Supplementary Material

Regioselective Substituent Effects upon the Synthesis of Dipyrrens from 2-Formyl Pyrroles

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General remarks

All chemicals were purchased and used as received unless otherwise indicated. Moisture sensitive reactions were performed in oven-dried glassware and under a positive pressure of nitrogen. Air- and moisture-sensitive compounds were introduced via syringe or cannula through a rubber septum. Flash chromatography was performed using Silicycle ultra-pure silica (230-400 mm). The NMR spectra were recorded using a 500 MHz spectrometer instrument using CDCl₃ as solvents and are reported in part per million (ppm). Internal solvent were referenced at 7.26 ppm for ¹H and at 77.16 ppm for ¹³C when using CDCl₃, at 5.31 ppm for ¹H and at 53.84 ppm for ¹³C when using CD₂Cl₂. Coupling constants (*J*) are given in Hertz (Hz). Mass spectra were obtained using TOF and LCQ Duo ion trap instruments operating in ESI^{+/-} mode, as indicated.

Experimental procedures

Compounds **1a**,¹ **1b**,¹ and **8**² were synthesized according to literature procedures.

Preparation of **1c*** Scheme S1. Synthesis of ²D-labelled **1c****tert*-Butyl 4,5-dimethyl-1*H*-pyrrole-2-carboxylate (**9**)

The title compound was synthesized following a modified literature procedure.³ Ethylene glycol (184 mL) and *p*-toluenesulfonic acid (959 mg, 5.6 mmol) were added to a solution of *tert*-butyl 4-acyl-3,5-dimethylpyrrole-2-carboxylate (**8**, 20 g, 84 mmol) in benzene (1 L), under N₂. The mixture was stirred and heated at reflux temperature for 18 h, cooled to room temperature, and water added (1 L). The resulting emulsion was extracted with CHCl₃ (2 x 1 L). The organic

fractions were washed with sat. NaHCO₃ (2 L), water (2 L), dried over anhydrous Na₂SO₄, and evaporated *in vacuo*. The residue was recrystallized from methanol/water and washed with hexanes to yield the desired product as a white solid (6.28 g, 38%). ¹H-NMR (300 MHz; CDCl₃) δ 8.49 (br s, 1H), 5.77 (m, 1H), 2.27 (s, 3H), 2.23 (s, 3H), 1.56 (s, 9H); ¹³C{¹H} NMR (125 MHz; CDCl₃) δ 161.4, 131.75, 131.68, 128.2, 119.2, 111.3, 80.3, 28.7, 13.20, 13.01. ¹H NMR data matches those previously reported.⁴ ¹³C NMR data have not been previously reported for this compound.

***tert*-Butyl 4-formyl-3,5-dimethyl-1*H*-pyrrole-2-carboxylate (10)**

The title compound was synthesized following a modified literature procedure.⁵ POCl₃ (4 mL) was added to DMF (8.5 mL), drop-wise, at 0 °C under N₂. The resulting mixture was stirred for 15 min while warming to 23 °C. The DMF/POCl₃ mixture was added to a solution of **9** (6.8 g, 35 mmol) in DMF (25mL) at 0 °C under N₂. The reaction mixture was stirred for 24 h at 23 °C, quenched with water (40 mL), and extracted with CH₂Cl₂ (3 x 150 mL). The combined organic layers were concentrated *in vacuo*. The residue was recrystallized from methanol/water to yield the desired product as a white solid (3.6 g, 46%). ¹H NMR (300 MHz; CDCl₃) δ 10.00 (s, 1H), 9.06 (br s, 1H), 2.54 (s, 6H), 1.58 (s, 9H); ¹³C{¹H} NMR (126 MHz; CDCl₃) δ 186.3, 161.3, 139.9, 129.4, 121.7, 120.1, 81.8, 28.6, 12.7, 10.5. ¹H NMR data matches that previously reported for this compound.⁴ ¹³C NMR data have not been previously reported for this compound.

