View Article Online / Journal Homepage / Table of Contents for this issue
Dynamic Article Links

ChemComm

Cite this: *Chem. Commun.*, 2012, **48**, 9983–9985

www.rsc.org/chemcomm

COMMUNICATION

Cooperativity of H-bonding and anion–π interaction in the binding of anions with neutral π-acceptors†

Michael Giese,[a] Markus Albrecht,*[a] Tim Krappitz,[a] Marius Peters,[a] Verena Gossen,[a] Gerhard Raabe,[a] Arto Valkonen[b] and Kari Rissanen[b]

Received 3rd July 2012, Accepted 23rd August 2012
DOI: 10.1039/c2cc34748b

Published on 04 September 2012. Downloaded by FORDHAM UNIVERSITY on 22/05/2013 20:02:43.

A rare anion–π complex between bromide and a neutral receptor is reported and related receptor systems are studied with a series of anions. The interaction is observed in the solid state and in solution, and further evidence for it is obtained by a computational study.

Due to their crucial role in biological and chemical processes anions have become the focus of intense recognition and sensing studies.[1] Common anion receptors are based on electrostatic attraction, hydrogen-bridges, hydrophobic effects or ion pair recognition and are more or less specific.[2] In recent years anion–π interaction was identified as an interesting new binding motif.[3] Many theoretical[4] and structural studies[3] have proven the existence of this weak interaction. However, the relevance and strength of anion–π interactions in solution still remain elusive.[5]

In 2008 we started systematic studies on anion–π interactions in pentafluorophenylammonium and -phosphonium salts.[6] Initial results revealed a certain flexibility in the position of the anion above the electron-deficient arene, which can be controlled by using directing substituents.[7] The spatial structure of the anion seems not to have an effect on the anion–π interaction.[8] However, anions which are of low stability or even unstable in the gas phase like the tetraiodide dianion can be stabilized in the crystal lattice by the support of electron-deficient arenes.[9] Just recently our results showed for the first time that the anion position depends on the fluorination degree of the arene in the solid state.[8]

In the present work anion–π interactions are studied by co-crystallizing a series of pentafluorophenyl derivatives with tetrabutylammonium halides (TBAX, X = Cl^-, Br^-, I^-, PF_6^-, BF_4^-). Pentafluorobenzamide with tetraethylammonium bromide (**1**) crystallizes in the monoclinic space group $P2_1/n$ (Fig. 1). In the solid state the bromide is fixed by N–HBr^- hydrogen bonds [N···Br^- = 3.431(3) Å] close to the π-system of the uncharged receptor. On the other hand, this directing hydrogen bond withdraws the Br^- from the center of the electron-deficient arene (Fig. 1). Furthermore, there is an additional intermolecular N–H···Br^- hydrogen bond from the adjacent molecule [N···Br^- = 3.392(3) Å]. The contacts between the carbon atoms of the pentafluorophenyl group and the bromide are in between 3.650(3) and 4.164(3) Å and the distance to the centroid of the C_6F_5 substituent is 3.67 Å.

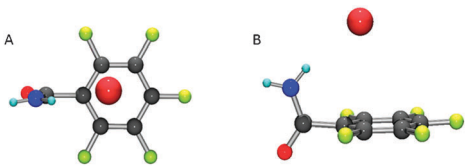


Fig. 1 Part of crystal structure of **1** showing the pentafluorobenzamide and the bromide (the TBA cation was removed for clarity).

Due to the low solubility of pentafluorobenzamide in chloroform the *N*-phenylbenzamides **2a–c** were synthesized (see ESI†) by reacting amine **3a** or **3b** with pentafluorobenzoyl chloride (**4a**) or 3,5-dichlorobenzoyl chloride (**4b**) in the presence of pyridine.

In order to determine the binding constants for **2a** or **2b** in chloroform the stoichiometry was checked using the Job plot (Fig. 2a).[10] By following the amide proton signal in the ^{1}H NMR spectra a 1 : 1 complex for **2a** as well as for **2b** was observed for various anions (Cl^-, Br^-, I^-, BF_4^-). Corresponding results can be obtained by following other signals in the ^{1}H or ^{19}F NMR spectra. The titration with $TBABF_4$ shows a different (2 : 1) ratio of receptor to anion (Fig. 2b and c).

