2-Amidopyrroles and 2,5-Diamidopyrroles as Simple Anion Binding Agents

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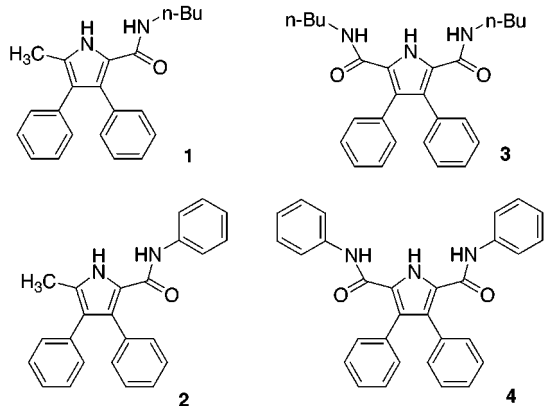
Four new 2-amidopyrroles and 2,5-diamidopyrroles have been synthesized and their anion complexation properties investigated. The crystal structures of these receptors have been elucidated and reveal hydrogen bonding in the solid state leading to dimer and network formation. Selectivity for oxo-anions has been demonstrated by ^{1}H NMR titration techniques.

Introduction and Background

Recent developments in the area of anion recognition and sensing have produced a variety of new selective receptors for anions.[1] However, the great variety of anionic species and their importance in the environment (pollutant anions from over use of agricultural fertilizers cause eutrophication of lakes and inland waterways[2]), in biological systems (misregulation of anion transport is responsible for a number of medical conditions including cystic fibrosis[3]), and in the clinic (the maintenance of sulfate anion concentration in dialysis patients continues to be problematic[4]) presents a continuing challenge to design selective receptors. The anion coordination ability of receptors containing pyrrole groups has been an area of increasing interest in the past decade. This area of chemistry has been led by Sessler and co-workers who have produced a variety of expanded porphyrins[5] and polypyrrolic[6] macrocycles capable of binding anions. A smaller subset of receptors containing both a pyrrole and an amide moiety have been described.[7] Many of these systems are quite complex, for example Sessler and Vögtle's elegant catenane for oxo-anion complexation.[8] More recently, Schmuck has shown that guanidinium groups that contain an appended pyrrole-amide moiety are useful in the selective complexation of amino acids.[9] We decided to 'extract' the pyrrole amide unit and synthesize a variety of simple pyrrole-amide ligands **1**−**4** in order to assess the anion complexation ability of this moiety alone.



Discussion

5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic acid ethyl ester was synthesized via a Paal−Knorr reaction

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(1) Gale, P. A. *Coord. Chem. Rev.* **2000**, *199*, 181−233. Gale, P. A. *Coord. Chem. Rev.* **2001**, *213*, 79−128. Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486-516. Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609−1646. Beer, P. D.; Smith, D. K. *Prog. Inorg. Chem.* **1997**, *46*, 1−96. Atwood, J. L., Holman, K. T.; Steed, J. W. *Chem. Commun.* **1996**, 1401−1407. Davis, A. P.; Gilmer, J. F.; Perry J. J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1312−1315. *Supramolecular Chemistry of Anions*; Bianchi, A.; Bowman-James, K.; García-España, E. Eds.; Wiley−VCH: New York, 1997. Sessler, J. L.; Allen, W. E. *Chemtech* **1999**, *29*, 16−24.

(2) Moss, B. *Chem., Ind.* **1996**, 407−411.

(3) *Chloride Trasport Coupling in Biological Membranes and Epithelia*; Gerenscer, G.; Ed.; Elsevier: Amsterdam, 1984; Boat, T. F.; Welsh, M. J.; Beaudet, A. L. In *The Metabolic Basis of Inherited Disease*, 6th ed.; Scriver, C. R.; Beaudet, A. L.; Sly, W. S.; Valle, D., Eds.; McGraw-Hill: New York, 1989; p 2649.

(4) Brunetti, M.; Terracina, L.; Timio, M.; Saronio, P.; Capodicasa, E. *J Nephrol.* **2001**, *14*, 27−31. Kajiyama, H.; Nojima, Y.; Mitsuhashi, H.; Ueki, K.; Tamura, S.; Sekihara, T.; Wakamatsu, R.; Yano, S.; Naruse, T. *J. Am. Soc. Nephrol.* **2000**, *11*, 923−7.