tert*-Butyl 4-(methyl-*d*₂)-3,5-dimethyl-1*H*-pyrrole-2-carboxylate (**11c)**

The novel title compound was synthesized following a modified literature procedure.⁶ NaBD₄ (175 mg, 4.2 mmol) was added to a cooled solution (-10 °C, salt/ice) of **10** (500 mg, 2.27 mmol) in THF (4.5 mL) under N₂. When almost all the NaBD₄ was dissolved, BF₃•OEt₂ (750 μL, 6.07 mmol) was added slowly drop-wise to avoid a dramatic increase in temperature. The resultant mixture was stirred for 1 h, monitoring using TLC (20% EtOAc/hexanes). 0.5 M HCl was added, until effervescence ceased, to destroy excess diborane. Water was added and the mixture was extracted into ether (3 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na₂SO₄ and concentrated *in vacuo*. The resulting residue was purified via column chromatography on silica, eluting with 20% EtOAc/hexanes, to yield the desired product as an off-white solid (60 mg, 12%). M.p. 136-138 °C; ¹H NMR (500 MHz; CDCl₃) δ 8.41 (br s, 1H), 2.22 (s, 3H), 2.17 (s, 3H), 1.91-1.86 (m, 1H), 1.56 (s, 9H); ¹³C{¹H} NMR (125 MHz; CDCl₃) δ 161.3, 128.5, 126.6, 117.9, 116.8, 80.0, 28.6, 11.4, 10.6, 8.24 (quin, *J* = 19.4 Hz); HRMS-ESI (*m/z*): [M+Na]⁺ calculated for C₁₂H₁₇D₂N₁O₂Na₁ 234.1434; found 234.1440.

tert*-Butyl 5-formyl-4-(methyl-*d*₂)-3-methyl-1*H*-pyrrole-2-carboxylate (**12c)**

The title compound was synthesized following a modified literature procedure.⁷ Lead tetraacetate (2.9g, 6.6 mmol) was slowly added to a solution of **11c*** (610 mg, 2.9 mmol) in AcOH (3 mL) over 20 min. The mixture was heated at 80 °C for 30 min, and then allowed to cool to 23

°C. Ethylene glycol (200 μ L) was then added to destroy excess oxidant. The reaction mixture was diluted with water (8 mL), and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were washed with water (10 mL). Solvent was removed *in vacuo* and the resulting residue was dissolved in aqueous THF (50%, 10 mL) and heated at reflux temperature for 2 h. The mixture was diluted with ether (5 mL). The organic layer was washed with sat. NaHCO_3 (20 mL), and brine (20 mL), and then dried over anhydrous Na_2SO_4 before the solvent was evaporated *in vacuo*. The resulting residue was purified via column chromatography on silica, eluting with a gradient of 20-30% EtOAc/hexanes, to yield the desired product as an off-white solid (350 mg, 54%). M.p. 100-102 °C; ^1H NMR (500 MHz; CDCl_3) δ 9.75 (s, 1H), 9.30 (br s, 1H), 2.28-2.24 (m, 1H), 2.24 (s, 3H), 1.57 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz; CDCl_3): δ 179.1, 160.4, 130.4, 129.7, 126.6, 126.0, 82.3, 28.5, 9.8, 8.2 (quin, $J = 19.7$ Hz); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{12}\text{H}_{15}\text{D}_2\text{N}_1\text{O}_3\text{Na}_1$ 248.1226; found 248.1221.

***tert*-Butyl 5-(2-cyano-3-ethoxy-3-oxo-1-propenyl)-4-(methyl- d_2)-3-methyl-1H-pyrrole-2-carboxylate (13c*)**

The title compound was synthesized following a modified literature procedure.⁸ A solution of methylamine (2 M in THF, 180 μ L) was added to a solution of **12c*** (350 mg, 1.6 mmol) and ethyl cyanoacetate (220 μ L, 2.1 mmol) in aqueous ethanol (95%, 800 μ L) at 80 °C. After several minutes of heating the product crystallized from solution, the mixture becoming thick with solid. The reaction mixture was cooled over ice and the product collected via Millipore™ suction filtration, rinsing with ice-cold ethanol, then hexanes, to yield the desired product as a brilliant

yellow solid (386 mg, 80%). M.p. 181-183 °C; ^1H NMR (500 MHz; CDCl_3) δ 10.19 (br s, 1H), 8.03 (s, 1H), 4.34 (q, $J = 7.1$ Hz, 2H), 2.26 (s, 3H), 2.15-2.12 (m, 1H), 1.59 (s, 9H), 1.37 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz; CDCl_3) δ 163.3, 159.6, 139.4, 133.5, 127.8, 126.5, 125.1, 118.3, 94.2, 82.6, 62.4, 28.4, 14.4, 10.0, 9.0 (quin, $J = 19.4$ Hz); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{17}\text{H}_{20}\text{D}_2\text{N}_2\text{O}_4\text{Na}_1$ 343.1597; found 343.1586.