The NMR titrations were performed in $CDCl_3$ using 0.01 M solutions of the receptors **2a** and **2b**. The TBA salts were added as 0.04 M solutions in chloroform. The binding constants were calculated by analyzing the titration curves *via* non-linear regression and are summarized in Table 1 (for full details see ESI†).[10]

A diagram for **2a** showing the binding constants for various anions reveals a decreasing binding constant in the order Cl^- > Br^- > I^- (Fig. 3a). The binding constants for BF_4^- (135–153 M^{-1}) are somewhat higher than for iodide while PF_6^- has very similar values. It should be noticed that the complex stoichiometry of the PF_6^- complex is not clear and that this value is estimated for a 1 : 1 complex. A deviation from the general trend is observed for the binding constants calculated by following the *ortho*-fluorine signals. This might

[a] *Institut für Organische Chemie, RWTH Aachen, Landoltweg 1, 52074 Aachen, Germany. E-mail: markus.albrecht@oc.rwth-aachen.de; Fax: +49 241 809 2385; Tel: +49 241 809 4678*
[b] *Department of Chemistry, Nanoscience Center, University of Jyväskylä, Survontie 9, 40014 Jyväskylä, Finland. E-mail: kari.t.rissanen@jyu.fi; Fax: +358 14 260 2672; Tel: +358 50 562 3721*

† Electronic supplementary information (ESI) available: Details of experimental procedures, solution investigations, crystallographic studies and computational investigations. CCDC 872223 and 872224. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc34748b

Published on 04 September 2012. Downloaded by FORDHAM UNIVERSITY on 22/05/2013 20:02:43.

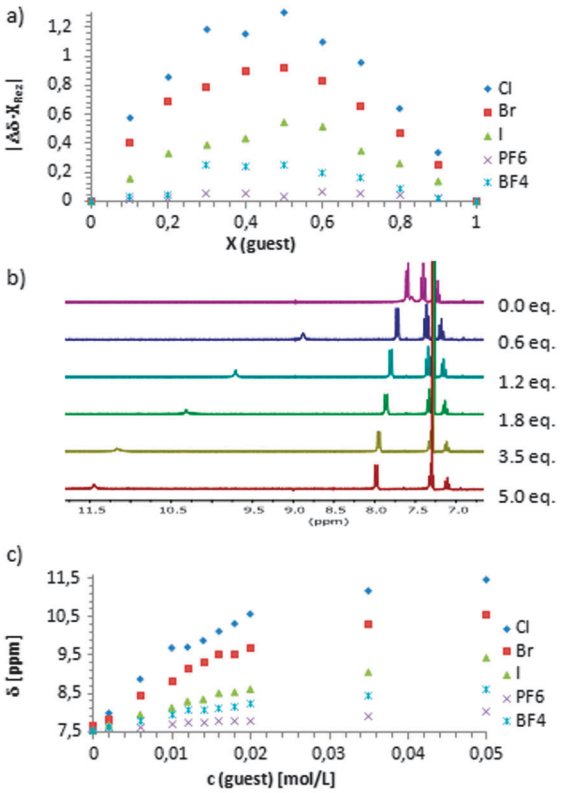


Fig. 2 (a) Representative Job plots for **2a** with various anions (Cl^-, Br^-, I^-, PF_6^-) added as *n*-Bu_4N salts in $CDCl_3$. (b) Selected ^{1}H-NMR spectra for the addition of *n*-Bu_4NCl to a solution of **2a** in $CDCl_3$. (c) Resulting titration curves obtained by following the shifting of the NH-signal for **2a** during the addition of TBA salts.

