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## 2,5-Diamidofuran anion receptors

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Abstract—3,4-Diphenylfuran-2,5-dicarboxylic acid bis-*N*-phenylamide 1 and 3,4-biphenyl-furan-2,5-dicarboxylic acid bis-*N*-butylamide 2 have been synthesised and shown to act as fluoride selective anion receptors in DMSO- $d_6/0.5\%$  water solution. © 2003 Elsevier Science Ltd. All rights reserved.

In 1997, Crabtree and co-workers reported that very simple isophthalamide type anion receptors form remarkably strong complexes with fluoride and chloride in organic solution.<sup>1</sup> This discovery has led to the incorporation of this hydrogen bond donor unit in a variety of anion<sup>2</sup> and ion-pair<sup>3</sup> receptors as well as in self-assembling systems.<sup>4</sup> With the aim of enhancing the anion affinity of this motif, we synthesised analogous receptors containing a central pyrrole ring (instead of a benzene) in order to introduce an additional hydrogen bond donor group. Our first generation 2,5-diamidopyrrole receptors were found to be selective for carboxylates in DMSO- $d_6/0.5\%$  water solution.<sup>5</sup> Second generation systems employed pendant arms containing amine, amide or ammonium groups to modulate the affinity of these systems and we found that amine functionalised receptors were selective for acidic oxo-anions such as  $HSO_4^{-.6}$  Crabtree found that introduction of a central pyridine ring increased the selectivity for smaller halides such as fluoride.<sup>7</sup> We have found that deprotonation of the central pyrrole ring in our 2,5-diamidopyrrole systems allowed the formation of an unusual interlocked dimer.8 We therefore wished to synthesise a variety of 2,5-diamidofurans and study their anion receptor and potential self-assembly properties.

3,4-Diphenylfuran-2,5-dicarboxylic acid was synthesised by literature methods.<sup>9</sup> This material was converted to the acid chloride and then coupled with aniline or *n*-butylamine affording the diamides  $1^{10}$  and  $2^{11}$  in 80 and 53% overall yields, respectively.



X-Ray quality crystals of **1** were obtained by slow evaporation of an acetonitrile solution of the receptor.<sup>12</sup> The receptor adopts a cleft conformation (Fig. 1). The molecules form chains along the a axis via NH $\cdots$ O hydrogen bond linkages (Fig. 2) such that the furan



Figure 1. The X-ray crystal structure of compound 1 (acetonitrile and certain hydrogen atoms omitted for clarity).

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Figure 2. Hydrogen bonding array present in the solid-state (certain atoms have been omitted for clarity).

rings adopt alternating orientations (in contrast to the 2,5-diamidopyrrole anion analogue which has been shown to form an interlocked dimer in the solid state<sup>8</sup>). There are two unique hydrogen bonds operating as independent pairs; the shorter pair (N2–H2…O1, 2.17 Å) link the molecules into centrosymmetric dimers and the longer pair (N1–H1…O3, 2.43 Å) connect the dimers into chains.

Dilution studies were conducted on both compounds in DMSO- $d_6/0.5\%$  water, however, no shifts in the amide NH resonances were observed. In dichloromethane, compound **2** appears to dimerise in solution but with a low dimerisation constant (1.7 M<sup>-1</sup>).<sup>13</sup> Anion binding studies were conducted in DMSO- $d_6/0.5\%$  water solution using <sup>1</sup>H NMR titration techniques.<sup>14</sup> The results, summarised in Table 1, reveal that both compounds show a high selectivity for fluoride under these conditions.

In contradistinction to the oxo-anion selective 2,5diamidopyrroles,<sup>5</sup> 2,5-diamidofurans show selectivity for fluoride in DMSO- $d_6/0.5\%$  water solution. The oxoanion selectivity of the former systems is believed to be due to the ability of the receptor to form three hydrogen bonds to the two oxygen atoms in an oxo-anion such as benzoate.<sup>15</sup> The absence of the central NH hydrogen bond donor group in **1** and **2** and the presence of an oxygen atom may introduce a repulsive component to the interaction of these species with

Table 1. NMR titrations were conducted in DMSO- $d_6/0.5\%$  water at 298 K

Added anion <sup>a</sup>	Association constant $(M^{-1})$ with compound $1^{b}$	Association constant $(M^{-1})$ with compound $2^{b}$
Fluoride <sup>c</sup>	1140	557
Dihydrogen phosphate	78	46
Benzoate	49	28
Chloride	47	14

<sup>a</sup> Anion added as tetrabutylammonium salt.

 $^{\rm b}$  Errors in association constants estimated to be a maximum of  $\pm 15\%.$ 

anions so favouring smaller anions such as fluoride which presumably resides further from the oxygen than larger bound anions.<sup>7</sup> We are continuing to study the anion-binding and assembly properties of 2,5-diamidofuran containing systems. The reports of these studies will be reported in due course.