(5) Sessler, J. L.; Cyr, M. J.; Lynch, V.; McGhee, E.; Ibers, J. A. *J. Am. Chem. Soc.* **1990**, *112*, 2810−2813. Shionoya, M.; Furuta, H.; Lynch, V.; Harriman, A.; Sessler, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 5714−5722. Král, V.; Furuta, H.; Shreder, K.; Lynch, V.; Sessler, J. L. *J. Am. Chem. Soc.* **1996**, *118*, 1595−1607. Král, V.; Andrievsky, A.; Sessler, J. L. *J. Am. Chem. Soc.* **1995**, *117*, 2953−2954. Sessler, J. L.; Andrievsky, A.; Král, V.; Lynch, V. *J. Am. Chem. Soc.* **1997**, *119*, 9385−9392. Furuta, H.; Cyr, M. J.; Sessler, J. L. *J. Am. Chem. Soc.* **1991**, *113*, 6677−6678. Sessler, J. L.; Král, V.; Genge, J. W.; Thomas, R. E.; Iverson, B. L. *Anal. Chem.* **1998**, *70*, 2516−2522. Sessler, J. L.; Genge, J. W.; Král, V.; Iverson, B. L. *Supramol. Chem.* **1996**, *8*, 45−52. Iverson, B. L.; Shreder, K.; Král, V.; Sessler, J. L. *J. Am. Chem. Soc.* **1993**, *115*, 11022−11023. Sessler, J. L.; Weghorn, S. J. *Expanded, Contracted and Isomeric Porphyrins*; Elsevier: Oxford, 1997.

(6) Gale, P. A.; Sessler, J. L.; Král, V. *Chem. Commun.* **1998**, 1−8. Anzenbacher, P., Jr.; Jursikova, K.; Lynch, V. M.; Gale, P. A.; Sessler, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 11020−11021. Sessler, J. L.; Gale, P. A. In *The Porphyrin Handbook*; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: San Diego, CA and Burlington, MA, 2000; Vol. 6, pp 257−278. Miyaji, H.; Sato, W.; Sessler, J. L. *Angew. Chem., Int. Ed.* **2000**, *39*, 1777−1780. Gale, P. A.; Sessler, J. L.; Allen, W. E.; Tvermoes, N. A.; Lynch, V. *Chem. Commun.* **1997**, 665−666. Sessler, J. L.; Andrievsky, A.; Gale, P. A.; Lynch, V. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2782−2785.

(7) Scherer, M.; Sessler, J. L.; Gebauer, A.; Lynch, V. *Chem. Commun.* **1998**, 85−86. Scherer, M.; Sessler, J. L.; Moini, M.; Gebauer, A.; Lynch, V. *Chem. Eur. J.* **1998**, *4*, 152−158.

(8) Andrievsky, A.; Ahuis, F.; Sessler, J. L.; Vögtle, F.; Gudat, D.; Moini, M. *J. Am. Chem. Soc.* **1998**, *120*, 9712−9713.

(9) Schmuck, C.; *Chem. Eur. J.* **2000**, *6*, 709−718. Schmuck, C. *Chem. Commun.* **1999**, 843−844.

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according to literature procedures,[10] giving characterization data in accord with a previously published synthesis.[11] This material was converted to 5-methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic acid butylamide **1** by reaction with an excess of butylamine (approximately 50 equiv) in the presence of catalytic quantities of cyanide[12] anions in 29% yield. Compound **2**, 5-methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic acid phenylamide, was obtained by reacting 5-methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic acid ethyl ester with an aluminum phenylamide derivative, prepared in situ by reaction of trimethylaluminum and aniline in 17% yield.[13]

3,4-Diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid was synthesized in five steps via literature procedures.[14,15] This material was then converted to the acid chloride by reaction with thionyl chloride with heating at reflux. The acid chloride was obtained by removal of the thionyl chloride in vacuo and used immediately, by addition of a dichloromethane solution containing either *n*-butylamine or aniline, together with triethylamine and a catalytic quantity of DMAP, affording the bis-amide clefts **3**, 3,4-diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid bis-butylamide, and **4**, 3,4-diphenyl-1*H*-pyrrole-2,5-dicarboxylic acid bis-phenylamide, respectively, in 18 and 47% yields as previously communicated.[16]

Compounds **1**−**4** are capable of both donating and accepting hydrogen bonds allowing for the formation of dimers and coordination polymers in the solid state.[17] Indeed, crystals of **1** obtained from a dichloromethane/methanol solvent mixture by slow evaporation form dimers in the solid state via pyrrole NH···amide O hydrogen bonds (Figure 1).[10] Similarly, crystals of compound **2** crystallized from dichloromethane/acetonitrile reveal dimer formation (Figure 2).

