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Imidazolium-Based [1$_4$]Heterophanes as Models for Anion Recognition

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The significance of the reported dicationic [1$_4$]imidazoliophanes **4·2X** relies on their ability to bind anions in polar media. Thus, imidazolium units represent the main structural motifs in the formation of unconventional (C–H)$^+$···Cl$^-$ charge-assisted hydrogen bonds which become the noncovalent forces driving the anionic interactions exhibited by dications **4·2X**. Herein, we report the "3+1" convergent synthesis of the title macrocycles **4a–d·2X**; their counteranion exchange using a strongly basic anion-exchange resin (OH$^-$ form) and their structures have been examined by NMR spectroscopy. Solution studies in CD_3CN and [D_6]DMSO by ^{1}H NMR spectroscopy have revealed the importance of the hydrogen bonds in controlling anion recognition.

Introduction

Over the last few years, imidazolium-based frameworks have been developed as part of the advances in N-heterocyclic carbene (NHC)[2] and anion recognition chemistry[3,4] and room-temperature ionic liquids (RILs).[5] Among them, recent developments in anion recognition include advances in anion templating and the design of artificial anion receptors, which frequently rely on cationic moieties.[4] In these positively charged systems, the primary noncovalent driving forces for binding are either electrostatic interactions or electrostatic interactions in combination with hydrogen bonding forces,[6] that is, by forming N–H···anion bonds[4a] or a novel type of charged hydrogen bond, (C–H)$^+$··· anion.[7,8]

As part of our ongoing research of imidazolium-based frameworks,[7,9] we have examined cyclophanes **1·2X** and **2**[9b] together with dicationic pincers **3·2X** (Figure 1);[9c] for bis(betaines) **2** and dications **1·2X**, quaternary imidazolium units were selected because of the recognized chemical stability of the methyleneimidazolium azolate betaine building blocks.[10] Maintaining the two imidazolium moieties present in the heterophanes **1·2X**, dicationic [1$_4$]imidazoliophanes **4·2X** arise as models for intermolecular interactions driven by unconventional (C–H)$^+$···X hydrogen bonds[7] (Figure 1). Dication **4a·2Cl·2H$_2$O** was the first reported example of nonclassical (C–H)$^+$···Cl$^-$ hydrogen bonds between the C–H group of the imidazolium rings and the chloride anions in the solid state,[1,7] and the ability of the [1$_4$]imidazoliophanes **4·2X** to bind chloride anions has been exploited during their synthesis.[9d]

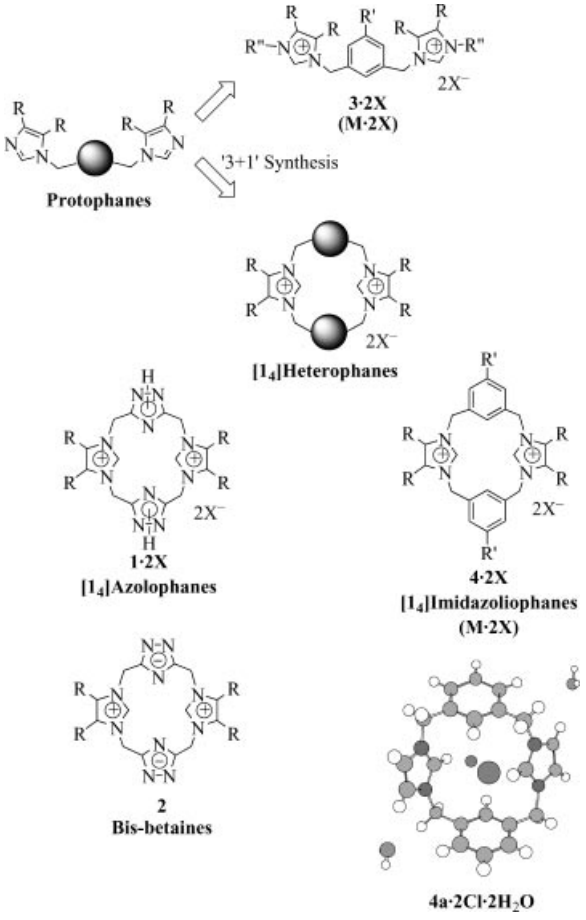

Figure 1. Imidazolium molecular motifs within [1$_4$]heterophane frameworks. The molecular structure of **4a·2Cl·2H$_2$O** shows nonclassical (C–H)$^+$···Cl$^-$ hydrogen bonds (see ref.[7]).

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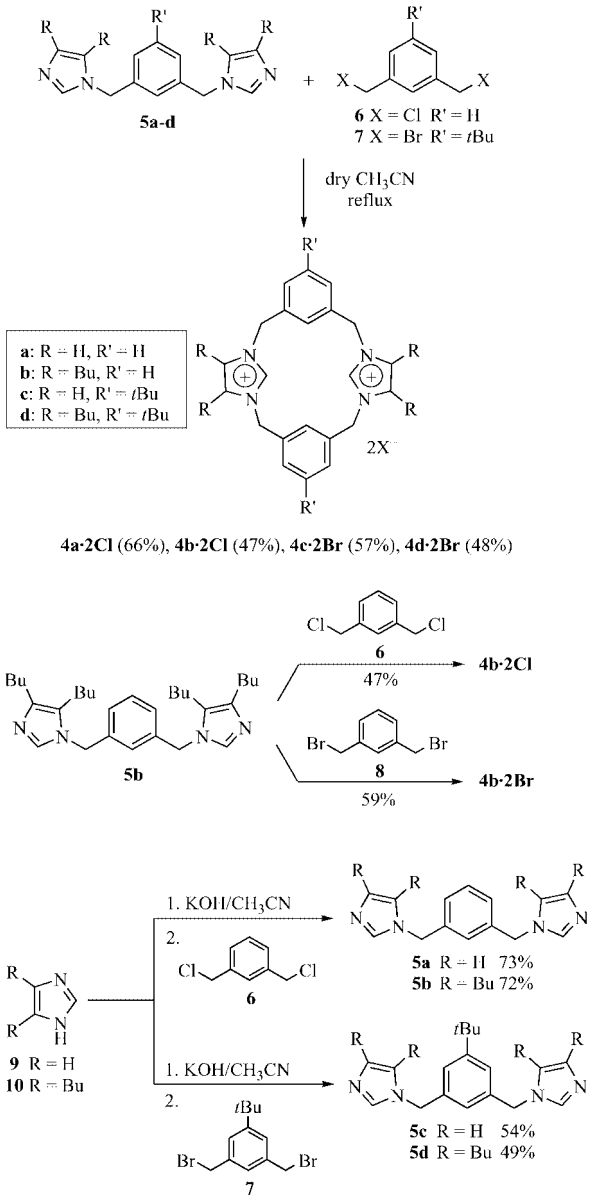
From dicationic prototypes **4·2X**, a variety of imidazolium-linked scaffolds have been investigated for anion binding driven by this new type of (C–H)$^+$···halide hydrogen bond.[8] The behavior in the gas phase of simple systems containing two imidazolium quaternary moieties, for example, **4·2X** (**M·2X**), has been examined by using positive-ion ESI-MS and direct electrospray mass spectrometric evidence has been obtained for singly charged imidazolylidene ions [M – H]$^+$ and the regiospecific deuteriated counterparts have produced the corresponding imidazolylidene species [M – D]$^+$.[11,12] In parallel, metal complexes of NHC-linked cyclophanes and pincers related to dications **4·2X** and **3·2X** have been reported, giving rise to active catalytic model systems for several reactions.[2,13]

