Supporting information

An Expedient Protecting Group-Free Total Synthesis of (±)-Dievodiamine

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General Information

All reactions were performed in oven-dried glassware under an atmosphere of argon unless specified otherwise. Anhydrous dichloromethane, DMF, toluene were obtained from an Innovative Technology Pure Solv solvent purification system by passing the solvent through activated alumina and copper catalyst columns, as appropriate. Anhydrous THF was obtained by distillation over sodium benzophenone ketyl immediately before use. Anhydrous benzene was obtained by distillation over calcium hydride and stored over 4 Å molecular sieves. All other reagents and solvents were used without further purification from commercial sources. Petrol refers to the fractions of petroleum ether which boil between 40 and 60 °C. Aqueous solutions are saturated unless specified otherwise. Flash column chromatography was carried out using Merck Kieselgel (40–63 μm particle size). Analytical thin layer chromatography (TLC) was performed using pre-coated plastic-backed plates (Fluka Kieselgel 60 F254), and visualised by ultra-violet irradiation (254 nm) and by staining with either basic aqueous potassium permanganate or ethanolic p- amialsaldehyde as appropriate. 1H NMR and 13C NMR spectra were recorded on a Jeol ECX-400 NMR or Jeol ECS400 spectrometer operating 400 MHz and 100 MHz, respectively, or on a Brucker DRX500 spectrometer, operating at 500 MHz and 125 MHz, respectively. All spectra was acquired at 295 K. Chemical shifts (δ) are quoted in parts per million (ppm). Couplings constants (J) are reported in Hertz (Hz) to the nearest 0.1 Hz. The multiplicity abbreviations used are: s, singlet; d, doublet; t, triplet; q, quartet; multiplet; br, broad or combinations of these. Where coincident coupling constants have been observed in the NMR spectrum, the apparent multiplicity of the proton resonance concerned is reported. Signal assignment was achieved by analysis of DEPT, COSY, NOESY, HMBC and HSQC experiments where required. The residual solvent peak, δH 7.26 and δC 77.0 for CDCl3 and δH 2.50 and δC 39.50 for (CD3)2SO was used as a reference. Infrared spectra (IR) were recorded on a ThermoNicolet IR-100 spectrometer with NaCl plates as a thin film or Perkin Elmer FT-IR spectrometer dispersed from either CH2Cl2 or CDCl3. High Resolution Mass Spectra (HRMS) were obtained by University of York Mass spectrometer Service, using ionisation (ESI) on a Bruker Daltonics, MicrOTOF spectrometer. Melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. All numbering on the structures below is for the benefit of structure characterization and does not conform to IUPAC rules. Compounds 7, 8, 10, 16 were all purchased from Sigma–Aldrich and used as supplied.
Experimental

2,3,4,9-Tetrahydro-1H-pyrido[3,4-b]indol-1-one (9):

Dimethylphosphoryl azide (3.42 mL, 15.8 mmol) was added dropwise to a stirred solution of indole-3-propionic acid 8 (3.00 g, 15.8 mmol) and NEt₃ (2.06 mL, 15.8 mmol) in toluene (47.6 mL) at RT under N₂. The reaction was then heated with stirring at 90 °C for 90 min. Most of the solvent was removed under reduced pressure to afford mobile oil. After cooling to 0 °C, BF₃·OEt₂ (7.95 mL, 193 mmol) was added dropwise to the rapidly stirred mixture, which was then warmed to RT and stirred for 16 h. The reaction was basified with 1 M aq. NaOH (to pH = 10) and EtOAc (64 mL) was added. The rapidly stirred mixture was heated at 50 °C for 1 h, until all the crude material was dissolved. The reaction mixture was cooled to RT and extracted with EtOAc (3 × 100 mL), washed with brine (100 mL), and then dried over MgSO₄. Purification by column chromatography (SiO₂, 1:1 petrol: ethyl acetate → pure EtOAc) afforded the title compound as a colorless oil. (2.78 g, 94%); Rf 0.3; δH (400 MHz, DMSO-d₆) 11.59 (1H, br s, NH-12), 7.59–7.57 (2H, m, H-6/9, NH-13), 7.38 (1H, d, J = 8.2 Hz, H-6/9), 7.21 (1H, dd, J = 8.2, 7.0 Hz, H-7/8), 7.05 (1H, dd, J = 8.2, 7.0 Hz, H-7/8), 3.50 (2H, t, J = 7.0 Hz, H-2), 2.91 (2H, t, J = 7.0 Hz, H-3); HRMS (ESI⁺): Found: 187.0861; C₁₁H₁₁N₂O (MH⁺) Requires: 187.0866 (2.4 ppm error); Found: 209.0685; C₁₁H₁₀N₂NaO (MH⁺) Requires: 209.0685 (1.4 ppm error); Spectral data corresponds to those reported in the literature.¹

