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N,*N*'-Disubstituted Methylenediimidazolium Salts: A Versatile Guest for Various Macrocycles

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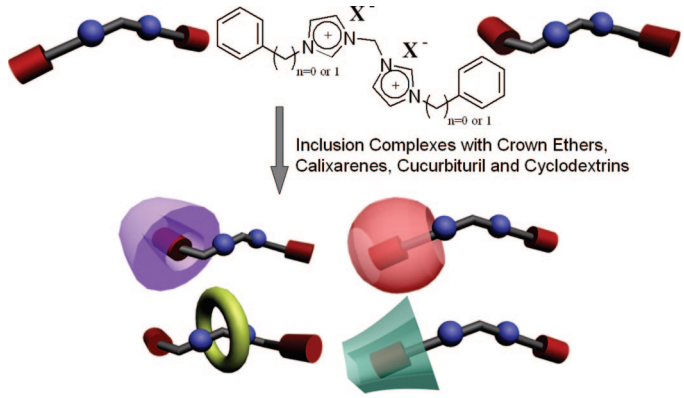

N,*N*'-Disubstituted methylenediimidazolium salts allow the formation of flexible inclusion complexes with β-cyclodextrin, cucurbit[7]uril, tetrapropoxycalix[4]arene, and dibenzo-24-crown-8 ether. Due to the salt nature of the imidazolium guest, the counterion largely determines its solubility in a given solvent. Moreover, by the judicious choice of the imidazolium substituents, inclusion complexes of guest salts were obtained with a variety of macrocyclic hosts, and the binding parameters of the inclusion were determined for each complex.

Introduction

One of the vital current tasks in supramolecular chemistry is to develop simple yet comprehensive and reliable methods to effectively hold together separate parts of complex architectures, exclusively through cooperative noncovalent interactions. For this purpose, it is beneficial to have a set of simple guest molecules which function as a molecular glue to bind a macrocycle as one complex architecture. It becomes more difficult to find an appropriate guest molecule capable of binding different host molecules with contrasting physicochemical properties and guest selectivities. Interactions such as hydrogen bonding, π-stacking, cation$-\pi$, charge transfer interactions, and electrostatic interactions play an important role in various templates, recognition, and complexation phenomena in supramolecular chemistry and in biological processes.[1] As an effective structural unit at the active sites of various proteins and nucleic acids, imidazole plays a key role in their biological function, in its nonprotonated or protonated form. The imidazolium cation has similar properties to the pyridinium cation such as holding a positive charge and possessing ionic liquid properties. It has also been exploited in the design of imidazolium-based hosts, but the methylenediimidazolium motif is absent from the literature.[2]

A literature survey helped us to identify *N*,*N*'-disubstituted methylenediimidazolium salts as valuable recognition motifs for the assembly of novel architectures with tunable physicochemical properties, in analogy with the imidazolium cation. To move closer to an understanding of molecular recognition in these systems, we have synthesized and studied the binding properties of host$-$guest complexes of new *N*,*N*'-disubstituted diimidazolium guests and a large diversity of macrocyclic hosts, including cyclodextrins, calixarenes, cucurbituril, and crown

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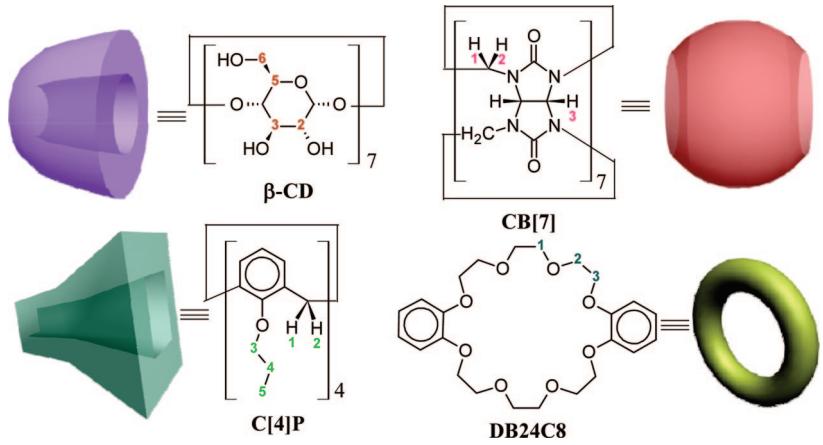

FIGURE 1. Structure and schematic representation of different macrocycles used in this work.

ethers. We have identified patterns in the binding constants of these diimidazolium salts, and we have established the interactions that are developed in each system.