The present study focuses on the convergent "3+1" synthesis of the title dications **4a**–**d·2X** and their counteranion exchange using a strongly basic anion-exchange resin (OH$^-$ form). The structures of these model imidazolium-based cyclophanes were examined by NMR spectroscopy and solution studies by ^{1}H NMR spectroscopy in CD_3CN and [D_6]-DMSO revealed the importance of the hydrogen bonds in controlling anion binding.

Results and Discussion

Synthesis

The dications **4a**–**d·2X** were prepared according to a "3+1" convergent approach, and the coupling of the trinucleating protophanes **5a**–**d** with the 1,3-bis(halomethyl)benzene **6** or **7** produced the dications **4a**–**d·2X** in ≥47% (Scheme 1). For **4b·2X**, the macrocyclization reaction was improved by using the more reactive 1,3-bis(bromomethyl)-benzene (**8**). Protophanes **5a**,**b** were obtained in ≥72% yield by treatment of 1,3-bis(chloromethyl)benzene (**6**) with imidazoles **9** or **10**, and reaction of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**7**) with imidazoles **9** or **10** gave **5c**,**d** in ≥49% yield (Scheme 1). Physical data for all the new compounds reported are listed in Table 1.



Scheme 1. "3+1" Convergent synthesis of imidazoliophanes **4·2X**.

Counteranion Exchange Using a Strongly Basic Anion-Exchange Resin (OH$^-$ Form)

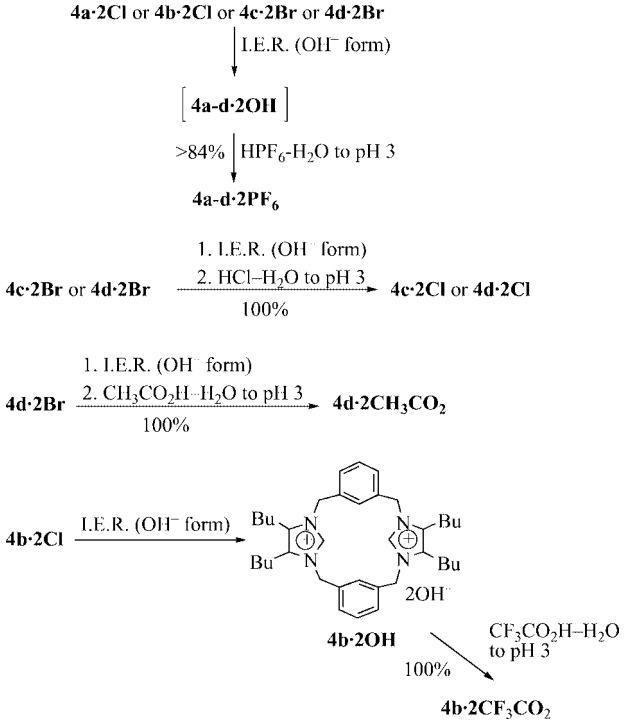
Exploiting our standard protocol,[9,10] the counteranions of dications **4a**–**d·2X** were changed by the use of a strongly basic anion-exchange resin (OH$^-$ form) followed by immediate collection of the eluates in acid solution in aq. HPF_6, aq. HCl, aq. HBr or aq. CH_3CO_2H to pH = 3 (Scheme 2 and Table 1). The anion exchange proceeded through the corresponding quaternary imidazolium hydroxides **4a**–**d·2OH** (see below).

The hexafluorophosphate counteranion enhances the solubility of the positively charged frameworks in relatively nonpolar solvents; Stoddart and co-workers observed that the solubility in organic solvents of the tetracationic cyclobis(paraquat-*p*-phenylene) (**M·4X**) increased considerably when the counteranions were hexafluorophosphates (**M·4PF$_6$**), whereas exchanging the counteranion to afford the tetrachloride macrocycle (**M·4Cl**) conferred aqueous solubility upon the tetracation but rendered it insoluble in Me_2CO, MeCN and $MeNO_2$.[14a] Similar hydrophobic behavior was also observed when the tetracation macrocycle counteranion was located within [2]catenane and rotaxane systems.[14b] Moreover, hydrophobic and hydrophilic ILs are of practical interest and the physical properties of these simple imidazolium salts can be modulated especially by changing the counteranions, with the hexafluorophosphate anion notably increasing the lipophilicity of ILs.[14c] Accordingly, the hexafluorophosphate counteranion notably increased the solubility of dicationic cyclophanes **4a**–**d·2X** in organic solvents and dications **4a**–**d·2PF$_6$** were much more soluble in acetonitrile and alcohols than their corresponding dichloride or dibromide counterparts. Note that dicationic macrocycles containing proton-ionizable 1*H*-

Table 1. Physical data for the macrocyclic salts **4a–d·2X** and protophanes **5b–d**.

