Organic & Biomolecular Chemistry

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Cite this: *Org. Biomol. Chem.*, 2012, **10**, 1181

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PAPER

Bis-amidocarbazolyl urea receptor for short-chain dicarboxylate anions†

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Received 6th September 2011, Accepted 27th October 2011
DOI: 10.1039/c1ob06540h

Urea receptor **1** based on two (1-amino-8-amido-3,6-dichloro)carbazole units shows a strong association with dicarboxylate anions such as oxalate, malonate and succinate guests through multiple hydrogen bonds from the carbazole, urea and amide NH groups. ^{1}H NMR complexation studies exhibit high values of association constants in DMSO-d_6. X-ray structures of the 1 : 1 complexes of **1** with oxalate and malonate as their ditetrabutylammonium salts were obtained. A modelling study of the complex of receptor **1** with succinate (as its diTBA salt) showed a more reduced geometric complementarity than its homologue malonate.

Introduction

In the field of molecular recognition, there remains a growing interest in developing receptors for anions,[1] which is motivated among others, by the relevance that anions have in biological and chemical processes.[2] Receptors for carboxylate anions are important for the recognition of a variety of biomolecules, dicarboxylates also have biosignificant relevance because they are implicated in various metabolic processes.[3] Hydrogen bonds are widely used in molecular receptors with preorganized clefts for effective anion recognition,[4] so dicarboxylates possessing multiple hydrogen bond accepting sites are very attractive guests for recognition through these interactions and several hosts have been found in the literature.[5]

NH-based hydrogen bonding heterocyclic compounds[6] have been broadly employed as hosts for a variety of molecules. Specifically, carbazole has been used as a versatile building block for the synthesis of anion receptors since Jurczak *et al*.[7] reported the advantages of 1,8-diamino-3,6-dichlorocarbazole derivatives as hydrogen bond donors. This diamine is the key substrate for the synthesis of amides, ureas and other carbazole-based anion receptors, which show very effective strong complexes with oxyanionic guests,[8] among others. So, 1,8-diamidocarbazole provides a binding site with three directional H-bonds to accommodate carboxylate anion guests. Recently, Gale and coworkers[9] have developed a series of carbazolyl ureas, like 1,3-dicarbazolylurea, that has high affinity for hydrogen carbonate and acetate anions and shows quenching of fluorescence for benzoate in DMSO–0.5% water.[10] Kim's group has synthesized a 1,8-(bis-*N*-ureido-*N*′-1-naphthyl)-carbazole receptor and the structure of its complex with acetate has been X-ray elucidated.[11] They have also published related monocarbazolylurea systems with very interesting colorimetric and fluorescent responses to anionic guests.[12]

Herein we report the synthesis of a new receptor **1**, 1,3-bis(8-carboxamido-3,6-dichloro-9*H*-dicarbazol-1-yl)urea, which has showed great ability in short-chain dicarboxylate anion recognition. Its binding properties with oxalate, malonate and succinate (as their ditetrabutylammonium salts, diTBA) have been studied in DMSO. We also report the analysis of the X-ray complexes, obtained between **1** and both oxalate and malonate dianions. To our knowledge, related carbazolyl ureas have not been used so far with the purpose of these dianions' recognition.

Results and discussion

Synthesis

The urea receptor **1** has been prepared from the 1,8-diamino-3,6-dichloro-9*H*-carbazole **2**, previously synthesized by Jurczak *et al*.[7a]

Diamine **2** was prepared from carbazole, *via* a three-step procedure: chlorination, nitration and hydrogenation, improving a previously described procedure.[13] The coupling of two units of monohexylcarboxamide derivative **3** was completed using the isocyanate **4**, yielding the urea receptor **1** (Scheme 1).

Monoacylated amine **3** was synthesized by treating diamine **2** with an equimolar amount of caproyl chloride in acetonitrile at 0 °C, yielding 45% of the desired monoamide **3** and recovering