5-(2-Cyano-3-ethoxy-3-oxo-1-propenyl)-4-(methyl- d_2)-3-methyl-1H-pyrrole-2-carboxylic acid (14c***)**

The title compound was synthesized following a modified literature procedure.⁸ TFA (300 μL) was added to a solution of **13c*** (387 mg, 1.21 mmol) in DCE (2.5 mL) at reflux temperature. The resulting solution was heated until the starting material was consumed, monitoring by TLC (25% EtOAc/hexanes). Product began to crystallize shortly after addition of TFA, and so more solvent was added as needed to the reaction mixture. The reaction mixture was cooled to 23 °C, and placed in a freezer for further precipitation. The mixture was filtered via Millipore™ suction filtration, washing with hexanes, to yield the desired product as a brilliant yellow solid (307 mg, 95%). M.p. 212-213 °C (decomp.); ^1H NMR (500 MHz; CDCl_3) δ 10.22 (br s, 1H), 8.08 (s, 1H), 4.37 (q, $J = 7.1$ Hz, 2H), 2.32 (s, 3H), 2.20-2.15 (m, 1H), 1.39 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz; CDCl_3) δ 164.4, 163.0, 139.4, 133.3, 128.8, 126.5, 125.1, 117.9, 96.0, 62.7, 14.4, 10.2, 9.1 (quin, $J = 19.1$ Hz); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{13}\text{H}_{12}\text{D}_2\text{N}_2\text{O}_4\text{Na}_1$ 287.0971; found 287.0981.

2-(2-Cyano-3-ethoxy-3-oxo-1-propenyl)-5-iodo-3-(methyl-*d*₂)-4-methyl-1*H*-pyrrole

The title compound was synthesized following a modified literature procedure.⁸ A mixture of **14c*** (253 mg, 0.96 mmol), anhydrous sodium acetate (337 mg, 3.3 mmol), acetic anhydride (195 μ L, 2.07 mmol), and acetic acid (2 mL) was heated, with stirring, until the solution became homogenous (~ 105 °C). Immediately thereafter, a solution of iodine chloride (1 M in AcOH, 2.0 mL, 2 mmol) was quickly added. The reaction mixture was boiled for 5 min, until the purple vapours of free iodine had ceased. Water (15 mL) was slowly added, causing the oiling and then crystallization of product. The solid was collected via Millipore™ suction filtration, washing extensively with water, and then dissolved in CH_2Cl_2 . Saturated aqueous sodium sulfite (1 mL) was added, with stirring, followed by addition of water, and cooling to 0 °C. The organic layer was separated, dried over anhydrous Na_2SO_4 and evaporated *in vacuo* to yield the crude product, which was used immediately in the subsequent reaction without further purification (product not stable for long periods of time).

2-(2-Cyano-3-ethoxy-3-oxo-1-propenyl)-3-(methyl-*d*₂)-4-methyl-1*H*-pyrrole (15c*)

The title compound was synthesized following a modified literature procedure.¹ Zinc dust (315 mg, 4.8 mmol) was added to a solution of 2-(2-cyano-3-ethoxy-3-oxo-1-propenyl)-5-iodo-3-(methyl-*d*₂)-4-methyl-1*H*-pyrrole (presumed 0.96 mmol) in AcOH (2.1 mL), swirling manually