Compd.	Yield [%][a]	M.p. [°C]	Solvent[b]	Molecular formula[c]
4a·2Cl	66	>300	MeCN	$C_{22}H_{22}N_4Cl_2·2H_2O$
4a·2PF$_6$	91	>300	–	$C_{22}H_{22}N_4P_2F_{12}·H_2O$
5b	72	[d]	–	$C_{30}H_{46}N_4·H_2O$
4b·2Br	59	262–264	–	$C_{38}H_{54}N_4Br_2·0.75HBr$
4b·2Cl	47	266	Me_2CO	$C_{38}H_{54}N_4Cl_2·1.75HCl$
4b·2PF$_6$	84	228–230	–	$C_{38}H_{54}N_4P_2F_{12}·4.5H_2O$
5c	54	72	toluene	$C_{18}H_{22}N_4$
4c·2Br	57	293	*i*PrOH	$C_{30}H_{38}N_4Br_2·2H_2O$
4c·2Cl	100	278–280	MeCN	$C_{30}H_{38}N_4Cl_2·3.5H_2O·0.5CH_3CN$
4c·2PF$_6$	99	>300	–	$C_{30}H_{38}N_4P_2F_{12}·H_2O$
5d	49	[d]	–	$C_{34}H_{54}N_4·0.25H_2O$
4d·2Br	48	278–280	–	$C_{46}H_{70}N_4Br_2·1.5H_2O$
4d·2Cl	100	236–238	–	$C_{46}H_{70}N_4Cl_2·2.5H_2O$
4d·2PF$_6$	99	288–290	MeCN	$C_{46}H_{70}N_4P_2F_{12}·H_2O$
4d·2AcO	100	[e]	–	$C_{50}H_{76}N_4O_4·4.5H_2O$

[a] Yields were not optimized. [b] Recrystallization solvent. [c] Satisfactory microanalyses were obtained (±0.4% for C, H, N). [d] Oily compound. [e] Foamy compound.



Scheme 2.

1,2,4-triazole fragments, such as heterophanes **1·2X**, are fairly insoluble compounds irrespective of the nature of their counteranions.[9b]

At this point, the stability of the dicationic hydroxides **4a–d·2OH** was then examined. The anion exchange for macrocycles **4a–d·2X** proceeds through the corresponding quaternary imidazolium hydroxides (**4a–d·2OH**) and the eluates had to be immediately collected in acid solution (see Scheme 2). Note that azolylimidazolium salts with different interannular spacers have been found to be very unstable, especially in the solid state, when the counteranion is hydroxide.[9,10] Prior to acidification, the eluates gave yellow-to-red solids and **4a**,**c**,**d·2OH** were unstable both in solution and in the solid state; after very short periods of time in solution products of decomposition and alteration were observed by ^{1}H NMR spectroscopy, ca. 20% for **4c**,**d·OH** and ca. 90% for **4a·OH**. In contrast, dication **4b·2OH** appeared to be rather stable and showed a clean ^{1}H NMR spectrum in [D$_6$]DMSO (see NMR spectroscopy and Figure 3); the relative stability of these dications in solution follows the relative order **4b·2OH** > **4c·2OH** ≈ **4d·2OH** >>> **4a·2OH**.

Structure and NMR Spectroscopy

The distinctive structural aspects of dicationic cyclophanes **4·2X** have been examined both in the gas phase by positive-ion electrospray mass spectrometry and in the solid state by X-ray crystallography.[7,11] Accordingly, macrocycles **4·2Cl** (**M·2Cl**) gave clean positive-ion ESI spectra; at low cone voltage V_c, the base peak corresponds in each case to the doubly charged ion $[M]^{2+}$ resulting from the loss of the two Cl$^-$ counterions. When the cone voltage was increased to 80 V, the base peak corresponded to the singly charged ion $[M - H]^+$.[11]

Notably, the single-crystal X-ray diffraction analysis of dication **4a·2Cl·2H$_2$O** typified the first example of the non-classic (C–H)$^+$···Cl$^-$ hydrogen bonds between the imidazolium rings and chloride anions; the shortest hydrogen bond interaction was H10···Cl1 (2.54 Å, θ = 157°) (see Figure 1). The hydrogen-bonding networks within the solid-state aggregates show that the chloride anions and water molecules are located among the dications in a channel fashion.[7]

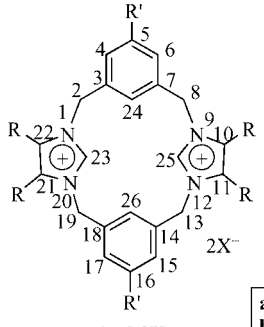
The IR spectra of dications **4a–d·2X** showed characteristic absorption bands of the counteranions, Cl$^-$, Br$^-$, PF$_6^-$ and AcO$^-$. The ^{1}H NMR spectra of **4a–d·2X** (X = Cl$^-$, Br$^-$, PF$_6^-$) showed a sharp singlet due to the methylene hydrogen atoms indicating a high degree of conformational flexibility comparable to that in dications **1·2X** and bis(betaines) **2**.[9b] The association behavior was examined in the concentration range of 0.5–38 mM (Table 2) and the variation in the

Table 2. Concentration dependence of **4a**–**d·2X** as determined by ^{1}H NMR spectroscopy.[a]

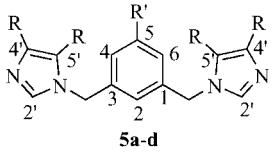
Compd.	Solvent	[**4a**–**d·2X**] [mM]	Nonaggregating [**4a**–**d·2X**]$_{max}$ [mM]
4a·2Cl	[D$_6$]DMSO	1.51–38.10	2.93
4a·2PF$_6$		1.36–18.60	[b]
4b·2Cl		0.71–23.63	2.85
4b·2PF$_6$		1.33–17.84	[b]
4c·2Br		1.39–25.11	12.55
4c·2Cl		0.59–25.55	1.09
4c·2PF$_6$		0.48–18.61	ca. 2[c]
4d·2Br		1.33–19.62	9.90
4d·2Cl		0.95–18.29	ca. 9[d]
4d·2PF$_6$		1.27–11.86	[b]
4d·2AcO		0.56–20.22	0.56
4d·2Br	CD$_3$CN	0.36–6.05[e]	0.36
4d·2Cl		0.40–6.37[e]	0.40
4d·2PF$_6$		1.49–14.14	[b]
4d·2AcO		0.37–22.28	0.37

[a] Aggregation occurred when the chemical shift difference ($\Delta\delta$) was > 0.1 ppm. [b] Aggregation was not observed. [c] $\Delta\delta \leq 0.1$ ppm for 1.53–2.89 mM. [d] $\Delta\delta \leq 0.1$ ppm for 4.76–9.71 mM. [e] At higher concentrations the compound was insoluble.

