

Rational synthesis of tripyrranes

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1. General methods

All chemicals were used as received unless otherwise noted. Reagent grade solvents (CH₂Cl₂, hexane) were distilled prior to use. All reported NMR spectra were recorded on 500 MHz spectrometer. UV-vis absorption and fluorescent spectra were recorded in toluene. Chromatography was performed on silica (200-400 mesh). Mass spectra were obtained via EI or electrospray MS (ESI-MS). The following compounds were prepared as described in the literature: **1**,^{S1} **9**,^{S2} **10**,^{S3} and **S1**.^{S4}

UV/Vis spectrophotometer and spectrofluorimeter were used to acquire absorption and emission spectra. Spectrophotometric grade solvents were used without further purification. For fluorescence spectra samples were excited at 530 nm.

2. Experimental procedures

[N-(Methylsulfonyl)pyrrol-2-yl]-(4-methylphenyl)methanon (2). To a solution of *N*-mesylpyrrole (**1**) (10 mmol, 1.45 g) and 4-methylbenzoic acid (20 mmol, 1.45 g) in dry ethylene chloride (10 ml) trifluoroacetic anhydride (7.5 ml) was added. After stirring for 20 hours at room temperature solvents were evaporated in vacuo and the oily residue was left in the refrigerator overnight. Filtration afforded pure product as white crystals (1.21 g, 46%): mp = 128-129°C; ¹H NMR (500 MHz, CDCl₃, Me₄Si, ppm): 2.52 (s, 3H), 3.93 (s, 3H), 6.39 (dd, 1H, J₁ = 3.3 Hz, J₂ = 3.5 Hz), 6.86 (dd, 1H, J₁ = 1.7 Hz, J₂ = 3.5 Hz), 7.36 (d,

2H, $J = 8.7$ Hz), 7.64 (dd, 1H, $J_1 = 1.7$ Hz, $J_2 = 3.3$ Hz), 7.88 (d, 2H, $J = 8.7$ Hz). ^{13}C NMR (125 MHz, CDCl_3 , Me_4Si , ppm): 21.7, 43.9, 110.2, 125.4, 129.0, 129.1, 130.1, 133.0, 135.0, 143.9, 184.9 HRMS (ESI): m/z calcd. for $\text{C}_{13}\text{H}_{13}\text{NO}_3\text{S}$: 286.0508; found 286.0500. Anal. calcd. for $\text{C}_{13}\text{H}_{13}\text{NO}_3\text{S}$: C, 59.30; H, 4.98; N, 5.32. Found: C, 59.35; H, 4.78; N, 5.29.

[N-[(4-Methylsulfonyl)-pyrrol-2-yl]-(4-methylphenyl)-methanol (3). To a solution of **2** (20 mmol, 5.27 g) in a mixture of methanol (60 ml) and THF (200 ml) NaBH_4 (100.0 mmol, 3.8 g) was slowly added. After 15 minutes solvents were evaporated in vacuo and the residue was washed with water (50mL) and extracted with CH_2Cl_2 ($3 \times 50\text{mL}$). The organic layer was dried (Na_2SO_4) and the solvent was evaporated in vacuum affording the product as a white solid (5.25 g, 99%): mp = 97°C ; ^1H NMR (500 MHz, CDCl_3 , Me_4Si , ppm): 2.37 (s, 3H), 2.86 (d, 1H, $J = 4.6$ Hz), 3.14 (s, 3H), 5.80–5.86 (m, 1H), 6.16 (t, 1H, $J = 3.5$ Hz), 6.20 (br d, 1H, $J = 4.6$ Hz), 7.14–7.20 (m, 1H), 7.19, 7.33 (AA'BB', $2 \times 2\text{H}$, $J = 8.1$ Hz). ^{13}C NMR (CDCl_3): 21.1, 42.9, 68.4, 110.9, 115.3, 123.5, 126.8, 129.0, 137.0, 137.8, 138.2, HRMS (ESI): m/z calcd. for $\text{C}_{13}\text{H}_{15}\text{NO}_3\text{S}$: 288.0665; found 288.0651. Anal. calcd. for $\text{C}_{13}\text{H}_{15}\text{NO}_3\text{S}$: C, 58.85; H, 5.70; N, 5.28. Found: C, 58.79; H, 5.78; N, 5.25.