until a spontaneous reaction set in and the temperature rose to ~50 °C, after which the reaction mixture was stirred mechanically for 30 min. The reaction mixture was filtered through Celite® to remove zinc, washing with methanol until the washings were colourless. Solvent was removed *in vacuo*, and the resulting residue was crystallized from methanol/water and collected via Millipore™ suction filtration to yield the desired product as a brilliant yellow solid (68 mg, 32% over two steps). M.p. 155-157 °C; ¹H NMR (500 MHz; CDCl₃) δ 9.66 (br s, 1H), 8.00 (s, 1H), 6.99-6.98 (m, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.18-2.14 (m, 1H), 2.04 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H); ¹³C{¹H} NMR (126 MHz; CDCl₃) δ 164.3, 139.5, 134.4, 127.6, 125.0, 122.1, 119.8, 88.7, 61.9, 14.5, 10.0, 8.9 (quin, *J* = 19.3 Hz); HRMS-ESI (*m/z*): [M+Na]⁺ calculated for C₁₂H₁₂D₂N₂O₂Na₁ 243.1073; found 243.1067.

3-(Methyl-*d*₂)-4-methyl-1*H*-pyrrole-2-carbaldehyde (1c*)

The title compound was synthesized following a modified literature procedure.¹ To a suspension of **15c*** (63 mg, 0.29 mmol) in methanol (1 mL) at reflux temperature was added NaOH (4M, 1mL) dropwise over several min, under N₂. The resulting mixture was heated at reflux temperature for 30 min. Methanol was removed *in vacuo*, water was added (1 mL), and the reaction mixture was heated at reflux temperature for 1.5 h. After cooling, the mixture was extracted with CH₂Cl₂ (3 x 5 mL) and the combined organic fractions were washed with water, brine, dried over anhydrous Na₂SO₄ and the solvent removed *in vacuo*. The resulting residue was purified via column chromatography on silica, eluting with a gradient of 20-30% EtOAc/hexanes, to yield the desired product as an off-white solid (19 mg, 52%). M.p. 131-132 °C; ¹H NMR (500 MHz; CDCl₃) δ 9.58 (s, 1H), 9.34 (s, 1H), 6.85-6.84 (m, 1H), 2.27-2.23 (m,

1H), 2.02 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz; CDCl_3) δ 177.3, 131.1, 129.7, 124.7, 121.1, 9.5, 8.1 (quin, $J = 19.5$ Hz); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_7\text{H}_7\text{D}_2\text{N}_2\text{O}_1\text{Na}_1$ 148.0702; found 148.0700.

Preparation of 1c

Scheme S2. Synthesis of 1c

tert-Butyl 3,4,5-dimethylpyrrole-2-carboxylate (11c)

The title compound was synthesized following a modified literature procedure.⁹ $\text{BH}_3 \cdot \text{THF}$ (1.66 mL, 1 M in THF 1.66 mmol) was added slowly, drop-wise, to a cooled solution (0 °C) of **10** (185 mg, 0.829 mmol) in THF (9 mL) under N_2 . Once the addition was complete, the reaction mixture was allowed to warm to room temperature and stir until all starting material was consumed, monitoring by TLC. The reaction mixture was then cooled to 0 °C and 1 M HCl was added, dropwise, until effervescence ceased. The resultant mixture was extracted into ethyl acetate (3 x

10 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified via column chromatography on silica, eluting with 5-25% EtOAc/hexanes, to yield the desired product as an off-white solid (42 mg, 24%). ^1H NMR (500 MHz; CDCl_3) δ 8.49 (br s, 1H), 2.23 (s, 3H), 2.18 (s, 3H), 1.91 (s, 3H), 1.56 (s, 9H). ^1H NMR data matches that previously reported for this compound.⁸

***tert*-Butyl 5-formyl-3,4-dimethyl-1*H*-pyrrole-2-carboxylate (12c)**

Following the same procedure used to prepare **11c***, lead tetra-acetate (26.2 g, 59 mmol) was added to a solution of *tert*-butyl 3,4,5-dimethylpyrrole-2-carboxylate (5.4 g, 26 mmol) in AcOH (26 mL). Following the same work-up used with **11c***, the desired product was obtained as an off-white solid (5.5 g, 95%). ^1H NMR (300 MHz; CDCl_3) δ 9.75 (s, 1H), 9.31 (br s, 1H), 2.28 (s, 3H), 2.24 (s, 3H), 1.58 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz; CDCl_3) δ 179.1, 160.4, 130.4, 129.7, 126.6, 126.0, 82.3, 28.5, 9.9, 8.7. ^1H NMR data matches that previously reported for this compound.⁸ ^{13}C NMR data have not been previously reported for this compound.

