View Online

PAPER

NJC

www.rsc.org/njc

Synthesis and anion binding behaviour of diamide derivatives of pyrrole-2,5-diacetic acid†

Rongqing Li,[a] Louise S. Evans,[b] David S. Larsen,[a] Philip A. Gale*[b] and Sally Brooker*[a]

[a] *Department of Chemistry, University of Otago, P.O. Box 56, Dunedin, New Zealand. E-mail: sbrooker@alkali.otago.ac.nz; Fax: +64 (0) 3 479 7906; Tel: +64 (0) 3 479 7919*
[b] *School of Chemistry, University of Southampton, Southampton, UK SO17 1BJ. E-mail: philip.gale@soton.ac.uk; Fax: +44 (0)23 8059 6805; Tel: +44 (0)23 8059 3332*

Received (in Durham, UK) 16th August 2004, Accepted 16th September 2004
First published as an Advance Article on the web 19th October 2004

Four examples of bis-amidopyrrole derivatives of pyrrole-2,5-diacetic acid have been prepared. The reaction of diethyl pyrrole-2,5-diacetate with a large excess (24 equiv.) of *N,N*-dimethylethylenediamine gave *N,N′*-bis(2-dimethylaminoethyl)-1*H*-pyrrole-2,5-diacetamide (**1**). Three further examples, *N,N′*-bis[2-(2-pyridyl)ethyl]-1*H*-pyrrole-2,5-diacetamide (**2**), *N,N′*-bis(2-pyridylmethyl)-1*H*-pyrrole-2, 5-diacetamide (**3**) and *N,N′*-dibenzyl-1*H*-pyrrole-2,5-diacetamide (**4**), were prepared in a one pot procedure by converting pyrrole-2,5-diacetic acid into the *N*-hydroxysuccinimide ester and then reacting this with four equivalents of the appropriate amine, 2-(2-aminoethyl)pyridine, 2-aminomethylpyridine or benzylamine, respectively. Compounds **1**–**4** are shown to be effective anion receptors in acetonitrile-d_3 solution, with comparable binding affinities to those found for simple pyrrole-2,5-dicarboxamides, despite possessing a more flexible hydrogen bonding array.

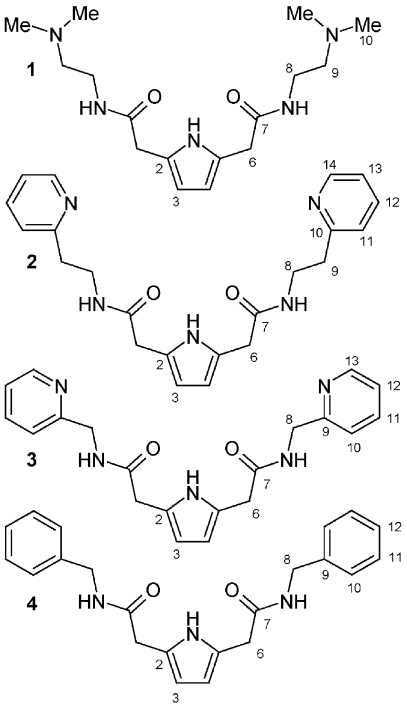
Published on http://pubs.rsc.org | doi:10.1039/B412654H
Downloaded on 22 December 2010

Introduction

Anion complexation chemistry is currently an area of intense interest.[1] Over the last few years, the anion complexation properties of mixed pyrrole–amide receptors have been investigated by the Southampton group[2] and others.[3] Pyrrole is particularly attractive as a hydrogen bond donor in such a receptor as: (a) unlike the amide or urea groups, pyrrole does not contain any built-in hydrogen bond acceptor sites and hence does not 'compete with itself' when forming a hydrogen bond to an anion; (b) the pyrrole N–H proton remains in place over a wide pK_a range and hence may function as a hydrogen bond donor group across a large pH window[4] and (c) pyrroles can be relatively easily functionalised and incorporated into elaborate cyclic and acyclic systems thus forming a variety of anion receptors. Recently attention has turned towards acyclic receptors and several types of pyrrole-containing anion binding systems have been reported, such as dipyrrolylquinoxalines,[5] guanidinium-containing amidopyrroles[6] and 2,5-dicarboxamidopyrroles.[2] Our interest in the 2,5-dicarboxamidopyrroles has led to the synthesis of a family of receptors with interesting binding, sensing and self-assembly properties.[2] We wished to extend this family to diamides synthesised from pyrrole-2,5-diacetic acid[7] in order to ascertain the effect of the extra methylene groups between the pyrrole and amide functionalities on the affinity of the resultant receptors for anions. Therefore the synthesis of four new bis-amidopyrrole derivatives, **1**–**4** (originally prepared due to our interest in them as potential ligands for transition metal ions[7]), from pyrrole-2,5-diacetic acid and their anion complexation properties, measured by ^{1}H NMR titration techniques, are reported here.

