COMMUNICATION

ChemComm
www.rsc.org/chemcomm

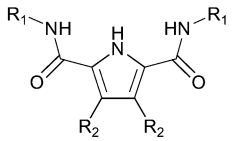
Solution and solid-state studies of 3,4-dichloro-2,5-diamidopyrroles: formation of an unusual anionic narcissistic dimer†

Salvatore Camiolo, Philip A. Gale,* Michael B. Hursthouse, Mark E. Light and Andy J. Shi
Department of Chemistry, University of Southampton, Southampton, UK SO17 1BJ.
E-mail: philip.gale@soton.ac.uk; Fax: +44 23 80596805; Tel: +44 23 80593332

Received (in Cambridge, UK) 29th January 2002, Accepted 21st February 2002
First published as an Advance Article on the web 12th March 2002

3,4-Dichoro-1*H*-pyrrole-2,5-dicarboxylic acid bis-phenylamide 3 and 3,4-dichoro-1*H*-pyrrole-2,5-dicarboxylic acid bis-butylamide 4 have been prepared and shown to deprotonate in the presence of basic anions: the X-ray crystal structure of the tetrabutylammonium salt of 3-H$^+$ reveals the formation of a dimer in the solid state.

Anion receptors[1] containing both pyrrole and amide groups have been shown to be effective and selective in their complexation properties.[2,3] Our interest in anion complexation[4] has recently led to the synthesis of simple 3,4-diphenyl-2,5-diamidopyrroles (*e.g.* **1** and **2**) which proved to be selective for oxo-anions in acetonitrile-d_3 and DMSO-d_6–water 0.5% solutions (binding benzoate, dihydrogen phosphate, fluoride and chloride in a 1 : 1 receptor : anion stoichiometry).[5] One strategy used to increase the affinity of a class of receptor for anions is to synthesise analogues containing electron withdrawing groups (frequently halogens) that will increase the acidity of NH hydrogen bond donor groups and hence form stronger complexes with anions.[6] In pursuit of this goal, we decided to synthesise analogues **3** and **4** and measure the affinity of these halogenated pyrroles for anions. We found however, that rather than binding certain anions more strongly, the putative receptor was deprotonated by basic anions such as fluoride, forming a dimer which may be of use as a precursor to new interlocked materials.



1 $R_1 = R_2 =$ Ph
2 R_1 = n-Bu, R_2 = Ph
3 R_1 = Ph, R_2 = Cl
4 R_1 = n=Bu, R_2 = Cl

Amides **3** and **4** were synthesised from 3,4-dichloro-1*H*-pyrrole-2,5-dicarboxylic acid diethyl ester **5**.[7] Compound **3** was synthesised in 11% yield by addition of compound **5** to an aluminium phenylamide in dichloromethane–hexane formed *via* the reaction of trimethylaluminium and aniline.[8] Compound **4** was synthesised in 71% yield by refluxing compound **5** in methanol in the presence of a catalytic quantity of NaCN and an excess of n-butylamine.[9] Further details and characterisation data for these compound are available on-line in the ESI.†

Crystals of compound **3** were obtained by crystallisation of the receptor from hot acetonitrile.‡ Compound **3** crystallises as a twisted dimer *via* two symmetry related hydrogen bonds (NH···O = 2.811(5) Å N–H···O = 169.9°) with the angle between the least squares planes being 70.51(9)° (Fig. 1). Interestingly, there are no phenyl CH···O=C hydrogen bonds in this material (interactions which have been observed in other amidopyrroles[5,10]).

Initial anion binding studies with compounds **3** and **4** were conducted using standard ^{1}H NMR titration procedures in a variety of deuteriated solvents. Upon addition of fluoride anions (added as the tetrabutylammonium salt) to dichloromethane-d_2 solutions of receptor **3**, an initial downfield shift of the amide NH protons was observed at low fluoride concentrations followed by an upfield shift between one and two equivalents of fluoride plateauing at approximately two equivalents of the anion (Fig. 2). Our initial interpretation of this data was to assume that the first equivalent of fluoride had deprotonated the pyrrole NH group (Fig. 3), whilst the second had bound to the deprotonated receptor. However, preparation of the tetrabutylammonium salt of **3** by addition of one equivalent of tetrabutylammonium hydroxide to the receptor in methanol, evaporation, drying and subsequent NMR analysis revealed that the chemical shift of the amide NH proton in dichloromethane-d_2 was 9.3 ppm, the same chemical shift as compound **3** in the presence of more than two equivalents of fluoride. Similar