Table 3. Selected ^{1}H NMR spectroscopic data for [1$_4$]imidazoliophanes **4a**–**d·2X** and protophanes **5a**–**d** in [D$_6$]DMSO at 300 MHz.[a]



4a-d·2X



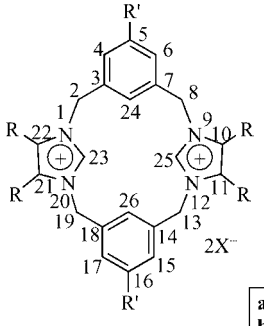
5a-d

a: R = H, R' = H
b: R = Bu, R' = H
c: R = H, R' = *t*Bu
d: R = Bu, R' = *t*Bu

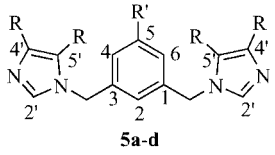
Compd.	Conc. [mM][a]	δ [ppm] *23-H*[b]	*24-H*[b]	–CH$_2$–
4a·2Cl[c]	1.51	9.42	7.09	5.42
4a·2PF$_6$	1.36	9.24	6.95	5.41
4b·2Cl	0.71	9.32	6.57	5.51
4b·2Br[d]	[e]	9.37	6.61	5.51
4b·OH	[e]	9.49	6.51	5.14–5.73
4b·2PF$_6$	1.33	9.34	6.60	5.50
4c·2Cl	0.59	9.36	6.69	5.42
4c·2Br[f]	1.39	9.34	6.67	5.42
4c·2PF$_6$	0.48	9.45	6.76	5.41
4d·2Cl	0.95	9.46	6.48	5.55
4d·2Br	1.33	9.33	6.41	5.50
4d·2PF$_6$	1.27	9.42	6.48	5.49
4d·2OAc	0.56	9.59	6.54	5.49
		2′-H	2-H	–CH$_2$–
5a	–	7.72	7.19	5.16
5b	–	7.46	6.82	5.05
5c	–	7.71	6.94	5.14
5d[d]	–	7.45	6.61	5.04

[a] At nonaggregating concentrations. [b] The equivalent proton atoms are abbreviated as follows: *23-H* = 23,25-H; *24-H* = 24,26-H. [c] Assignment by NOESY. [d] Recorded at 500 MHz. [e] At a concentration of ca. 2 mM. [f] Assignment by NOE.

Table 4. Selected ^{13}C NMR spectroscopic data for [1$_4$]metaimidazoliophanes **4a**–**d·2X** and protophanes **5a**–**d** in [D$_6$]DMSO at 50.3 MHz.



4a-d·2X



5a-d

a: R = H, R' = H
b: R = Bu, R' = H
c: R = H, R' = *t*Bu
d: R = Bu, R' = *t*Bu

Compd.	δ [ppm] *C-23*[a]	*C-24*[a]	–CH$_2$–
4a·2Cl[b]	136.4	127.1	52.0
4a·2PF$_6$	136.4	126.0	52.1
4b·2Cl	137.2	124.3	49.7
4b·2Br[b]	136.8	123.9	49.7
4b·2PF$_6$	136.7	123.6	49.8
4c·2Cl	136.4	123.1	52.2
4c·2Br	136.3	122.7	52.2
4c·2PF$_6$	136.4	123.5	52.2
4d·2Cl	137.0	121.5	50.0
4d·2Br	136.7	121.1	50.1
4d·2PF$_6$	136.7	121.1	50.1
4d·2OAc	137.7	121.8	49.9
	C-2′	C-2	–CH$_2$–
5a[b]	137.7	126.9	49.5
5b	136.2	125.2	47.6
5c	137.6	124.1	49.8
5d[b]	136.2	122.3	47.9

[a] The equivalent carbon atoms are abbreviated: *C-23* = C-23,25; *C-24* = C-24,26. [b] Assignment by hetcor (hmqc, hmbc).

chemical shift was studied for protons 23,25-H and 24,26-H; the chemical shifts of the macrocycles **4a**–**d·2PF$_6$** remained essentially constant upon changing the concentration from ca. 1 to ca. 18 mM.

Selected ^{1}H NMR spectroscopic data at 300 MHz (298 K) in [D$_6$]DMSO under nonaggregation conditions are listed in Table 3 and ^{13}C NMR spectroscopic data in Table 4.

Qualitative ^{1}H NMR observations have shown the importance of the imidazolium structural motifs for anion binders **4·2X**. At nonaggregating concentrations, the proton chemical shifts of the imidazolium protons 23-H and 25-H together with 24-H and 26-H (the aromatic fragments) were the most affected mainly due to structural factors, the nature of the counteranion and solvent polarity. Representative data are gathered in Table 5 and Figure 2. The presence of substituents led to significant shielding of these protons, possibly due to diminished conformational flexibility. For example, in [D$_6$]DMSO the $\Delta\delta$(24,26-H) between **4d·2Cl** and **4a·2Cl** was –0.61 ppm (183 Hz) and this effect was maintained on changing the counteranion, $\Delta\delta$(24,26-H) between **4d·2PF$_6$** and **4a·2PF$_6$** being –0.47 ppm (141 Hz) (see Figure 2a).

Table 5. Selected ^{1}H NMR spectroscopic data for **4a**–**d·2X** in [D$_6$]-DMSO and CD$_3$CN.

Compd.[a]	Conc. [mM]	δ [ppm]	
		23,25-H	24,26-H
4a·2Cl	1.51	9.42	7.09
4a·2PF$_6$	1.36	9.24	6.95
4b·2Cl	0.71	9.32	6.57
4b·2PF$_6$	1.33	9.34	6.60
4c·2Br	1.39	9.34	6.67
4c·2Cl	0.59	9.36	6.69
4c·2PF$_6$	0.48	9.45	6.76
Compd.[a]	Conc. [mM]	23,25-H	24,26-H
4d·2Br	1.33	9.33	6.41
4d·2Cl	0.95	9.46	6.48
4d·2PF$_6$	1.27	9.42	6.48
4d·2AcO	0.56	9.59	6.54
Compd.[b]	Conc. [mM]	23,25-H	24,26-H
4d·2Br	0.36	9.43	6.80
4d·2Cl	0.40	9.48	6.81
4d·2PF$_6$	1.49	8.87	6.32
4d·2AcO	0.37	9.96	6.97

[a] ^{1}H NMR (300 MHz) data in [D$_6$]DMSO. [b] ^{1}H NMR (300 MHz) data in CD$_3$CN.

