/aldehyde, indicating *G. oxydans* had produced less than 3 mM aldehyde from 10 mM alcohol over 24 h. This shows that *G. oxydans* do not oxidize 2-phenylethanol at requisite concentrations under comparable conditions and timeframe to the tandem system.

**Figure S3.** ¹HNMR spectrum (CDCl₃, 500 MHz) of the extract from the *G. oxydans* oxidation of 2-phenylethanol. The alpha proton signals (2-phenylethanol, δ 3.86 ppm, 2H; phenylacetaldehyde, δ 9.75 ppm, 1H) were integrated to gauge relative abundance of the two species.

**Pictet-Spengler reactions of Tryptamines**

5-methoxytryptamine and butyraldehyde were used as model tryptamine and aldehyde substrates, respectively, to explore the potential for tryptamines to participate in phosphate-catalyzed Pictet-Spengler annulation. 5-methoxytryptamine was selected...
because Callaway et al. found that it outperformed serotonin and tryptamine in the annulation with acetaldehyde under physiological conditions.

**Figure S4.** Time-course conversion of 5-methoxytryptamine to 15 in the Pictet-Spengler reaction with butyraldehyde for HEPES buffer and KPi buffer at different concentrations. Shown are time-course plots for 10 mM KPi (blue triangles), 50 mM KPi (orange squares), 250 mM KPi (black circles), and 50 mM HEPES (yellow diamonds). Reaction conditions: Aqueous buffer (10 mL), 5-methoxytryptamine·HCl (68 mg), butyraldehyde (54 µL), pH 6.7, 28 °C, 180 rpm. The reaction was sampled for HPLC at each timepoint and promptly returned to the incubator. Conversion was determined by HPLC.
Figure S5. Time-course conversion of 5-methoxytryptamine to 15 in the Pictet-Spengler reaction with butyraldehyde. Shown are product distributions at the indicated timepoint for 15 (grey), intermediate (orange), and starting 5-methoxytryptamine (blue). Reaction conditions: KPi (10 mL, 250 mM), 5-methoxytryptamine·HCl (68 mg), butyraldehyde (54 µL), pH 6.7, 28 °C, 180 rpm. The reaction was sampled for HPLC at each timepoint and promptly returned to the incubator. The species distribution was determined by HPLC.

Synthesis and isolation of tetrahydroisoquinolines (m-tyramine adducts)

General protocol: The β-arylethylamine·HCl salt (300 µmol) and alcohol (600 µmol) were added to live G. oxydans cells suspended in 10 mL 250 mM pH 6.7 KPi in a 250 mL flask under air. For reactions of dopamine, ascorbic acid (10 mM) was also included as a sacrificial reductant. The flask was capped and incubated at 28 °C and 180 rpm for 48 h. At 12 h, the reaction was sampled for HPLC. To the reaction mixture, 3 g NaCl, 1 g Na₂SO₃, and 1 g K₂CO₃ were added. The aqueous mixture was extracted with 3 × 10 mL ethyl acetate. This selectively extracted tetrahydroisoquinoline products while unreacted m-tyramines remained in the aqueous phase. Centrifugation (20,000 g × 5 min) was used to break the emulsion at each extraction. The combined ethyl acetate layers were washed with pH 10 NaCl/Na₂SO₃/K₂CO₃ brine. Solvent removal via low-vacuum warm rotary evaporation caused product to oxidize, as evidenced by yellowing. Instead, the solvent was removed with high-vacuum on a Schlenk line, and the sample allowed to cool from solvent evaporation. This afforded the isolated product as mixed regioisomers. Only the major a regioisomer is depicted and assigned. All spectra contain a water peak (3.3 ppm in CD₃OD, and in DMSO) in addition to the DMSO or CD₃OD solvent peak.