Cyclodextrins (CDs) are water-soluble hosts that contain a hydrophobic cavity which are able to accommodate a variety of small organic molecules (Figure 1).[3] α-Cyclodextrin is composed of six glucose residues, while *β*-cyclodextrin has seven and *γ*-cyclodextrin has eight. This means that each type of cyclodextrin provides a cavity with slightly different geometric properties and a preference for particular-sized molecules. Cyclodextrins have been reported in the literature to form inclusion complexes with imidazole, but there are no examples of complexation of imidazolium cations in the presence of these hosts.

Another synthetic host able to form host−guest complexes in water is cucurbituril (CB).[4] CBs are cyclic oligomers consisting of glycoluril repeat units. CBs recognize positively charged molecules such as dipyridinium, ammonium, imidazolium, dialkylimidazolium, and bis(imidazolium) cations.[5]

Calixarenes have a typical cone structure that allows them to sequester a variety of hydrophobic molecules and ions, making them useful to form host−guest complexes.[6] As in the case of CDs, there are no examples of imidazolium cations complexed by this type of hosts.

Crown ethers have the ability to strongly solvate cationic compounds.[7] It is already known that the imidazolium cation can form inclusion complexes with large crown-ether-type hosts via H-bonding.[8] New motifs for the complexation of linear cations through crown ethers are being reported regularly; recently, other types of linear cations, like *N*-benzylanilinium[9] and bis(benzimidazolium)ethane[10] cations, were shown to bind to dibenzo-24-crown-8 ether with approximately the same range of association constants (10^3 M^{-1} in acetonitrile at 25 °C) as 1,2-bis(pyridinium)ethane and dibenzylammonium cations.[11]

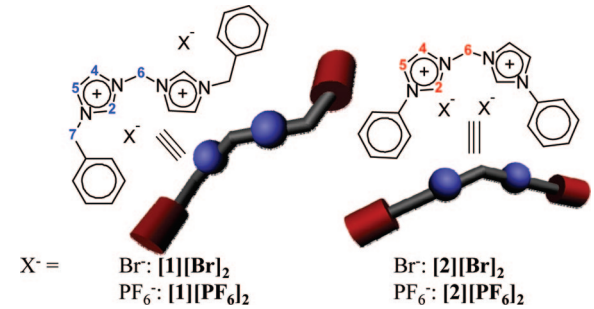

FIGURE 2. Diimidazolium salts and their schematic representation (blue, polar groups; and red, apolar groups).

In this paper, we describe a flexible toolkit for the host−guest chemistry based on the inclusion complexes of *N,N'*-disubstituted diimidazolium salts with various macrocycles (*β*-cyclodextrin, cucurbit[7]uril, tetrapropyloxycalix[4]arene, and dibenzo-24-crown-8 ether) (Figure 2). In fact, by the judicious choice of the counterion and the substituent, the solubility of the guest and the association parameters can be changed. For each complex, the stoichiometry, the association constant, and the complex geometries are discussed on the basis of 1D and 2D NMR data, mass spectrometry (MS), and molecular modeling studies.

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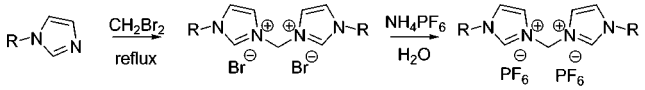
SCHEME 1. Synthesis of the *N,N'*-Disubstituted Methylenediimidazolium Compounds



R = Bn : [1][Br]$_2$; 78 %
R = Ph : [2][Br]$_2$; 54 %

R = Bn : [1][PF$_6$]$_2$; 83 %
R = Ph : [2][PF$_6$]$_2$; 72 %

Results and Discussion

Cucurbit[7]uril (**CB[7]**) and β-cyclodextrin (***β*-CD**) hosts are only soluble in water. Herein, we used dibromide diimidazolium salts for the recognition of **CB[7]** and ***β*-CD** in D_2O. Tetrapropyloxycalix[4]arene (**C[4]P**) and dibenzo-24-crown-8 ether (**DB24C8**) are soluble in various organic solvents. Complexation studies were performed in pure CD_3CN for hexafluorophosphate cations with **DB24C8** and in a mixture of $CDCl_3/CD_3CN$ (80/20 V/V) for **C[4]P**. The methylenediimidazolium cations can provide enough noncovalent interactions to bind all the macrocycles described above, and strong association was observed in the majority of the cases. The complexation of different substituted methylenediimidazolium salts with the different hosts is described in the following sections.