As a consequence of the hydrogen bonding of the anions present in the dicationic macrocycle **4a**–**d·2X**, the signals of the acidic imidazolium 23-H and 25-H atoms were shifted downfield up to about 10 ppm in comparison with the usual values of the chemical shifts for these imidazolium protons in azolophanes (e.g., **1·2X**) and in a variety of *N*-azolylimidazolium salts with different spacers.[9,10] Depending on the nature of the anion, large differences in the chemical shifts were observed; for instance, in [D$_6$]DMSO between **4a·2Cl** and **4a·2PF$_6$** $\Delta\delta$(23,25-H) = +0.18 ppm (54 Hz) and $\Delta\delta$(24,26-H) = +0.14 ppm (42 Hz), while in CD$_3$CN between **4d·2CH$_3$CO$_2$** and **4d·2PF$_6$** $\Delta\delta$(23,25-H) = +1.09 ppm (327 Hz) and $\Delta\delta$(24,26-H) = +0.65 ppm (195 Hz) (see Figure 2b).

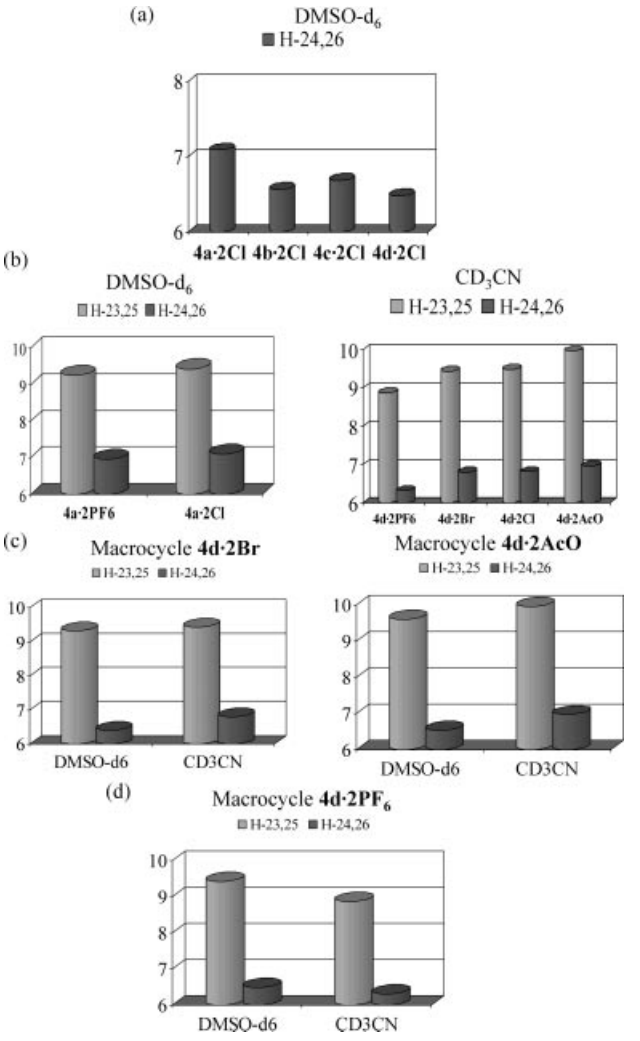


Figure 2. ^{1}H NMR chemical shift variations of 23,25-H and/or 24,26-H (300 MHz): (a) **4a**–**d·2Cl** in [D$_6$]DMSO; (b) **4a·2PF$_6$**/**4a·2Cl** in [D$_6$]DMSO and **4d·2X** in CD$_3$CN; (c) **4d·2Br** and **4d·2CH$_3$CO$_2$** in [D$_6$]DMSO and CD$_3$CN; (d) **4d·2PF$_6$** in [D$_6$]-DMSO and CD$_3$CN.

Owing to solvent effects,[4a,9c,15] dications **4d·2X** exhibited greater deshielding of the acidic 23-H and 25-H protons in a less polar solvent, for example, **4d·2Br** for which $\Delta\delta$(23,25-H) (in CD$_3$CN/[D$_6$]DMSO) = +0.1 ppm (30 Hz) and **4d·2CH$_3$CO$_2$** for which $\Delta\delta$(23,25-H) (in CD$_3$CN/[D$_6$]-DMSO) = +0.37 ppm (111 Hz) (see Figure 2c). When the counteranions were hexafluorophosphates, the dications **4**$^{2+}$ showed very weak or no hydrogen bonding between the PF_6^- counteranions; similar behavior has been reported for the heterophanes **1·2PF$_6$**[9b] and protophanes **3·2PF$_6$**[9c] in solution and has been confirmed in the solid state by X-ray diffraction analysis of protophane **3c·2PF$_6$** (see Figure 1; R = H, R′ = *t*Bu). On the whole, the title imidazolium-based dicationic cyclophanes **4a**–**d·2X** are simple prototypes for noncovalent intermolecular ion interactions driven by hydrogen bonds, taking into account both the operation of

the chloride template effect in the formation of these macrocyclic dications though a "3+1" macrocyclization reaction[9d] and their structural properties.

A meaningful ^{1}H NMR result deals with the macrocycle **4b·2OH**, which exhibits two pairs of doublets in a ratio of 1:1 for the methylene spacer signals, which is indicative of a partial cone conformation. Addition of 5% trifluoroacetic acid to the NMR solution sample gave a singlet for the methylene protons as a result of the conversion of **4b·2OH** into the corresponding bis(trifluoroacetate) **4b·2CF$_3$CO$_2$** (Figure 3). Significantly, modulation of the nature of the counteranion can be applied as a "brake" in a reversible manner to the conformational equilibria.