1-methyl-1,2,3,4-tetrahydroisoquinolin-6-ol (2): m-tyramine·HCl (54 mg) and ethanol (45 µL) were used in the general protocol. HPLC indicated 100% conversion after 12 h with 27:1 2a/2b. The combined ethyl acetate layers were concentrated in vacuo to give 2 as a white solid (32 mg, 63% yield). ¹H NMR (500 MHz, CDCl₃) δ 6.95 (d, J = 9.2 Hz, 1H), 6.56 (d, J = 8.8 Hz, 1H), 6.48 (s, 1H), 3.93 (q, J = 6.8 Hz, 1H), 1.39 (d, J = 6.5 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 155.37, 135.32, 130.54, 126.63, 115.09, 113.24, 50.46, 42.05, 28.93, 21.01.
1-ethyl-1,2,3,4-tetrahydroisoquinolin-6-ol (3): *m*-tyramine·HCl (53 mg) and 1-propanol (50 µL) were used in the general protocol. HPLC indicated 92% conversion after 12 h with 32:1 3a/3b. The combined ethyl acetate layers were concentrated in vacuo to give 3 as a white solid (49 mg, 91% yield). $^1$H NMR (500 MHz, CDCl$_3$) δ 6.94 (d, J = 8.1 Hz, 1H), 6.56 (dd, J = 2.6, 8.5 Hz, 1H), 6.48 (d, J = 2.9 Hz, 1H), 3.76 (m, 1H), 3.15 (dt, J = 4.5, 11.8 Hz, 1H), 2.85 (m, 1H), 2.75 (m, 1H), 2.64 (m, 2H), 1.88 (m, 1H), 1.67 (m, 1H), 0.97 (t, J = 7.6 Hz, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 155.38, 135.79, 129.88, 114.76, 113.19, 55.95, 39.93, 28.97, 28.39, 9.28.

1-propyl-1,2,3,4-tetrahydroisoquinolin-6-ol (4): *m*-tyramine·HCl (55 mg) and 1-butanol (55 µL) were used in the general protocol. HPLC indicated 97% conversion after 12 h with 30:1 4a/4b. The combined ethyl acetate layers were concentrated in vacuo to give 4 as a white solid (38 mg, 62% yield). $^1$H NMR (500 MHz, CDCl$_3$) δ 6.94 (d, J = 8.2 Hz, 1H), 6.55 (d, J = 8.7 Hz, 1H), 6.47 (s, 1H), 3.83 (m, 1H), 3.14 (m, 1H), 2.84 (m, 1H), 2.75 (m, 1H), 2.65 (m, 1H), 1.78 (m, 1H), 1.64 (m, 1H), 1.43 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 155.25, 135.70, 130.41, 127.41, 114.73, 113.15, 55.57, 39.56, 38.31, 29.49, 18.85, 13.63.

4 was also prepared from *m*-tyramine and butyraldehyde according to a protocol adapted from Pesnot et al. $^1$ *m*-tyramine·HCl (63 mg) and butyraldehyde (32 µL) were incubated in pH 6.0 100 mM KPi at 50 °C for 24 h. After 24 h, the reaction was sampled for HPLC, which showed 20:1 4a/4b and incomplete conversion. K$_2$CO$_3$ brine was used to adjust the pH to 10, and the reaction was extracted into 2 mL CDCl$_3$. The solvent was removed in vacuo to give 4 as a white solid. $^1$H NMR and HPLC were performed in order to confirm product identity and purity, respectively. 4 generated in this manner was used to generate calibration curves for Figure S1.

1-butyl-1,2,3,4-tetrahydroisoquinolin-6-ol (5): *m*-tyramine·HCl (54 mg) and 1-pentanol (65 µL) were used in the general protocol. HPLC indicated 100% conversion after 12 h with 28:1 5a/5b. The combined ethyl acetate layers were concentrated in vacuo to give 5 as a white solid (45 mg, 70% yield). $^1$H NMR (500 MHz, CDCl$_3$) δ 6.93 (d, J = 8.6 Hz, 1H), 6.56 (d, J = 8.2 Hz, 1H), 6.48 (s, 1H), 3.82 (m, 1H), 3.14 (m, 1H), 2.83 (m, 1H), 2.76 (m, 1H), 2.65 (m, 1H), 1.82 (m, 1H), 1.65 (m, 1H), 1.37 (m, 4H), 0.93 (t, J = 6.1 Hz, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 155.96, 135.71, 130.41, 127.41, 114.73, 113.17, 55.12, 40.95, 35.72, 30.02, 27.90, 22.63, 15.93.