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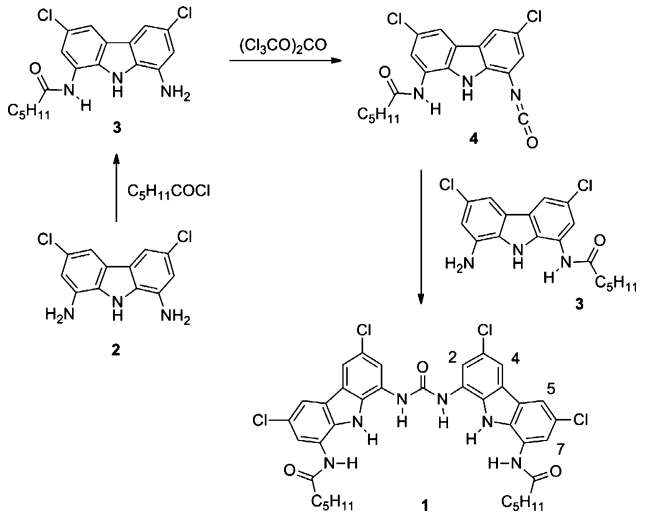
† Electronic supplementary information (ESI) available: Copies of NMR, IR and MS spectra of the compounds, selected binding curves, X-ray characterization data and modelling studies. CCDC reference numbers 837724 and 837725. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob06540h



Scheme 1 Preparation of receptor **1**.

the unreacted diamine **2**. Subsequent treatment with triphosgene afforded isocyanate **4**, which was directly used in the final reaction with **3** to yield the 1,3-dicarbazolylurea **1** (85%).

The structural symmetry of the molecule was confirmed by the number of signals present in the ^{1}H and ^{13}C NMR spectra (DMSO-d_6). The ^{1}H NMR spectrum showed three downshifted singlet signals at δ = 10.67 ppm (carbazole NH), δ = 10.12 ppm (amide NH) and δ = 9.25 ppm (urea NH). The remaining signals are three other singlets at δ = 8.08 ppm (H-4 and H-5), δ = 7.80 ppm (H-7) and δ = 7.64 ppm (H-2). For 2D ROESY spectrum and total characterization of compound **1** see the ESI.†

Molecular modelling of receptor 1

In order to know the arrangement of the core skeleton of this receptor, we have previously carried out the molecular modelling[13] of the bis(8′-hexylamido-1′-carbazolyl)-1,3-urea, whose more stable conformation is shown in Fig. 1.

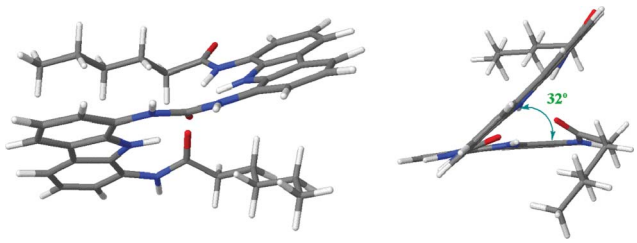


Fig. 1 Molecular model of 1,3-bis(8-hexylamido-9*H*-dicarbazol-1-yl)urea. The carbazole sheets form a dihedral angle of 32°.

The urea and amide carbonyl groups form intramolecular hydrogen-bonds with the NH of the carbazolic units, forcing the structure to adopt a helix-shaped disposition, with both urea NH in outer disposition and the carbazole sheets forming a dihedral angle of 32°.

However, this arrangement does not allow the simultaneous association of the two carboxylate groups of one short-chain dicarboxylate guest, one of the carbazoles rotates, upon binding, to adopt the favourable conformation of the urea group. This is necessary to form a single cavity capable of binding the dianions in solution through all the H-bonds of the system.

Table 1 N*H* shifts of receptor **1** protons involved in H-bonds with dicarboxylate guests and association constants (M^{-1}) of the complexes formed at 293 K in DMSO-d_6

Dianion[a]	Δδ (ppm) carbazole N*H*	Δδ (ppm) amide N*H*	Δδ (ppm) urea N*H*	K_{ass}(M^{-1})[b]
oxalate	3.08	1.51	1.36	[c]
malonate	3.84	1.78	1.11	9.2×10^4
succinate	4.02	1.61	1.18	3.1×10^4

[a] Added as ditetrabutylammonium salt. [b] Errors estimated to be no more than ±10%. [c] Data could not be fitted to a 1 : 1 or 1 : 2 binding stoichiometry.

Binding studies

Complexation studies of dianions were performed using ^{1}H NMR titration technique,[14] in DMSO-d_6 at constant concentration of receptor **1** (4.0×10^{-3} M), by the addition of increasing amounts of guest until saturation (see Fig. 2). All the NH protons were involved in the association event according to the observed shift changes shown in Table 1. So that, the addition of oxalate, malonate and succinate guests took place with high downfield shifts for the signals of the protons implicated in H-bonds. Significantly, higher changes were observed for the carbazole NH (3 to 4 ppm) (Table 1).