The *N,N'*-disubstituted diimidazolium salts were obtained by a double S_N2 reaction involving *N*-substituted imidazoles and dibromomethane,[12] followed by ion exchange with a hexafluorophosphate counterion (Scheme 1).

1. Methylenediimidazolium Cation/Cyclodextrin Complexes. The H_2 proton for both **[1][Br]$_2$** and **[2][Br]$_2$** was not observed in D_2O because of deuterium exchange. In the presence of the ***β*-CD**, the chemical shifts of all the other protons of the diimidazolium cations were modified (Figures 3a,b and 4a,b). This is evidence for the formation of a "host−guest" complex.[13] This feature, which is related to the geometry of the complex, is generally caused by a combination of contributions from H-bonds (expressed as a downfield) and aromatic shielding (expressed as an upfield). In the case of **[1][Br]$_2$·*β*-CD** and **[2][Br]$_2$·*β*-CD** complexes, the H_4/H_5 protons on the imidazolium moiety as well as H_6 are shifted downfield, which, in this case, is indicative of H-bonds and a more hydrophobic environment, consistent with the proximity of the ***β*-CD**'s cavity. For these complexes, the aromatic protons of phenyl or benzyl groups are also shifted downfield. The chemical shifts of the imidazolium protons and the split of the aromatic protons of **[1][Br]$_2$** and **[2][Br]$_2$** demonstrate the formation of inclusion complexes.[13] In addition to 1D NMR experiments, mass spectrometry was used to demonstrate the formation of the inclusion complexes. Electrospray ionization (ESI) is used to "fish" loosely bonded supramolecular complexes in solution and to transfer them to a mass spectrometer to investigate their assemblies. The positive ions are formed in solution and then transferred by ESI directly to the gas phase. ESI is characterized by the gentleness by which the gaseous ions are formed, and loosely bonded supramolecules can be observed, such as hydrogen-bonded amino acid assemblies.[14] The ESI mass spectra, in the positive ion mode, of equimolar solutions of ***β*-CD/[1][Br]$_2$** or **[2][Br]$_2$** give *m/z* peaks at 1545.1 that correspond to (**[1][Br]·*β*-CD**)$^+$ and at 1517.0 that correspond to (**[2][Br]·*β*-CD**)$^+$.

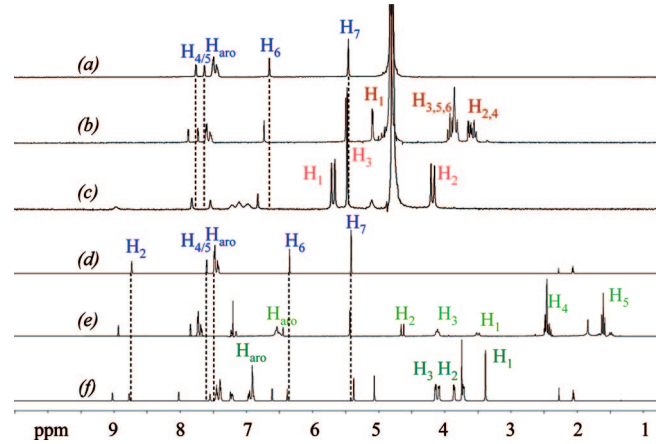


FIGURE 3. ^{1}H NMR spectra at 25 °C of: (a) 4 mM **[1][Br]$_2$** (D_2O); (b) 4 mM **[1][Br]$_2$** and 4 mM ***β*-CD** (D_2O); (c) 4 mM **[1][Br]$_2$** and 4 mM **CB[7]** (D_2O); (d) 25 mM **[1][PF$_6$]$_2$** (CD_3CN); (e) 25 mM **[1][PF$_6$]$_2$** and 25 mM **C[4]P** ($CDCl_3/CD_3CN$ (80/20 V/V)); (f) 25 mM **[1][PF$_6$]$_2$** and 25 mM **DB24C8** (CD_3CN).