***tert*-Butyl 5-(2-cyano-3-ethoxy-3-oxo-1-propenyl)-3,4-dimethyl-1*H*-pyrrole-2-carboxylate (13c)**

Following the same procedure used to prepare **13c***, a solution of methylamine (2 M in THF, 2.9 mL) was added to a solution of **12c** (5.4 g, 25 mmol) and ethyl cyanoacetate (3.5 mL, 33 mmol) in aqueous ethanol (95%, 20 mL). Following the same work-up used with **13c***, the desired product was obtained as a brilliant yellow solid (6.2 g, 80%). ^1H NMR (300 MHz; CDCl_3) δ 10.19 (br s, 1H), 8.04 (s, 1H), 4.35 (q, $J = 7.1$ Hz, 2H), 2.27 (s, 3H), 2.17 (s, 3H), 1.59 (s, 9H), 1.38 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz; CDCl_3) δ 163.3, 159.6, 139.4, 133.5, 127.8, 126.5, 125.1, 118.3, 94.2, 82.6, 62.4, 28.4, 14.4, 10.0, 9.5. ^1H NMR data matches that previously reported for this compound.⁸ ^{13}C NMR data have not been previously reported for this compound.

5-(2-Cyano-3-ethoxy-3-oxo-1-propenyl)-3,4-dimethyl-1H-pyrrole-2-carboxylic acid
(14c)

Following the same procedure used to prepare **14c***, TFA (6 mL) was added to a solution of **13c** (6.00 g, 18.9 mmol) in DCE (40 mL) at reflux temperature. Following the same work-up used with **14c*** the desired product was obtained as a brilliant yellow solid (3.55 g, 72%). ^1H NMR (500 MHz; CDCl_3) δ 10.22 (br s, 1H), 8.08 (s, 1H), 4.37 (q, $J = 7.1$ Hz, 2H), 2.32 (s, 3H), 2.20 (s, 3H), 1.39 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz; CDCl_3) δ 164.0, 163.0, 139.4, 133.3, 128.7, 126.5, 125.0, 117.9, 96.0, 62.7, 14.4, 10.2, 9.5. ^1H NMR data matches that previously reported for this compound.⁸ ^{13}C NMR data have not been previously reported for this compound.

2-(2-Cyano-3-ethoxy-3-oxo-1-propenyl)-5-iodo-3,4-dimethyl-1H-pyrrole

Following the procedure used to prepare 2-(2-cyano-3-ethoxy-3-oxo-1-propenyl)-5-iodo-3-(methyl- d_2)-4-methyl-1H-pyrrole, a solution of iodine chloride (1 M in AcOH, 27 mL) was quickly added to a solution of **14c** (3.55 g, 13.5 mmol), anhydrous sodium acetate (45 g, 44.2 mmol), and acetic anhydride (2.7 mL) in AcOH (27 mL) at reflux temperature. Following the same work-up for 2-(2-cyano-3-ethoxy-3-oxo-1-propenyl)-5-iodo-3-(methyl- d_2)-4-methyl-1H-pyrrole, the desired crude product was obtained and used immediately in the subsequent reaction without further purification (product not stable for long periods of time).

2-(2-Cyano-3-ethoxy-3-oxo-1-propenyl)-3,4-dimethyl-1H-pyrrole (15c**)**

Following the same procedure used to prepare **15c***, zinc dust (4.4 g, 67.5 mmol) was added to a solution of 2-(2-cyano-3-ethoxy-3-oxo-1-propenyl)-5-iodo-3-(methyl- d_2)-4-methyl-1H-pyrrole (presumed 13.5 mmol) in AcOH (30 mL). Following the same work-up as with **15c***, the desired product was obtained as brilliant yellow solid (1.69 g, 57% over two steps). ^1H NMR (300 MHz; CDCl_3) δ 9.66 (br s, 1H), 8.00 (s, 1H), 6.99-6.98 (m, 1H), 4.31 (t, J = 7.1 Hz, 2H), 2.18 (s, 3H), 2.04 (s, 3H), 1.35 (d, J = 7.1 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (126 MHz; CDCl_3) δ 164.3, 140.0, 139.5, 134.5, 127.6, 122.4, 122.1, 119.8, 61.9, 14.5, 10.0, 9.6; HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calculated

for $C_{12}H_{14}N_2O_2Na$ 241.0947; found 241.0952. HRMS, 1H and ^{13}C NMR data have not been previously reported for this compound.