Results and discussion

N , N′-Bis(2-dimethylaminoethyl)-1*H*-pyrrole-2,5-diacetamide (**1**) was synthesised in high yield (95%) by reacting freshly prepared diethyl pyrrole-2,5-diacetate[7] with an excess of *N,N*-dimethylethylenediamine (24 equiv.) in dry ethanol under reflux for 96 h. Evaporation of the solvent and excess amine gave a brown oil which, on pumping under high vacuum at 50 °C, solidified to produce **1** as a very hygroscopic brown solid. The use of different amounts of the amine was examined. ^{1}H NMR spectra of the resulting reaction products revealed



† Electronic supplementary information (ESI) available: table of association constants of anions with receptors **1**, **2**, **3** and **4** in acetonitrile-d_3 and ^{1}H NMR titration curves for compounds **1**–**4** and anions. See http://www.rsc.org/suppdata/nj/b4/b412654h/

DOI: 10.1039/b412654h

This journal is © The Royal Society of Chemistry and the Centre National de la Recherche Scientifique 2004

View Online

Published on http://pubs.rsc.org | doi:10.1039/B412654H
Downloaded on 22 December 2010

that the use of lesser amounts of the amine (10 equiv. or 20 equiv.) resulted in mixtures of the desired diamide (**1**) and small amounts of the monoamide. The monoamide can be removed by washing an aqueous solution of the crude reaction product with dichloromethane. The ^{1}H NMR spectrum of the stoichiometric reaction (1 : 2 ratio of diester to amine) showed that almost no reaction had occurred.

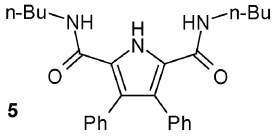
Initially a similar procedure was employed in attempts to synthesise *N,N′*-bis[2-(2-pyridyl)ethyl]-1*H*-pyrrole-2,5-diacetamide (**2**) and *N,N′*-bis(2-pyridylmethyl)-1*H*-pyrrole-2,5-diacetamide (**3**), simply replacing *N,N*-dimethylethylenediamine with 2-(2-aminoethyl)pyridine or 2-aminomethylpyridine, respectively. However, no reaction occurred in either case. Hence, instead of the diester, use of the more reactive precursor, 1*H*-pyrrole-2,5-diacetyl chloride, was considered. Attempts to prepare this reagent failed, presumably due to instability of the diacid chloride. Flitsch and co-workers[8] had successfully prepared two cyclic diamides from pyrrole-2,5-diacetic acid using a reactive, but unstable, mixed anhydride as the intermediate. Instead we turned our attention to the use of a stable activated diester as the precursor, employing the coupling method which has been widely used for both peptide synthesis and in general for amide bond formation. The coupling agent is usually added to the mixture of the carboxylic acid component and the amine component so that activation and coupling proceed simultaneously to form the amide product. Among the many possible coupling agents, dicyclohexylcarbodiimide (DCC), first introduced by Sheehan and Hess in 1955,[9,10] is one of the most commonly used.[11,12] In the present work, however, the coupling reaction did not take place as instead transfer of a proton from 1*H*-pyrrole-2,5-diacetic acid to the amines of interest [*e.g.* 2-(2-aminoethyl)-pyridine, 2-aminomethylpyridine] was fast enough to result in the quantitative precipitation of the ammonium salt of the amine. This observation is also found for other compounds in the literature.[13] Therefore, we decided to use the activated ester method to synthesise the pyrrole-2,5-diacetic acid diamides, employing the DCC coupling agent to prepare this ester from the diacid. The *N*-hydroxysuccinimide ester was chosen to be the activated ester because of its high reactivity and hence ease of formation of amide and peptide bonds,[12,14,15] and also because *N*-hydroxysuccinimide (HOSu) is commercially available. The DCC coupling method[14,15] was used to prepare the *N*-hydroxysuccinimide ester of pyrrole-2,5-diacetic acid. The main drawback of the HOSu–DCC method is the difficulty of purifying the activated ester product from the dicyclohexylurea (DCU) which forms as a by-product, since DCU is somewhat soluble in most organic solvents commonly used for coupling reactions. Fortunately in the present work we found that it was not necessary to isolate the activated ester and that the subsequent addition of the amines to this reaction mixture resulted in the formation of the desired pyrrole-2,5-diacetic acid diamides which could be purified more easily. The general procedure for the synthesis of the pyrrole-2,5-diacetic acid diamides **2**–**4** using the HOSu–DCC coupling method, is as follows. One equivalent of pyrrole-2,5-diacetic acid, two equivalents of HOSu and two equivalents of DCC are mixed together in THF (HPLC grade) and stirred for *ca.* 30 h at 0 °C. Then the ice–water bath is removed and four equivalents of the amine [2-(2-aminoethyl)pyridine, 2-aminomethylpyridine or benzylamine] are added to the reaction mixture, which is stirred for a few hours at room temperature. Removal of most of the DCU by-product, as a white solid, by filtration and subsequent evaporation of the filtrate gives the crude products still contaminated with small amounts of DCU. Subsequent extractions and recrystallisation (recrystallisation needed for **4** only) give the desired products, the pyrrole-2,5-diacetic acid diamides **2**, **3** and **4** in pure form and in good yield (60–70%). Like compound **1**, analytically pure solid *N,N′*-bis[2-(2-pyridyl) ethyl]-1*H*-pyrrole-2,5-diacetamide **2** was obtained by putting the initially oily product on a high vacuum line at 50 °C for a few days due to the compound being very hygroscopic.