Methoxytripyrin 6, tripyrinone 7 and methoxydipyrin 8. Tripyrrane **4** (24.7 mmol, 10 g) was dissolved in a methanol (350 mL) solution of KOH (446 mmol, 25 g) and stirred at room temperature in an open flask for 1 week. The solvent was evaporated in vacuum, water (300 ml) was added and extracted with CH_2Cl_2 (3×100 mL). The organic layer was separated, dried (Na_2SO_4) and the solvent was evaporated. The residue was chromatographed (silica, CH_2Cl_2 :hexanes = 1:3 up to 3:1) giving dipyrane **8** (first main fraction) as yellow glassy solid (865 mg, 12.8%). The use of stronger eluent system (CH_2Cl_2 :MeOH = 8:2) allowed to collect fraction containing products **6** and **7**. The second chromatography (silica, hexanes:ethyl acetate = 9:1) afforded pure product **6** as a dark purple solid (100 mg, 1%) and product **7** as a dark blue solid (150 mg, 1.5%). **2-Methoxy-6,11-di(4-methylphenyl)tripyrin 6:** R_f (CH_2Cl_2 :MeOH=95:5) = 0.33; ^1H NMR (500 MHz, CDCl_3 , Me_4Si , ppm): 2.34 (s, 3H), 2.36 (s, 3H), 4.32 (s, br) 6.06 (d, 1H, $J = 4.0$ Hz), 6.17 (d, 1H, $J = 4.7$ Hz), 6.20 (s, br), 6.46 (d, 1H, $J = 4.5$ Hz), 6.69 (d, 1H, $J = 4.7$ Hz), 6.75 (d, 1H, $J = 4.5$ Hz), 7.13 (d, 2H, $J = 8.0$ Hz), 7.15 (d, 2H, $J = 7.9$ Hz), 7.22 (d, 2H, $J = 8.0$ Hz), 7.29 (d, 2H, $J = 7.9$ Hz), 7.87 (s, 1H), 10.1 (s, br, 1H); ^{13}C NMR

(125 MHz, CDCl₃, ppm): 21.2, 21.3, 56.7, 119.2, 122.9, 124.3, 128.2, 128.4, 130.9, 131.0, 131.4, 134.2, 134.9, 135.1, 137.1, 138.1, 138.3, 138.8, 140.9, 141.4, 147.8, 150.6, 159.2, 176.7; HRMS (ESI) calcd for C₂₉H₂₅N₃O [M+H⁺] 431.1998, found 431.2005; λ_{max} (THF)/nm 354 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ (26400), 512 (20700) and 546 (23300); λ_{max} (THF)/nm 354($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ (26400), 512 (20700) and 546 (23300).

Tripyrrinone 7: R_f (CH₂Cl₂:MeOH=95:5) = 0.60; ¹H NMR (500 MHz, CDCl₃, Me₄Si, ppm): 2.42 (s, 3H), 2.45 (s, 3H), 6.22 (d, 1H, J = 5.6 Hz), 6.29 (d, 1H, J = 4.5 Hz), 6.37 (dd, 1H, J₁ = 3.8 Hz, J₂ = 2.5 Hz), 6.53 (d, 1H, J = 3.1 Hz), 6.77 (d, 1H, J = 4.5 Hz), 6.99 (d, 1H, J = 5.6), 7.23 (s, 4H), 7.25 (d, 2H, J = 7.9 Hz), 7.40 (d, 2H, J = 7.9 Hz), 7.45 (s, 1H), 10.1 (s, br, 1H), 11.9 (s, br, 1H); ¹³C NMR (125 MHz, CDCl₃, ppm): 21.2, 21.4, 112.6, 120.4, 123.9, 124.6, 126.1, 128.4, 128.7, 130.3, 131.0, 131.5, 133.4, 133.5, 134.6, 135.3, 137.4, 138.1, 139.4, 139.7, 142.8, 149.9, 166.0, 172.1; HRMS (ESI) calcd for C₂₈H₂₅N₃O [M+H⁺] 418.1914, found 418.1911; λ_{max} (THF)/nm 308($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 17260), 352 (20000) and 534 (19500).