Table 1 Binding constants K_a [M^{-1}] for the 1 : 1 complexes of **2a** and **2b** with various anions TBAX, X = Cl^-, Br^-, I^-, PF_6^-). The binding constants were determined by following the amide proton in the ^{1}H NMR in $CDCl_3$ (errors are estimated to be lower than 20%)

	Cl^-	Br^-	I^-	BF_4^{-a}	PF^-_6
2a	237	173	99	135	89
2b	163	114	82	102	74

[a] Estimated for a 1 : 1 complex stoichiometry.

be due to intramolecular interactions of the *ortho*-fluorine atoms with the amide protons. For **2b** an analogous trend was observed. The binding constants are slightly higher for receptor **2a** (Table 1, Fig. 3b). There are two possible explanations for this behaviour: the cooperativity of NH–anion and anion–π interaction or the acidification of the NH-group by the electron-withdrawing C_6F_5—compared to the C_6H_5 unit. Proton NMR is able to confirm the H-bonding, but we cannot definitely confirm anion–π interactions in solution.

Attempts to perform similar studies in solution for **2c** failed due to the very low solubility of **2c** in chloroform. Interestingly, **2c** becomes soluble in chloroform by adding 1.0 eq. of TBACl. Solid state structure of **2c** revealed the stacking of the molecules by N–H···O=C hydrogen bonds of the amide groups (see ESI†). The strong double N–H···O=C H-bonds form robust columns resulting in the low solubility of **2c**. By adding the tetrabutylammonium salt to the solution the

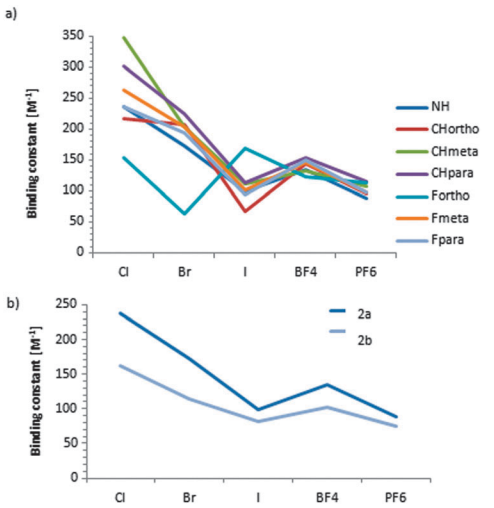


Fig. 3 (a) Binding constants for **2a** obtained by following the signal in the NMR for various anions (Cl^-, Br^-, I^-, BF_4^-, PF_6^-). (b) Comparison of the binding constants of **2a** and **2b** for various anions (Cl^-, Br^-, I^-, BF_4^-, PF_6^-).

hydrogen bonds are broken and the phenylbis(pentafluorobenzamide) complex becomes soluble.

Job plots confirm a 1 : 1 ratio for **2c** with chloride, bromide and iodide in deuterated acetonitrile. For hexafluorophosphate no significant shifting of the signals could be observed in the NMR spectra. The binding constants obtained for **2c** are summarized in Table 2.

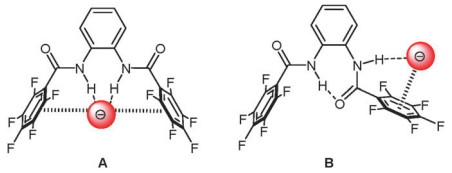
The binding constants for **2c** and various anions confirm the expected binding order of $Cl^- > Br^- > I^-$ (Table 2). In this case the *ortho*-fluorine signals lead to slightly higher values. The binding constants for **2c** in CD_3CN are significantly higher than for **2a** in $CDCl_3$. This mainly arises from the strong anion binding capability of two amide hydrogens, which is further enhanced by the electron-withdrawing effect of the pentafluorophenyl groups. In addition, cation solvation is stronger in CD_3CN leaving a "free" anion (and not an ion pair) for binding to the receptor. Moreover, binding of the anions is further strengthened by direct anion–π interactions. It should be noticed that due to the different solubility of **2a** and **2b** the binding constants were determined in different solvents. Nevertheless, the higher binding constant for **2c** in CD_3CN compared to the binding constants of **2a** and **2b** determined in $CDCl_3$ is even more surprising due to the stronger solvation of the anion in polar acetonitrile. However, there are two different opportunities for **2c** to interact with an anion (see Scheme 1, **A** and **B**). In **A** the anion is bound to a cleft by hydrogen bonds *via* the two amidic protons and anion–π interactions to the two C_6F_5 moieties, while **B** allows the

Table 2 Binding constants K_a [M^{-1}] for the 1 : 1 complexes of **2c** with various anions (Cl^-, Br^-, I^-). The binding constants were determined by following the proton signals in the ^{1}H NMR in CD_3CN (errors are estimated to be lower than 20%)

	Cl^-	Br^-	I^-
NH	3345	637	182
H_{ortho}	3198	645	203
H_{meta}	3060	606	148
F_{ortho}	4683	800	134
F_{meta}	3401	602	156
F_{para}	3660	625	186

This journal is © The Royal Society of Chemistry 2012

Published on 04 September 2012. Downloaded by FORDHAM UNIVERSITY on 22/05/2013 20:02:43.