It was found that the addition of two (stoichiometric amount), not four, equivalents of 2-(2-aminoethyl)pyridine to the activated ester resulted in the instantaneous formation of a white precipitate which could be filtered off. The ^{1}H NMR spectrum of this precipitate indicates that it is the 2-(2-pyridyl) ethylammonium salt of HOSu.[16–19] The ^{1}H NMR spectrum of the residue obtained by taking the filtrate to dryness showed that it was the monoamide, not the desired diamide. In summary, the use of just two equivalents of the amine (stoichiometric reaction) is not sufficient, and instead four equivalents are needed to fully convert the activated ester to the various diamides.

Anion binding studies

The anion binding properties of compounds **1**–**4** were studied by ^{1}H NMR titration techniques. Anions were added as their tetrabutylammonium salts to solutions of the receptors in deuterated acetonitrile. Association constants for the receptors **1**–**4** with a variety of anionic guests are shown in Table 1. Titration curves were plotted following either the pyrrole or amide NH proton resonance. In some cases, these proton resonances broadened during the titration, and in these cases a CH proton in the receptor was followed (see ESI†). The curves were fitted successfully to 1 : 1 receptor : anion binding models using the EQNMR computer program.[20]

Compounds **2**, **3** and **4** show the following selectivity order: $BzO^- > H_2PO_4^- > Cl^-$ (Table 1) which has been observed previously with dicarboxamidopyrroles in acetonitrile-d_3 (see below).[2] We have yet to obtain crystallographic evidence of the mode of complexation of the oxo-anions with these hosts. The X-ray crystal structure of compound **5** with benzoate was elucidated in 2002 and revealed that one oxygen of the benzoate anion was bound to one amide NH and the pyrrole NH in the plane of the pyrrole ring whilst the other oxygen was out of the plane of the pyrrole being bound by the other amide group which was twisted out of plane by 38°.[21] This twist presumably introduces strain into the complex. The new compounds reported here are more flexible than the previous generation receptors and hence might be expected to have lower affinities for anionic guests. However, the similar to moderately higher affinities for anions (compound **5** binds anions with the following stability constants in acetonitrile-d_3: $K_a(F^-)$ 85 M^{-1}; (Cl^-) 138 M^{-1}; ($H_2PO_4^-$) 357 M^{-1}; (benzoate) 2500 M^{-1}) of the new receptors suggest that the expanded hydrogen bonding site is closer to being optimal for these anions despite its increased flexibility.