Single crystals of compounds **3** and **4** were obtained by slow evaporation of CH_2Cl_2/EtOH and acetonitrile solutions of the receptors, respectively. The two independent molecules in crystals of **3** differ only in the conformation of the butyl chains and form pseudo centrosymmetric dimers via chemically equivalent *amide*−*amide* hydrogen bonds. The oxygen atoms then each accept a second *pyrrole* NH hydrogen bond to bridge the dimers into chains that extend along the *c* axis (Figure 3). Both independent molecules in the crystal structure of **4** form centrosymmetric dimers (Figure 4) via both N−H···O hydrogen bonds and C−H···O hydrogen bonds as has been observed by Schmuck and Lex in the crystal structure of methyl 5-amidopyrrole-2-carboxylate.[18] Interestingly, when compound **4** is crystallized from DMSO, a different 'semicleft like' conformation is adopted wherein pyrrole and one amide NH group form hydrogen bonds to a bound DMSO guest (Figure 5).

It has been previously shown that a single pyrrole ring is ineffective at complexing anions in solution.[19] Therefore, the ability of these receptors to act as anion complexation agents must rely upon the formation of a cleft-like conformation[20] involving either two or three hydrogen bond donors. The crystal structure of the DMSO complex of **4** illustrates the formation of a 'bidentate' cleft, and it may also be possible for the other amide to flip conformation and allow for the formation of three hydrogen bonds to a putative guest species. Unlike urea, a commonly used receptor for carboxylate anions,[21] these receptors form a convergent binding site (Figure 6).

Anslyn and co-workers have synthesized poly-aza cleft systems containing pyrrole rings functionalized in the 2-position with amine groups; however, these systems are

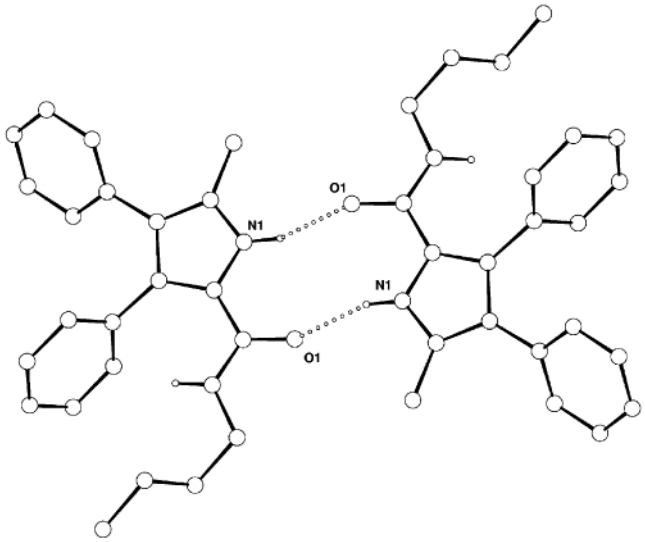

Figure 1. The X-ray crystal structure of compound **1** (dimerization via amide C═O···HN pyrrole hydrogen bonds N1−O1 distance 2.766(6) Å).

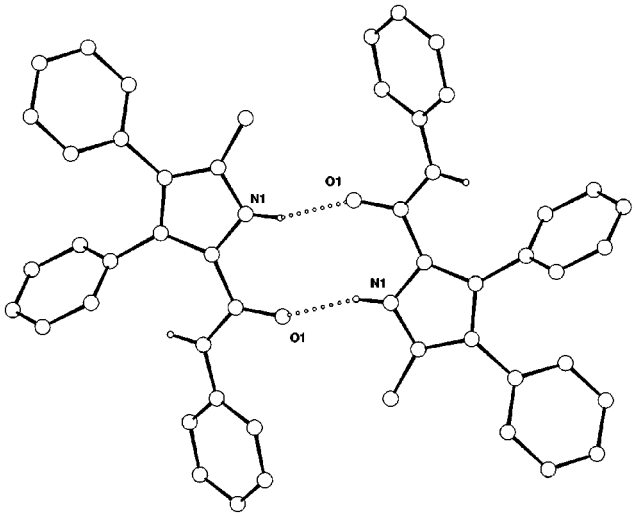

Figure 2. The X-ray crystal structure of compound **2** (dimerization via amide C═O···HN pyrrole hydrogen bonds N1−O1 2.875(5) Å).