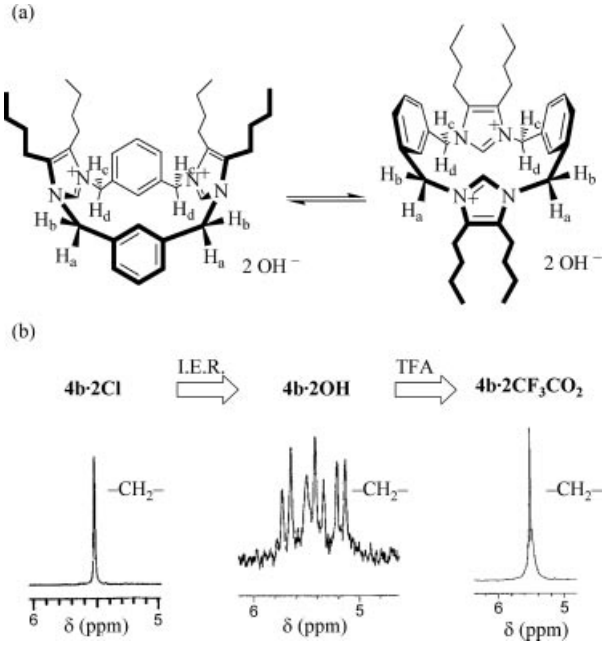


Figure 3. Dication **4b·2OH**: (a) Partial cone conformations; (b) ^{1}H NMR spectra of **4b·2Cl**, **4b·2OH** and **4b·2CF$_3$CO$_2$** in [D$_6$]DMSO at 200 MHz between δ = 5 and 6 ppm.

On the whole, the simple imidazolium-based cyclophanes **4·2X** can be considered as models for intermolecular anion interactions driven by hydrogen bonds since there is a good parallel between the experimental trends observed in liquid solution and in the solid state as well as in the gas phase by ESI-MS in the negative mode. As a consequence, we decided to delve into the anion-receptor behavior of the targeted dications. Macrocycle **4d·2PF$_6$** was selected as the model as a result of its solubility in both nonpolar solvents, such as chloroform, and polar solvents, for example, acetonitrile and dimethyl sulfoxide, despite its insolubility in water. The concentration dependence of the chemical shift was studied for protons 23-H and 25-H together with 24-H and 26-H. In [D$_6$]DMSO, no aggregation was observed in the range of 1.27–11.86 mM, whereas in CD$_3$CN no aggregation was observed between 1.49 and 14.14 mM; in aggregation and binding studies, the experimental error was evaluated to be $\Delta\delta \leq 0.1$ ppm.

Complexation Studies

The anion-binding behavior of dication **4d·2PF$_6$** was then examined by ^{1}H NMR spectroscopy.[1,7a,16] Significant changes in δ_H were induced by the addition of various tetrabutylammonium salts (ca. 6 mM) to a solution of dication **4d·2PF$_6$** (ca. 3 mM) either in [D$_6$]DMSO or CD$_3$CN and the major deshielding effect was observed at the ring protons 23,25-H and 24,26-H, respectively (Figure 4). The host **4d·2PF$_6$** showed a preference for the anions in the order of $F^- > H_2PO_4^- > CH_3CO_2^- > CN^- > Cl^- > Br^- > I^- >> PF_6^-$ in [D$_6$]DMSO, whereas in CD$_3$CN the trend was $CN^- > CH_3CO_2^- > F^- > H_2PO_4^- > Cl^- > Br^- > I^- >> PF_6^-$. The largest chemical shift difference observed after the addition of 1 equiv. of TBA·CH$_3$CO$_2$ in CD$_3$CN to **4d·2X** corresponds to 23,25-H with $\Delta\delta$ = +1.61 ppm (483 Hz) and to 24,26-H with $\Delta\delta$ = +0.83 ppm (249 Hz), whereas under anion saturation conditions the maximum chemical shift registered for 23,25-H is $\Delta\delta$ = +2.02 ppm (606 Hz) and for 24,26-H is $\Delta\delta$ = +0.81 ppm (243 Hz).

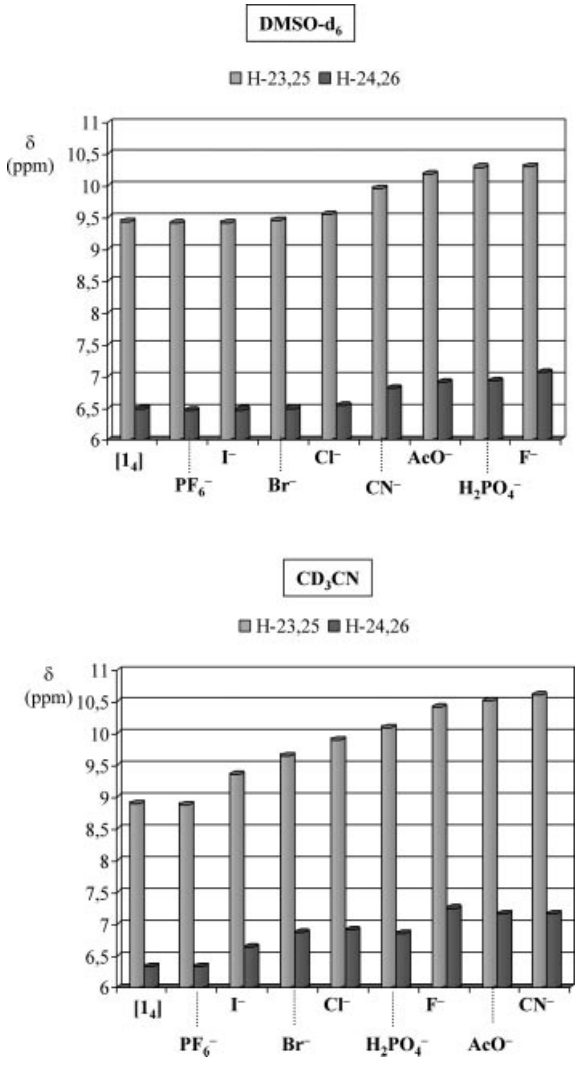


Figure 4. ^{1}H NMR chemical shift deshielding $\Delta\delta$ at 300 MHz for 23,25-H and 24,26-H for ca. 3 mM **4d·2PF$_6$** after the addition of 1 equiv. of different **TBA·X** salts in [D$_6$]DMSO and CD$_3$CN.