1-isobutyl-1,2,3,4-tetrahydroisoquinolin-6-ol (8): *m*-tyramine·HCl (49 mg) and isoamyl alcohol (65 µL) were used in the general protocol. HPLC indicated 100% conversion after 12 h with 28:1 8a/8b. The combined ethyl acetate layers were concentrated in vacuo to give 8 as a white solid (43 mg, 74% yield). $^1$H NMR (500 MHz, CDCl$_3$) δ 6.90 (d, J = 8.6 Hz, 1H), 6.56 (d, J = 8.2 Hz, 1H), 6.48 (s, 1H), 3.88 (dd, J = 4.1, 9.9 Hz, 1H), 3.12 (dt, J = 5.3, 12.4 Hz, 1H), 2.85 (m, 1H), 2.75 (m, 1H), 2.67 (m, 1H), 1.83 (m, 1H), 1.56 (m, 2H), 0.97 (dd, J = 6.7, 17.1 Hz, 6H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 155.19, 136.14, 131.11, 126.91, 115.79, 113.14, 53.86, 45.82, 40.12, 28.92, 24.30, 23.08, 20.44.
1-isobutyl-1,2,3,4-tetrahydroisoquinolin-6-ol (9): m-tyramine·HCl (47 mg) and 2-methoxy ethanol (47 µL) were used in the general protocol. HPLC indicated 65% conversion after 12 h with 5:1 9a/9b. The combined ethyl acetate layers were concentrated in vacuo to give 9 as an off-white solid (30 mg, 57% yield). The high proportion of the minor regioisomer convoluted the NMR spectra (Figure S20-21). ¹H NMR (500 MHz, CDCl₃) δ 6.96 (d, J = 7.8 Hz, 1H), 6.57 (d, J = 8.6 Hz, 1H), 6.50 (s, J = Hz, 1H), 4.01 (m, 1H), 3.60 (m, 1H), 3.52 (m, 1H), 3.38 (s, 3H), 2.86 (m, 2H), 2.72 (t, J = 12.0 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 156.34, 135.29, 130.41, 127.10, 114.97, 113.86, 74.86, 59.91, 55.41, 39.93, 29.81.

Synthesis and isolation of tryptolines (tryptamine adducts)

General protocol: The tryptamine·HCl salt (300 µmol) and 1-butanol (600 µmol, 55 µL) were added to live K. pastoris cells suspended in 10 mL 200 mM pH 6.3 KPi in a 250 mL flask under air. The flask was capped and incubated at 28 °C and 180 rpm for 48 h. At 48 h the reaction was sampled for HPLC. To the reaction mixture, 3 g NaCl, 1 g Na₂SO₃, and 1 g K₂CO₃ were added. The aqueous mixture was extracted with 3 × 10 mL ethyl acetate. This extracted both the tryptoline products and unreacted tryptamine starting material. Centrifugation (20,000 g × 5 min) was used to break the emulsion at each extraction. The ethyl acetate layers were combined and the solvent removed by rotary evaporation at 45 °C to yield the crude product as a yellow oil. The crude product was taken up into 10% methanol in methylene chloride and then purified by flask chromatography on silica, eluting with 10% methanol in methylene chloride.

1-propyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (13): Tryptamine·HCl (58 mg) was used in the general protocol. HPLC indicated 12% conversion after 48 h. The fractions containing only the tryptoline product were identified by TLC with I₂ staining and concentrated in vacuo to give a yellow wax (7 mg, 11% yield). ¹H NMR (500 MHz, DMSO-D₆) δ 10.89 (s, 1H), 7.36 (d, J = 10.0 Hz, 1H), 7.02 (t, J = 10 Hz, 1H), 6.94 (t, J = 7.5 Hz, 1H), 4.26 (d, J = 5 Hz, 1H), 3.32 (m, 1H), 3.03 (m, 1H), 2.37 (m, 2H), 1.97 (m, 1H), 1.70 (m, 1H), 1.47 (m, 1H), 0.92 (t, J = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 136.86, 134.23, 126.96, 122.87, 119.98, 118.20, 113.51, 108.59, 55.32, 43.98, 37.08, 25.69, 18.84, 14.48.