Compound 8: R_f (CH₂Cl₂:Hexanes=4:1) = 0.40; ¹H NMR (500 MHz, CDCl₃, Me₄Si, ppm): 2.36 (s, 3H), 2.37 (s, 3H), 4.16 (s, 3H), 6.17-6.22 (m, 2H), 6.71-6.74 (m, 1H), 6.76 (d, 1H, J₁ = 2.7 Hz), 7.18 and 7.26 (AA'BB', 2 x 2H), 7.22 and 7.40 (AA'BB', 2 x 2H, J = 7.96 Hz), 12.76 (s, 1H); ¹³C NMR (125 MHz, CDCl₃, ppm): 21.3, 21.6, 56.4, 117.6, 118.3, 119.5, 128.6, 129.0, 129.1, 130.8, 131.4, 133.5, 134.3, 135.9, 137.7, 138.4, 138.5, 142.5, 147.3, 176.5, 184.5; HRMS (EI) m/z calcd for C₂₅H₂₂N₂O₂ (M)⁺ 382.1681. Found: 382.1701; λ_{max} (CH₂Cl₂)/nm 281, 310, 418.

1-N-(4-Methylphenyl)sulfonyl-6-(methylphenyl)-dipyrrane (11). Alcohol **S3** (9.0 mmol, 3.07 g) was dissolved in pyrrole (0.27 mol, 18.5 ml) and TFA (2.0 mmol, 160 μ l) was added. Then the reaction mixture was stirred at room temperature for 20 hours and pyrrole was distilled out. The residue was dissolved in CH₂Cl₂, washed with water, dried (Na₂SO₄), and evaporated affording pure product as pink solid (3.19 g, 91%): IR (KBr, ν_{max} /cm) 592, 667, 1 722, 1147, 1173, 1366, 1512, 1592, 2922, 3435; ¹H NMR (400 MHz, CDCl₃, Me₄Si, ppm): δ 2.29 (s, 3H), 2.33 (s, 3H), 5.60 (t, 1H, J = 2.8 Hz), 5.80 (ddd, 1H, J₁ = 0.8 Hz, J₂ = 1.8 Hz, J₃ = 3.4 Hz), 6.01–6.03 (m, 2H), 6.19 (dt, 1H, J₁ = 0.5 Hz, J₂ = 3.4 Hz), 6.58 (d, 1H, J = 1.3 Hz) 6.86 (d, 2H, J = 8.2 Hz), 6.94 (d, 2H, J = 7.9 Hz), 7.01–7.03 (m, 2H), 7.24–7.26 (m, 2H), 7.30 (ddd, 1H, J₁ = 0.3 Hz, J₂ = 1.8 Hz, J₃ = 3.4 Hz), 7.73 (s, br, 1H); ¹³C NMR (125 MHz, CDCl₃, ppm): δ 21.0, 21.5, 41.6, 107.5, 108.2, 111.2, 115.0, 116.7, 122.9, 126.7, 128.4, 128.9, 129.4, 132.4, 135.8, 136.2,

137.0, 138.2, 144.1; HRMS (EI) m/z calcd for $C_{23}H_{22}N_2O_2S$ (M)⁺ 390.1402. Found: 390.1398; Anal. Calcd for $C_{23}H_{22}N_2O_2S$: C, 70.74; H, 5.68; N, 7.17; S, 8.21. found: C, 70.60; H, 5.68; N, 7.11; S, 8.03.