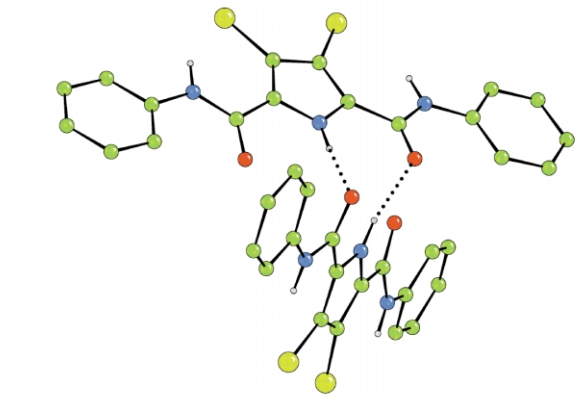


Fig. 1 X-ray crystal structure of **3** revealing NH···O=C hydrogen bonds in the solid state (colour key: carbon – green, oxygen–red, nitrogen–blue, hydrogen–white, chlorine–yellow).

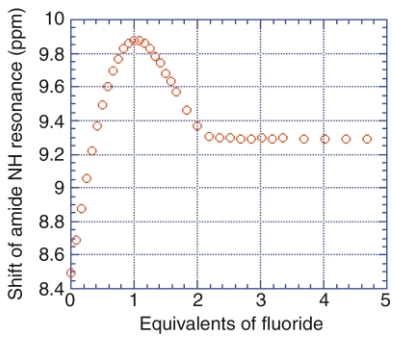


Fig. 2 NMR titration curve for compound **3** (amide NH protons) with fluoride in dichloromethane-d_2.

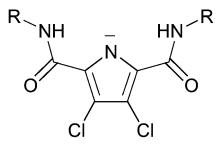


Fig. 3 Pyrrolate anion formed upon addition of fluoride to solutions of **3** and **4**.

† Electronic supplementary information (ESI) available: synthesis and characterisation of compounds **3** and **4**. See http://www.rsc.org/suppdata/cc/b2/b200980c/

DOI: 10.1039/b200980c

titration curves were obtained in dichloromethane-d_2 for compounds **3** and **4** with fluoride, dihydrogenphosphate and benzoate and in acetonitrile-d_3 for compound **4** with these anions. We are continuing to investigate the deprotonation process occurring in these systems.

In contradistinction to these results, addition of less basic chloride to solutions of **3** in dichloromethane-d_2 and compound **4** in acetonitrile-d_3 or dichloromethane-d_2 gave ^{1}H NMR titration curves indicative of 1:1 receptor:anion complex formation.[11] For example, compound **4** binds chloride with an association constant of K_a = 2015 M^{-1} in acetonitrile-d_3. The 3,4-diphenyl analogue of compound **4**, compound **2**, is a much weaker anion receptor binding chloride in acetonitrile-d_3 with an association constant of 138 M^{-1}.[5]

Crystals of the tetrabutylammonium salt of **3**-H$^+$ were obtained by slow evaporation from a dichloromethane solution of **3** in the presence of excess tetrabutylammonium fluoride.§ The X-ray crystal structure (Fig. 4) revealed that the pyrrole heterocycle has indeed been deprotonated and the receptor, now in the *syn–syn* conformation, forms a narcissistic dimer *via* amide NH···N$^-$(pyrrole) hydrogen bonds. The hydrogen atoms in this structure were located from the difference map and then constrained during the refinement confirming the deprotonation of the pyrrole ring (Fig. 3). In addition to the N–H···N hydrogen bonds there are π–H interactions between the *ortho* phenyl hydrogen atoms and the pyrole ring in the range 2.4627(42)–2.6401(44) Å.