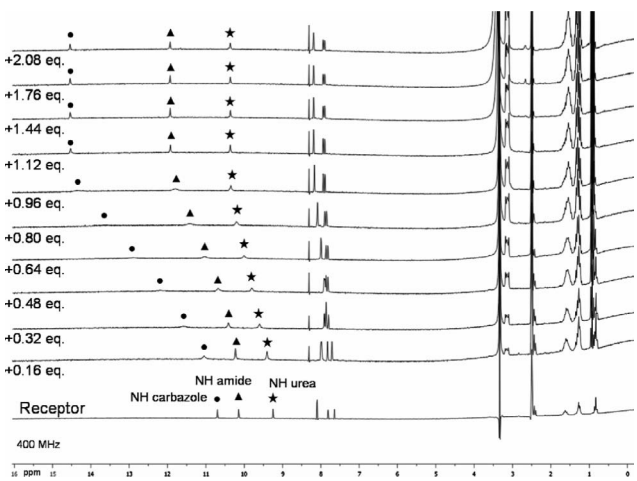


Fig. 2 Effect of the addition of increasing amounts of diTBA malonate to receptor **1** on the ^{1}H NMR spectrum in DMSO-d_6.

The stoichiometries of complexes were analyzed by Job's plot method,[15] which showed 1 : 1 receptor : guest complexes for malonate and succinate dianions as their diTBA salts. However, this was not the case for diTBA oxalate showing that 1 : 1 and 1 : 2 host : guest stoichiometries were formed simultaneously. At a 1 : 1 molar ratio of this dianion and receptor **1**, a mixture of both 1 : 1 and 1 : 2 host : guest complexes are formed in an almost equal amount, in agreement with the titration data that could not be fitted adequately to a single binding model (see ESI†).

In addition, smaller but fairly observable shifts of the aromatic protons revealed different conformational changes of the receptor

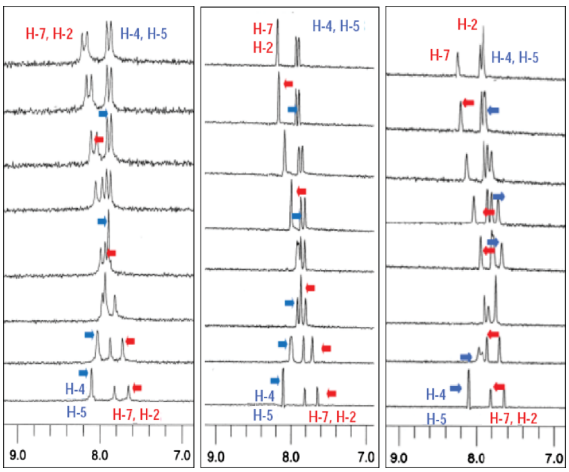


Fig. 3 ^{1}H NMR spectrum regions showing shift changes of aromatic protons of receptor **1** upon association with diTBA oxalate (left), malonate (middle) and succinate (right).

for each complex. Fig. 3 shows the shift changes of H-2 and H-7 (red) and H-4 and H-5 (blue).

Crystallographic and modelling studies

In order to obtain the crystallographic structures of the complex, receptor **1** and an equimolar amount of ditetrabutylammonium oxalate were dissolved in methylene chloride–ethanol (2 : 1) but this procedure was unsuccessful. Only when an excess of guest was added were single crystals suitable for X-ray analysis of the complex formed between **1** and diTBA oxalate obtained.

By performing the crystallographic study, a complex **1**·oxalate, with 1 : 1 stoichiometry, was identified. X-ray structure analysis revealed that the receptor adopts a *syn–syn* conformation. Fig. 4 displays two representations of the X-ray structure, in order to achieve a better view of the arrangement of the host and guest in the complex. Thus, in Fig. 4 (left) the ORTEP diagram is displayed, where the concave disposition of the host and the orthogonal arrangement of both carboxylates of the guest can be appreciated. Fig. 4 (right) shows a crystal structure of the complex where the indicated H-bond distances are better observed.

Six hydrogen bonds shorter than 3 Å (2.73–2.87 Å, green) were established between host NHs and guest carboxylate oxygen atoms. Each carboxylate was equally placed in the receptor, one oxygen was H-bonded to one amide NH and the other one to carbazole and urea NHs. Similarities in hydrogen bond lengths may indicate that the oxalate dianion matches almost symmetrically the receptor binding site.