Tripyrrane 12. Ketone **10**^{S3} (5.54 mmol, 1.8 g) was dissolved in the mixture of methanol (20 ml) and THF (70 ml). Then $NaBH_4$ (27.7 mmol, 1 g) was added. After 15 minutes the solvents were distilled out and water was added (50 ml). Next that suspension was extracted with CH_2Cl_2 , the organic layer was dried (Na_2SO_4) and the solvent was evaporated affording pure [N-(phenylsulfonyl)-pyrrol-3-yl]-(4-methylphenyl)-methanol as a colorless solid (1.8 g, 99%). Crude alcohol (5.5 mmol, 1.8 g) and dipyrane **11** (5.4 mmol, 2.11 g) were dissolved in CH_2Cl_2 (125 ml). Then TFA (2.6 mmol, 200 μ l) was added and the reaction mixture was stirred for 2 hours at room temperature. After that reaction mixture was washed with water and organic layer was dried (Na_2SO_4) and evaporated. The residue was passed through silica pad and evaporated affording pure product as a pale orange solid (2.3 g, 60%): IR (KBr, ν max /cm) 589, 671, 727, 755, 1059, 1097, 1117, 1148, 1173, 1366, 1448, 1512, 2922, 3401; 1H NMR (200 MHz, $CDCl_3$, Me_4Si , ppm): δ 2.30 (s, 3H), 2.31 (s, 3H), 2.32 (s, 3H), 5.06 (s, br, 2H), 5.31–5.35 (m, 1H), 5.46–5.52 (m, 1H), 5.79 (s, br, 1H), 5.89 (d, 1H J = 3.3 Hz), 6.09 (dd, 1H, J_1 = 1.6 Hz, J_2 = 3.3 Hz), 6.19–6.24 (m, 1H), 6.78 (s, br, 1H), 6.81 (d, 1H, J = 1.8 Hz), 7.06–7.09 (m, 3H), 7.21 (d, 2H, J = 8.4 Hz), 7.29–7.32 (m, 4H), 7.43–7.61 (m, 13 4H), 7.75–7.79 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 21.0, 21.5, 26.9, 41.6 41.7, 42.7, 106.9, 107.0, 107.6, 107.7, 111.1, 111.2, 114.7, 114.8, 118.7, 118.8, 121.3, 146 122.9, 126.6, 126.7, 128.1, 128.4, 128.8, 129.1, 129.3, 131.9, 132.0, 132.1, 132.2, 132.6, 132.7, 133.7, 133.8, 135.8, 135.9, 136.1, 136.4, 137.0, 137.1, 137.9, 138.0, 139.0, 139.3, 139.4, 144.1 ; HRMS (EI) m/z calcd for $C_{41}H_{37}N_3O_4S_2$ (M)⁺ 699.2225. Found: 699.2201; Anal. Calcd for $C_{41}H_{37}N_3O_4S_2$: C, 70.36; H, 5.33; N, 6.00; S, 9.16. found: C, 70.49; H, 5.50; N, 5.80; S, 8.98.

2-(4-Methylbenzoyl)-N-tosylpyrrole (S2): To a solution of *N*-tosylpyrrole (**S1**, 11.05 g, 50 mmol) in 1,2-dichloromethane (100 mL), 4-methylbenzoic acid (13.6 g, 100 mmol) was added followed by trifluoroacetic anhydride (75 mL). The mixture has been stirred at 20°C for 3hrs and then refluxed for the next 18 hrs. After cooling down to room temperature the reaction mixture was concentrated and placed in the refrigerator. Filtration of the resulting solid afforded product (15.4 g, 91%). 1H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 6.32 (dd, J_1 = 3.6 Hz, J_2 = 3.2 Hz, 1H, pirol), 6.68 (dd, J_1 =