(10) Motekaitis, R. J.; Heinert, D. H.; Martell, A. E. *J. Org. Chem.* **1970**, *35*, 2504−2511.
(11) Chang, C. K.; Bag, N. *J. Org. Chem.* **1995**, *60*, 7030−7032.
(12) Hogberg, T.; Strom, P.; Ebner, M.; Ramsby, S. *J. Org. Chem.* **1986**, *52*, 2033−2036.
(13) Basha, A.; Lipton, M.; Weinreb, S. M. *Tetrahedron Lett.* **1977**, *48*, 4171−4174.
(14) Medforth, C. J.; Senge, M. O.; Smith, K. M.; Sparks, L. D.; Shelnutt, *J. Am. Chem. Soc.* **1992**, *114*, 9859−9869.
(15) Friedman, M. *J. Org. Chem.* **1965**, *30*, 859−863.
(16) Gale, P. A.; Camiolo, S.; Chapman, C. P.; Light, M. E.; Hursthouse, M. B. *Tetrahedron Lett.* **2001**, *42*, 5095−5097.
(17) Allen W. E.; Fowler C. J.; Lynch V. M.; Sessler J. L. *Chem. Eur. J.* **2001**, *7*, 721−729.
(18) Schmuck, C.; Lex, J. *Eur. J. Org. Chem.* **2001**, 1519−1523.
(19) Gale, P. A.; Sessler, J. L.; Král, V.; Lynch, V. *J. Am. Chem. Soc.* **1996**, *118*, 5140−5141.
(20) Kavallieratos, K.; de Gala, S. R.; Austin, D. J.; Crabtree, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 2325−2326.
(21) For a recent examples of the use of urea for carboxylate complexation, see: Julian, V.; Shepherd, E.; Gelbrich, T.; Hursthouse, M. B.; Kilburn, J. D. *Tetrahedron Lett.* **2000**, *41*, 3963−3966. Pelizzi, N.; Casnati, A.; Friggeri, A.; Ungaro, R. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1307−1311 and references therein.

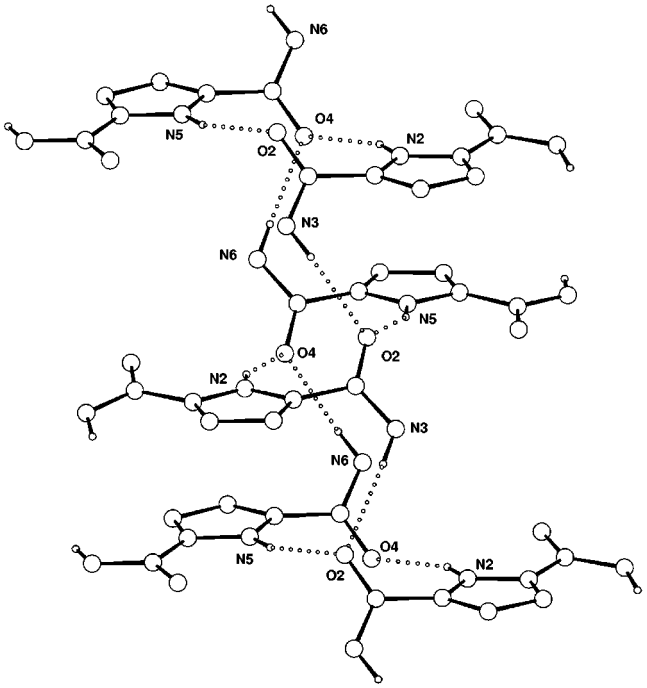

Figure 3. The X-ray crystal structure of compound **3** (hydrogen-bonding distances: N6−O4 2.982(4) Å; N5−O2 2.938(4) Å; N3−O2 3.060(4) Å; N2−O4 2.984(4) Å). Phenyl and butyl groups omitted for clarity.

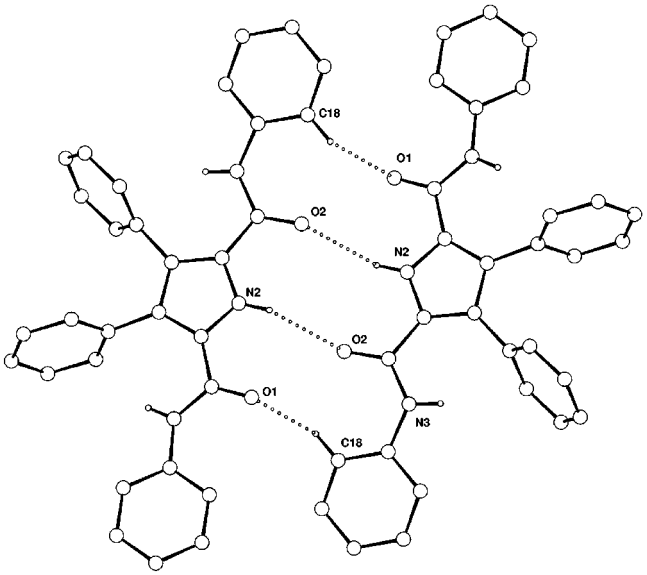

Figure 4. The X-ray crystal structure of compound **4** (dimerization via amide C═O···HN pyrrole and amide C═O···HC aromatic hydrogen bonds N2−O2 3.238(4); N5−O4 3.127(4) Å, C18−O1 3.271(4) Å).

more reminiscent of urea, as the hydrogen bond donor array is more nearly parallel that in the systems discussed in this paper.[22] The *possible* binding modes of receptors **1**−**4** with anions are illustrated in Figure 7. For the mono-amide receptors, **1** and **2**, only two 'bidentate' binding modes i and ii with carboxylates are possible. With the bis-amide systems, modes iii and iv are similar to i and ii while modes v and vi are unique to these systems.