Dehydroevodiamine hydrochloride (4):²

To a round bottom flask containing 2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-one 9

¹ Judd, K.E.; Mahon, M.F.; Caggiano, L. Synthesis 2009, 2809.
(8.85 g, 47.5 mmol) in toluene (400 mL), methyl atryanilate 10 (9.27 mL, 63.2 mmol) was added at RT. Then POCl₃ (29.4 mL, 316 mmol) was added and the resulting pale orange solution was heated at 110 °C for 1 h before pouring carefully into ice cold water (2 L). The resultant precipitate was isolated by filtration, washed with water (1 L) and collected with MeOH, concentrated and dried under high vacuum, affording the title compound as a yellow solid (16.1 g, 88 %); mp: 204–207 °C νmax (thin film)/cm⁻¹ 1703, 1544, 1499, 1425, 1335, 1207, 1103, 769, 683, 520; δH (400 MHz, DMSO-d6) 8.35 (1H, dd, J = 7.9, 1.5 Hz, ArH), 8.20–8.11 (2H, m, ArH), 7.88 (1H, d, J = 8.1 Hz, ArH), 7.82–7.78 (1H, m, ArH), 7.73 (1H, d, J = 8.3 Hz, ArH), 7.52 (1H, ddd, J = 8.3, 6.9, 1.0 Hz, ArH), 7.27 (1H, ddd, J = 8.1, 6.9, 1.0 Hz, ArH), 4.47 (2H, t, J = 6.7 Hz, H-2), 4.41 (3H, s, H-19), 3.33 (2H, t, J = 6.7 Hz, H-3); δC (100 MHz, DMSO-d6) 158.2 (C-12), 150.0 (Ar-C), 141.4 (Ar-C), 139.6 (Ar-C), 136.6 (Ar-CH), 130.1 (Ar-C), 128.7 (Ar-CH), 128.6 (Ar-CH), 127.7 (Ar-CH), 123.3 (Ar-C), 121.6 (Ar-CH), 121.5 (Ar-CH), 120.1 (Ar-C), 118.7 (Ar-C), 118.5 (Ar-CH), 113.6 (Ar-CH), 42.0 (C-2), 41.0 (C-19), 18.5 (C-3); HRMS (ESI⁺): Found: 302.1274; C₁₉H₁₆N₃O (MH⁺) Requires: 302.1288 (4.7 ppm error);


**Procedure A:**
n-BuLi (1.6 M, 2.78 mL, 4.44 mmol) was added to a solution of trimethylsilylacetylene (0.84 mL, 5.92 mmol) in THF (15 mL) at −78 °C and the mixture was stirred for 30 min. The resulting ((trimethylsilyl)ethynyl) lithium solution was then added to a suspension of DHED salt 4 (500 mg, 1.48 mmol) in THF (15 mL) at −78 °C via cannula. The mixture was stirred at −78 °C for 30 min and then allowed to stir at RT for another 30 min before quenching with water (30 mL). Following extraction with DCM (3 x 30 mL), the organic phase was washed with water (2 x 20 mL) and brine (20 mL), and then dried over MgSO₄, filtered and concentrated in vacuo affording 14-methyl-13b-[(trimethylsilyl)ethynyl]-8,13,13b,14-tetra hydro indolo [2′,3′:3,4] pyrido [2,1b] quinazoli-5(7H)-one 11 as an orange solid. The crude material was used directly to the next step without further purification. TBAF (1 M, 1.78 mL, 1.78 mmol) was added to a solution of alkyne 11 at 0 °C in THF (15.8 mL) and the resulting solution was stirred at 0 °C for 10 min. Then, the reaction mixture was poured into the water, extracted with ether (3 x 30
ml) and then dried over MgSO₄, filtered and concentrated in vacuo affording the title compound as an orange solid (435 mg, 90%).