5

Table 1 Stability constants of hosts **1**–**4** in acetonitrile-d_3[a]

	Anions				
	F^-	Cl^-	BzO^-	$H_2PO_4^-$	HSO_4^-
1	430	135	1450	$>10^4$	$>10^4$
2	425	150	3370	1080	420
3	6060	190	5270	1590	250
4	1500	190	2500	460	80

[a] Anions added as their tetrabutylammonium salts. Errors estimated to be less than 15%.

View Online

Compound **1** shows apparent enhanced affinities for dihydrogen phosphate and hydrogen sulfate as compared to the other three compounds. This suggests that proton transfer is occurring in these cases from the anion to the amine moieties present in this receptor. Thus in the case of hydrogen sulfate, the measured complexation process corresponds to a protonated receptor binding a dinegative sulfate anion and the measured stability constant must be considered only an 'apparent' value. This phenomenon of enhanced binding in organic solutions of acidic oxo-anions by mixed amide–amine receptors has been observed previously by Bowman-James[22] and ourselves.[23] It is difficult to rationalise the different stabilities observed with fluoride with **1**–**4**. Compounds **1** and **2** show very similar affinities and these compounds have two methylene groups between the pyridine or amine groups and the amide. Compounds **3** and **4** only have one methylene group spacer and in both these cases we see a higher affinity for fluoride (and in fact compound **3** binds fluoride more strongly than benzoate).

Conclusions

Pyrrole amide derivatives, **1**–**4**, based on the pyrrole-2,5-diacetic acid skeleton have been synthesised and shown to be effective anion receptors in acetonitrile-d_3 solution. These systems show comparable anion binding affinities to those obtained for simple pyrrole-2,5-dicarboxamides such as **5** and yet possess a more flexible hydrogen bonding array. Pyrrole-2,5-diacetic acid therefore offers great promise as a new moiety for inclusion in future anion receptors.

Experimental

General

A Varian 500 MHz Inova spectrometer was used to record the ^{1}H and ^{13}C NMR spectra in $CDCl_3$ and these were referenced to $CHCl_3$ at 7.26 ppm and 77.08 ppm, respectively. Binding studies were performed using a Bruker AV 300 NMR spectrometer, in acetonitrile-d_3, and referenced to solvent at 1.94 ppm. Infrared spectra were obtained on a Perkin Elmer Spectrum BX FT-IR System as pressed KBr discs. MS spectra were collected on a Shimadzu QP8000 alpha with an ESI probe. Melting points were determined on a Mettler Toledo FP62 melting block and are not corrected. Elemental analyses were carried out by the Campbell Microanalytical Laboratory at the University of Otago. Ethanol was dried by the standard method (Mg). HPLC grade tetrahydrofuran (THF) was used as supplied. All other chemicals and solvents were of reagent grade and were used as received.

Preparation of *N,N′*-bis(2-dimethylaminoethyl)-1*H*-pyrrole-2,5-diacetamide (1)

To freshly prepared diethyl pyrrole-2,5-diacetate (0.2270 g, 0.949 mmol), 24 equiv. of *N,N*-dimethylethylenediamine (2.007 g, 22.8 mmol) were added, followed by dry ethanol (15 mL). The resulting solution was then refluxed for 96 h. Evaporation of the solvent and excess amine *in vacuo* gave a brown oil, which solidified to produce a hygroscopic brown solid after pumping at 50 °C for 96 h (0.2924 g, 95%) (Found: C, 59.15; H, 9.14; N, 21.84. Calc. for $C_{16}H_{29}N_5O_2$: C, 59.42; H, 9.04; N, 21.65%). IR (KBr disc) ν_{max}/cm^{-1}: 3290, 3091, 2984, 2950, 2867, 2831, 2786, 1651, 1551, 1465, 1363, 1257, 1189, 1171, 1099, 1037, 941, 775, 582. δ_H ($CDCl_3$): 9.48 (1H, pyrrole N–H, broad s), 6.26 (2H, amide N–H, broad t, $J \approx 4.7$ Hz), 5.90 ($2H_3$, d, $J = 2.6$ Hz), 3.49 ($4H_6$, s), 3.29 ($4H_8$, q, $J = 5.8$ Hz), 2.37 ($4H_9$, t, $J = 6.0$ Hz), 2.19 ($12H_{10}$, s). δ_C ($CDCl_3$): 170.5 (C_7), 124.9 (C_2), 107.6 (C_3), 57.8 (C_9), 45.2 (C_{10}), 37.1 (C_8), 35.8 (C_6). ES-MS [*m*/*z*]: 324 $[M + H]^+$, 346 $[M + Na]^+$, 362 $[M + K]^+$.