2-Formyl-3,4-dimethylpyrrole (1c)

Following the same procedure used to prepare **1c***, aqueous NaOH (4 M, 9.5 mL) was added dropwise to a suspension of **15c** (1.65 g, 7.56 mmol) in methanol (18 mL) at reflux temperature, under N_2 . Following the same work-up as for **1c***, the desired product was obtained as an off-white solid (534 mg, 57%). 1H NMR (300 MHz; $CDCl_3$) δ 9.63 (br s, 1H), 9.57 (s, 1H), 6.87-6.86 (m, 1H), 2.27 (s, 3H), 2.01 (s, 3H), in accordance with literature.¹⁰

Preparation of 1d

Scheme S3. Synthesis of **1d**

3,4-Diethylpyrrole (16)

The title compound was synthesized according to a literature procedure¹¹ and was isolated as a colourless liquid (1.58 g, 59%). 1H NMR (500 MHz; $CDCl_3$) δ 7.81 (br s, 1H), 6.66-6.55 (m,

2H), 2.50 (q, $J = 7.5$ Hz, 4H), 1.24 (t, $J = 7.5$ Hz, 6H). ^1H NMR data matches those previously reported.¹²

3,4-Diethylpyrrole (1d)

Using 3,4-diethyl pyrrole, the title compound was synthesized according to the literature procedure⁵ and was isolated as an olive green solid (1.37 g, 75%). ^1H NMR (300 MHz; CDCl_3)

δ 9.60 (d, $J = 0.9$ Hz, 1H), 9.19 (s, 1H), 6.87-6.86 (m, 1H), 2.74 (q, $J = 7.6$ Hz, 2H), 2.46 (qd, $J = 7.5, 0.6$ Hz, 2H), 1.25-1.18 (m, 6H). ^1H NMR data matches those previously reported.¹³

Deduction of ratio of deuterated dipyrins

The theoretical integration of each signal was calculated assuming the symmetrical and asymmetric products were in a 1:1 ratio, and differences analysed thereupon. The sum was based on all contributing protons from D_8 , D_7 , and D_6 species taking into account the original pyrrole ratio and the corresponding dipyrin ratios (e.g. **2d'*** - $\text{D}_4:\text{D}_3$ is 1:0.7, therefore $\text{D}_8:\text{D}_7:\text{D}_6$ is 1:0.7:0.49). When the absolute value of either integral was set to the calculated value, the opposing signal matched the theoretical value indicating that there was no surplus or deficit of protons i.e. all dipyrins were there in expected amounts. The key to this assertion is that the fully deuterated **sym-2d'*** (Figure 1) contributes no protons to the integration of the signal at δ 2.7. As this is the case, if any product, symmetrical vs. asymmetric, was not there in the expected 1:1 ratio, we should see a notable difference in the actual integrations compared to the expected. As we do not see this in the spectra of **2d'***, nor **2d***, we are confident in concluding the product ratio is 1:1 for both.

Figure 1 ^1H NMR signal integrations of **2d**, **sym-2d'***, and **asym-2d'***

¹H NMR spectrum of a solution of **1c*** dissolved in CDCl₃

¹³C NMR spectrum (top):

- 177.468
- 131.202
- 129.828
- 124.833
- 121.196
- 77.160

¹H NMR spectrum (bottom):

- 9.622
- 8.474
- 8.379
- 8.279
- 8.169
- 8.069
- 7.914
- 8.474
- 8.379
- 8.228
- 8.069
- 7.914

^1H NMR spectrum of a solution of **3** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **3** dissolved in CDCl_3

^1H NMR spectrum of a solution of **4** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **4** dissolved in CDCl_3

^1H NMR spectrum of a solution of **7** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **7** dissolved in CDCl_3