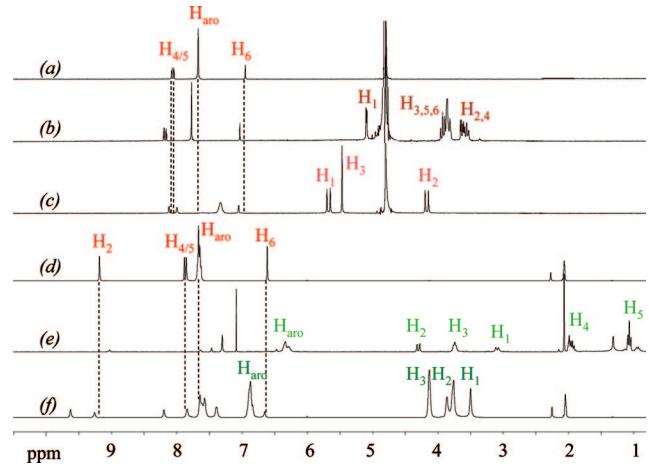


FIGURE 4. ^{1}H NMR spectra at 25 °C of: (a) 4 mM **[2][Br]$_2$** (D_2O); (b) 4 mM **[2][Br]$_2$** and 4 mM ***β*-CD** (D_2O); (c) 4 mM **[2][Br]$_2$** and 4 mM **CB[7]** (D_2O); (d) 25 mM **[2][PF$_6$]$_2$** (CD_3CN); (e) 25 mM **[2][PF$_6$]$_2$** and 25 mM **C[4]P** ($CDCl_3/CD_3CN$ (80/20 V/V)); (f) 25 mM **[2][PF$_6$]$_2$** and 25 mM **DB24C8** (CD_3CN).

To gain insight into the molecular interactions and the geometry of the host−guest complex, we performed a 2D NMR study in addition to the 1D NMR data presented above. NOESY experiments are well suited for the purpose; even though the COSY peaks are intense at the concentrations used, it is possible to assign the NOE signals between the diimidazolium salts and the macrocycles. The spatial distance must be less than 5 Å to observe cross peaks between two protons. The NOESY spectrum of an equimolar mixture of ***β*-CD** with **[1][Br]$_2$** or with **[2][Br]$_2$** in D_2O gave intense cross peaks between the aromatic protons of phenyl or benzyl groups and the internal H_3 and H_5 protons of the CD (Figures 5a and 6a). These cross peaks are evidence for the formation of an inclusion complex between the ***β*-CD** and **[1][Br]$_2$** or **[2][Br]** in aqueous solution. Moreover, the

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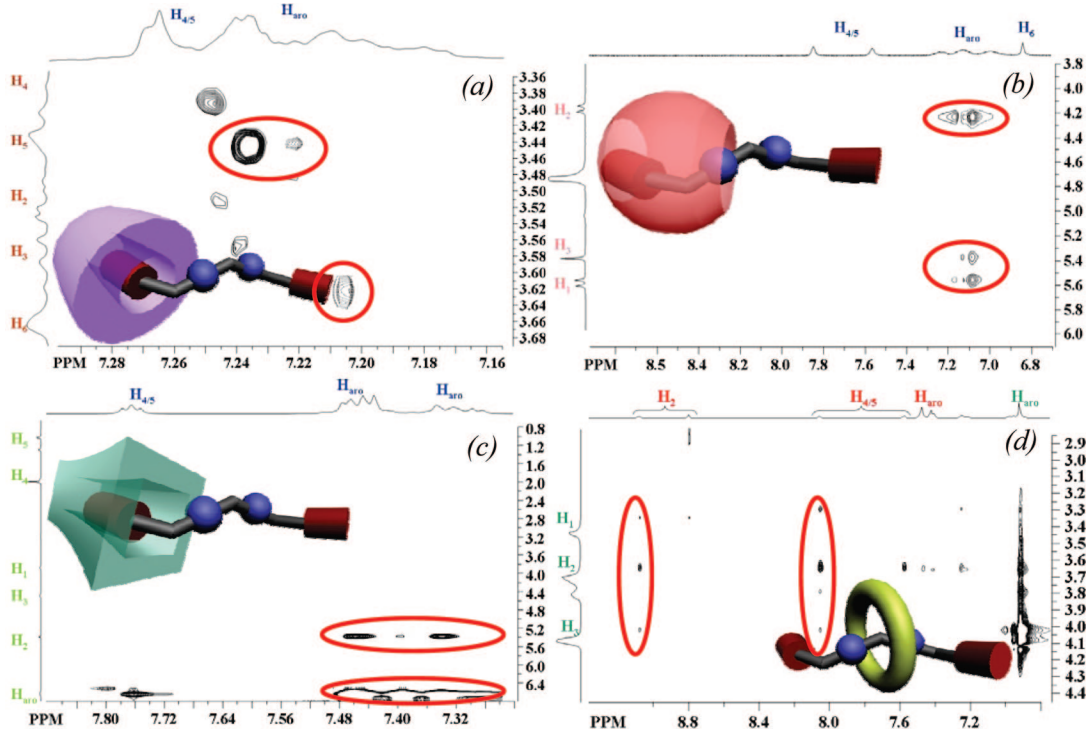

