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Ion-pair recognition of amidinium salts by partially hydrogen-bonded heteroditopic cyclo[6]aramide†

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Convergent heteroditopic cyclo[6]aramide demonstrates efficient ion-pair recognition of amidinium salts in 10% methanolic chloroform (>10^4 M^{-1}) as confirmed by NMR and conductivity experiments. As predicted by density functional theory (DFT) method simulations, cyclo[6]aramide **1a** is able to bind amidinium salts **G1–G5** with varying binding affinity in 1 : 1 stoichiometry through hydrogen bonding interactions involving both anion-recognizing amide H-atoms and cation-binding amide carbonyl O-atoms. Particularly, the binding affinities for **G1**, **G2** and **G3** are found to decrease with increasing the size of substituents in the amidinium ion in the order of **G1** > **G2** > **G3**. Moreover, the association ability for simultaneous binding of cationic and anionic guest species depends considerably on the counterions. Among the four formamidinium salts (Cl^-, Br^-, I^- and BPh_4^-) examined, formamidinium chloride is best encapsulated as a contact ion-pair species in the macrocycle. The reduced association constants with increasing the size of counterions in the order of **G1** > **G6** > **G7** > **G4** underscore the importance of ion paring in effecting the host–guest interaction. Comparative conductivity studies provide a convenient approach to differentiate between contact and loose ion pairs for these amidinium complexes. This work provides a rare example of binding biologically important types of amidinium cations as ion pairs by a synthetic receptor.

Introduction

Recognition of amidinium cations by artificial receptors has been a subject of research interest for the last two decades[1] due to their importance in implementing biological functions in DNA-binding and inhibitor drugs. For example, pentamidine isethionate, which contains two amidinium residues, has been widely used for the treatment of pneumocystosis, babesiosis, trypanosomiasis, and leishmaniasis.[2] However, very few synthetic receptors are available so far for use in binding the amidinium group.[1,3] Among the very limited examples reported up to 2003 and afterwards, only one recognition motif involves the utilization of a highly preorganized multi pyridine-based macrocycle.[1] Therefore, the design and creation of new macrocyclic host–guest systems for amidinium complexation represents a great challenge, particularly when the development of new receptor systems for amidinium ions[4] has been untouched by supramolecular scientists during the past decade. Furthermore, all artificial receptors are only concerned with complexation of amidinium cation alone, other than binding concomitantly both cationic species and its counteranion, which is widely known as ion-pair recognition. Ion-pair recognition is considered as an efficient approach to enhance binding affinities as shown by salt solubilisation, extraction and membrane transport.[5] Despite the realization of designed molecules for coordinating zwitterionic amino acids and peptides,[6] complexation of biologically relevant amidinium ions by synthetic receptors as ion pair in a convergent fashion is still unknown. With widespread use of amidines and their salts,[7] development of such ion-pair recognition systems may have important implications for medicinal chemistry.

Hydrogen-bonded aromatic amide macrocycles[8] have received increasing attention because of their interesting host–guest chemistry.[9] Among them, cyclo[6]aramides, a class of shape-persistent cyclic compounds with amide oxygen atoms inwardly oriented,[10] are of particular interest in their binding affinity towards organic cations. Our recent work has revealed the strong ability of these macrocycles to bind secondary ammonium salts,[11] diquat[12] and tropylium.[13] Their unique host–guest chemistry is also revealed by their capability to specifically discriminate native arginine[14] and to manipulate liquid crystal properties.[15] Interestingly, depletion of partial hydrogen bonds leads to convergent heteroditopic cyclo[6]aramides that have shown high association ability for intimate organic ion pairs.[16] The recent advance of ditopic receptors[17]

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aroused our intense interest to probe the possibility of binding amidinium salt as ion pair by convergent H-bonded macrocycles. We report herein that heteroditopic cyclo[6]aramide **1a** (Fig. 1) is able to recognize a series of amidinium salts **G1–G5** with varying binding affinity through hydrogen bonding (H-bonding) interactions. Particularly, **G1**, **G2** and **G3** with different steric hindrance in the central carbon of the cation are bound as contact ion pair where the amidinium and chloride are present essentially as one entity as evidenced by NMR and conductivity experiments.

Results and discussion

Density functional theory (DFT) calculation results

The feasibility of binding a contact ion-pair species amidinium chloride is examined based on density functional theory (DFT) method simulations of the complex system comprising cyclo[6]aramide **1b** and amidinium **G1**, **G2**. Our computational results on the calculated binding energies reveal that **G1** fits well in the cavity of the host molecule (Fig. 2a and S37, ESI†). The chloride anion is engaged in four H-bonds (H, I, J and K), three of which are associated with the anion-binding cleft formed by three H-bond donors from the macrocycle (two amide NH and one aromatic H) with the remaining charge-assisted H-bond formed with the cationic NH group of **G1**. The ion-pair complexation is further strongly stabilized by four charge-assisted H-bonds (D, E, F, I). With this optimized conformation stabilized by cooperative H-bonding interactions, the amidinium chloride is perfectly engulfed as a contact ion-pair species in the macrocycle. Computer simulations on **G2** produce a similar result that shows the acetamidinium chloride stays somewhat above the macrocyclic platform due to the presence of additional methyl substituent (Fig. 2b and S38, ESI†).