^1H NMR spectrum of a solution of **7'** dissolved in CDCl_3

 ^{13}C NMR spectrum of a solution of **7'** dissolved in CDCl_3

^1H NMR spectrum of a solution of **1d*(D₄)** and **1d*(D₃)** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **1d*(D₄)** and **1d*(D₃)** dissolved in CDCl_3

Chemical structures of **trans-1c*** (**D₄**) and **trans-1c*** (**D₃**) are shown above the corresponding NMR spectra. The structures indicate the positions of deuterium (D) and hydrogen (H) atoms, and the presence of a bromine atom (Br) in the **trans-1c*** (**D₄**) structure.

The NMR spectra show the chemical shifts (ppm) and integration values for the peaks. The x-axis represents the chemical shift in ppm, ranging from 1 to 14.

Key peaks and integration values:

- Peak at ~13.5 ppm (integration: 5.87)
- Peak at ~7.7 ppm (integration: 6.4)
- Peak at ~7.3 ppm (integration: 3.24)
- Peak at ~2.7 ppm (integration: 10.7)
- Peak at ~2.3 ppm (integration: 5.53)
- Peak at ~1.2 ppm (integration: 20.4)

The integration values are consistent with the expected molecular formula and the presence of deuterium and hydrogen atoms in the structures.

Chemical shifts (ppm) listed on the right side of the spectrum:

- 148.978
- 141.737
- 131.711
- 127.409
- 123.165
- 77.160
- 18.407
- 18.025
- 17.941
- 17.840
- 17.775
- 17.755
- 17.614
- 17.547
- 17.386
- 17.384
- 17.216
- 16.879
- 16.821
- 13.932
- 13.913
- 13.894
- 13.764
- 13.713
- 13.558
- 13.474

HSQC NMR spectrum of dipyrins from **1d*** (CDCl₃)

HMBC NMR spectrum of dipyrins from **1d*** (CDCl₃)

^1H spectrum of **1d'*(D₄)** and **1d'*(D₃)** (CDCl₃)

^{13}C NMR spectrum of **1d'*(D₄)** and **1d'*(D₃)** (CDCl₃)

^1H NMR spectrum of **sym-2d*** and **asym-2d*** (CDCl_3)

^{13}C NMR spectrum of **sym-2d*** and **asym-2d*** (CDCl_3)

^{13}C NMR spectrum of a solution of **9** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **10** dissolved in CDCl_3

^1H NMR spectrum of a solution of **11c*** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **11c*** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **12** dissolved in CDCl_3

^1H NMR spectrum of a solution of **12c*** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **12c*** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **13c** dissolved in CDCl_3

^1H NMR spectrum of a solution of **13c*** dissolved in CDCl_3

^1H NMR spectrum of a solution of **14c** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **14c** dissolved in CDCl_3

^1H NMR spectrum of a solution of **14c*** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **14c*** dissolved in CDCl_3

^1H NMR spectrum of a solution of **15c** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **15c** dissolved in CDCl_3

^1H NMR spectrum of a solution of **15c*** dissolved in CDCl_3

^{13}C NMR spectrum of a solution of **15c*** dissolved in CDCl_3

X-ray data

Empirical formula	$C_{17}H_{25}BrN_2$
Formula weight	337.30 g/mol
Crystal description	clear red-orange thin rectangular plate
Temperature	298(2) K
Crystal system	Triclinic
Space group	$P-1$
Unit cell dimensions	$a = 8.8132(4) \text{ \AA}$ $b = 9.1511(4) \text{ \AA}$ $c = 12.1393(6) \text{ \AA}$
	$\alpha = 111.160(3)^\circ$ $\beta = 103.282(3)^\circ$ $\gamma = 95.888(3)^\circ$
Volume	$869.85(7) \text{ \AA}^3$
Z	2
ρ (calculated)	1.288 Mg/m^3
μ (Mo $K\alpha$)	2.357 mm^{-1}
Crystal size	$0.300 \times 0.150 \times 0.050 \text{ mm}^3$
Reflections collected	15590 (4216 unique, $R_{\text{int}} = 0.0325$)
Goodness-of-fit	1.014
$R(F)$	0.0359
$Rw(F)$	0.0721

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