Next we examined the ability of the model heterophane **4d·2PF$_6$** based on imidazolium units to act as a molecular recognition motif for anions and its quantitative complexation with five tetrabutylammonium salts (TBA·X) was studied in polar solvents ([D$_6$]dimethyl sulfoxide and [D$_3$]-acetonitrile) by ^{1}H NMR titration (see Table S6 and Figure S5 in the Supporting Information). In several cases the stoichiometry of solution complexation was 1:1 which was determined by the mol ratio method. Among the 1:1 complexes, the maximum association constant (K_a) was observed for the complex formed between **4d·2PF$_6$** and TBA·CH_3CO_2: $K_a = 359 \pm 42\ M^{-1}$, $-\Delta G° = 14.5 \pm 0.3$ kJ/mol.[1,17]

Conclusions

Dicationic [1$_4$]imidazoliophanes **4·2X** are simple prototypes for the examination of the intermolecular interactions driven by hydrogen bonds in which the halide counteranions, for example, X = Cl, are noncovalently bound to the macrocyclic framework. For their preparation, a "3+1" convergent stepwise synthesis was applied and, by exploiting our standard protocol, the counteranions of dications **4a**–**d·2X** were changed by the use of a strongly basic anion-exchange resin (OH^- form) followed by immediate collection of the eluates in acid solution; the anion exchange proceeded through the corresponding quaternary imidazolium hydroxides **4a**–**d·2OH**. Their structures were examined in solution by ^{1}H NMR spectroscopy and there is a good parallel between the experimental trends observed in the solid state by X-ray crystallography of **4a·2Cl·2H$_2$O** and in liquid solution by ^{1}H NMR spectroscopy. Efforts are currently being directed towards the use of imidazolium-linked systems for processes controlled either by hydrogen-bonding networks or by their (imidazol-2-ylidene)metal complexes.

Experimental Section

General Methods: Melting points: CTP-MP 300 hot-plate apparatus with ASTM 2C thermometer (given in Table 1). IR (KBr disks): Nicolet 205 FT spectrophotometer. ^{1}H NMR: Varian Gemini 200 and 300 spectrometers (200 and 300 MHz) at 298 K. ^{13}C NMR: Varian Gemini 200 spectrometer (50.3 MHz) at 298 K. HMQC and HMBC: Varian VXR 500 spectrometer (500 MHz). NMR spectra were determined in [D$_6$]dimethyl sulfoxide or [D$_3$]acetonitrile and chemical shifts are expressed in parts per million (δ) relative to the central peak of [D$_6$]dimethyl sulfoxide or [D$_3$]acetonitrile. The pH was monitored with a CRISON micro-pH 2001 apparatus. TLC was performed on Merck precoated 60 F_{254} silica gel plates in methanol/ammonium chloride (2 M)/nitromethane (6:3:1) as developing solvent; the spots were located with UV light and developed with a 10% aqueous solution of potassium iodide or a 3% aqueous solution of hexachloroplatinic acid. Chromatography: SDS silicium oxide 60 ACC (30–75 μm) and Merck aluminium oxide 90 standardized. A standard protocol was applied for counteranion exchange using a strongly basic anion-exchange resin (hydroxide form).[9c] When a rotary evaporator was used, the bath temperature was 25 °C. In general, the compounds were dried at 25 °C in a vacuum oven overnight. Microanalyses were performed with a Carlo Erba 1106 analyzer.

Materials: 1,3-Bis(chloromethyl)benzene (**6**), 1,3-bis(bromomethyl)-benzene (**8**) and 1*H*-imidazole (**9**) were purchased from commercial sources. 1,3-Bis(bromomethyl)-5-*tert*-butylbenzene (**7**)[18] and 4,5-dibutylimidazole hydrochloride (**10·HCl**)[19] were prepared as described in the literature. Counterion exchange was performed by treatment of the [1$_4$]heterophanes **4a**–**d·2X** with a strongly basic anion-exchange resin followed by immediate collection of the eluates in acid solutions (either with aq. HCl, aq. HBr, aq. HPF_6 or aq. CH_3CO_2H) to pH = 3 according to a standard protocol.[9,10]

Protophane 5a (Scheme 1):[20] A suspension of 1*H*-imidazole (**9**; 2.0 g, 29.4 mmol) and finely powdered 85% potassium hydroxide (2.5 g, 37.9 mmol) in dry acetonitrile (200 mL) was vigorously stirred under nitrogen at room temperature for 1 h. A solution of 1,3-bis(chloromethyl)benzene (**6**; 2.6 g, 14.7 mmol) in dry acetonitrile (50 mL) was then added dropwise and the mixture stirred at room temperature for 6 h. The reaction mixture was cooled, filtered and the solvent removed to dryness. The resulting oil was dissolved in dichloromethane (100 mL) and washed with water (3 × 100 mL) The organic layer was dried (anhydrous Na_2SO_4), filtered and the solvent evaporated to provide protophane **5a**.

Protophane 5b (Table 1): A suspension of 4,5-dibutylimidazole hydrochloride (**10·HCl**; 1.8 g, 8.3 mmol) and finely powdered 85% potassium hydroxide (1.4 g, 21.5 mmol) in dry acetonitrile (60 mL) was vigorously stirred under nitrogen at room temperature for 1 h. A solution of 1,3-bis(chloromethyl)benzene (**6**; 0.8 g, 4.1 mmol) in dry acetonitrile (25 mL) was then added dropwise and the mixture stirred at room temperature for 7 h. The reaction mixture was cooled, filtered and the solvent removed to dryness. The resulting oil was dissolved in dichloromethane (150 mL) and washed with water (3 × 150 mL). The organic layer was dried (anhydrous Na_2SO_4), filtered and the solvent evaporated. The oily residue was purified by column chromatography (Al_2O_3) with dichloromethane/ethanol mixtures of increasing polarity as eluents to provide protophane **5b**.

Protophane 5c (Table 1): A suspension of 1*H*-imidazole (**9**; 2.0 g, 29.4 mmol) and finely powdered 85% potassium hydroxide (2.5 g, 37.9 mmol) in dry acetonitrile (200 mL) was vigorously stirred under nitrogen at room temperature for 1 h. A solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**7**; 4.6 g, 14.5 mmol) in dry acetonitrile (50 mL) was then added dropwise and the mixture stirred at room temperature for 4 d. The reaction mixture was cooled, filtered, and the solvent removed to dryness. The resulting oil was dissolved in dichloromethane (200 mL) and washed with water (3 × 250 mL). The organic layer was dried (anhydrous Na_2SO_4), filtered, and the solvent evaporated. The oily residue was purified by column chromatography (SiO_2) with dichloromethane/ethanol mixtures of increasing polarity as eluents to provide protophane **5c**.

Protophane 5d (Table 1): A suspension of 4,5-dibutylimidazole hydrochloride (**10·HCl**; 3.3 g, 15.0 mmol) and finely powdered 85% potassium hydroxide (2.6 g, 39.0 mmol) in dry acetonitrile (90 mL) was vigorously stirred under nitrogen at room temperature for 1 h. A solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**7**; 2.4 g, 7.5 mmol) in dry acetonitrile (50 mL) was then added dropwise and the mixture stirred at room temperature for 24 h. The reaction mixture was cooled, filtered and the solvent removed to dryness. The resulting oil was dissolved in dichloromethane (100 mL) and washed with water (3 × 200 mL). The organic layer was dried (anhydrous Na_2SO_4), filtered and the solvent evaporated. The oily residue was purified by column chromatography (Al_2O_3) with dichlo-

romethane/ethanol mixtures of increasing polarity as eluents to provide protophane **5d**.