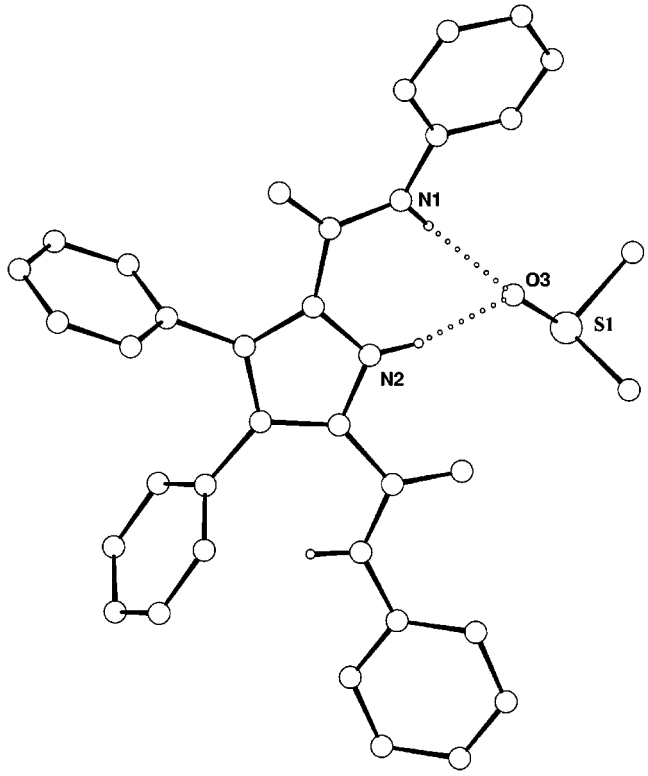

Figure 5. In the presence of DMSO, compound **4** crystallizes in a 'semicleft' conformation (N1−O3 2.831(4) Å; N2−O3 Å 2.757(4) Å).

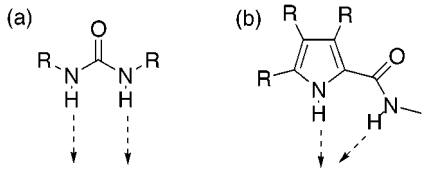

Figure 6. 2-Amidopyrroles provide a convergent binding site.

^{1}H NMR titration studies were used to assess the anion complexation properties of the receptors with association constants being obtained via the EQNMR computer program.[23] Initial dilution studies with the receptors in the solvent media used for anion binding studies showed no evidence for aggregation under the relevant concentration ranges used in the anion binding studies. Job plot analyses[24] revealed the formation of solely 1:1 receptor: anion solution complexed species. Unfortunately, precipitation (and crystallization) problems prevented studies being successfully completed in a quantitative manner with compound **2**. However, downfield shifts of the amide NH proton revealed the formation of anion complexes with this receptor. Compounds **1** and **3** were studied in acetonitrile-d_3 solution, while solubility problems with compound **4** forced the use of DMSO-d_6 and in fact DMSO-d_6/0.5% water was used. Direct comparisons may therefore be drawn between the data for compounds **1** and **3** only. The association constants for these receptors with benzoate, dihydrogen phosphate, fluoride, chloride, and bromide (as their tetrabutylammonium salts) are presented in Table 1. Both receptors **1** and **3** show selectivity for benzoate in acetonitrile-d_3 solution, binding

(22) Kelly-Rowley, A. M.; Lynch, V. M.; Anslyn, E. V. *J. Am. Chem. Soc.* **1995**, *117*, 3438−3447.

(23) Hynes, M. J. *J. Chem. Soc., Dalton Trans.* **1993**, 311−312.
(24) Huang, C. Y. *Methods Enzymol.* **1982**, *87*, 509−525.