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- 3,4-Diphenylfuran-2,5-dicarboxylic acid bis-N-phenylamide 1

<sup>&</sup>lt;sup>c</sup> Dried under high vacuum without heating. The fluoride was assumed to be anhydrous when calculating the concentrations used in the fitting procedure, however, this is unlikely to be the case and these values must therefore be treated with a certain degree of caution. However, the titration profiles clearly indicate the selectivity of these receptors for fluoride.

3,4-Diphenylfuran-2,5-dicarboxylic acid (2.0 g, 0.0048 mol) was suspended in freshly distilled thionyl chloride (50 ml) and heated at reflux overnight. The thionyl chloride was removed in vacuo and the resulting solid dried under high vacuum for 2 h. The resulting 3,4diphenylfuran-2,5-dicarbonyl dichloride was dissolved in dry dichloromethane (80 mL). Triethylamine (2.0 g, 0.0198 mol), DMAP (catalytic quantity) and aniline (1.27 g, 0.0136 mol) were added whilst the solution was stirred under a nitrogen atmosphere. The reaction mixture was stirred overnight and the organic solution was then washed with water (4×100 ml), dried with magnesium sulfate and the dichloromethane removed in vacuo. The product was recrystallised from acetonitrile (200 ml) affording the final product (1.77 g, 80%) as a white powder. (Found: C, 75.82; H, 5.11; N, 5.69. C<sub>30</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>+H<sub>2</sub>O requires C, 75.61; H, 5.08; N, 5.88%). <sup>1</sup>H NMR in DMSO- $d_6$  300 MHz,  $\delta$  (ppm): 7.24–7.83 (m, 20H, ArH), 10.49 (s, 2H, NH). <sup>13</sup>C NMR in DMSO-d<sub>6</sub> 400 MHz  $\delta$  (ppm): 121.3, 124.8, 128.0, 128.2, 129.3, 130.5, 130.8, 132.7, 138.3, 141.9, 156.2. ES+ mass spectrum, m/z, 560 (M+Et<sub>3</sub>NH<sup>+</sup>), 917 (2M<sup>+</sup>) HRES MS  $C_{60}H_{44}N_4O_6Na$  calcd 939.3153, found 939.3180,  $\Delta = 2.8$ ppm. Mp =  $278^{\circ}$ C.

11. 3,4-Diphenylfuran-2,5-dicarboxylic acid bis-*N*-butylamide **2** 

3,4-Diphenylfuran-2,5-dicarboxylic acid (2.0 g, 0.0048 mol) was suspended in freshly distilled thionyl chloride (50 ml) and heated at reflux overnight. The thionyl chloride was removed in vacuo and the resulting solid dried under high vacuum for 2 h. The 3,4-diphenylfuran-2,5-dicarbonyl dichloride was dissolved in dry

dichloromethane (80 ml). Triethylamine (2.0 g, 0.0198 mol), DMAP (catalytic quantity) and *n*-butylamine (1.00 g, 0.0136 mol) were added whilst the solution was stirred under a nitrogen atmosphere. The reaction mixture was stirred overnight and the organic solution was then washed with water (4×100 ml), dried with magnesium sulfate and the dichloromethane removed in vacuo. The yellow residue was crystallised from diethyl ether (200 ml) resulting in a white crystalline material (1.07 g, 53%). (Found: C, 73.79; H, 7.16; N, 6.51. C<sub>26</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub>+0.33 MeOH requires C, 73.69; H, 7.36; N, 6.53%). <sup>1</sup>H NMR in CDCl<sub>3</sub> 300 MHz,  $\delta$  (ppm): 0.88 (t, J = 7.3 Hz, 6H, CH<sub>3</sub>), 1.24 (m, 4H, CH<sub>2</sub>), 1.43 (m, 4H, CH<sub>2</sub>), 3.32 (m, 4H, CH<sub>2</sub>), 6.28 (t, J=5.5 Hz, 2H, NH), 7.17–7.30 (m, 10H, ArH). <sup>13</sup>C NMR in CDCl<sub>3</sub> 400 MHz  $\delta$  (ppm): 13.7, 20.0, 31.4, 39.0, 128.3, 128.4, 130.2, 130.3, 131.0, 142.4, 158.2.  $ES^+$  mass spectrum, m/z, 520 (M+Et<sub>3</sub>NH<sup>+</sup>), 837 (2M+H<sup>+</sup>) HRES MS  $C_{52}H_{60}N_4O_6Na$  calcd 859.4405, found 859.4408,  $\Delta = 0.4$  ppm. Mp = 144°C.

- 12. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 195420. Copies of the data can be obtained free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
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