1-propyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-7-ol (18): Serotonin·HCl (59 mg) was used in the general protocol. HPLC indicated 53% conversion after 48 h. The fractions containing only the tryptoline product were identified by TLC with I₂ staining and concentrated in vacuo to give an off-white solid (28 mg, 44% yield). ¹H NMR (500 MHz, DMSO-D₆) δ 10.35 (s, 1H), 8.51 (bs, 1H), 7.02 (d, J = 10 Hz, 1H), 6.63 (d, J = 2.3 Hz, 1H), 6.49 (dd, J = 8.4, 2.3 Hz, 1H), 3.96 (d, J = 5.5 Hz, 1H), 3.15 (dt, J = 12.5, 2.5 Hz), 2.85 (m, 1H), 2.50 (m, 2H), 1.84 (m, 1H), 1.55 (m, 1H), 1.42 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 151.91, 138.12, 131.19, 128.08, 112.52, 110.47, 106.13, 102.29, 54.68, 45.46, 37.03, 26.55, 19.85, 19.85, 19.85, 14.62.
7-methoxy-1-propyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (19): 5-methoxytryptamine·HCl (61 mg) used in the general protocol. HPLC indicated 56% conversion after 48 h. The fractions containing only the tryptoline product were identified by TLC with I$_2$ staining and concentrated in vacuo to give a white solid (27 mg, 41% yield). $^1$H NMR (500 MHz, DMSO-D$_6$) δ 10.55 (s, 1H), 7.13 (d, $J$ = 8.6 Hz, 1H), 6.83 (d, $J$ = 2.1 Hz, 1H), 6.62 (dd, $J$ = 8.9, 2.7 Hz, 1H), 4.02 (d, $J$ = 7.2 Hz, 1H), 3.70 (s, 3H), 3.20 (dt, $J$ = 12.4, 4.6 Hz, 1H), 2.89 (m, 1H), 2.58 (m, 2H), 1.87 (m, 1H), 1.58 (m, 1H), 1.43 (m, 2H), 0.90 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 153.56, 137.01, 131.30, 127.64, 113.87, 110.76, 107.17, 102.57, 63.45, 51.65, 42.26, 37.73, 22.00, 20.19, 15.15.
Figure S10. $^1$HNMR spectrum of 2 in CD$_3$OD.
Figure S11. $^{13}$CNMR spectrum of 2 in CD$_3$OD.
Figure S12. $^1$HNMR spectrum of 3 in CD$_3$OD.
Figure S13. $^{13}$CNMR spectrum of 3 in CD$_3$OD.
Figure S14. $^1$H NMR spectrum of 4 in CD$_3$OD.
Figure S15. $^{13}$C NMR spectrum of 4 in CD$_3$OD.
Figure S16. $^1$H NMR spectrum of 5 in CD$_3$OD.
Figure S17. $^{13}$C NMR spectrum of 5 in CD$_3$OD.
Figure S18. $^1$HNMR spectrum of 8 in CD$_2$OD.
Figure S19. $^{13}$C NMR spectrum of 8 in CD$_3$OD.
Figure S20. $^1$HNMR spectrum of 9 in CD$_3$OD. This reaction gave an unusually high proportion of the minor regioisomer (5:1 vs. the usual 30:1), which complicated NMR spectra.
Figure S21. $^{13}$CNMR spectrum of 9 in CD$_3$OD. This reaction gave an unusually high proportion of the minor regioisomer (5:1 vs. the usual 30:1), which complicated NMR spectra.
Figure S22. $^1$HNMR spectrum of 17 in DMSO-d$_6$. 
Figure S23. $^{13}$CNMR spectrum of 17 in DMSO-d$_6$
Figure S24. $^1$HNMR spectrum of 18 in DMSO-d$_6$. 
Figure S25. $^{13}$C NMR spectrum of 18 in DMSO-d$_6$. 
Figure S26. $^1$HNMR spectrum of 19 in DMSO-d$_6$. 
Figure S27. $^{13}$C NMR spectrum of 19 in DMSO-$d_6$. 