Scheme 1 Binding motifs for the interaction of **2c** with an anion.

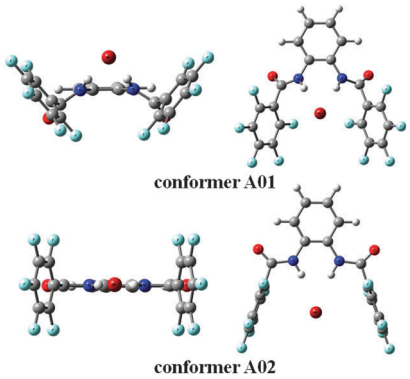


Fig. 4 Conformers **A01** (C_1) and **A02** (C_{2v}) of **2c** with bromide optimized at the HF/6-311++G** level of theory.

anion to interact only with one H-bond and one electron-deficient unit. In order to determine whether **A** or **B** is the preferred structural motif for the anion binding, low-temperature NMR studies of **2c**·Br as well as computational studies were performed. The low-temperature NMR measurements show highly symmetric NMR spectra and in addition with the computational results **A** seems to be the favoured binding mode for the anion (see ESI†). The shielding of the anion in **A** also could be the reason for enhanced solubility of **2c** by addition of TBACl in chloroform solution. However, it should be mentioned that the DFT studies are performed in the gas phase and no solvent effects are considered. Based on the observed binding constants and the low-temperature measurements, the interaction between the anion and the pentafluorophenyl groups can be considered as an attractive force. To further support this assumption, both conformers **A** and **B** (Scheme 1) were geometrically optimized with Gaussian 09[11] at the MP2/6-31G* level of theory.

Conformer **A** (**A02**) adopting C_{2v} symmetry is 5.90 kcal mol^{-1} lower in energy than **B** with C_1 symmetry. At the HF/6-311++G** level an even more stable conformer (**A01**) could be found (Fig. 4). The energy difference between conformer **A01** and **A02** is 3.85 kcal mol^{-1}. Normal mode analyses resulted in two imaginary frequencies for conformer **A02** and none for conformer **A01**. Therefore, **2c** would most likely adopt the structure of conformer **A01**.

In conclusion we were able to show that pentafluorobenzamides are appropriate systems for studying anion–π interactions in the solid state as well as in solution. To the best of our knowledge the crystal structure of **1**·Br$^-$ is the first example of anion–π interactions between an uncharged pentafluorophenyl derivative and an anion. Moreover, our investigations in solution show a slight difference between an electron-rich and -poor system, which can be explained by a cooperative effect of N–H···anion and anion–π interaction and the enhanced acidity of the amide proton by the electron-withdrawing C_6F_5-unit. So far we were not able to clarify this point sufficiently. However, the differences in the binding constants between **2a** and **2b** are quite small and might be insignificant. Nevertheless, for receptor **2c** with various anions, an attractive interaction between the anion and the pentafluorophenyl moieties can be expected in solution.

Notes and references

1 A. Bianchi, K. Bowman-James and E. Garcia-Espana, *Supramolecular Chemistry of Anions*, Wiley-VCH, New York, 1997; Special issue: P. Gale, T. Gunnlaugsson, (Edts.) *Chem. Soc. Rev.* **2010**, *39*, Issue 10.