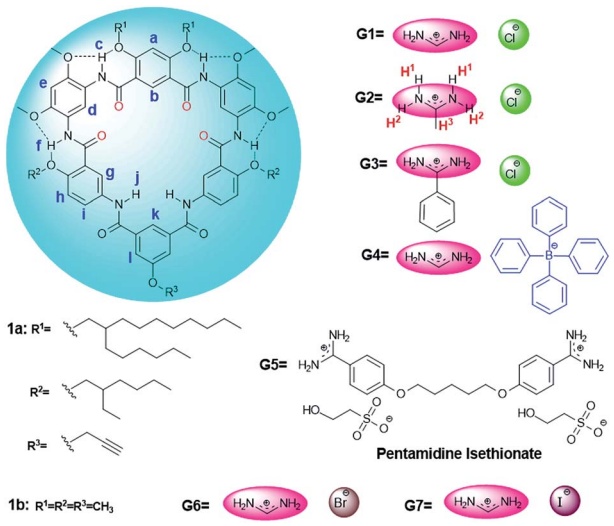

Fig. 1 Chemical structures and proton designations of heteroditopic cyclo[6]aramide **1** and amidinium salt **G1–G7**. Green and pink represent chloride anion and amidinium cations, respectively.

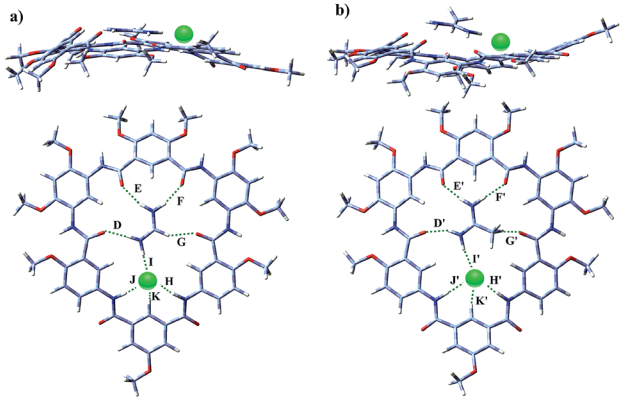

Fig. 2 Side (up) and top (down) views of optimized geometry of (a) **1b**·**G1** and (b) **1b**·**G2** at the RB3PW91/6-31G (d, p) level; all side chains of **1a** are replaced by methyl groups for simplicity (gray = C, white = H, red = O and blue = N). The chloride anion is shown as a CPK model. The dashed green lines indicate intermolecular H-bonds **D**–**K** with **D** = 1.888 Å, **E** = 1.965 Å, **F** = 1.889 Å, **G** = 2.311 Å, **H** = 2.283 Å, **I** = 1.982 Å, **J** = 2.308 Å and **K** = 2.464 Å; **D′** = 1.976 Å, **E′** = 1.911 Å, **F′** = 2.114 Å, **G′** = 2.202 Å, **H′** = 2.360 Å, **I′** = 2.040 Å, **J′** = 2.295 Å and **K′** = 2.581 Å.

Ion-pair complexation studies

With the theoretical prediction for the stability of ion-pair complex, ditopic cyclo[6]aramide **1a** was synthesized *via* a multi-step pathway (Scheme S1, ESI†).[16] An acetylene chain was incorporated to improve the solubility of the macrocycle. Since **G1** is very hygroscopic and not easy to handle in experiments, guest **G2** was tested first for its binding ability with **1a**. The first sign of binding with **G2** as ion pair came from ^{1}H NMR experiments. Addition of one equivalent of **G2** to a $CDCl_3$ solution of **1a** leads to the downfield shifts in the signals arising from amide and aromatic protons H_j, H_k, H_b and H_g on **1a** by 1.39, 0.55, 0.20 and 0.27 ppm, respectively (Fig. 3).

This implies that both the cationic and anionic guests are associated primarily with the cavity of this receptor.[18] Particularly, the substantial change of amide proton resonance ($\Delta\delta$ = 1.39 ppm for H_j) relative to other proton resonances strongly suggests the H-bonding interaction of amide hydrogen with chloride anion, and thus its residing in the core of the macrocycle. Moreover, a binding constant of 6.08×10^3 M^{-1} in $CDCl_3$–CD_3OH (v/v, 9 : 1) was obtained by fitting the concentration-dependent change of the chemical shifts of proton **1a**-H_d (Fig. 4 and Table 1).

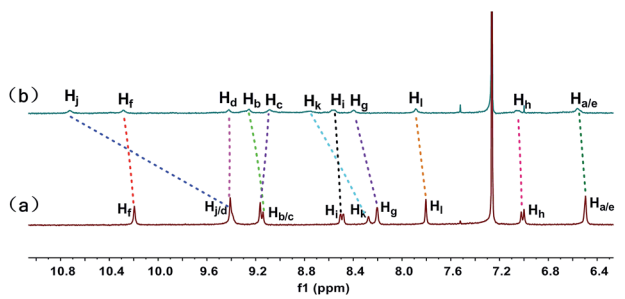

Fig. 3 Partial ^{1}H NMR spectra of (a) 1.0 mM cyclo[6]aramide **1a**; (b) 1.0 mM cyclo[6]aramide **1a**·**G2** (400 MHz, $CDCl_3$, 298 K).

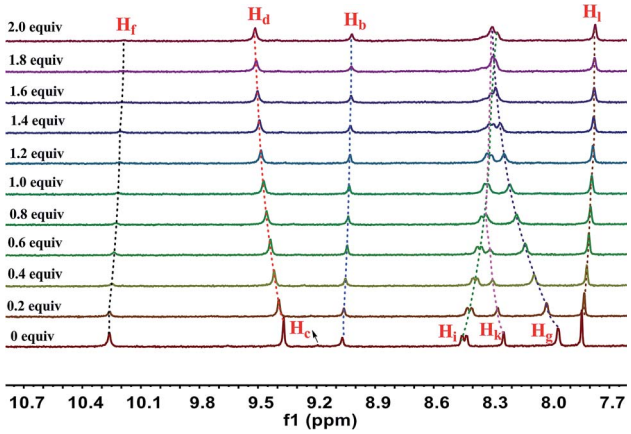

Fig. 4 Partial stacked ^{1}H NMR spectra of cyclo[6]aramide **1a** (1.0 mM) titrated by **G2** (0–2.0 equiv.) in (400 MHz, 9 : 1, $CDCl_3$–CD_3OD, 298 K).