FIGURE 5. Partial NOESY NMR spectra at 25 °C of: (a) 5 mM **[1][Br]$_2$** and 5 mM ***β*-CD** (D_2O); (b) 4 mM **[1][Br]$_2$** and 4 mM **CB[7]** (D_2O); (c) 10 mM **[1][PF$_6$]$_2$** and 10 mM **C[4]P** ($CDCl_3/CD_3CN$ (80/20 V/V)); (d) 10 mM **[1][PF$_6$]$_2$** and 10 mM **DB24C8** (CD_3CN).

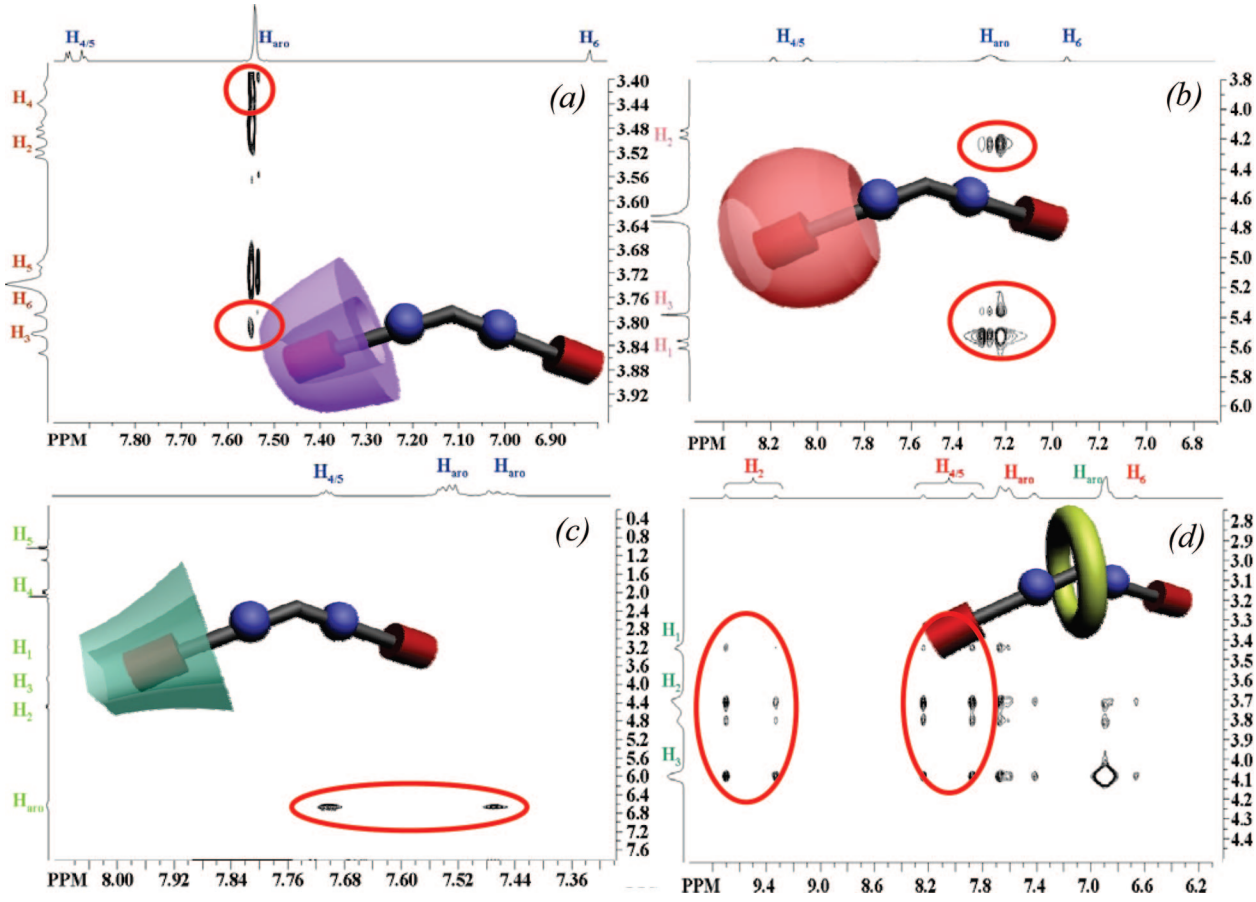

FIGURE 6. Partial NOESY NMR spectra at 25 °C of: (a) 5 mM **[2][Br]$_2$** and 5 mM ***β*-CD** (D_2O); (b) 4 mM **[2][Br]$_2$** and 4 mM **CB[7]** (D_2O); (c) 10 mM **[2][PF$_6$]$_2$** and 10 mM **C[4]P** ($CDCl_3/CD_3CN$ (80/20 V/V)); (d) 10 mM **[2][PF$_6$]$_2$** and 10 mM **DB24C8** (CD_3CN).

absence of cross-peaks between the hydrogens of the ***β*-CD** and the hydrogens located on the imidazolium residue ($H_{4/5}$) clearly shows that the interaction between the ***β*-CD** and the imidazolium cation occurs with the aromatic substituent of the diimi-

dazolium cation. As both imidazolium salts contain aromatic groups at the extremities, the binding interactions seem to be dominated by the hydrophobic forces.

The stoichiometry of the inclusion complexes was determined by the NMR continuous variation method.[15] A series of solutions were prepared in which the sum of **β-CD** and **[1][Br]$_2$** or **[2][Br]$_2$** concentrations was kept constant (10 mM in the present case) but in which the concentrations of **β-CD** and the imidazolium salts were systematically varied. From the variation of chemical shifts of the ^{1}H NMR spectra of various **β-CD**/imidazolium salt mixtures, two Job's plots were drawn, one for each host−guest complex. For each imidazolim salt (**[1][Br]$_2$** and **[2][Br]**), the maximum observed at 50% of total concentration and the highly symmetric shape of the curve revealed a 1:1 stoichiometry. The **β-CD** forms inclusion complexes