The structure of the complex formed between receptor **1** and ditetrabutylammonium malonate was also solved by X-ray diffraction. Quality crystals were obtained by slow evaporation of methylene chloride from a methylene chloride–ethanol (2 : 1) solution containing equimolar amounts of host and guest, conditions that in this case were successful. Fig. 5 shows the structure of the complex, where both carboxylates of the guest are located inside the H-bond pocket while the malonate methylene is positioned outside.

In this case, the guest was placed less symmetrically inside the receptor cavity. The complex was stabilized by five hydrogen bonds shorter than 3 Å, (2.73–2.90 Å, green), the association being more effective for one of the carboxylates bonded through three H-bonds than the other, bonded only through two. Other weaker interactions (3.20 and 3.22 Å, purple) are shown from one of the urea NHs and two oxygens of different carboxylates (Fig. 5, right).

In the absence of crystals of receptor **1**·succinate complex, models for the receptor : guest complexes were generated by means of molecular dynamics simulations.[16] This study showed that the increase of the chain length of the guest up to four atoms produces a change in the arrangement of the host and guest. In this case only one of the carboxylates is fixed inside the H-bond pocket by four H-bonds, whereas the other is located outside, establishing a H-bond with one amide NH (Fig. 6) (For another view showing H-bonds, see the ESI†).

This means that the size of the cavity is slightly too small to accommodate the succinate dianion, in agreement with the three times smaller association constant value obtained for the **1**·succinate complex *versus* its homologue with malonate (Table 1).

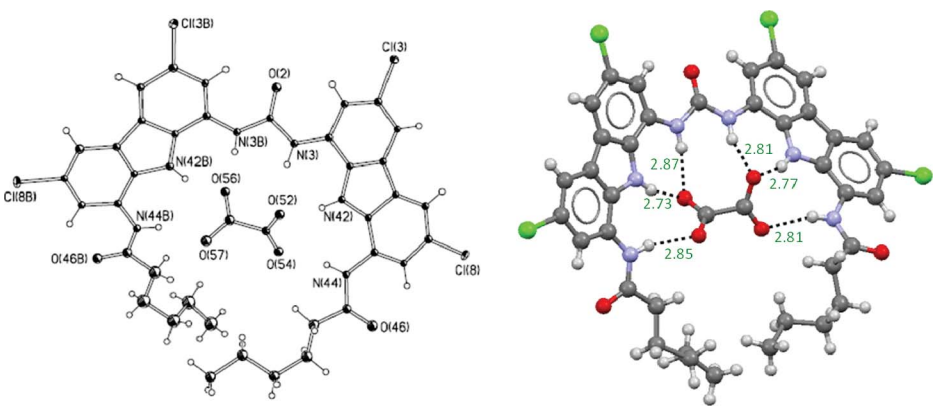


Fig. 4 ORTEP plots of the crystal structure of the receptor **1**·oxalate complex. Thermal ellipsoids are drawn at the 50% probability level. Ditetrabutylammonium counter-cations have been omitted for clarity. Crystal structure of receptor **1**·oxalate complex. Distances between the nitrogen and oxygen atoms involved in hydrogen-bonding are given in Å.

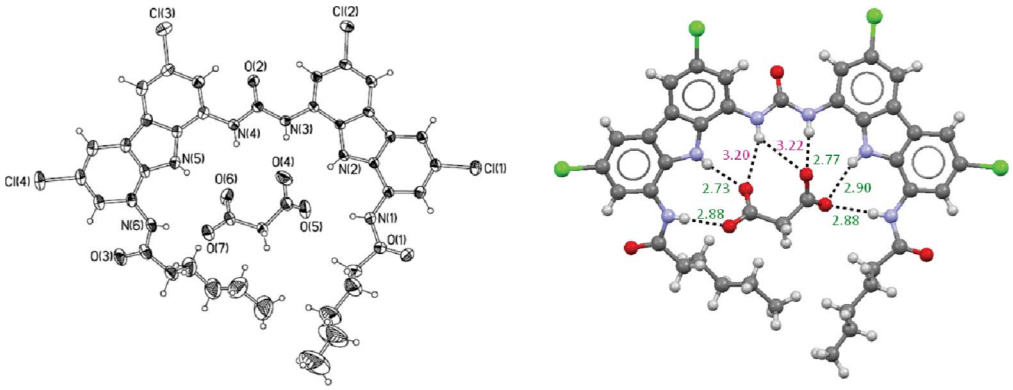


Fig. 5 ORTEP plots of the crystal structure of the receptor **1**·malonate complex. (Details as in Fig. 4.)