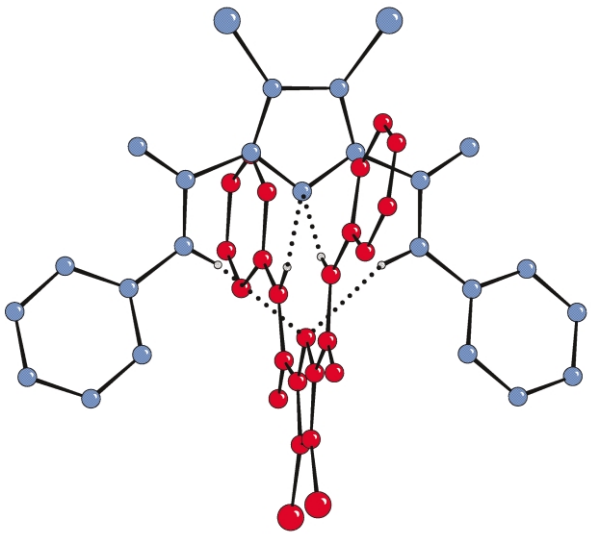


Fig. 4 X-ray crystal structure of the tetrabutylammonium salt of **3**-H$^+$ revealing NH···N$^-$ hydrogen bonds (tetrabutylammonium counter cations omitted for clarity).

A ^{1}H NMR dilution study was performed upon the tetrabutylammonium salt of **3**-H$^+$ in dichloromethane-d_2 observing the shift of the amide NH resonance as a function of concentration between 1 × 10^{-3}M and 4 × 10^{-2}M. Over this concentration range the NH proton shifts from 9.25 ppm to 9.35 ppm, data consistent with the formation of the hydrogen bonded dimer in solution.

The serendipitous discovery that the pyrrolate anions of 3,4-dichloro-2,5-diamidopyrroles assemble in solution and in the solid state may lead to a new class of interlocked materials[12] based upon this hydrogen bonding motif. For example, we are currently investigating the potential of these amido-pyrroles to form pH switchable catenanes. The results of these studies will be presented in due course.

P. A. G. would like to thank the Royal Society for a University Research Fellowship and the EPSRC for a project studentship (to S. C.) and for use of the X-ray facilities at the University of Southampton.

Notes and references

‡ Data for both crystal structures were collected on a Bruker Nonius Kappa CCD area detector diffractometer with a rotating molybdenum anode following standard procedures. Crystal data for **3** $C_{18}H_{13}Cl_2N_3O_2$, M_r = 374.21, T = 120(2) K, orthorhombic, space group *Pbcn*, a = 33.485(2), b = 7.9757(4), c = 12.4468(6) Å, V = 3324.1(3) Å^3, ρ_{calc} = 1.495 g cm^{-3}, μ = 0.408 mm^{-1}, Z = 8, reflections collected: 13422, independent reflections: 2792 (R_{int} = 0.1635), final *R*indices [$I > 2\sigma I$]: $R1$ = 0.2061, $wR2$ = 0.1576, *R*indices (all data): $R1$ = 0.0796. $wR2$ = 0.1351. CCDC 178607. See http://www.rsc.org/suppdata/cc/b2/b200980c/ for crystallographic files in .cif format.

§ *Crystal data* for tetrabutylammonium salt of **3**: $C_{68}H_{96}Cl_4N_8O_4$, M_r = 1231.33, T = 120(2) K, monoclinic, space group *Pn*, a = 13.2385(2), b = 16.9228(5), c = 15.0678(4) Å, β = 99.944(2), V = 3324.96(17) Å^3, ρ_{calc} = 1.230 g cm^{-3}, μ = 0.231 mm^{-1}, Z = 2, reflections collected: 19094, independent reflections: 10094 (R_{int} = 0.0588), final R indices [$I > 2\sigma I$]: $R1$ = 0.0476, $wR2$ = 0.0868, R indices (all data): $R1$ = 0.0819. $wR2$ = 0.0984. CCDC 178608.

1 P. A. Gale, *Coord. Chem. Rev.*, 2000, **199**, 181; P. A. Gale, *Coord. Chem. Rev.*, 2001, **213**, 79; P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486; J. L. Sessler and W. E. Allen, *Chemtech.*, 1999, **29**, 16; F. P. Schmidtchen and M. Berger, *Chem. Rev.*, 1997, **97**, 1609; P. D. Beer and D. K. Smith, *Prog. Inorg. Chem.*, 1997, **46**, 1; J. L. Atwood, K. T. Holman and J. W. Steed, *Chem. Commun.*, 1996, 1401; K. Kavallieratos, S. R. de Gala, D. J. Austin and R. H. Crabtree, *J. Am. Chem. Soc.*, 1997, **119**, 2325; A. P. Davis, J. F. Gilmer and J. J. Perry, *Angew. Chem., Int. Ed.*, 1996, **35**, 1312; *Supramolecular Chemistry of Anions*, eds. A. Bianchi, K. Bowman-James and E. García-España, Wiley-VCH, New York, 1997.

