Isophthalamides and pyridine-2,6-dicarboxamides with pendant indole groups: a ‘twisted’ binding mode for selective fluoride recognition

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Synthesis

Pyridine-2,6-dicarboxylic acid bis-[{(2,3-dimethyl-1H-indol-7-yl)-amide}], 1

2,3-Dimethyl-7-nitroindole (0.7 g, 3.7 mmol) was dissolved in ethanol (100 mL) with 10% Pd/C (100 mg) and hydrazine monohydrate (2 mL). The reaction was refluxed for 2 hours then filtered through celite and washed with ethanol. The filtrate was concentrated in vacuo and the solid residue was used immediately. The solid was dissolved in acetonitrile (50 mL) with triethylamine (5 mL) and a catalytic amount of DMAP. To this was added a solution of pyridine-2,6-dicarbonylchloride (0.37 g, 1.8 mmol) in acetonitrile (50 mL) and the reaction was stirred overnight during which time a solid precipitate had formed. This was collected by filtration and washed with further acetonitrile followed by ether. The product was isolated as a yellow solid. Yield 0.52g (63 %, 1.2 mmol)

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 2.19 (s, 3H, CH$_3$), 2.36 (s, 3H, CH$_3$), 6.99 (t, 2H, $J=7.5$Hz, Ar-H), 7.15 (d, 2H, $J=7.3$Hz, Ar-H), 7.30 (d, 2H, $J=7.5$Hz, Ar-H), 8.32 (q, 1H, $J=7$, 8.5Hz, Ar-H), 8.43 (d, 2H, $J=7.5$Hz, Ar-H), 10.55 (s, 2H, amide NH), 11.13 (s, 2H, indole NH); $^{13}$C NMR (100 Mhz, DMSO-$d_6$) $\delta$: 8.22 (CH$_3$), 11.02 (CH$_3$), 105.26 (C), 115.20 (Ar-CH), 116.84 (Ar-CH), 117.57 (Ar-CH), 120.54 (Ar-C), 124.68 (Ar-CH), 129.98 (Ar-C), 130.12 (Ar-C), 131.35 (Ar-C), 139.40 (Ar-CH), 148.77 (Ar-C), 161.63 (C=O); LRMS ES$: 450.2 (M+H)$; IR $\nu$ cm$^{-1}$ 3381s, 3256s, 2915s, 1644s, 1544s, 1456s, 1412s, 1343s, 1148s, Microanalysis for C$_{27}$H$_{25}$N$_5$O$_2$+0.15CH$_2$Cl$_2$. Calc. (%) C = 70.20, H = 5.49, N = 15.07. Found (%) C = 70.19, H = 5.60, N = 15.02; Mp: decomposed $\sim$220°C
Figure S1 $^1$H NMR of compound 1

Figure S2 $^{13}$C NMR of compound 1
**N,N'-Bis-(2,3-dimethyl-1H-indol-7-yl)-isophthalamide, 2**

2,3-Dimethyl-7-nitroindole (0.7 g, 3.7 mmol) was dissolved in ethanol (100 mL) with 10% Pd/C (100 mg) and hydrazine monohydrate (2 mL). The reaction was refluxed for 2 hours then filtered through celite and washed with ethanol. The filtrate was concentrated *in vacuo* and the solid residue was used immediately. The solid was dissolved in acetonitrile (50 mL) with triethylamine (5 mL) and a catalytic amount of DMAP. To this was added a solution of isophthaloyl chloride (0.37 g, 1.8 mmol) in acetonitrile (50 mL) and the reaction was stirred overnight during which time a solid precipitate had formed. This was collected by filtration and washed with further acetonitrile followed by ether. The product was isolated as a white solid. Yield 0.49 g (60%, 1.1 mmol)