with one of the aromatic rings, and supplementary stabilizing interactions with the imidazolium cations occur. However, it seems that these **β-CD** are too bulky to allow the formation of 2:1 complexes. For the **β-CD·[1][Br]$_2$** complex, binding constants of 6500 ± 20 M^{-1} and 3000 ± 10 M^{-1} for the **β-CD·[2][Br]$_2$** complex were further calculated at 25 °C by the ^{1}H NMR titration technique (constant concentration of imidazolium salt while varying the concentration of the **β-CD**). The difference between the two association constants must be due to the diimidazolium cation geometry. To confirm this assertion, we performed a computational study using the semiempirical PM3 energy minimization calculation using the Hyperchem 7.5 program. Previous success in treating inclusion phenomena with semiempirical methods[16] suggested that treating these systems empirically would be a judicious approximation. For computational expediency, solvent effects were neglected in this work. This approximation appears not to have a significant deleterious impact on the results, a finding also reported previously by Ricketts et al.[17] All structures were optimized at the molecular mechanics level to clean the physically distant contacts. To ensure thorough conformational searching, the macrocycle in the initial inclusion complex was successively rotated around and translated along the diimidazolium component manually. The rotation was performed with 36° step size and 360° range. The translation of the macrocycle for each of these 10 rotations was carried out with a step size of 1 Å and a range of 0−20 Å. The most stable complexes are formed when the cyclodextrin is positioned on the aromatic group of both imidazolium salts and the complex is more stable in the case of **β-CD·[1][Br]$_2$**.