**Procedure B:**

Ethynylmagnesium chloride (0.750 mL, 0.375 mmol) was added to a stirred suspension of DHED salt 4 (42.2 mg, 0.125 mmol) in toluene (1.5 mL) at 0 °C. Then LiCl (16.9 mg, 0.400 mmol) was added. The reaction mixture was stirred for 5 mins at 0 °C and then allowed to warm at RT and stirred for an additional 1 h before quenching with water (20 mL). Following extraction with DCM (3 x 20 mL), the organic phase was washed with water (2 x 20 mL) and brine (20 mL), and then dried over MgSO₄, filtered and concentrated in vacuo affording the title compound as an orange solid (30.3 mg, 74%).

Rf 0.4 (3:1 petrol: ethyl acetate); mp: 220–223 °C; νmax (thin film)/cm⁻¹ 3194, 1597, 1554, 1443, 1397, 1329, 1294, 1243, 1219, 740, 717; δH (400 MHz, DMSO-d₆) 11.64 (1H, br s, NH), 7.98 (1H, dd, J = 7.7, 1.5 Hz, ArH), 7.64–7.59 (2H, m, ArH), 7.46 (1H, d, J = 8.1 Hz, ArH), 7.31–7.21 (m, 3H), 7.1 (1H, ddd, J = 7.1, 7.1, 1.0 Hz, ArH), 4.90–4.86 (1H, m, H-2a), 3.60 (1H, s, H-21), 3.10–2.99 (2H, m, H-2b, H3a), 2.87–2.78 (1H, m, H-3b), 2.58 (3H, s, H-19); δC (100 MHz, DMSO-d₆) 162.8 (C-12), 148.7 (Ar-C), 136.9 (Ar-C), 133.6 (Ar-CH), 128.5 (Ar- C), 127.8 (Ar-CH), 125.1 (Ar-CH), 123.0 (Ar-CH), 122.6 (Ar-CH), 121.8 (Ar-C), 121.2 (Ar-CH), 119.1 (Ar-CH), 118.9 (Ar-CH), 111.9 (Ar-C/CH), 111.8 (Ar-C/CH), 82.0 (C-1/20), 75.1 (C-1/20), 69.7 (C-21), 38.0 (C-2), 36.9 (C-19), 20.1 (C-3); HRMS (ESI⁺): Found: 328.1453; C₂₁H₁₈N₃O (MH⁺) Requires: 328.1444 (2.5 ppm error).


Tributyltin hydride (1.02 mL, 3.77 mmol) was added to a mixture of alkyne 12 (1.00 g, 3.05 mmol) and AIBN (94.2 mg, 0.611 mmol) in degassed benzene (15.3 mL). The rapidly stirred suspension was heated at 100 °C for 1 h. The solvent was removed in vacuo. Purification by column chromatography (SiO₂, pure petrol → 19:1 petrol:ethyl acetate → 10:1 petrol: ethyl acetate) afforded the title compound as an orange oil (1.02 g, 54 %); Rf 0.5 (3:1 petrol:ethyl acetate); mp: 148–154 °C; νmax (thin film)/cm⁻¹ 2911, 2879, 2826, 2808, 1607, 1581, 1446,
H, Ar – H, 0.68 (m, 6 H, Ar-H), 7.28 (1H, m, ArH), 7.19–7.11 (3H, m, ArH), 6.18 (1H, d, J = 18.9 Hz, H-20/21), 5.97 (1H, d, J = 18.9 Hz, H-20/21), 5.16 (1H, ddd, J = 12.9, 4.9, 1.6 Hz, H-2eq), 3.21 (1H, ddd, J = 12.9, 11.5, 4.4 Hz, H-2ax), 3.03–2.88 (2H, m, H-3a,b), 2.45 (3H, s, H-19), 1.27–1.08 (12H, n-Bu (CH_2)), 0.81–0.77 (m, 9H, n-Bu (CH_3)), 0.72–0.68 (m, 6H, n-Bu (CH_2)); δ_C (100 MHz, CDCl_3) 163.7 (C-2), 152.3 (Ar-C), 144.7 (C-20/21), 136.7 (Ar-C), 132.9 (Ar-CH), 130.5 (C-20/21), 130.3 (Ar-CH), 128.4 (Ar-CH), 126.3 (Ar-C), 125.0 (Ar-C), 124.3 (Ar-CH), 123.9 (Ar-CH), 123.0 (Ar-CH), 120.0 (Ar-CH), 119.0 (Ar-CH), 113.2 (Ar-C), 111.4 (Ar-C), 100.0 (C-1), 40.1 (C-19), 38.8 (C-2), 28.9 (n-Bu (CH_2)), 27.2 (n-Bu (CH_2)), 20.7 (C-3), 13.7 (n-Bu (CH_3)), 9.5 (n-Bu (CH_2)); HRMS (ESI^+): Found: 620.2641; C_{33}H_{46}N_3OSn (MH^+) Requires: 620.2664 (2.7 ppm error).