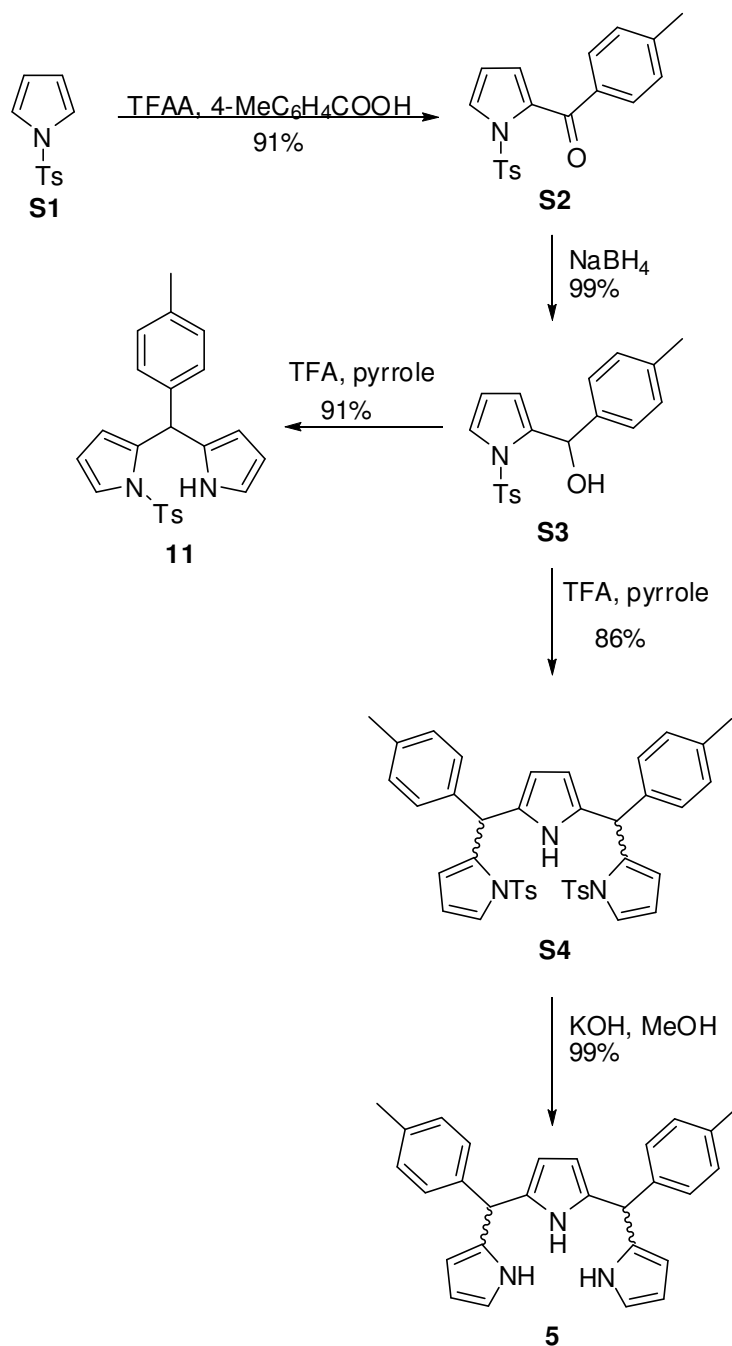
3.6 Hz, $J_2 = 1.7$ Hz, 1H, pirol), 7.24 (AA'BB', $J = 8.5$ Hz, 2H), 7.36 (AA'BB', $J = 8.6$ Hz, 2H), 7.73 (AA'BB', $J = 8.1$ Hz, 2H), 7.74 (dd, $J_1 = 3.6$ Hz, $J_2 = 1.7$ Hz, 1H, pirol), 8.01 (AA'BB', $J = 8.4$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.62, 21.70, 110.51, 124.55, 128.38, 128.92, 129.06, 129.44, 129.98, 133.18, 135.19, 136.27, 143.53, 144.89, 184.42. HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{17}\text{O}_3\text{NS}$ (M) $^+$ 339.0929. Found: 339.0922. El. anal. calcd $\text{C}_{19}\text{H}_{17}\text{O}_3\text{NS}$: C, 67.24; H, 5.05; N, 4.13. Found: C, 67.00; H, 5.25; N, 4.00.