Preparation of *N,N′*-bis[2-(2-pyridyl)ethyl]-1*H*-pyrrole-2,5-diacetamide (2)

To a solution of freshly prepared pyrrole-2,5-diacetic acid (0.1782 g, 0.974 mmol) in THF (50 mL, HPLC grade), cooled to 0 °C using an ice–water bath, was added a solution of *N*-hydroxysuccinimide (HOSu) (0.2242 g, 1.948 mmol) in THF (15 mL). After 20 min stirring *N,N′*-dicyclohexylcarbodiimide (DCC) (0.4019 g, 1.948 mmol) in THF (5 mL) was added. The resulting solution was stirred at 0 °C for 71 h, over which time a white precipitate, dicyclohexylurea (DCU), was produced. The ice–water bath was then removed and the reaction mixture warmed to room temperature. To this mixture 2-(2-aminoethyl)pyridine (0.4760 g, 3.896 mmol) in THF (10 mL) was added dropwise, causing the instantaneous formation of more white solid. The resulting mixture was stirred for 80 min at room temperature and then concentrated *in vacuo* to about 40 mL. Removal of the solid and evaporation of the remaining solvent *in vacuo* gave a yellow residue. This crude product was taken up in CH_2Cl_2 (10 mL) and the remaining DCU contaminant removed by filtration. After removal of the CH_2Cl_2 *in vacuo* the oily residue was then taken up in water (100 mL) and all of the water insoluble impurities filtered off with a no. 4 frit. Evaporation of the filtrate *in vacuo* gave a yellow oil which was dissolved in CH_2Cl_2 (80 mL) and washed with water (10 mL × 3). The organic phase was separated, dried over Na_2SO_4, and then taken to dryness *in vacuo* to produce an oil. The oil solidified to give the pure product as a hygroscopic yellow solid, after pumping on a high vacuum line at 50 °C for 48 h (0.2368 g, 63%) (Found: C, 67.57; H, 6.65; N, 17.91. Calc. for $C_{22}H_{25}N_5O_2$: C, 67.50; H, 6.44; N, 17.89%). IR (KBr disc) ν_{max}/cm^{-1}: 3285, 3070, 3015, 2927, 1649, 1592, 1568, 1541, 1473, 1435, 1401, 1344, 1291, 1242, 1149, 1102, 1051, 1033, 994, 917, 775, 752, 702, 566, 504. δ_H ($CDCl_3$): 9.50 (1H, pyrrole N–H, broad s), 8.41 ($2H_{14}$, broad d, $J = 4.2$ Hz), 7.58 ($2H_{12}$, td, $J = 7.6$ and 1.7 Hz), 7.12–7.08 (4H, H_{13} and H_{11}, m), 6.75 (2H, amide N–H, broad t, $J \approx 5.2$ Hz), 5.89 ($2H_3$, d, $J = 2.5$ Hz), 3.56 ($4H_8$, q, $J = 6.1$ Hz), 3.48 ($4H_6$, s), 2.89 ($4H_9$, t, $J = 6.3$ Hz). δ_C ($CDCl_3$): 170.4 (C_7), 159.5 (C_{10}), 149.1 (C_{14}), 136.8 (C_{12}), 125.1 (C_5), 123.5 and 121.7 (C_{11} and C_{13}), 108.2 (C_3), 39.0 (C_8), 36.9 (C_9), 36.0 (C_6). ES-MS [*m*/*z*]: 392 $[M + H]^+$, 414 $[M + Na]^+$, 430 $[M + K]^+$.