2-(1H-Indol-2-yl)-1-methylquinazolin-4(1H)-one (15):

To a solution of indole-2-carboxylic acid 7 (5.00 g, 31.0 mmol) in CHCl_3, (352 mL) oxalyl chloride (4.42 mL, 52.3 mmol) and 2 drops of DMF were added. The reaction was heated to reflux (70 °C) for 1 h. Then the solvent was evaporated to dryness in vacuo to give indole-2-carbonyl chloride 13. The residue was taken up with CHCl_3 (763 mL) and DMAP (462 mg, 3.78 mmol) and aniline 6 (16.0 g, 107 mmol) were added. The reaction mixture was stirred at 70 °C for 1 h, before quenching with water (800 mL). Following extraction with DCM (3 x 800 mL), the organic phase was washed with water (2 x 500 mL) and brine (500 mL), and then dried over MgSO_4, filtered and concentrated in vacuo affording amide 14 as an orange solid. [mp: 185–188 °C; ν_{max} (thin film)/cm^{-1} 3128, 1643, 1596, 1550, 1497, 1400, 1371, 1322, 738, 723; δ_H (400 MHz, DMSO-d_6) 11.51 (1H, br s, NH), 7.69 (1H, br, NH), 7.64–7.62 (1H, m, ArH), 7.55–7.52 (2H, m, ArH), 7.39–7.36 (3H, m, ArH, H-2), 7.27 (1H, d, J = 7.3 Hz, ArH), 7.10 (1H, dd, J = 7.3, 7.3 Hz, ArH), 6.90 (1H, dd, J = 7.3, 7.3 Hz, ArH), 5.28 (1H, br, NH), 3.35 (3H, s, H-16); δ_C (100 MHz, DMSO-d_6) 168.9 (C-9), 162.0 (C-17), 142.2 (Ar-C), 136.1 (Ar-C), 135.8 (Ar-C), 131.7 (Ar-CH), 130.8 (Ar-C), 130.3 (Ar-CH), 129.3 (Ar-CH), 128.9 (Ar-CH), 127.4 (Ar-C), 122.0 (C-2), 119.9 (Ar-CH), 112.6 (Ar-CH), 39.09 (C-16); HRMS (ESI^+): Found: 294.1236; C_{17}H_{16}N_3O_2 (MH^+) Requires: 294.1237 (0.4 ppm error);] The crude product (10.4 g) was added to in 1M aq. KOH (13.6 g in 242 mL, 241

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mmol) and was stirred for 1 h at 105 °C. The resultant solid was isolated by filtration and washed with cold water (800 mL), HCl 10 % (300 mL), ether (300 mL) and dried in vacuo, affording the title compound as a yellow solid. (7.69 g, 90 %); mp: decompose at 210 °C; $\nu_{\text{max}}$ (thin film)/cm$^{-1}$ 1604, 1576, 1498, 1482, 1464, 1422, 1410, 1365, 1324, 1241, 1129; $\delta$H (400 MHz, DMSO-d$_6$) 12.02 (br, 1H, NH), 8.13 (1H, dd, J = 7.9, 1.4 ArH), 8.13 (1H, dd, J = 7.9, 1.4, ArH), 7.91 (1H, ddd, J = 8.4, 7.0, 1.6, ArH), 7.83 (1H, d, J = 8.4 Hz, ArH), 7.69 (1H, dd, J = 7.9, 0.7, ArH), 7.60–7.55 (2H, m, ArH), 7.30–7.25 (2H, m, ArH/H-2), 7.10 (1H, ddd, J = 7.9, 7.0, 1.0 Hz, ArH), 4.09 (3H, s, H-17); $\delta$C (100 MHz, DMSO-d$_6$) 167.1 (C-9/10), 154.4 (C-9/10), 142.2 (Ar-C), 136.8 (Ar-C), 134.0 (Ar-CH), 129.2 (Ar-C), 127.9 (Ar-C), 126.9 (Ar-CH), 126.1 (Ar-CH), 124.3 (C-2), 121.6 (Ar-CH), 120.1 (Ar-C), 119.9 (Ar-CH), 117.1 (Ar-CH), 112.6 (Ar-CH), 108.8 (Ar-CH), 38.3 (C-17); HRMS (ESI$^+$): Found: 276.1134; C$_{17}$H$_{12}$N$_3$O (MH$^+$) Requires: 276.1131 (-0.9 ppm error); Found: 298.0965; C$_{17}$H$_{13}$N$_3$NaO (MNa$^+$) Requires: 298.0951 (4.7 ppm error).