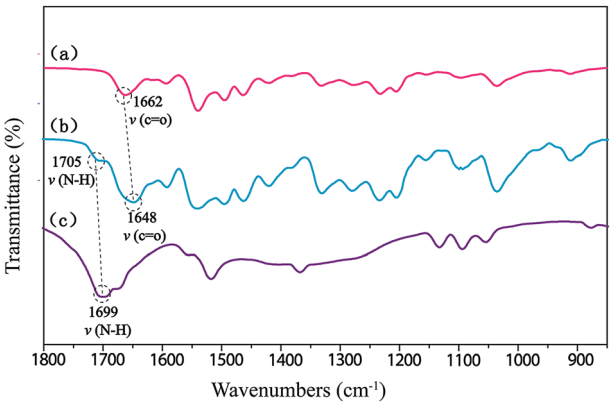

Fig. 5 FT-IR transform infrared spectra of cyclo[6]aramide **1a** (a), complex**1a**·**G2** (b) and **G2** (c).

Table 1 Electrical conductivity (σ/μS cm^{-1})^{a,b} and association constants (K_a/M^{-1})^c for complexation of various guests (**G1**–**G7** and TBACl) by **1a** at 298 K

		σ/μS cm^{-1}		
Guest	Ion pair	Guest^a	Complex^b	$K_a{}^c$/M^{-1}
G1	Contact	63.5	50.3	$(5.98 \pm 0.89) \times 10^4$
G2	Contact	69.1	57.2	$(6.08 \pm 1.72) \times 10^3$
G3	Contact	77.2	68.5	$(4.08 \pm 0.73) \times 10^3$
G4	Loose	333.1	311.8	$(2.04 \pm 0.48) \times 10^3$
G5	Loose	351.2	319.4	$(5.91 \pm 0.60) \times 10^3$
G6	Contact	67.8	55.6	$(1.45 \pm 0.58) \times 10^4$
G7	Contact	78.4	66.8	$(5.46 \pm 1.49) \times 10^3$
TBACl	Loose	411.2	392.5	$(3.81 \pm 0.83) \times 10^2$

^{a} The electrical conductivity σ values were obtained in $CDCl_3$–CD_3CN (v/v, 1 : 1). ^{b} The electrical conductivity σ values were obtained in $CDCl_3$–CD_3CN (v/v, 1 : 1). ^{c} The association constant K_a values were obtained by ^{1}H NMR titration in $CDCl_3$–CD_3OD (v/v, 9 : 1).

The involvement of carbonyl oxygen atoms in forming intermolecular hydrogen bonds was corroborated by the infrared experiments of the complex prepared from a mixture of **1a** and **G1**, **G2**, **G3** in a molar ratio 1 : 1. The strong band at 1662 cm^{-1} of ν(C=O) in **1a** shifts to 1648 cm^{-1} in the complex, revealing a change of 14 cm^{-1} from vibration of carbonyl oxygen. On the other hand, the band of amidinium N–H vibrations appears at 1699 cm^{-1} in free **G2** and merges into a band at 1705 cm^{-1} in the complex of **1a**·**G2** (Fig. 5), suggestive of the interaction of aramide N–H with the oxygen atoms. Similar results were obtained for the complexation of **1a**·**G1** and **1a**·**G3** (Fig. S34 and S35, ESI†).

Furthermore, results from the high resolution electrospray ionization mass spectrometry (HRESI-MS) show a highly intense fragment ion of $[\mathbf{1a} + \mathbf{G2} - \mathrm{Cl}]^+$ at $m/z = 1685.1021$ for **1a**·**G2** in the positive ion mode (Fig. 6a). Importantly, a peak at $m/z = 1661.6003$, corresponding to $[\mathbf{1a} + \mathrm{Cl}]^-$, is observed in the negative ion mode (Fig. 6b). This result indicates the binding of chloride anion as ion pair in the complex and a 1 : 1 stoichiometry. Similar results were obtained for the ion-pair complexation of **G1** (Fig. S30 and S31, ESI†) and **G3** (Fig. S32 and S33, ESI†). The method of Job's plot supplied information on the binding stoichiometry of **1a** and **G2** in solution. The maximum absorbance in UV-vis spectra is observed at 0.5, indicating a macrocycle–ion pair ratio of 1 : 1 in the complex (Fig. 7). In fact, the stoichiometry of all host–guest complexes was found to be 1 : 1 by the Job's plot method (Fig. S5, S17, S21 and S25, ESI†).

Evidence in support of chloride ion binding in solution came from the observation that the K_a value (~10^4 M^{-1}) obtained by ^{1}H NMR titrations (Fig. 8) for **G1** is larger by over one order of magnitude than the value for **G4** (~10^3 M^{-1}) bearing a bulky anion, BPh_4^- (Table 1). Thus, the small chloride anion greatly enhances the complexation as compared to a larger anion, indicating its essential contribution to the enhanced cation binding *via* a positive cooperativity effect. In sharp contrast to **G1**, TBACl, which shares the same anion but contains a large tetrabutylammonium cation, is bound with a significantly lowered binding constant (~10^2 M^{-1}). (Fig. S3–S24, ESI†). The drastic reduction of the binding affinity in the presence of the non-coordinated cationic species TBA or tetramethylammonium,[19] underscores the important cooperative action for ion paring of the formamidinium cation ($HC(NH_2)_2^+$) with the chloride to retain its high binding affinity in the recognition process. In addition, replacing the counterions of **G1** with halide anions (bromide and iodide) led to **G6** and **G7** with K_a values in the decreasing order: **G1** > **G6** > **G7** > **G4** (Table 1, Fig. S3–S11, ESI†). This indicates that a larger anion tends to screw the anion out of the cavity, which in turn diminishes the binding affinity of the complex. Among the four anions examined above, the smallest anion chloride is mostly likely to be well accommodated in the cavity as ion pair. Results from conductivity study are consistent with ion paring of chloride (vide post). Unfortunately, all attempts to obtain suitable crystals of **1a** with amidinium salts failed. However, from 2D ^{1}H NMR experiments the information on the structure of the complex can be retrieved. The NOESY spectrum of a solution containing an equimolar mixture of **1a**·**G2** in $CDCl_3$–CD_3CN (v/v, 1 : 1) shows correlations between the signals attributable to the amidinium ion H^1, H^2 and aromatic protons H_k, H_g and H_b