Preparation of *N,N′*-bis(2-pyridylmethyl)-1*H*-pyrrole-2,5-diacetamide (3)

To a stirred solution of freshly prepared pyrrole-2,5-diacetic acid (1.2769 g, 6.972 mmol) in THF (80 mL, HPLC grade), cooled to 0 °C using an ice–water bath, was added a solution of *N*-hydroxysuccinimide (HOSu) (1.6048 g, 13.94 mmol) in THF (480 mL). After 15 min stirring *N,N′*-dicyclohexylcarbodiimide (DCC) (2.8771 g, 13.94 mmol) in THF (30 mL) was added. The resulting solution was stirred at 0 °C for 29 h over which time a white precipitate, DCU, formed. The ice–water bath was removed and 2-aminomethylpyridine (3.0158 g, 27.89 mmol in THF (20 mL) was added, resulting in the formation of more white solid. The resulting mixture was stirred for 20 h at room temperature and the solid then filtered off. Evaporation of the orange filtrate *in vacuo* gave an orange residue. The residue was taken up in water (300 mL) and all of the water insoluble impurities filtered off with a no. 4 frit. Removal of the water *in vacuo* gave an oily brown residue. The residue was taken up in CH_2Cl_2 (320 mL), washed with water (40 mL × 3), dried over Na_2SO_4, and evaporated to dryness *in vacuo* to yield a yellow brown solid which was dried *in vacuo* for about two weeks (1.7877 g, 71%) (Found: C, 65.80; H, 5.84; N, 19.00. Calc. for $C_{20}H_{21}N_5O_2$: C, 66.10; H, 5.82; N, 19.27%). Mp 139 °C. IR (KBr disc) ν_{max}/cm^{-1}: 3284, 3183, 3077, 2932, 2896, 1648, 1595, 1571, 1545, 1475, 1435, 1396, 1340, 1292, 1238, 1176, 1148, 1049, 1017, 1001, 756, 602, 558, 503. δ_H ($CDCl_3$): 9.67

Published on http://pubs.rsc.org | doi:10.1039/B412654H
Downloaded on 22 December 2010

View Online

(1H, pyrrole N–H, s), 8.46 ($2H_{13}$, ddd, $J = 4.9$, 1.7 and 0.9 Hz), 7.60 ($2H_{11}$, td, $J = 7.7$ and 1.8 Hz), 7.17–7.12 (4H, H_{10} and H_{12}, m), 6.97 (2H, amide N–H, broad t, $J \approx 5.1$ Hz), 5.98 ($2H_3$, d, $J = 2.6$ Hz), 4.46 ($4H_8$, d, $J = 5.3$ Hz), 3.61 ($4H_6$, s). δ_C ($CDCl_3$): 170.7 (C_7), 156.4 (C_9), 149.0 (C_{13}), 136.8 (C_{11}), 125.0 (ES-MS [m/z]: 364 $[M + H]^+$, 386 $[M + Na]^+$, 402 $[M + K]^+$.

Preparation of *N,N′*-dibenzyl-1*H*-pyrrole-2,5-diacetamide (4)