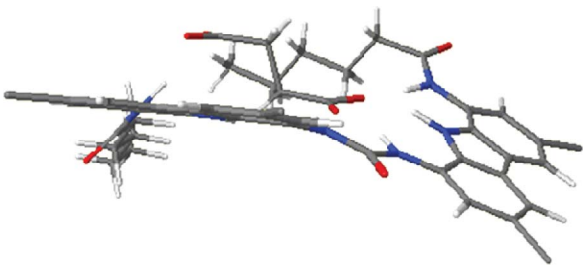


Fig. 6 Optimized structure of receptor **1**·succinate complex.

Conclusions

In summary, we conclude that neutral receptor **1** has a binding pocket where up to six strong NH-bonds could be formed due to the presence of different NH-bond donor units: two carbazoles, one urea and two amide functions. Receptor **1** is very suitable to associate with malonate and succinate ditetrabutylammonium salts (1 : 1 stoichiometry) in DMSO-d_6 with association constants up to 9.2×10^4 M^{-1}.

However, with oxalate a mixture of 1 : 1 and 1 : 2 host : guest complexes are formed in almost the same ratio. X-ray crystallographic studies of the complexes of receptor **1** with oxalate and malonate also show the 1 : 1 stoichiometry in the solid state. The K_{ass} for succinate turned out to be three times smaller than its homologue malonate due to the limited size of the cavity formed by receptor **1**.

Experimental

***N*-(8-Amino-3,6-dichloro-9*H*-carbazol-1-yl)hexanamide (3).** To a solution of 1,8-diamino-3,6-dichloro-9*H*-carbazole **2** (5 g,18.8 mmol) in acetonitrile (140 cm^3) at 0 °C, a solution of caproyl chloride (2.6 cm^3, 2.5 g, 18.8 mmol) in acetonitrile (20 cm^3) was added slowly. After stirring for 10 h at room temperature the precipitate was removed by filtration and it was identified as diacyl carbazole. The solvent was evaporated off under reduced pressure. The crude product obtained in this way was a mixture of starting diaminocarbazole **2** and monoacyl carbazole **3**, which was purified *via* column chromatography over silica gel using CH_2Cl_2 : MeOH (99 : 1) as eluent, yielding the desired compound **3** (3.0 g, 43%); mp 225 °C decomposition; ν_{max}(nujol/cm^{-1}) 3253, 2954, 2854, 1640, 1513, 1488, 1401, 1301, 1224 and 842; δ_H (200 MHz, DMSO-d_6) 10.47 (1H, broad s, carbazole N*H*), 9.89 (1H, s, amide N*H*), 7.95 (1H, s, H-2), 7.55 (1H, s, H-4), 7.43 (1H, s, H-5), 6.67 (1H, s, H-7), 5.60 (2H, broad s, -NH_2), 2.44 (2H, t, *J* 7.4, NHCO–CH_2-), 1.70 (2H, m, *J* 7.4 Hz, -CH_2-), 1.35 (4H, m, -CH_2–CH_2-), 0.90 (3H, t, *J* 6.7, CH_3) ppm. δ_C (50 MHz, DMSO-d_6) 171.6 (s), 135.2 (s), 131.2 (s), 127.6 (s), 124.5 (s), 124.0 (s), 122.8 (s), 122.6 (s), 118.8 (d), 116.2 (d), 109.6 (d), 107.8 (d), 36.0 (t), 30.9 (t), 24.7 (t), 21.9 (t), 13.8 (c) ppm; HRMS-ESI: ($M+Na^+$) calcd for $C_{18}H_{19}Cl_2N_3ONa$: 386.0797; found: 386.0787.