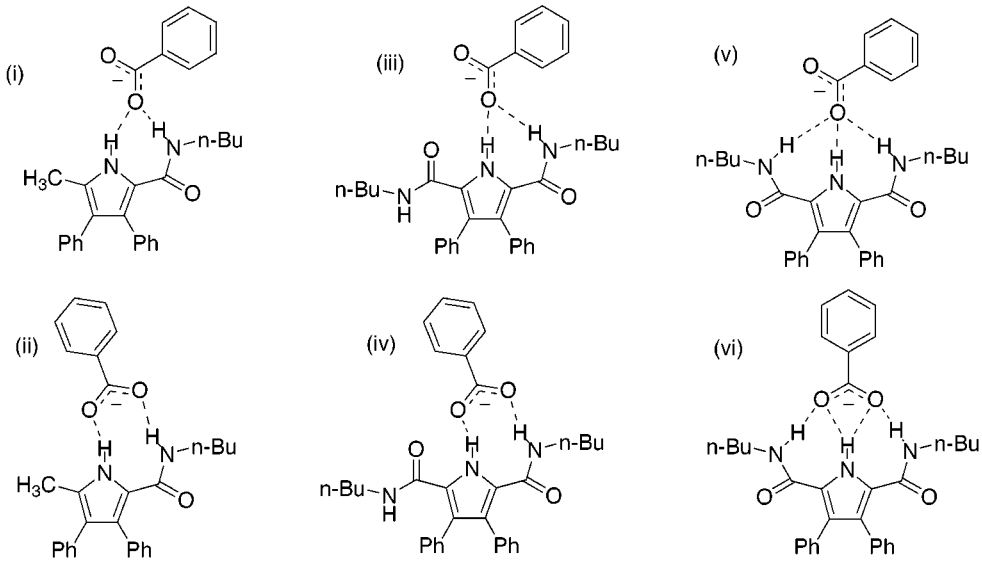

Figure 7. Possible binding modes of benzoate with compounds **1** and **3**.

Table 1. Association Constants of 1, 3, and 4 (M^{-1}) with Various Anionic Guest Species at 25 °C[a]

compound	anion[a]	solvent	K_a (M^{-1})[b]
1	fluoride	CD_3CN	134
1	chloride	CD_3CN	28
1	bromide	CD_3CN	<10
1	dihydrogen phosphate	CD_3CN	89
1	benzoate	CD_3CN	202
3	fluoride[c]	CD_3CN	85
3	chloride[c]	CD_3CN	138
3	bromide	CD_3CN	<10
3	dihydrogen phosphate	CD_3CN	357
3	benzoate	CD_3CN	2500
4	fluoride	DMSO/H_2O 0.5%	74
4	chloride	DMSO/H_2O 0.5%	11
4	bromide	DMSO/H_2O 0.5%	<10
4	dihydrogen phosphate	DMSO/H_2O 0.5%	1450
4	benzoate	DMSO/H_2O 0.5%	560

[a] Anions added as tetrabutylammonium salts dried under high vacuum with heating at 70 °C for 24 h prior to use. Acetonitrile water content = 0.03%. Solubility problems prevented studies on compound **4** from being conducted in acetonitrile solution. [b]Errors estimated to be <15%. [c]The amount of water present in the acetonitrile can have a dramatic effect on fluoride/chloride selectivity. In the presence of 0.5% water, fluoride is bound with a stability constant of 37.5 M^{-1} whereas chloride is bound more weakly (K = 12.5 M^{-1}).

this anion with association constants of 202 and 2500 M^{-1}, respectively. Dihydrogen phosphate is also complexed by these receptors albeit with smaller association constants (89 and 357 M^{-1}, respectively). There is little discrimination between the halides with compound **3** binding chloride most strongly (K_a = 138 M^{-1}) while compound **1** binds fluoride most strongly from this subgroup of guests with an association constant of 134 M^{-1}. Compound **4** in wet DMSO is selective for dihydrogen phosphate (K_a = 1450 M^{-1}) while also binding benzoate reasonably strongly (K_a = 560 M^{-1}) in this polar solvent medium. The difference in the benzoate and dihydrogen phosphate association constants for compounds **1** and **3** suggests that a different binding mode may be operating in each case and therefore suggests that compound **3** is forming a cleftlike conformation when binding carboxylate in solution. This may either be mode v or mode vi in Figure 7, both of which involve a higher degree of hydrogen bond formation than is possible of the mono-amide species.

Conclusion

In conclusion, we have shown that 2-amidopyrroles and particularly 2,5-diamidopyrroles *on their own* function as effective receptors for oxo-anions. We are currently incorporating this binding moiety into a variety of supramolecular anion complexation and sensing devices, and the results of these studies will be presented in due course.