[N-[(4-Methylphenyl)sulfonyl]-pyrrol-2-yl]-(4-methylphenyl)methanol (S3). Ketone **S2** (11.8 mmol, 4.0 g) was dissolved in the mixture of methanol (40 ml) and THF (150 ml). Then NaBH_4 (59.0 mmol, 2.18 g) was added. After 15 minutes the solvents were distilled out and water was added (50 ml). Subsequently resulted suspension was extracted with CH_2Cl_2 , the organic layer was dried (Na_2SO_4) and the solvent was evaporated affording pure product as a colorless solid (4.0 g, 99%): ^1H NMR (500 MHz, CDCl_3 , Me_4Si , ppm): δ 2.33 (s, 3H), 2.41 (s, 3H), 3.12 (d, 1H, $J = 4.8$ Hz), 5.83 (ddd, 1H, $J_1 = 0.8$ Hz, $J_2 = 1.8$ Hz, $J_3 = 3.4$ Hz), 6.03 (d, 1H, $J = 3.4$ Hz), 6.17 (t, 1H, $J = 3.4$ Hz), 7.07 (d, 2H, $J = 8.0$ Hz), 7.13 (d, 2H, $J = 8.0$ Hz), 7.25 (d, 2H, $J = 8.4$ Hz), 7.60 (d, 2H, $J = 8.4$ Hz); ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 21.1, 21.6, 68.0, 115.3, 123.8, 126.5, 128.8, 129.9, 136.2, 137.9, 137.9, 138.3, 145.0; HRMS (EI) calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_3\text{S}[\text{M}^+]$ 341.1086, found 341.1078.

1,17-Bis-N,N-(4-methylphenyl)sulphonyl-6,12-bis-(4-methylphenyl)-tripyrane (S4). Alcohol **S3** (20 mmol, 6.79 g) and pyrrole (9.5 mmol, 660 μl) were dissolved in CH_2Cl_2 , then TFA (1.5 mmol, 115 μl) was added. The reaction mixture was stirred at room temperature for 72 hours and washed with water. The organic layer was washed with water, dried (Na_2SO_4) and evaporated. The residue was passed through silica pad affording pure product as a pale orange solid (5.7 g, 86%): IR (KBr, ν_{max} / cm^{-1}) 590, 671, 1054, 1089, 1116, 1148, 1173, 1369, 1512, 1596, 2921, 3400; ^1H NMR (500 MHz, CDCl_3 , Me_4Si , ppm): δ 2.28 (s, 6H), 2.30 (s, 3H) 2.33 (s, 3H), 5.30 (dd, 2H, $J_1 = 2.7$ Hz, $J_2 = 12.9$ Hz), 5.79 (dd, 2H, $J_1 = 1.6$ Hz, $J_2 = 5.1$ Hz), 5.85 (d, 2H, $J = 3.4$ Hz), 6.18 (q, 2H, $J = 3.4$ Hz), 6.81 (dd, 4H, $J_1 = 2.8$ Hz, $J_2 = 8.0$ Hz), 6.91 (dd, 4H, $J_1 = 3.9$ Hz, $J_2 = 8.0$ Hz), 6.99 (dd, 4H, $J_1 = 8.4$ Hz, $J_2 = 11.6$ Hz), 7.23 (dd, 4H, $J_1 = 2.5$ Hz, $J_2 = 8.4$ Hz), 7.28 (s, br, 1H); ^{13}C NMR (125 MHz, CDCl_3 , ppm): δ 21.0, 21.4, 41.7, 107.6, 111.1, 114.8, 122.9, 128.4, 128.8, 129.3, 131.9, 135.9, 136.1, 136.6, 137.0, 138.0, 144.1, 144.2; HRMS (EI) calcd for

$C_{42}H_{39}N_3O_4S_2$ [M^{+}] 713.2382, found 713.2403; Anal. Calcd for $C_{42}H_{39}N_3O_4S_2$: C, 70.66; H, 5.51; N, 5.89; S, 8.98. found: C, 70.53; H, 5.45; N, 5.75; S, 8.97.

Scheme S1



4. References

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5. Spectral data