2-(3-ido-1H-indol-2-yl)-1-methyl-2,3-dihydroquinazolin-4(1H)-one (5):

To a solution of quinazolinone 15 (4.00 g, 14.5 mmol) in acetone (500 mL) was added N-iodosuccinimide (3.43 g, 15.3 mmol). After stirring for 2 h at RT, sat. aq. Na$_2$S$_2$O$_3$ (300 mL) was added and the mixture was stirred for an additional 5 mins at RT. The resulting precipitate was isolated by filtration and washed with cold water (1 L). The resulting white solid was collected and dried in vacuo. Purification by column chromatography (DCM $\rightarrow$ 100:1 $\rightarrow$ 50:1 $\rightarrow$ 25:1 DCM:MeOH) afforded the title compound as a white solid (4.94 g, 85%); R$_f$ 0.5 (18:1 DCM:MeOH); mp 214–219 °C; $\nu_{\text{max}}$ (thin film)/cm$^{-1}$ 1625, 1572, 1503, 1469, 1445, 1425, 1410, 1377, 1353, 1157, 1129, 1057, 755; $\delta$H (400 MHz, DMSO-d$_6$) 12.41 (1H, br, NH), 8.22 (1H, dd, J = 8.0, 1.6 Hz, ArH), 7.99 (1H, ddd, J = 8.4, 7.1, 1.6 Hz, ArH), 7.91 (1H, dd, J = 8.4, 1.0 Hz, ArH), 7.69 (1H, ddd, J = 8.0, 7.1, 1.0 Hz, ArH), 7.55 (1H, dd, J = 8.2, 0.9 Hz, ArH), 7.47 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.37 (1H, ddd, J = 8.2, 7.0, 1.2 Hz, ArH), 7.27 (1H, ddd, J = 8.0, 7.0, 0.9 Hz, ArH), 3.81 (3H, s, H-17); $\delta$C (100 MHz, DMSO-d$_6$) 167.8 (C-9/10), 155.8 (C-9/10), 141.9 (Ar-C), 136.7 (Ar-CH), 134.9 (Ar-C), 133.1 (Ar-C), 130.2 (Ar-C), 127.8 (Ar-CH), 127.3 (Ar-CH), 124.9 (Ar-CH), 121.5 (Ar-CH), 121.5 (Ar-CH), 120.4 (Ar-C), 117.5 (Ar-CH), 113.1 (Ar-CH), 62.8 (C-2), 38.0 (C-17); HRMS (ESI$^+$): Found: 402.0090; C$_{17}$H$_{13}$N$_3$O (MH$^+$) Requires: 402.0098 (1.9 ppm error);
1-Methyl-2-(3-vinyl-1H-indol-2-yl)quinazolin-4(1H)-one (17):