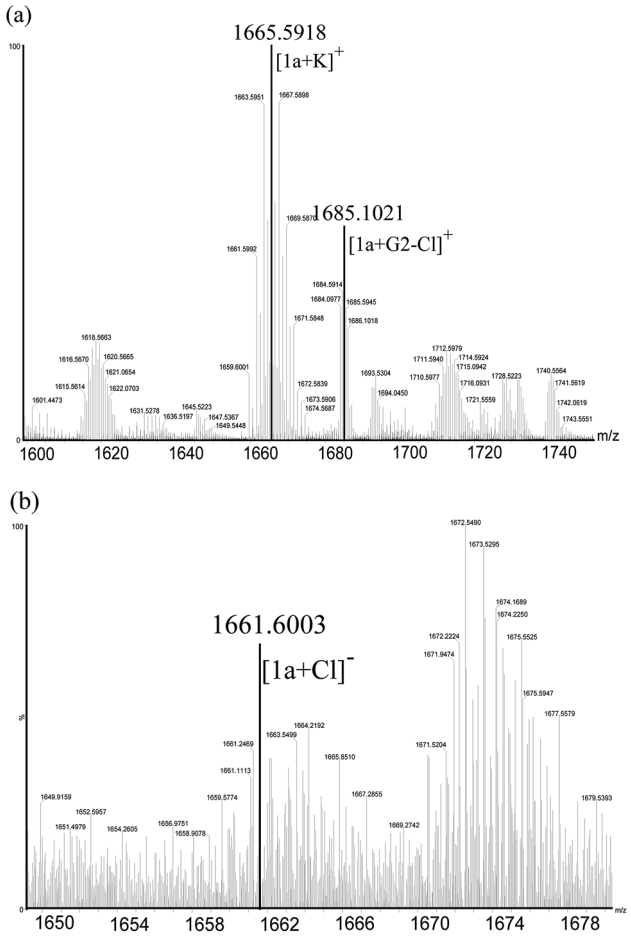

Fig. 6 HRESI-MS spectra of an equimolar solution of **1a** and **G2** in methanol in the positive ion mode (a) and negative ion mode (b).

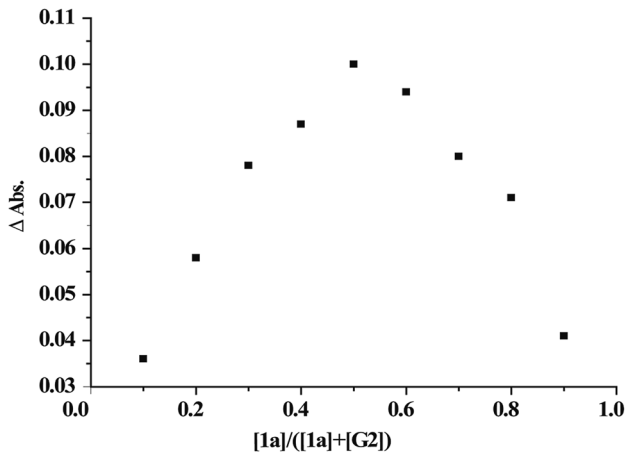

Fig. 7 Job's plot for the complexation of **1a** and **G2** in $CDCl_3$–CD_3OD (v/v, 9 : 1) based on the absorbance at 365 nm, indicating a 1 : 1 stoichiometry. The total concentration is 3×10^{-4} M.

of **1a** (Fig. 9a). Meanwhile, two correlations are observed between the signals of aromatic protons H_b, H_j and methyl proton H^3 on the amidinium ion (Fig. 9b). In contrast, no cross-peaks associated with the interaction between exterior aromatic

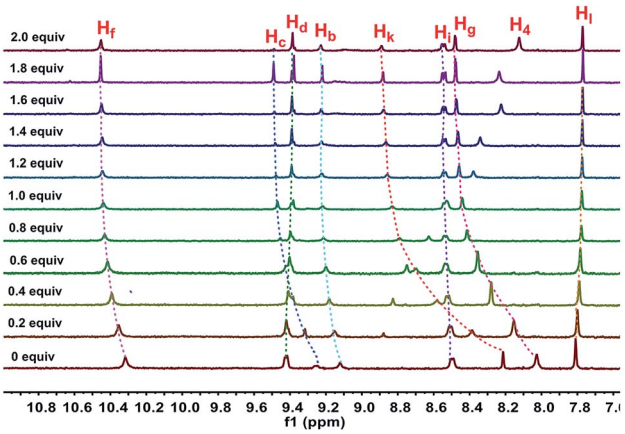

Fig. 8 Partial stacked ^{1}H NMR spectra of cyclo[6]aramide **1a** (1.0 mM) titrated by **G1** (0–2.0 equiv.) in (400 MHz, 9 : 1, $CDCl_3$–CD_3OD, 298 K).