To a stirred solution of freshly prepared pyrrole-2,5-diacetic acid (0.9644 g, 5.265 mmol) in THF (HPLC grade) (50 mL), cooled to 0 °C using an ice–water bath, was added a solution of *N*-hydroxysuccinimide (HOSu) (1.210 g, 10.53 mmol) in THF (230 mL). After 20 min stirring *N,N′*-dicyclohexylcarbodiimide (DCC) (2.1728 g, 10.53 mmol) in THF (30 mL) was added. The resulting solution was stirred at 0 °C for 30 h. The ice–water bath was then removed and the white precipitate of DCU filtered off. To the filtrate was added benzylamine (2.2569 g, 21.06 mmol) in THF (30 mL), resulting in a white precipitate. The mixture was stirred at room temperature overnight (17 h). The white precipitate was filtered off and evaporation of the yellow filtrate *in vacuo* gave a pale yellow solid. This was taken up in CH_3CN (400 mL), stirred for 40 min and the solid (DCU) was filtered off. The yellow filtrate was rotary evaporated to dryness and the yellow solid residue was dissolved in CH_2Cl_2 (200 mL), washed with water (200 mL × 2), dried over Na_2SO_4, and the yellow filtrate evaporated *in vacuo* to yield the crude product as a pale yellow solid. Purification of the crude product by recrystallisation from chloroform produced a white crystalline solid (1.210 g, 63%) (Found: C, 72.93; H, 6.29; N, 11.57. Calc. for $C_{22}H_{23}N_3O_2$: C, 73.11; H, 6.41; N, 11.63%). Mp 158 °C. IR (KBr disc) ν_{max}/cm^{-1}: 3347, 3281, 3062, 3030, 2923, 2886, 1659, 1631, 1588, 1526, 1499, 1454, 1436, 1399, 1371, 1332, 1293, 1248, 1228, 1150, 1069, 1018, 759, 740, 692, 630, 604, 575, 555, 498. δ_H ($CDCl_3$): 9.24 (1H, pyrrole N–H, broad s), 7.32–7.19 (10H, $H_{10} + H_{11} + H_{12}$, m), 6.07 (2H, amide N–H, broad t, $J \approx 5.3$ Hz), 5.92 ($2H_3$, d, $J = 2.8$ Hz), 4.38 ($4H_8$, d, $J = 5.9$ Hz), 3.54 ($4H_6$, s). δ_C ($CDCl_3$): 170.3 (C_7), 138.0 (C_9), 128.8, 127.63 and 127.59 ($C_{10} + C_{11} + C_{12}$), 125.0 (C_2), 108.2 (C_3), 43.7 (C_8), 35.8 (C_6). ES-MS [m/z]: 384 $[M + Na]^+$, 400 $[M + K]^+$.

Acknowledgements

We would like to thank the University of Otago for a Prestigious Postgraduate Scholarship (RL) and for funding this research (including a Bridging Grant), EPSRC for a DTA studentship (LSE) and the Royal Society for a University Research Fellowship (PAG).

References

1 For example: (*a*) *Supramolecular Chemistry of Anions*, ed. A. Bianchi, K. Bowman-James and E. Gracia-España, Wiley-VCH, New York, 1997; (*b*) P. A. Gale, *Coord. Chem. Rev.*, 2000, **199**, 181; (*c*) P. A. Gale, *Coord. Chem. Rev.*, 2001, **213**, 79; (*d*) P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486; (*e*) G. J. Kirkovits, J. A. Shriver, P. A. Gale and J. L. Sessler, *J. Inclusion Phenom. Mol. Recognit. Chem.*, 2001, **41**, 69; (*f*) P. A. Gale, *Coord. Chem. Rev.*, 2003, **240**, 17; (*g*) *Fundamentals and Applications of Anion Separations*, ed. B. Moyer and R. Singh, Kluwer Academic/Plenum Publishers, New York, 2004; (*h*) M. Berger and F. P. Schmidtchen, *J. Am. Chem. Soc.*, 1996, **118**, 8947; (*i*) B. Turner, M. Botoshansky and Y. Eichen, *Angew. Chem., Int. Ed.*, 1998, **37**, 2475; (*j*) G. Cafeo, F. H. Kohnke, G. L. L. Torre, A. J. P. White and D. J. Williams, *Angew. Chem., Int. Ed.*, 2000, **39**, 1496; (*k*) J. L. Sessler, P. Anzenbacher Jr., J. A. Shriver, K. Jursíková, V. M. Lynch and M. Marquez, *J. Am. Chem. Soc.*, 2000, **122**, 12061; (*l*) K. Kavallieratos, S. R. de Gala, D. J. Austin and R. H. Crabtree, *J. Am. Chem. Soc.*, 1997, **119**, 2325; (*m*) A. P. Davis, J. F. Gilmer and J. J. Perry, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1312; (*n*) K. J. Wallace, W. J. Belcher, D. R. Turner, K. F. Syed and J. W. Steed, *J. Am. Chem. Soc.*, 2003, **125**, 9699.

2 (*a*) P. A. Gale, S. Camiolo, C. P. Chapman, M. E. Light and M. B. Hursthouse, *Tetrahedron Lett.*, 2001, **42**, 5095; (*b*) P. A. Gale, S. Camiolo, G. J. Tizzard, C. P. Chapman, M. E. Light, S. J. Coles and M. B. Hursthouse, *J. Org. Chem.*, 2001, **66**, 7849; (*c*) G. Denuault, P. A. Gale, M. B. Hursthouse, M. E. Light and C. N. Warriner, *New J. Chem.*, 2002, **26**, 811.