***N*^{1},*N*^{3}-Bis(3,6-dichloro-8-hexanamido-9*H*-carbazol-1-yl)urea (1).** A solution of **3** (200 mg, 0.55 mmol) in CH_2Cl_2 (20 cm^3) was added dropwise to a stirring solution of triphosgene (196 mg, 0.66 mmol) in a two phase solution of CH_2Cl_2 (20 cm^3) and saturated $NaHCO_3$ aq (40 cm^3). The solution was stirred vigorously under argon overnight. The organic phase was then washed with water (200 cm^3), dried with anhydrous Na_2SO_4 and evaporated to dryness to give the isocyanate **4** which was used immediately due to its high reactivity. A solution of **3** (200 mg, 0.55 mmol) in THF (15 cm^3) was added over **4**. The reaction was stirred for 4 h and a white precipitate was collected by filtration and was dried under vacuum to afford receptor **1** (350 mg, 85%); mp 270 °C decomposition; ν_{max}(nujol/cm^{-1}) 3247, 2954, 1646, 1562, 1490, 1298, 1274, 1239, 943 and 896; δ_H (200 MHz, DMSO-d_6) 10.67 (2H, s, N*H* carbazole), 10.11 (2H, s, N*H* amide), 9.22 (2H, s, N*H* urea), 8.08 (4H, s, H-4 and H-5 carbazole), 7.80 (2H, s, H-7 carbazole), 7.64 (2H, s, H-2 carbazole), 2.42 (4H, t, *J* = 7.3 Hz, NHCO–CH_2-), 1.62 (4H, m, *J* = 7.3 Hz, -CH_2-), 1.27 (8H, m, -CH_2–CH_2-), 0.83 (6H, t, *J* = 6.7 Hz, CH_3) ppm; δ_C (50 MHz, DMSO-d_6) 171.8 (s), 153.2 (s), 131.6 (s), 130.4 (s), 124.7 (s), 124.5 (s), 124.2 (s), 123.5 (s), 123.4 (s), 119.4 (d), 118.2 (d), 116.0 (d), 115.9 (d), 36.1 (t), 30.9 (t), 24.7 (t), 21.9 (t), 13.8 (c) ppm. Elemental analysis: calcd (%) for $C_{37}H_{36}Cl_4N_6O_3$: C, 58.90; H, 4.81; N, 11.14; found: C, 58.20; H, 4.70; N, 10.90.

Ditetrabutylammonium salts. Tetrabutylammonium salts were prepared by adding 2 equiv. of tetrabutylammonium hydroxide in methanol to a solution of the corresponding dicarboxylic acid (1 equiv.) in methanol. The mixture was stirred at room temperature for 2 h, evaporated to dryness under reduced pressure and then dried under high vacuum.

Acknowledgements

We thank the Spanish Junta de Castilla y León (Grant SA125 A06) and the Spanish MICINN (CTQ2008-01771) for supporting this research. M. B. Jiménez thanks the Junta de Castilla y León for a Ph.D. grant and the Ministerio de Educación is acknowledged by A. L. F. A. for a FPU grant.

Notes and references

1 For more recent reviews, see: themed issue on Supramolecular Chemistry of Anionic Species, Ed. P. A. Gale and T. Gunnlaugsson, *Chem. Soc. Rev.*, 2010, **39**, 3581; J. L. Sessler, P. A. Gale and W.-S. Cho, *Anion Receptor Chemistry*, Royal Society of Chemistry, Cambridge, UK, 2006; G. W. Bates and P. A. Gale, *Struct. Bonding*, 2008, **129**, 1; Z. Zhang and P. R. Schreiner, *Chem. Soc. Rev.*, 2009, **38**, 1187; C. Caltagirone and P. A. Gale, *Chem. Soc. Rev.*, 2009, **38**, 520; P. A. Gale, S. E. García-Garrido and J. Garric, *Chem. Soc. Rev.*, 2008, **37**, 151; P. Prados and R. Quesada, *Supramol. Chem.*, 2008, **20**, 201; P. A. Gale and R. Quesada, *Coord. Chem. Rev.*, 2006, **250**, 3219; P. A. Gale, *Acc. Chem. Res.*, 2006, **39**, 465; N. Gimeno and R. Vilar, *Coord. Chem. Rev.*, 2006, **250**, 3161; J. Yoon, S. K. Kim, N. J. Singh and K. S. Kim, *Chem. Soc. Rev.*, 2006, **35**, 355; M. A. Hossain, *Curr. Org. Chem.*, 2008, **12**, 1231; E. A. Katayev, P. J. Melfi and J. L. Sessler, *Mod. Supramol. Chem.*, 2008, 315; R. Vilar, *Eur. J. Inorg. Chem.*, 2008, 357; S. Kubik, *Chem. Soc. Rev.*, 2009, **38**, 585; P. Dydio, D. Lichosyt and J. Jurczak, *Chem. Soc. Rev.*, 2011, **40**, 2971; V. Amendola, M. Bonizzoni, D. Esteban-Gomez, L. Fabbrizzi, M. Licchelli, F. Sancenon and A. Taglietti, *Coord. Chem. Rev.*, 2006, **250**, 1451; V. Amendola, D. Esteban-Gomez, L. Fabbrizzi and M. Licchelli, *Acc. Chem. Res.*, 2006, **39**, 343; P. A. Gale, *Amide- and Urea-Based Anion Receptors in Encyclopedia of Supramolecular Chemistry*, ed. J. L. Atwood and J. W. Steed, Marcel Dekker, New York, 2004, 31E. Bianchi, K. Bowman-James and E. García-España, ed., *Supramolecular Chemistry of Anions*, Wiley-VCH, New York, 1997.