Experimental Section

5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic Acid Ethyl Ester. Literature methods[25] have been found unsuitable for large-scale synthesis. A modification of another pyrrole synthesis[10] led to the desired compound. Ethyl benzoylacetate (49.3 g, 0.256 mol) was dissolved in acetic acid (100 mL) and cooled in an ice bath. A solution of sodium nitrite (21.25 g, 0.307 mol) in water (32 mL) was added dropwise and the solution and the mixture allowed to stand overnight. Phenyl methyl ketone (34.5 g, 0.256 mol) was added followed by portionwise addition of zinc powder (36.5 g, 0.557 mol). The resulting orange suspension was then heated at 120 °C for 30 min. After being cooled to 50 °C, the solution was poured in 300 mL of ice/water and stirred for 1 h. The water was decanted, and addition of ethanol (200 mL) led to a white solid that was collected by filtration, washed twice with ethanol (30 mL), and dried in vacuo (14.8 g, 18.9%). The compound gave characterization data in accordance with material produced via an alternative route.[11]

5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic Acid Butylamide (1). 5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic acid ethyl ester (1 g, 3.3 mmol), butylamine (13 g, 0.18 mol), and sodium cyanide[12] (18 mg, 3 mmol) were dissolved in dry methanol (20 mL) and refluxed for 5 days. The solvent was removed in vacuo and the residue purified by column chromatography (dichloromethane:methanol 95:5) (320 mg, 29%). ^{1}H NMR 300 MHz in CD_2Cl_2 δ (ppm): 0.83 (t, J = 7.29, 3H, CH_2CH_3), 1.13 (m, 2H, CH_2CH_3), 1.29 (m, 2H, $CH_2CH_2CH_3$), 2.39(s, 3H, CH_3), 3.25 (m, 2H, $NHCH_2$), 5.52 (s, 1H, CONH), 7.07−7.42 (m, 10H, arom.), 11.17 (s, 1H, NH). ^{13}C NMR 75.4 MHz in CD_2Cl_2 δ (ppm): 12.26, 13.97, 20.41, 31.86, 39.32, 121.36, 126.12, 128.12, 128.35, 129.31, 130.64, 131.52, 135.87,

(25) Fisher, H.; Fink, E. *Z. Physiol. Chem.* **1948**, *283*, 152−156.

136.23, 162.11. ES^+ mass spectrum, *m*/*z*, 333 ($M + H^+$), 374 ($M^+ + CH_3CN$), 396 ($M + CH_3CN + Na^+$) 665 ($2M + H^+$), 687 ($2M + Na^+$). HRMS calculated ($M + H^+$) 333.1961, found 333.1964 (Δ 0.7 ppm). Anal. Found for $C_{22}H_{24}N_2O \cdot 0.25H_2O$ (Calcd): C, 78.68 (78.42); H, 7.12 (7.33); N, 8.31 (8.31). Mp 158 °C (decomp). R_f 0.64 (dichloromethane:methanol, 20:1).

5-Methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic Acid Phenylamide (2). Aniline (305 mg, 3.3 mmol) was dissolved in freshly distilled dichloromethane (10 mL), and a 2 M solution of $AlMe_3$ in hexane[13] (1.65 mL, 3.3 mmol) was added dropwise. After stirring for 30 min, 5-methyl-3,4-diphenyl-1*H*-pyrrole-2-carboxylic acid ethyl ester (1 g, 3.3 mmol) was added and the solution refluxed for 3 days. The solution was then washed with 2 M HCl (20 mL), and the organic and aqueous layers were separated. The aqueous layer was washed with 20 mL of dichloromethane, and the organic phases were combined, dried over $MgSO_4$, and filtered. The solvent was removed in vacuo, and crystallization from acetonitrile led to the desired compound (200 mg, 17%). ^1H NMR 300 MHz in DMSO-d_6 δ (ppm): 2.38 (s, 3H, CH_3), 7.09−7.43 (m, 15H, arom.), 8.20 (s, 1H, CONH), 11.92 (s, 1H, NH). ^{13}C NMR 75.4 MHz in DMSO-d_6 δ (ppm): 11.65, 118.59, 120.80, 122.15, 122.96, 125.53, 126.93, 127.12, 127.15, 127.81, 128.27, 128.72, 129.00, 129.65, 130.76, 134.76, 134.90,138.54. ES^+ mass spectrum, *m*/*z*, 353 ($M + H^+$), 705 ($2M + H^+$). HRMS calculated ($M + H^+$) 353.1648, found 353.1655 (Δ 1.9 ppm). Anal. Found for $C_{24}H_{20}N_2O \cdot 1.07CH_2Cl_2$ (Calcd): C, 67.65 (67.91); H, 5.55 (5.03); N, 6.01 (6.32). Mp 212 °C (decomp). R_f 0.5 (dichloromethane:methanol, 99:1).