3 (*a*) J. L. Sessler, G. Berthon-Gelloz, P. A. Gale, S. Camiolo, E. V. Anslyn, P. Anzenbacher Jr., H. Furuta, G. J. Kirkovits, V. M. Lynch, H. Maeda, P. Morosini, M. Scherer, J. Shriver and R. S. Zimmerman, *Polyhedron*, 2003, **22**, 2963; (*b*) A. Andrievsky, F. Ahuis, J. L. Sessler, F. Vogtle, D. Gudat and M. Moini, *J. Am. Chem. Soc.*, 1998, **120**, 9712.

4 (*a*) Electron-withdrawing groups can enhance the acidity of pyrrole derivatives such that they may be deprotonated by basic anions in organic solution: S. Camiolo, P. A. Gale, M. B. Hursthouse, M. E. Light and A. J. Shi, *Chem. Commun.*, 2002, 758; (*b*) P. A. Gale, K. Navakhun, S. Camiolo, M. E. Light and M. B. Hursthouse, *J. Am. Chem. Soc.*, 2002, **124**, 11228; (*c*) S. Camiolo, P. A. Gale, M. B. Hursthouse and M. E. Light, *Org. Biomol. Chem.*, 2003, **1**, 741.

5 C. B. Black, B. Andrioletti, A.C. Try, C. Ruiperez and J. L. Sessler, *J. Am. Chem. Soc.*, 1999, **121**, 10438.

6 (*a*) C. Schmuck, *Chem.–Eur. J.*, 2000, **6**, 709; (*b*) C. Schmuck and J. Lex, *Eur. J. Org. Chem.*, 2001, 1519.

7 R. Li, D. S. Larsen and S. Brooker, *New J. Chem.*, 2003, **27** 1353.

8 M. Bohusch, W. Flitsch and H.-G. Kneip, *Liebigs Ann. Chem.*, 1991, 67.

9 J. C. Sheehan and G. P. Hess, *J. Am. Chem. Soc.*, 1955, **77**, 1067.

10 J. C. Sheehan, M. Goodman and G. P. Hess, *J. Am. Chem. Soc.*, 1956, **78**, 1367.

11 Y. S. Klausner and M. Bodansky, *Synthesis*, 1972, 453.

12 M. Bodanszky, *Peptide chemistry—A practical textbook*, Springer-Verlag, Berlin Heidelberg, 1988.

13 H. R. Hoveyda, V. Karunaratne, C. J. Nichols, S. J. Rettig, A. K. W. Stephens and C. Orvig, *Can. J. Chem.*, 1998, **76**, 414.

14 G. W. Anderson, J. E. Zimmerman and F. M. Callahan, *J. Am. Chem. Soc.*, 1963, **85**, 3039.

15 G. W. Anderson, J. E. Zimmerman and F. M. Callahan, *J. Am. Chem. Soc.*, 1964, **86**, 1839.

16 R. Chinchilla, D. J. Dodsworth, C. Nájera and J. M. Soriano, *Tetrahedron Lett.*, 2003, **44**, 463.

17 C. Somlai, G. Szókán and L. Baláspiri, *Synthesis*, 1992, 285.

18 C. Somlai, G. Szókán and B. Penke, *Synthesis*, 1995, 683.

19 J. Wang, F. Meersman, R. Esnouf, M. Froeyen, R. Busson, K. Heremans and P. Herdewijn, *Helv. Chim. Acta*, 2001, **84**, 2398.

20 M. J. Hynes, *J. Chem. Soc., Dalton Trans.*, 1993, 311.

21 S. Camiolo, P. A. Gale, M. B. Hursthouse and M. E. Light, *Tetrahedron Lett.*, 2002, **43**, 6995.

22 M. A. Hossain, J. M. Llinares, D. Powell and K. Bowman-James, *Inorg. Chem.*, 2001, **40**, 2936.

23 K. Navakhun, P. A. Gale, S. Camiolo, M. E. Light and M. B. Hursthouse, *Chem. Commun.*, 2002, 2084.

Published on http://pubs.rsc.org | doi:10.1039/B412654H
Downloaded on 22 December 2010