2 Z. Y. Zeng, Y. B. He, J. L. Wu, L. H. Wei, X. Liu, L. Z. Meng and X. Yang, *Eur. J. Org. Chem.*, 2004, 2888; R. J. Fitzmaurice, G. M. Kyne, D. Douheret and J. D. Kilburn, *J. Chem. Soc., Perkin Trans. 1*, 2002, 841.

3 S. J. Brooks, P. R. Edwards, P. A. Gale and M. A. Light, *New J. Chem.*, 2006, **30**, 65; S. González, R. Peláez, F. Sanz, M. B. Jiménez, J. R. Morán and M. C. Caballero, *Org. Lett.*, 2006, **8**, 4679; A. Gonzalez-Alvarez, I. Alfonso, P. Diaz, E. Garcia-Espana, V. Gotor-Fernandez and V. Gotor, *J. Org. Chem.*, 2008, **73**, 374; M. W. Hosseini and J. M. Lehn, *J. Am. Chem. Soc.*, 1982, **104**, 3525.

4 F. M. Muñiz, V. Alcázar, F. Sanz, L. Simón, Á. L. Fuentes de Arriba, C. Raposo and J. R. Morán, *Eur. J. Org. Chem.*, 2010, 6179; F. M. Muñiz, V. Alcázar, L. Simón, C. Raposo, E. Calle and J. R. Morán, *Eur. J. Org. Chem.*, 2009, 1009; F. M. Muñiz, L. Simón, V. Alcázar, C. Raposo, A. L. Fuentes de Arriba and J. R. Morán, *Eur. J. Org. Chem.*, 2009, 5350; F. M. Muñiz, L. Simón, S. Saez, C. Raposo, V. Alcázar and J. R. Morán, *Sensors*, 2008, **8**, 1637; A. I. Oliva, L. Simón, F. M. Muñiz, F. Sanz and J. R. Morán, *Org. Lett.*, 2004, **6**, 1155; A. I. Oliva, L. Simón, F. M. Muñiz, F. Sanz and J. R. Morán, *Eur. J. Org. Chem.*, 2004, 1698.