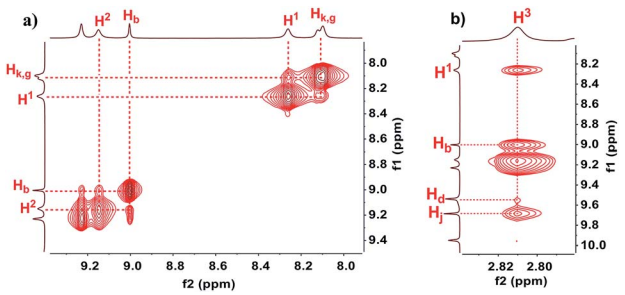

Fig. 9 Expanded 2D NOESY spectra of 1 : 1 complex **1a**·**G2** showing correlations between aromatic protons of **1a** and (a) NH_2 of **G2** and (b) CH_3 of **G2** (10 mM, 1 : 1, $CDCl_3$–CD_3CN, 400 MHz, 298 K).

protons of **1a** and any protons of **G2** are observed (Fig. S36, ESI†). These findings, combined with the facts above, strongly support the residing of both cation and anion as contact ion pair inside the cavity of the host molecule. In addition, the binding affinities are found to decrease with increasing the size of the substituent in the amidinium ion in the order of **G1** > **G2** > **G3**, reflecting the decreased steric demands for efficient complexation.

Conductometric studies for the intimacy of ion-pairs

Variation in conductivity of analytes is known to reflect the propensity of host–guest inclusion and ion-pair interaction in solution,[20] which can consequently be used to evaluate the intimacy of ion pairs formed by the amidinium ion and the anion. Therefore, conductivity experiments were performed at 5 mM of the host **1a** in $CHCl_3$–CH_3CN (v/v, 1 : 1) for the complexes (Tables 1 and S10, ESI†). Di-*n*-butylammonium chloride (DBACl) and di-*n*-butylammonium hexafluorophosphate (DBAH), which are known to be contact ion pair and loose (or separated) ion pair,[21] respectively, are used as a control. Their conductivity values were determined to be 63.4 and 594.5 μS cm^{-1} respectively, revealing a tremendous difference in conductivity ($\Delta\sigma$ = 531.1 μS cm^{-1}) between the contact and loose ion pairs. Correspondingly, their complexes **1a**·DBACl

and **1a**·DBAH also show a significant difference in conductivity ($\Delta\sigma$ = 515.9 μS cm^{-1}). Interestingly, the crystal structure of **1a**·DBACl in our previous work reveals contact ion-pair complexation[16] *via* hydrogen bonding where the distance between one hydrogen of the charge-assisted H-bonds of the di-*n*-butylammonium cation and the chloride anion measures 2.177 Å. Therefore, the lower conductivity as observed for **1a**·DBACl should point to the presence of a highly associated species or a contact ion pair in solution, and conversely, the higher conductivity should correspond to the formation of a loose ion-pair. In these cases, the ion-pair behaviour of the salts and complexes could be well distinguished by the difference of conductivity. It is envisioned that the simultaneous complexation of both amidinium and chloride as contact ion pair by the macrocyclic ditopic receptor would lead to low conductivity. Indeed, upon complexation, **G1–G3** offer a conductivity value by *ca.* five to six-fold lower than **G4**, and also TBACl, a typical example of loose ion-pair[22] (Table 1). These comparative data indicate that amidinium salts with small chloride are bound as contact ion pair in the cavity of **1a**, while **1a**·**G4** having the large anion as the counterion is prone to exist as loose ion pair. The extent to which the anion as contact ion pair is bound inside the cavity is revealed by the increased conductivity with increasing the size of anions in the order of **G1** < **G6** < **G7**. Formation of contact ion pair is particularly interesting as this avoids the energetically unfavourable separation of the two ions.[23] Of particular relevance to biological molecules is benzamidinium **G3**, a structural mimic of arginine and a potent inhibitor.[4] To the best of our knowledge, implementation of ion-pair recognition of amidinium salts by synthetic receptors is still unknown.

Pentamidine (PAM) isethionate (**G5**) is a bisamidinium salt that has found extensive use against pneumonia and even for AIDS therapy. Given its structural feature involving two benzamidinium moieties in the molecule, the complexation of PAM by **1a** was examined by ^{1}H NMR spectroscopy. Signals for the aromatic protons H^7 and H^8 ($\Delta\delta$ = +0.18 and −0.14 ppm) of **G5** undergo downfield shifts in $CDCl_3$–CD_3OD (v/v, 9 : 1), consistent with its participation in forming the complex with the macrocycle (Fig. S29, ESI†). However, the complex was found to be present in 1 : 1 stoichiometry by both mass spectrometry (MALDI-TOF) (Fig. 10) and the Job's plot method in solution (Fig. 11), and its binding constant with host **1a** was found to be (5.91 ± 0.60) × 10^3 M^{-1} (Fig. S26 and S27, ESI†). The close conductivity values between the two complexes **1a**·**G5** and **1a**·**G4** (Table 1) indicate that PAM exists as loose ion-pair in solution due to the bulky counterion. The decreased conductivity ($\Delta\sigma$ = −31.8 μS cm^{-1}) of **1a**·**G5** as compared to the free loose ion-pair of **G5** is ascribed to the confinement of the cation in the macrocyclic lumen.

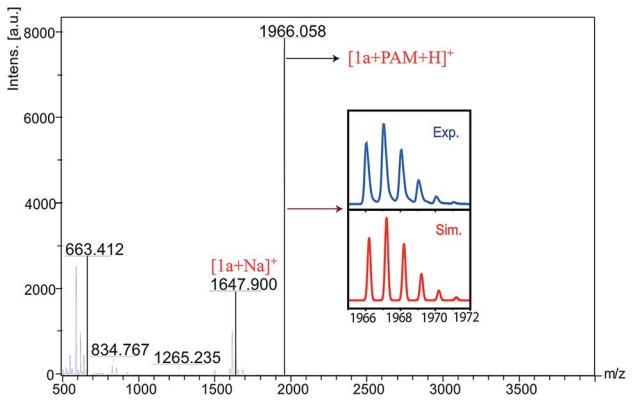

Fig. 10 MALDI-TOF spectrum of an equimolar solution $CHCl_3$–CH_3OH (v/v, 9 : 1) of **1a** and **G5**, showing the presence of 1 : 1 charge-transfer complex [inset: experimental isotope distribution (blue) and computer simulation (red)].