3,4-Diphenyl-1*H*-pyrrole-2,5-dicarboxylic Acid Butylamide (3). 3,4-Diphenylpyrrole-2,5-dicarboxylic acid (1 g, 3.2 mmol) was refluxed in thionyl chloride (25 mL) overnight to obtain the acid chloride. The excess of thionyl chloride was removed by rigorous drying under high vacuum. After dissolving the resulting acid chloride in dichloromethane (30 mL), triethylamine (711 mg, 7.04 mmol) and DMAP (10 mg, 0.08 mmol) were added followed by butylamine (528 mg, 7.04 mmol). The reaction was stirred for 48 h, leading to a red suspension. The solvent was removed in vacuo and the residue purified by column chromatography on silica gel (dichloromethane:methanol 95:5) to yield compound **3** (240 mg, 18%). ^1H NMR 300 MHz in DMSO-d_6 δ (ppm): 0.91 (t, J = 7.26, 6H, CH_3), 1.23 (m, 4H, CH_2CH_3), 1.37 (m, 4H, CH_2), 3.20 (m, 4H, NCH_2), 7.10 (t, J = 5.46, 2H, Ar), 7.18 (m, 4H, Ar), 7.30 (m, 4H, Ar), + obscured amide CONH, 2H), 12.03 (s, 1H, NH). ^{13}C NMR 75.4 MHz in DMSO-d_6 δ (ppm):13.7, 19.9, 31.2, 39.0, 124.1, 125.7, 128.1, 128.9, 130.9, 133.6, 160.4. ES^+ mass spectrum, *m*/*z*, 418 ($M + H^+$), 440 ($M + Na^+$), 857.6 ($2M + Na^+$), 1274 ($3M + Na^+$), 1290 ($M + K^+$). HRMS calculated ($M + Na^+$) 440.2308, found 440.2322 (Δ 2.7 ppm) ($2M + Na$); calculated 857.4725, found 857.4716 (Δ 1.0 ppm). Anal. Found for $C_{26}H_{31}N_3O_2 \cdot {}^1/_2H_2O$ (Calcd): C, 72.82 (73.21); H, 7.37 (7.56); N, 9.75 (9.85). Mp 162 °C (decomp). R_f 0.5 (dichloromethane: methanol, 20:1).

3,4-Diphenyl-1*H*-pyrrole-2,5-dicarboxylic Acid Phenylamide (4). 3,4-Diphenylpyrrole-2,5-dicarboxylic acid (1 g, 3.2 mmol) was refluxed in thionyl chloride (25 mL) overnight to obtain the acid chloride. The excess of thionyl chloride was removed by rigorous drying under high vacuum. After dissolving the resulting acid chloride in dichloromethane (30 mL), triethylamine (711 mg, 7.04 mmol) and DMAP (10 mg, 0.08 mmol) were added followed by aniline (654 mg, 7.04 mmol). The reaction was stirred for 48 h, leading to a red suspension. The solvent was removed in vacuo and the residue purified by column chromatography on silica gel (dichloromethane/methanol 96:4 v/v) to yield compound **4** (687 mg, 47%). ^1H NMR 300 MHz in DMSO-d_6 δ (ppm): 7.15 (t, J = 7.29, 2H, Ar), 7.34 (m, 14H, Ar), 7.55 (d, J = 8.19, 4H, Ar), 9.37 (s, 2H, CONH), 12.67 (s, 1H, NH). ^{13}C NMR 75.4 MHz in DMSO-d_6 δ (ppm): 119.3, 123.5, 124.7, 126.8, 127.2, 127.8, 128.7, 130.5, 133.7, 138.5, 158.6. ES^+ mass spectrum, *m*/*z*, 480 ($M + Na^+$)-937.4 ($2M + Na^+$), 1394 ($3M + Na^+$), 1413 ($3M + K^+$). HRMS calculated ($M + Na^+$) 480.1682, found 480.1681 (Δ 0.2 ppm). Anal. Found for $C_{26}H_{31}N_3O_2 \cdot {}^1/_2H_2O$ (Calcd): C, 77.90 (77.73); H, 4.76 (5.15); N, 8.80 (9.07). Mp 206 °C (decomp). R_f 0.56 (dichlorometane:methanol 99:1).

Supporting Information Available: Crystallographic data, ^1H NMR, ^{13}C NMR, and mass spectroscopic data for compounds **1**, **2**, **3**, and **4** together with ^1H NMR titration curves for the anion complexation titrations. This material is available free of charge via Internet at http://pubs.acs.org.

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