2 M. Scherer, J. L. Sessler, A. Gebauer and V. Lynch, *Chem. Commun.*, 1998, 85; M. Scherer, J. L. Sessler, M. Moini, A. Gebauer and V. Lynch, *Chem. Eur. J.*, 1998, **4**, 152; A. Andrievsky, F. Ahuis, J. L. Sessler, F. Vögtle, D. Gudat and M. Moini, *J. Am. Chem. Soc.*, 1998, **120**, 9712.

3 C. Schmuck, *Chem. Eur. J.*, 2000, **6**, 709; C. Schmuck, *Chem. Commun.*, 1999, 843–844.

4 S. J. Coles, P. A. Gale and M. B. Hursthouse, *Cryst. Eng. Commun.*, 2001, 53; C. R. Bondy, S. J. Loeb and P. A. Gale, *Chem. Commun.*, 2001, 729; S. Camiolo, P. A. Gale, M. I. Ogden, B. W. Skelton and A. H. White, *J. Chem. Soc., Perkin Trans. 2*, 2001, 1294; P. A. Gale, M. B. Hursthouse, M. E. Light, J. L. Sessler, C. N. Warriner and R. S. Zimmerman, *Tetrahedron Lett.*, 2001, **42**, 6759; S. Camiolo and P. A. Gale, *Chem. Commun.*, 2000, 1129; S. Camiolo, S. J. Coles, P. A. Gale, M. B. Hursthouse, T. A. Mayer and M. A. Paver, *Chem. Commun.*, 2000, 275; P. A. Gale, L. J. Twyman, C. I. Handlin and J. L. Sessler, *Chem. Commun.*, 1999, 1851.

5 P. A. Gale, S. Camiolo, C. P. Chapman, M. E. Light and M. B. Hursthouse, *Tetrahedron Lett.*, 2001, **42**, 5095; 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.

6 P. Anzenbacher Jr., A. C. Try, H. Miyaji, K. Jursíková, V. M. Lynch, M. Marquez and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 10268; J. L. Sessler, P. Anzenbacher Jr., J. A. Shriver, K. Jursíková, V. M. Lynch and M. Marquez, *J. Am. Chem. Soc.*, 2000, **122**, 12061; P. A. Gale, J. L. Sessler, W. E. Allen, N. A. Tvermoes and V. Lynch, *Chem. Commun.*, 1997, 665.

7 R. J. Motekaitis, D. H. Heinert and A. E. Martell, *J. Org. Chem.*, 1970, **35**, 2504.

8 A. Basha, M. Lipton and S. M. Weinreb, *Tetrahedron Lett.*, 1977, **48**, 4171.

9 T. Hogberg, P. Strom, M. Ebner and S. Ramsby, *J. Org. Chem.*, 1986, **52**, 2033.

10 C. Schmuck and J. Lex, *Eur. J. Org. Chem.*, 2001, 1519.

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

12 A. R. Pease, J. O. Jeppesen, J. F. Stoddart, Y. Luo, C. P. Collier and J. R. Heath, *Acc. Chem. Res.*, 2001, **34**, 433; G. M. Hübner, J. Glaser, C. Seel and F. Vögtle, *Angew. Chem., Int. Ed.*, 1999, **38**, 3477; J. A. Wisner, P. D. Beer and M. G. B. Drew, *Angew. Chem., Int. Ed.*, 2001, **40**, 3606; C. O. Dietrich-Buchecker, J. P. Sauvage and J. M. Kern, *J. Am. Chem. Soc.*, 1984, **106**, 3043; D. A. Leigh, P. J. Lusby, S. J. Teat, A. J. Wilson and J. K. Y. Wong, *Angew. Chem., Int. Ed.*, 2001, **40**, 1538; H. Adams, F. J. Carver and C. A. Hunter, *J. Chem. Soc., Chem. Commun.*, 1995, 809.