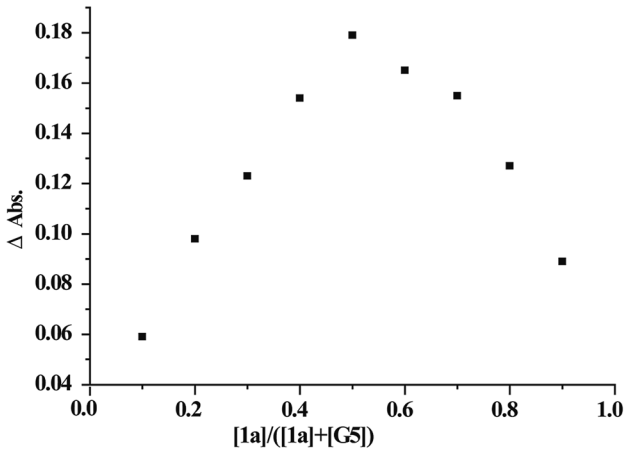

Fig. 11 Job's plot for the complexation of **1a** and **G5** in $CDCl_3$–CD_3OD (v/v, 9 : 1) based on the absorbance at 365 nm, indicating a 1 : 1 stoichiometry. The total concentration is 3 × 10^{-4} M.

Conclusions

In summary, we have demonstrated a modular system based on convergent heteroditopic cyclo[6]aramide for ion-pair recognition of amidinium chlorides. The association ability for simultaneous binding of cationic and anionic guest species depends considerably on the counterions and the size of amidinium ions. Comparative conductivity studies offer a convenient methodology to discriminate between contact and loose ion pairs for these amidinium complexes. Our findings provide a rare example of ion-pair recognition for formamidinium salts and their kindred compounds by synthetic receptors. Further work may lead to cycloaramide-based receptors for transport, controlled release, and detection of these compounds.

Experimental

Materials and reagents

Compound **1** was synthesised following the reported procedure.[16] Dichloromethane, anhydrous Na_2SO_4 and anhydrous Mg_2SO_4 were purchased from Chengdu Kelong Chemical Factory. CH_2Cl_2 was dried over CaH_2. Column chromatography was carried out using silica gel (300–400 mesh). All other solvents and chemicals used for the synthesis were of reagent grade and used as received. The complex samples for ESI-MS

determination were prepared by mixing a CH_3OH solution. Solvents for extraction and chromatography were of reagent grade.

Synthetic procedure of 1a

Pentamer **7** (300 mg, 0.20 mmol) was hydrogenated in the presence of 20% Pd/C (60 mg) in $CHCl_3/CH_3OH$ (80 mL, v/v = 5 : 1) for 10 h at 40 °C. The solution was filtered in darkness as fast as possible followed by immediate removal of the solvent. The reduced diamine **8** was used for the immediate coupling reaction. DMF (5 uL) was added to a suspension of 5-(prop-2-yn-1-yloxy)isophthalic acid **10** (58 mg, 0.20 mmol) and oxalyl chloride (87.5 mg, 0.70 mmol) in CH_2Cl_2. The mixture was stirred for 40 min at room temperature. The solvent was evaporated and the resulting residue was dried in vacuum at room temperature for 30 min. The acid chloride **11** thus obtained was dissolved in CH_2Cl_2 (60 mL) and added dropwise to a mixture of **8** and Et_3N (162 mg, 1.60 mmol) in CH_2Cl_2 (20 mL) at 0 °C. The solution was stirred under N_2 for 7 h. The organic layer was washed with water (20 mL × 3) and dried over anhydrous Na_2SO_4 and filtered. The crude product was purified by chromatography on silica gel (CH_2Cl_2/MeOH = 20 : 1) to provide the product **1a** as a white solid (241 mg, 73%). ^{1}HNMR (400 MHz, $CDCl_3$, 298 K) (ppm): 10.19 (s, 2H), 9.14 (s, 4H), 9.16 (s, 2H), 9.14 (s, 1H), 8.51 (d, 2H, J = 12 Hz), 8.28 (s, 1H), 8.20 (s, 2H), 7.80 (s, 2H), 7.02 (d, 2H, J = 8 Hz), 6.50 (s, 3H), 4.79 (s, 2H), 4.10 (d, 8H, J = 10 Hz), 3.91 (d, 12H, J = 16 Hz), 2.25 (t, 1H, J = 4 Hz), 1.54–1.26 (m, 74H), 0.94–0.86 (m, 24H); ^{13}C NMR (101 MHz, $CDCl_3$, 298 K): δ 164.55, 163.18, 162.38, 159.92, 159.72, 153.40, 145.87, 135.19, 132.31, 124.98, 124.25, 122.13, 120.92, 118.95, 117.90, 117.81, 112.81, 94.58, 77.22, 72.45, 72.29, 55.89, 55.50, 38.52, 37.86, 31.87, 30.96, 30.35, 30.06, 29.72, 29.72, 29.59, 29.35, 29.08, 28.65, 26.72, 26.38, 23.44, 23.15, 23.09, 22.67, 14.13, 10.35, 10.32; MALDI-TOF MS (m/z) calcd for $C_{97}H_{136}N_6O_{15}$ $[M + Na]^+$ 1647.996, found $[M + Na]^+$ 1647.900.