5 J. M. Benito, M. Gomez-Garcia, J. L. J. Blanco, C. O. Mellet and J. M. G. Fernandez, *J. Org. Chem.*, 2001, **66**, 1366; M. H. Filby, T. D. Humphries, D. R. Turner, R. Kataky, J. Kruusma and J. W. Steed, *Chem. Commun.*, 2006, 156; K. Ghosh and G. Masanta, *Tetrahedron Lett.*, 2008, **49**, 2592; K. Ghosh, I. Saha, G. Masanta, E. B. Wang and C. A. Parish, *Tetrahedron Lett.*, 2010, **51**, 343; K. Ghosh and A. R. Sarkar, *Tetrahedron Lett.*, 2009, **50**, 85; H. S. Kim, K. S. Moon and D. O. Jang, *Supramol. Chem.*, 2006, **18**, 97; V. Kral, A. Andrievsky and J. L. Sessler, *J. Am. Chem. Soc.*, 1995, **117**, 2953; Y. Liu, L. Fang, Y. B. He, W. H. Chan, K. T. Yeung, Y. K. Cheng and R. H. Yang, *Org. Lett.*, 2005, **7**, 5825; S. Y. Liu, Y. B. He, J. L. Wu, L. H. Wei, H. J. Qin, L. Z. Meng and L. Hu, *Org. Biomol. Chem.*, 2004, **2**, 1582; V. Ruangpornvisuti, *Journal of Molecular Structure-Theochem*, 2004, **686**, 47; L. Sebo, B. Schweizer and F. Diederich, *Helv. Chim. Acta*, 2000, **83**, 80; J. L. Sessler, A. Andrievsky, V. Kral and V. Lynch, *J. Am. Chem. Soc.*, 1997, **119**, 9385; N. Singh, G. W. Lee and D. O. Jang, *Tetrahedron*, 2008, **64**, 1482; Y. P. Tseng, G. M. Tu, C. H. Lin, C. T. Chang, C. Y. Lin and Y. P. Yen, *Org. Biomol. Chem.*, 2007, **5**, 3592; Q. Q. Wang, V. W. Day and K. Bowman-James, *Chem. Sci.*, 2011, **2**, 1735; J. L. Wu, Y. B. He, Z. Y. Zeng, L. H. Wei, L. Z. Meng and T. X. Yang, *Tetrahedron*, 2004, **60**, 4309; Y. P. Yen and K. W. Ho, *Tetrahedron Lett.*, 2006, **47**, 7357; Y. P. Yen and K. W. Ho, *Tetrahedron Lett.*, 2006, **47**, 1193; Z. Y. Zeng, Y. B. He, J. L. Wu, L. H. Wei, S. Y. Liu, Y. Y. Huang, L. Z. Meng and L. Hu, *Supramol. Chem.*, 2004, **16**, 233; Z. Y. Zeng, Y. B. He, J. L. Wu, L. H. Wei, X. Liu, L. Z. Meng and X. Yang, *Eur. J. Org. Chem.*, 2004, 2888; X. B. Zhou, Y. W. Yip, W. H. Chan and A. W. M. Lee, *Beilstein J. Org. Chem.*, 2011, **7**, 75.

6 C. Caltagirone, P. A. Gale, J. R. Hiscock, S. J. Brooks, M. B. Hursthouse and M. E. Light, *Chem. Commun.*, 2008, 3007; T. Zielinski, P. Dydio and J. Jurczak, *Tetrahedron*, 2008, **64**, 568.

7 M. J. Chmielewski, M. Charon and J. Jurczak, *Org. Lett.*, 2004, **6**, 3501; D. E. Gross, V. Mikkilineni, V. M. Lynch and J. L. Sessler, *Supramol. Chem.*, 2010, **22**, 135; T. D. Thangadurai, N. J. Singh, I.-C. Hwang, J. W. Lee, R. P. Chandran and K. S. Kim, *J. Org. Chem.*, 2007, **72**, 5461.

8 P. Dydio, D. Lichosyt and J. Jurczak, *Chem. Soc. Rev.*, 2011, **40**, 2971.

9 J. R. Hiscock, C. Caltagirone, M. E. Light, M. B. Hursthouse and P. A. Gale, *Org. Biomol. Chem.*, 2009, **7**, 1781; P. A. Gale, *Chem. Commun.*, 2008, 4225.

10 J. R. Hiscock, P. A. Gale, C. Caltagirone, M. B. Hursthouse and M. E. Light, *Supramol. Chem.*, 2010, **22**, 647.

11 T. D. Thangadurai, N. J. Singh, I. Hwang, J. W. Lee, R. P. Chandran and K. S. Kim, *J. Org. Chem.*, 2007, **72**, 5461.

12 S. K. Kim, N. J. Singh, S. J. Kim, K. M. K. Swamy, S. H. Kim, K.-H. Lee, K. S. Kim and J. Yoon, *Tetrahedron*, 2005, **61**, 4545.

13 F. Muzik, Z. Allan and J. Poskocil, *Collect. Czech. Chem. Commun.*, 1958, **23**, 770.

14 K. A. Connors, *Binding Constants*, John Wiley & Sons: New York, 1987; p. 24; L. Fielding, *Tetrahedron*, 2000, **56**, 6151.

15 M. T. Blanda, J. H. Horner and M. Newcomb, *J. Org. Chem.*, 1989, **54**, 4626; H. J. Scheneider, A. K. Yatsimirsky, *Principles and Methods in Supramolecular Chemistry*, John Wiley & Sons: New York, 2000.

16 Systematic conformational searches for the free receptor using Monte Carlo MM3 as molecular force field were performed with Macromodel v. 5.1 and clustering of the resulting conformations was performed with XCluster on Silicon Graphics workstations. For receptor : guest complexes, up to 10 ns molecular dynamics simulations were also carried out with Macromodel v. 5.1, and the resulting conformations were subsequently minimized.