NEt₃Cl (59.7 mg, 0.360 mmol) was added to a Schlenk tube under Ar and flame dried in vacuo. PdCl₂(PPh₃)₂ (12.6 mg, 0.0170 mmol), iodide 5 (200 mg, 0.489 mmol) and stannane 16 (273 mg, 0.748 mmol) were then added to the Schlenk tube under Ar. Degassed DMF (3.9 mL) was added and the reaction mixture was stirred at RT until everything dissolved. The rapidly stirred mixture was then heated at 80 °C for 10 min before CuI (142.5 mg, 0.748 mmol) was added. The reaction mixture was stirred at 80 °C for 2 h, before cooling and quenching with water (20 mL). Following extraction with DCM (3 x 20 mL), the organic phase was washed with water (20 mL) and then dried over MgSO₄. Purification by column chromatography (10% K₂CO₃ in SiO₂⁴, DCM → 50:1 → 33.3:1 DCM:MeOH) afforded the title compound as a yellow solid. (89 mg, 82 %); Rf 0.6 (DCM, 10 % MeOH); mp: 182–186 °C; νmax (thin film)/cm⁻¹: 3109, 2923, 1629, 1605, 1519, 1492, 1448, 1397, 1339, 1260, 765, 748; δH (400 MHz, DMSO-d₆): 12.00 (1H, br s, NH), 8.17 (1H, d, J = 7.7 Hz, ArH), 7.98 (1H, d, J = 8.0 Hz, ArH), 7.92 (1H, dd, J = 8.4, 8.5 Hz, ArH), 7.81 (1H, d, J = 8.4 Hz, ArH), 7.61 (1H, dd, J = 8.5, 7.7 Hz, ArH), 7.51 (1H, d, J = 8.1 Hz, ArH), 7.30 (1H, dd, J = 8.1, 7.9 Hz, ArH), 7.19 (1H, dd, J = 8.0, 7.9 Hz, ArH), 6.90 (1H, dd, J = 17.8, 11.5 Hz, H-17), 5.73 (1H, dd, J = 17.8, 1.2 Hz, H-18a), 5.27 (1H, dd, J = 11.5, 1.2 Hz, H-18b), 3.70 (3H, s, H-19); δC (100 MHz, DMSO-d₆): 167.3 (C-9/10), 155.2 (C-9/10), 141.6 (Ar-C), 136.4 (Ar-C), 134.1 (Ar-CH), 128.8 (C-17), 128.7 (Ar-CH), 127.1 (Ar-CH), 126.4 (Ar-CH), 124.8 (Ar-C), 123.7 (Ar-CH), 120.7 (Ar-CH), 120.6 (Ar-C), 119.8 (Ar-C), 116.9 (Ar-CH), 114.7 (Ar-CH), 113.5 (C-18), 112.3 (Ar-CH), 37.3 (C-19); HRMS (ESI⁺): Found: 302.1286; C₁₉H₁₆N₃O (MH⁺) Requires: 302.1288 (0.8 ppm error);

(±)-Dievodiamine (1):

N\textsubscript{Et\textsubscript{3}}Cl (82.5 mg, 0.498 mmol) was added to a Schlenk tube under Ar and flame dried in vacuo. PdCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (17.4 mg, 0.0249 mmol), iodide 5 (100 mg, 0.249 mmol) and stannane 3 (231 mg, 0.374 mmol) were then added to the Schlenk tube under Ar. Degassed DMF (2.5 mL) was added and the reaction mixture was stirred at RT until everything dissolved. The rapidly stirred mixture was then heated at 80 °C for 10 min and then a second batch of PdCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (17.4 mg, 0.0249 mmol) and Cul (71.2 mg, 0.374 mmol) were added. The reaction mixture was stirred at 80 °C for 2 h, before cooling and quenching with water (20 mL). Following extraction with EtOAc (3 x 20 mL), the organic phase was then dried over MgSO\textsubscript{4}. Purification by column chromatography (SiO\textsubscript{2}, DCM → 100:1 → 50:1 DCM:MeOH) followed by recrystallisation (DCM/hexane) afforded the title compound as a pale yellow solid. (98 mg, 65 %); R\textsubscript{f} 0.6 (DCM, 10 % MeOH); mp: 229–233 °C (no literature mp has been reported); v\textsubscript{max} (thin film)/cm\textsuperscript{-1} 3216, 3057, 2928, 1629, 1604, 1522, 1490, 1446, 1396, 1396, 1355, 1299, 1262, 1174, 1150, 733, 761. 703, 693; δ\textsubscript{H} (400 MHz, DMSO-d\textsubscript{6}) 12.00 (1H, br s, NH), 11.42 (1H, br s, NH), 8.18 (1H, d, J = 7.9 Hz, H-19\textsuperscript{′}), 7.93 (1H, t, J = 8.3, 7.2 Hz, H-17\textsuperscript{′}), 7.78 (1H, d, J = 7.7 Hz, H-19), 7.70–7.64 (2H, m, H-9\textsuperscript{′}, 18\textsuperscript{′}), 7.55–7.50 (2H, m, H-9, 16\textsuperscript{′}), 7.43 (1H, d, J = 8.1 Hz, H-12\textsuperscript{′}), 7.37–7.32 (2H, m, H-12, 17), 7.23 (1H, t, J = 8.1, 7.4 Hz, H-11\textsuperscript{′}), 7.17–7.03 (5H, m, H-11, 10\textsuperscript{′}, 16, 10, 18), 6.55 (1H, d, J = 16.0 Hz, H-6\textsuperscript{′}), 6.35 (1H, d, J = 16.0 Hz, H-5\textsuperscript{′}), 4.91–4.88 (1H, m, H-5eq), 3.28 (3H, s, H-5ax), 3.16–3.10 (1H, m, H-22\textsuperscript{′}), 2.95–2.91 (1H, m, H-6eq), 2.82–2.73 (1H, m, H-6ax), 2.47 (3H, m, H-22); δ\textsubscript{C} (100 MHz, DMSO-d\textsubscript{6}) 167.3 (C-21\textsuperscript{′}), 162.6 (C-21), 154.9 (C-3\textsuperscript{′}), 149.1 (C-15), 141.4 (C-15\textsuperscript{′}), 136.8 (C-13), 136.3 (C-12\textsuperscript{′}), 134.1 (C-17\textsuperscript{′}), 133.2 (C-17), 130.7 (C-2), 128.9 (C-2\textsuperscript{′}), 128.4 (C-5\textsuperscript{′}), 127.5 (C-19), 127.1 (C-19\textsuperscript{′}), 126.5 (C-18\textsuperscript{′}), 125.5 (C-8), 124.5 (C-8\textsuperscript{′}), 123.8 (C-11\textsuperscript{′}), 123.3 (C-18), 122.9 (C-20), 122.4 (C-16), 122.2 (C-11), 121.5 (C-6\textsuperscript{′}), 120.7 (C-10\textsuperscript{′}), 120.3 (C-9\textsuperscript{′}), 119.9 (C-20\textsuperscript{′}), 118.9 (C-10), 118.6 (C-9), 116.9 (C-16\textsuperscript{′}), 112.8 (C-7\textsuperscript{′}), 112.4 (C-12\textsuperscript{′}), 111.7 (C-
A comparison of the $^1$H NMR data of the natural (δ$_h$ ref) and synthetic (δ$_h$ exp) dievodiamine