^1H NMR (400 MHz, DMSO-d$_6$) δ: 2.18 (s, 3H, CH$_3$), 2.34 (s, 3H, CH$_3$), 6.96 (t, 2H, J=7.8Hz, Ar-H), 7.24 (d, 2H, J=7.5Hz, Ar-H), 7.33 (d, 2H, J=7.5Hz, Ar-H), 7.73 (t, 1H, J=7.8Hz, Ar-H), 8.24 (d, 2H, J=7.6Hz, Ar-H), 8.70 (s, 1H, Ar-H), 10.14 (s, 2H, amide NH), 10.47 (s, 2H, indole NH);

^13C NMR (100 Mhz, DMSO-d$_6$) δ: 8.40 (CH$_3$), 11.20 (CH$_3$), 105.58 (C), 114.67 (Ar-CH), 115.01 (Ar-CH), 117.93 (Ar-CH), 121.93 (Ar-C), 127.42 (Ar-CH), 128.35 (Ar-CH), 128.72 (Ar-C), 130.43 (Ar-C), 130.69 (Ar-CH), 131.28 (Ar-C), 135.08 (Ar-C), 161.85 (C=O);

LRMS ES*: 473.3 (M+Na)$^+$, LRMS ES$: 485.2, 487.2 (M+Cl)$^-$; IR ν cm$^{-1}$: 3415s, 3271s, 2916s, 1631s, 1544s, 1456s, 1413s, 1346s, Microanalysis for C$_{28}$H$_{26}$N$_4$O$_2$+0.12CH$_2$Cl$_2$. Calc. (%) C = 73.33, H = 5.74, N = 12.17; Found (%) C = 73.30, H = 5.88, N = 12.17; Mp: decomposed ~215°C

![Figure S3 ^1H NMR of compound 2](image-url)
Anion Binding Experiments

Figure S5 Fit plot for titration experiment of 1 with TBA acetate in DMSO/0.5% water
Figure S6 Fit plot for titration experiment of 1 with TBA dihydrogen phosphate in DMSO/0.5% water

Figure S7 Fit plot for titration experiment of 1 with TBA benzoate in DMSO/0.5% water

Figure S8 Fit plot for titration experiment of 1 with TBA chloride in DMSO/0.5% water
Figure S9 Fit plot for titration experiment of 1 with TBA fluoride in DMSO/0.5% water

Figure S10 Fit plot for titration experiment of 1 with TBA fluoride/5% water

Figure S11 Fit plot for titration experiment of 1 with TBA chloride/5% water
Figure S12 Fit plot for titration experiment of 2 with TBA acetate in DMSO/0.5% water

Figure S13 Fit plot for titration experiment of 2 with TBA dihydrogen phosphate in DMSO/0.5% water

Figure S14 Fit plot for titration experiment of 2 with TBA benzoate in DMSO/0.5% water
Figure S15 Fit plot for titration experiment of 2 with TBA chloride in DMSO/0.5% water

Figure S16 Fit plot for titration experiment of 2 with TBA fluoride/5% water

Figure S17 Fit plot for titration experiment of 2 with TBA chloride/5% water
Figure S18 Fit plot for titration experiment of 2 with TBA acetate/5% water

Figure S19 Fit plot for titration experiment of 2 with TBA dihydrogen phosphate/5% water

Figure S20 Fit plot for titration experiment of 2 with TBA benzoate/5% water
Figure S21 $^1$H NMR stack plot of compound 1 with increasing concentrations of TBAF in DMSO/5% water (from bottom – free ligand, 1 eq., 1.5 eq, 5 eq).

Figure S22 $^1$H NMR stack plot of compound 2 with increasing concentrations of TBAF in DMSO/5% water (from bottom – free ligand, 1 eq., 1.5 eq, 5 eq).
Figure S23 Job plot of Compound 2 with fluoride showing predominant 1:1 binding in DMSO-d$_6$/0.5% water.

Figure S24 $^1$H NMR stack plot of compound 2 with increasing concentrations of TBAF in DMSO-d$_6$/0.5% water.
Figure S25 $^1$H NMR titration data plot of compound 2 with TBAF DMSO-$d_6$/ 0.5% water. Following amide NH (red proton on above spectra).

Figure S26 N–F–N angles in 1-F
Figure S27 N–F–N angles in 2–F