2 C. H. Park and H. E. Simmons, *J. Am. Chem. Soc.*, 1968, **90**, 2431; D. Quinonero, C. Garau, C. Rotger, A. Frontera, P. Ballester, A. Costa and P. M. Deyà, *Angew. Chem.*, 2002, **114**, 3539 (*Angew. Chem., Int. Ed.*, 2002, **41**, 3389); P. D. Beer and P. A. Gale, *Angew. Chem.*, 2001, **113**, 502 (*Angew. Chem., Int. Ed.*, 2001, **40**, 486); S. O. Kang, R. A. Begum and K. Bowman-James, *Angew. Chem.*, 2006, **118**, 8048 (*Angew. Chem., Int. Ed.*, 2006, **45**, 7882); H. J. Schneider, F. Werner and T. Blatter, *J. Phys. Org. Chem.*, 1993, **6**, 590; M. Cametti and K. Rissanen, *Chem. Commun.*, 2009, 2809.

3 P. Ballester, *Struct. Bonding*, 2008, **129**, 127–174; B. L. Schottel, H. T. Chifotides and K. R. Dunbar, *Chem. Soc. Rev.*, 2008, **37**, 68–83; B. P. Hay and V. S. Bryantsev, *Chem. Commun.*, 2008, 2417–2428; P. Gamez, T. J. Mooibroek, S. J. Teat and J. Reedijk, *Acc. Chem. Res.*, 2007, **40**, 435–444; A. Robertazzi, F. Krull, E.-W. Knapp and P. Gamez, *CrystEngComm*, 2011, **13**, 3293–3300; P. Gamez, M. Mascal, T. J. Mooibroek and J. Reedijk, *Angew. Chem.*, 2011, **123**(41), 9736 (*Angew. Chem., Int. Ed.*, 2011, **50(41)**, 9564).

4 For selected computational studies on anion–π interactions see: I. Alkorta, I. Rozas and J. Elguero, *J. Am. Chem. Soc.*, 2002, **124**, 8593; M. Mascal, A. Armstrong and M. D. Bartberger, *J. Am. Chem. Soc.*, 2002, **124**, 6274; C. Garau, A. Frontiera, P. Ballester, D. Quinonera, A. Costa and P. M. Deya, *Eur. J. Org. Chem.*, 2005, 179; O. B. Berryman, V. S. Bryantsev, D. P. Stay, D. W. Johnson and B. P. Hay, *J. Am. Chem. Soc.*, 2007, **129**, 48.

5 H. Maeda, A. Osuka and H. Furuta, *J. Inclusion Phenom. Macrocyclic Chem.*, 2004, **49**, 33; H. Maeda and H. Furuta, *J. Porphyrins Phthalocyanines*, 2004, **8**, 67; O. B. Berryman, F. Hof, M. Hynes and D. W. Johnson, *Chem. Commun.*, 2006, 506; M. Staffilani, K. S. B. Hancock, J. W. Steed, K. T. Holman, J. L. Atwood, R. K. Juneja and R. S. Burkhalter, *J. Am. Chem. Soc.*, 1997, **119**, 6324; D.-X. Wang, Q.-Y. Zheng, Q.-Q. Wang and M.-X. Wang, *Angew. Chem.*, 2008, **120**, 7595 (*Angew. Chem., Int. Ed.*, 2008, **47**, 7485).

6 M. Albrecht, C. Wessel, M. de Groot, K. Rissanen and A. Lüchow, *J. Am. Chem. Soc.*, 2008, **130**, 4600.

7 M. Albrecht, M. Müller, O. Mergel, A. Valkonen and K. Rissanen, *Chem.–Eur. J.*, 2010, **16**, 5062.

8 M. Giese, M. Albrecht, G. Ivanova, A. Valkonen and K. Rissanen, *Supramol. Chem.*, 2012, **1**, 48–55.

9 M. Müller, M. Albrecht, V. Gossen, T. Peters, A. Hoffmann, G. Raabe, A. Valkonen and K. Rissanen, *Chem.–Eur. J.*, 2010, **16**, 12446.

10 K. A. Connors, *Binding Constants*, Wiley, New York, 1987; C. S. Wilcox, in *Frontiers in Supramolecular Chemistry and Photochemistry*, ed. H.-J. Schneider and H. Dürr, Wiley-VCH, Weinheim, 1991, p. 123.

11 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, *Gaussian 09, Revision A.1*, Gaussian, Inc., Wallingford, CT, 2009.