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<th>The 1H NMR data of DIEVODIAMINE (DMSO-d$_6$ at 300 MHz)</th>
<th>δ$_h$ ref</th>
<th>δ$_h$ exp (Ref. DMSO-d$_6$ at δ$_h$ 2.50)</th>
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<tbody>
<tr>
<td>NH</td>
<td>1H, br s</td>
<td>11.92</td>
<td>12.00</td>
</tr>
<tr>
<td>NH</td>
<td>1H, br s</td>
<td>11.34</td>
<td>11.42</td>
</tr>
<tr>
<td>19'</td>
<td>1H, d, J = 6.6 Hz</td>
<td>8.16</td>
<td>8.18</td>
</tr>
<tr>
<td>17'</td>
<td>1H, t, J = 8.4, 7.8 Hz</td>
<td>7.88</td>
<td>7.93</td>
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<td>1H, d, J = 16.0 Hz</td>
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<td>1H, dt, J = 12.6, 4.5, 5.1 Hz</td>
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<td>1H, dd, J = 11.1, 3.9, 5.1 Hz</td>
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<td>6ax</td>
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<td>3H, s</td>
<td>2.47</td>
<td>3H, s</td>
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[Diagram of DIEVODIAMINE molecule]
A comparison of the $^{13}$C NMR data of the natural ($\delta_{c \text{ ref}}$) and synthetic ($\delta_{c \text{ exp}}$) dievodiamine

<table>
<thead>
<tr>
<th>$\delta_{c \text{ ref}}$</th>
<th>$\delta_{c \text{ exp}}$ (Ref. DMSO-$d_6$ at $\delta_{c} 39.50$)</th>
<th>$\Delta \delta_{c}$</th>
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Note that all of $^{13}$C peaks for the synthetic material were all ca. 0.3–0.4 ppm lower than those of the natural product. Given that all of the resonances differed to approximately the same degree, we believe that it is highly likely that the difference is caused by a difference in the reference peak of the NMR spectra. (We referenced DMSO-$d_6$ at $\delta_{c}$ 39.50 for the center of the septet)
The image contains two NMR spectra with molecular structures labeled with numbers corresponding to peaks in the spectra. The spectra are labeled r9566chk_PROTON-2.jdf and r9565chk_CARBON-2.jdf.

The upper spectrum is labeled ppm (t1) and shows peaks at various ppm values, ranging from 0.00 to 2.00.

The lower spectrum is labeled ppm (t1) and shows peaks at various ppm values, ranging from 170 to 10.