Instruments and apparatus

^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE AV II-400 MHz (^{1}H: 400 MHz; ^{13}C: 100 MHz) (Karlsruhe, Germany). High resolution mass spectra (HR-MS) data were collected by WATERS Q-TOF Premier (California, USA). UV-vis spectra were measured by SHIMADZU UV-2450 (Tokyo, Japan). Chemical shifts are reported in δ values in ppm using tetramethlysilane (TMS). HR-MS data were obtained by WATERS Q-TOF Premier. The geometry optimizations were carried out in gas phase by employing the Gaussian09 program. Fourier transform infrared (FT-IR) data were collected by a Thermo Nicolet NEXUS 670 FT-IR spectrophotometer. MALDI-TOF MS spectra were recorded on Bruker Autoflex III MS spectrometer.

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Notes and references

1 T. W. Bell and V. J. Santora, *J. Am. Chem. Soc.*, 1992, **114**, 8300.

2 M. T. Cushion, P. D. Walzer, M. S. Collins, S. Rebholz, J. J. Vanden Eynde, A. Mayence and T. L. Huang, *Antimicrob. Agents Chemother.*, 2004, **48**, 4209.

3 (*a*) T. Grawe, G. Schäfer and T. Schrader, *Org. Lett.*, 2003, **5**, 1641; (*b*) S. Rudra and A. V. Eliseev, *J. Am. Chem. Soc.*, 1998, **120**, 11543; (*c*) S. C. Zimmerman, Y. Wang, P. Bharathi and J. S. Moore, *J. Am. Chem. Soc.*, 1998, **120**, 2172; (*d*) A. Kraft and A. Reichert, *Tetrahedron*, 1999, **55**, 3923; (*e*) A. Kraft, L. Peters and H. R. Powell, *Tetrahedron*, 2002, **58**, 3499.

4 T. Schrader and M. Maue, in *Functional Synthetic Receptors*, ed. T. Schrader and A. D. Hamilton, Wiley, Weinheim, 2005, p. 111.

5 (*a*) J. Scheerder, J. P. M. van Duynhoven, J. F. J. Engbersen and D. N. Reinhoudt, *Angew. Chem., Int. Ed.*, 1996, **35**, 1090; (*b*) P. D. Beer, P. Hopkins and J. McKinney, *Chem. Commun.*, 1999, **13**, 1253; (*c*) S. G. Galbraith, P. G. Plieger and P. A. Tasker, *Chem. Commun.*, 2002, **22**, 2662; (*d*) P. R. Webber and P. D. Beer, *Dalton Trans.*, 2003, **22**, 2249; (*e*) C. C. Tong, R. Quesada, J. L. Sessler and P. A. Gale, *Chem. Commun.*, 2008, **47**, 6321; (*f*) P. A. Gale, *Chem. Soc. Rev.*, 2010, **39**, 3746; (*g*) S. K. Kim, G. I. Vargas-Zúñiga, B. P. Hay, N. J. Young, L. H. Delmau, C. Masselin, C.-H. Lee, J. S. Kim, V. M. Lynch, B. A. Moyer and J. L. Sessler, *J. Am. Chem. Soc.*, 2012, **134**, 1782; (*h*) M. Yano, C. C. Tong, M. E. Light, F. P. Schmidtchen and P. A. Gale, *Org. Biomol. Chem.*, 2010, **8**, 4356; (*i*) X. D. Wang, S. Li, Y. F. Ao, Q. Q. Wang, Z. T. Huang and D. X. Wang, *Org. Biomol. Chem.*, 2016, **14**, 330.

6 (*a*) M. A. Hossain and H.-J. Schneider, *J. Am. Chem. Soc.*, 1998, **120**, 11208; (*b*) H. Tsukube, M. Wada, S. Shinoda and H. Tamiaki, *Chem. Commun.*, 1999, **11**, 1007; (*c*) A. P. Silva, H. Nimalá Gunaratne, E. Glenn and R. Pamela, *Chem. Commun.*, 1996, **18**, 2191.

7 (*a*) T. Yu and R. G. Weiss, *Green Chem.*, 2012, **14**, 209; (*b*) R. Talhout and J. B. Engberts, *Org. Biomol. Chem.*, 2004, **2**, 3071; (*c*) A. Clark, T. Hemmelgarn, L. Danziger-Isakov and A. Teusink, *Pediatr. Transplant.*, 2015, **19**, 326; (*d*) P. A. Nguewa, M. A. Fuertes, V. Cepeda, S. Iborra, J. Carrión, B. Valladares, C. Alonso and J. M. Pérez, *Chem. Biodiversity*, 2005, **2**, 1387.

8 For selected reviews, see: (*a*) D.-W. Zhang, X. Zhao, J.-L. Hou and Z.-T. Li, *Chem. Rev.*, 2012, **112**, 5271; (*b*) K. Yamato, M. Kline and B. Gong, *Chem. Commun.*, 2012, **48**, 12142; (*c*) B. Gong and Z. F. Shao, *Acc. Chem. Res.*, 2013, **46**, 2856; (*d*) H. L. Fu, Y. Liu and H. Q. Zeng, *Chem. Commun.*, 2013, **49**, 4127.

9 (*a*) A. R. Sanford, L. H. Yuan, W. Feng, K. Yamato, R. A. Flowers and B. Gong, *Chem. Commun.*, 2005, **37**, 4720;

(*b*) Y. Liu, J. Shen, C. Sun, C. L. Ren and H. Q. Zeng, *J. Am. Chem. Soc.*, 2015, **137**, 12055.