Macrocycle 4a·2Cl (Table 1): A stirred solution of 1,3-bis(chloromethyl)benzene (**6**; 0.53 g, 3.0 mmol) in dry acetonitrile (50 mL) was added dropwise to a suspension of protophane **5a** (0.7 g, 3.0 mmol) in dry acetonitrile (550 mL) at 25 °C under nitrogen, and the mixture was then maintained in a bath at about 85 °C for 4 d. The solvent was removed by rotary evaporation and the solid residue was triturated with dry acetone (3 × 5 mL) and filtered to afford macrocycle **4a·2Cl**.

Macrocycle 4b·2Cl (Table 1): A stirred solution of 1,3-bis(chloromethyl)benzene (**6**; 0.23 g, 1.3 mmol) in dry acetonitrile (50 mL) was added dropwise to a solution of protophane **5b** (0.62 g, 1.3 mmol) in dry acetonitrile (50 mL) at 25 °C under nitrogen and the mixture was then maintained in a bath at about 85 °C for 2 d. The solvent was removed by rotary evaporation and the solid residue was triturated with dry acetone (3 × 5 mL) and filtered to afford macrocycle **4b·2Cl**.

Macrocycle 4b·2Br (Table 1): A stirred solution of 1,3-bis(bromomethyl)benzene (**8**; 0.9 g, 3.4 mmol) in dry acetonitrile (100 mL) was added dropwise to a solution of protophane **5b** (1.5 g, 3.4 mmol) in dry acetonitrile (900 mL) at 25 °C under nitrogen and the mixture was then maintained in a bath at about 85 °C for 24 h. The solvent was removed by rotary evaporation and the solid residue was triturated with dry acetone (3 × 5 mL) and filtered to afford macrocycle **4b·2Br**.

Macrocycle 4b·2OH (Scheme 2): A solution of macrocycle **4b·2Cl** (0.1 g, 0.16 mmol) in ethanol (90%, 50 mL) was passed through a column packed with a strongly basic anion-exchange resin. The eluates were concentrated to dryness to afford the hydroxide **4b·2OH**.

Macrocycle 4c·2Br (Table 1): A stirred solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**7**; 0.32 g, 1.0 mmol) in dry acetonitrile (50 mL) was added dropwise to a solution of protophane **5c** (0.3 g, 1.0 mmol) in dry acetonitrile (200 mL) at 25 °C under nitrogen and the mixture was then maintained in a bath at about 85 °C for 4 d. The solvent was removed by rotary evaporation and the solid residue was triturated with dry acetone (3 × 5 mL) and filtered to afford macrocycle **4c·2Br**.

Macrocycle 4d·2Br (Table 1): A stirred solution of 1,3-bis(bromomethyl)-5-*tert*-butylbenzene (**7**; 0.7 g, 2.2 mmol) in dry acetonitrile (50 mL) was added dropwise to a solution of protophane **5d** (1.1 g, 2.2 mmol) in dry acetonitrile (600 mL) at 25 °C under nitrogen and the mixture was then maintained in a bath at about 85 °C for 24 h. The solvent was removed by rotary evaporation and the solid residue was triturated with dry acetone (3 × 5 mL) and filtered to afford macrocycle **4d·2Br**.

Supporting Information (see footnote on the first page of this article): Physical data and elemental analysis for protophanes **5b**–**d** and [1$_4$]metaimidazoliophanes **4a**–**d·2X**. ^{1}H NMR spectroscopic data for [1$_4$]metaimidazoliophanes **4a**–**d·2X** and protophanes **5a**–**d** in [D$_6$]DMSO (300 MHz) at 298 K. ^{13}C NMR spectroscopic data for [1$_4$]metaimidazoliophanes **4a**–**d·2X** and protophanes **5a**–**d** in [D$_6$]-DMSO (50.3 MHz) at 298 K. All ^{1}H NMR data for the concentration dependence of **4a**–**d·2X** in [D$_6$]DMSO (300 MHz) at 298 K. ^{1}H NMR data for the concentration dependence of **4d·2X** in CD_3CN (300 MHz) at 298 K. ^{1}H NMR data for dications **4a**–**d·2OH** in [D$_6$]-DMSO and [D$_6$]DMSO + TFA. ^{1}H NMR spectroscopic data for mixtures of the imidazoliophane **4d·2PF$_6$** (3 mM) and several guests in [D$_6$]DMSO (300 MHz) at 298 K. ^{1}H NMR spectroscopic data for mixtures of the imidazoliophane **4d·2PF$_6$** (3 mM) and several tetrabutylammonium salts (6 mM) in [D$_6$]DMSO (300 MHz) at 298 K. Data for ^{1}H NMR titration experiments with the imidazoliophane **4d·2PF$_6$** (3 mM) and several tetrabutylammonium salts in [D$_6$]DMSO (300 MHz) at 298 K. ^{1}H NMR spectroscopic data for mixtures of imidazoliophane **4d·2PF$_6$** (3 mM) and several tetrabutylammonium salts (6 mM) in CD_3CN (300 MHz) at 298 K. Data for ^{1}H NMR titration experiments with the imidazoliophane **4d·2PF$_6$** (3 mM) and several tetrabutylammonium salts in CD_3CN (300 MHz) at 298 K. Determination of the stoichiometry between **4d·2PF$_6$** (R) and TBA·CN (S) in CD_3CN (200 MHz) at 298 K by Job's method. Stoichiometry values by the mol ratio method between the receptor **4d·2PF$_6$** and TBA·X in CD_3CN and [D$_6$]DMSO (300 MHz) at 298 K (Table S6). Plots of the stoichiometry between **4d·2PF$_6$** and TBA·CN in CD_3CN. Scatchard plots for 1:1 complexation between **4d·2PF$_6$** and TBA·X (X = $CH_3CO_2^-$ or CN^- or F^-) (Figure S5).Thermodynamic parameters for complexes formed between the imidazoliophane **4d·2PF$_6$** and tetrabutylammonium salts (TBA·X).

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