10 (*a*) L. H. Yuan, W. Feng, K. Yamato, A. R. Sanford, D. G. Xu, H. Guo and B. Gong, *J. Am. Chem. Soc.*, 2004, **126**, 11120; (*b*) W. Feng, K. Yamato, L. Q. Yang, J. S. Ferguson, L. J. Zhong, S. L. Zou, L. H. Yuan, X. C. Zeng and B. Gong, *J. Am. Chem. Soc.*, 2009, **131**, 2629; (*c*) Y. A. Yang, W. Feng and L. H. Yuan, *Chem. J. Chin. Univ.*, 2011, **32**, 1950; (*d*) Y. A. Yang, W. Feng, J. C. Hu, S. L. Zou, R. Z. Gao, K. Yamato, M. Kline, Z. H. Cai, Y. Gao, Y. B. Wang, Y. B. Li, Y. L. Yang, L. H. Yuan, X. C. Zeng and B. Gong, *J. Am. Chem. Soc.*, 2011, **133**, 18590; (*e*) L. J. Zhong, L. Chen, W. Feng, S. L. Zou, Y. Y. Yang, N. Liu and L. H. Yuan, *J. Inclusion Phenom. Macrocyclic Chem.*, 2012, **72**, 367.

11 J. C. Hu, L. Chen, Y. Ren, P. C. Deng, X. W. Li, Y. J. Wang, Y. M. Jia, J. Luo, X. S. Yang, W. Feng and L. H. Yuan, *Org. Lett.*, 2013, **15**, 4670.

12 M. Xu, L. Chen, Y. M. Jia, L. J. Mao, W. Feng, Y. Ren and L. H. Yuan, *Supramol. Chem.*, 2015, **27**, 436.

13 L. Chen, Z. Y. Peng, S. Liu, X. W. Li, R. Z. Chen, Y. Ren, W. Feng and L. H. Yuan, *Org. Lett.*, 2015, **17**, 5950.

14 Y. Z. He, M. Xu, R. Z. Gao, X. W. Li, F. X. Li, X. D. Wu, D. G. Xu, H. Q. Zeng and L. H. Yuan, *Angew. Chem., Int. Ed.*, 2014, **53**, 11834.

15 X. W. Li, B. Li, L. Chen, J. C. Hu, C. D. Wen, Q. D. Zheng, L. X. Wu, H. Q. Zeng, B. Gong and L. H. Yuan, *Angew. Chem., Int. Ed.*, 2015, **54**, 11147.

16 J. C. Hu, L. Chen, J. Shen, J. Luo, P. C. Deng, Y. Ren, H. Q. Zeng, W. Feng and L. H. Yuan, *Chem. Commun.*, 2014, **50**, 8024.

17 (*a*) A. J. McConnell and P. D. Beer, *Angew. Chem., Int. Ed.*, 2012, **51**, 5052; (*b*) S. K. Kim and J. L. Sessler, *Acc. Chem. Res.*, 2014, **47**, 2525; (*c*) S. K. Kim and J. L. Sessler, *Chem. Soc. Rev.*, 2010, **39**, 3784; (*d*) R. Custelcean, L. H. Delmau, B. A. Moyer, J. L. Sessler, W. S. Cho, D. Gross, G. W. Bates, S. J. Brooks, M. E. Light and P. A. Gale, *Angew. Chem., Int. Ed.*, 2005, **117**, 2593; (*e*) M. H. Filby, T. D. Humphries, D. R. Turner, R. Kataky, J. Kruusma and J. W. Steed, *Chem. Commun.*, 2006, **2**, 156; (*f*) J. W. Steed and J. L. Atwood, in *Supramolecular Chemistry*, John Wiley Sons, Ltd, 2009, p. 285; (*g*) M. F. Ni, Y. F. Guan, L. Wu, C. Deng, X. Y. Hu, J. L. Jiang, C. Lin and L. Y. Wang, *Tetrahedron Lett.*, 2012, **53**, 6409; (*h*) B. Qiao, A. Sengupta, Y. Liu, K. P. McDonald, M. Pink, J. R. Anderson, K. Raghavachari and A. H. Flood, *J. Am. Chem. Soc.*, 2015, **137**, 9746; (*i*) Y. Y. Fang, X. Y. Yuan, L. Wu, Z. Y. Peng, W. Feng, N. Liu, D. G. Xu, S. J. Li, A. Sengupta, P. K. Mohapatra and L. H. Yuan, *Chem. Commun.*, 2015, **51**, 4263.

18 K. L. Zhu, S. J. Li, F. Wang and F. H. Huang, *J. Org. Chem.*, 2009, **74**, 1322.

19 M. D. Lankshear, A. R. Cowley and P. D. Beer, *Chem. Commun.*, 2006, **6**, 612.

20 (*a*) Y. A. Gao, Z. H. Li, J. M. Du, B. X. Han, G. Z. Li, W. G. Hou, D. Shen, L. Q. Zheng and G. Y. Zhang, *Chem.–Eur. J.*, 2005, **11**, 5875; (*b*) B. Datta and M. N. Roy, *Phys. Chem. Liq.*, 2015, **53**, 574; (*c*) H. Shekaari and F. Jebali, *Phys. Chem. Liq.*, 2011, **49**, 572.

21 (*a*) J. W. Jones and H. W. Gibson, *J. Am. Chem. Soc.*, 2003, **125**, 7001; (*b*) H. W. Gibson, J. W. Jones, L. N. Zakharov, A. L. Rheingold and C. Slebodnick, *Chem.–Eur. J.*, 2011, **17**, 3192; (*c*) M. Montalti and L. Prodi, *Chem. Commun.*, 1998, **14**, 1461.

22 A. Arduini, E. Brindani, G. Giorgi, A. Pochini and A. Secchi, *J. Org. Chem.*, 2002, **67**, 6188.

23 (*a*) J. M. Mahoney, A. M. Beatty and B. D. Smith, *Inorg. Chem.*, 2004, **43**, 7617; (*b*) M. Cametti, M. Nissinen, A. Dalla Cort, L. Mandolini and K. Rissanen, *J. Am. Chem. Soc.*, 2005, **127**, 3831.