2. Methylenediimidazolium Cation/Cucurbit[7]uril Complexes. CB[7] is slightly more voluminous than **β-CD** and thus can bind a wider range of guests than lower order homologues (CB[5] or CB[6]). The ability of **[1][Br]$_2$** and **[2][Br]$_2$** salts to form inclusion complexes in water with **CB[7]** was studied. In aqueous solution, the aromatic protons of **[1][Br]$_2$** and **[2][Br]$_2$** are upfield shifted, consistent with the formation of an inclusion complex into the electron-rich inner cavity of the **CB[7]** (Figures 3a,c, and 4a,c). The effect of the complexation on the imidazolium ring proton is weaker, which suggests that the complexation occurs primarily wiyh the aromatic group of **[1][Br]$_2$**and **[2][Br]$_2$**. In fact, in **CB[7]**, there are two different binding regions:[4] (i) the hydrophobic cavity and (ii) the outer disk formed by the oxygen atoms that can stabilize the positive charge. Here, the aromatic phenyl or benzyl residues are positioned in the hydrophobic cavity, and the cations are situated in the cation binding region. In parallel to ^{1}H NMR experiments, the inclusion complexes were also observed by MS (positive ionization mode) at *m*/*z* 1491.4 (**[1]·CB[7]**)$^+$ and 1463.3 (**[2]·CB[7]**)$^+$. We also observed that one of the positive charges is screened by the presence of **CB[7]**.

The NOESY spectra of **CB[7]** with **[1][Br]$_2$** or **[2][Br]$_2$** in D_2O also show cross peaks between the aromatic protons and the H_1, H_2, and H_3 protons of the **CB[7]** (Figures 5b and 6b). The absence of cross-peaks between the hydrogens of the **CB[7]** and the $H_{4/5}$ hydrogens of the imidazolium residue shows once again that the interaction between the macrocycle and the imidazolium ring occurs with the aromatic substituent of the diimidazolium cation. The position of the **CB[7]** in these complexes is more surprising because this macrocycle is known to complex imidazolium or pyridinium residue.[4,5] However, in our case, the aromatic group is included in the cavity. We believe that the methylene group between the two imidazolium rings destabilizes the formation of the complex directly on the diimidazolium moiety.

For both diimidazolium salts **[1][Br]$_2$** and **[2][Br]$_2$**, association constants were calculated and Job's Plots were constructed. The complex **[1][Br]$_2$·CB[7]** gives a 1:1 stoichiometry, whereas the **[2][Br]$_2$·CB[7]** complex gives a 1:2 stoichiometry. In the case of the latter, two macrocycles can be complexed on each aromatic side, probably due to a more flexible geometry of the phenyl groups attached to the imidazolium rings. The association constants were determined to be 4200 ± 25 M^{-1} for **[1][Br]$_2$·CB[7]** and 2100 ± 50 M^{-1} for **([2][Br]$_2$)$_2$·CB[7]** at 25 °C. As in the case of the CD complexes, the PM3 calculations show that the most stable conformer is obtained when the **CB[7]** is positioned on the aromatic groups.

3. Methylenediimidazolium Cation/Tetrapropoxycalix[4]arene Complexes. The hexafluorophosphate diimidazoliums **[1][PF$_6$]$_2$** and **[2][PF$_6$]$_2$** are not soluble in water but highly soluble in polar organic solvents such as acetonitrile, methanol, or nitromethane. The **C[4]P** possesses an aromatic cavity, ideal for π−π interactions and cation−π interactions with the diimidazolium groups. In the case of the **C[4]P** complexes, all the signals in the ^{1}H NMR spectrum are shifted downfield for **[1][PF$_6$]$_2$** and shifted upfield for **[2][PF$_6$]$_2$** (Figures 3d,e and 4d,e). In the second case, it is clearly due to aromatic stacking between the aromatic rings of the **C[4]P** and aromatic rings of **[2][PF$_6$]$_2$**. However, the geometry of the complex is unclear because of the aromatic and imidazolium proton shifts. For **[1][PF$_6$]$_2$**, the downfield shift is probably due to the formation of H-bonds between the oxygen atoms of **C[4]P** and the imidazolium ring protons of **[1][PF$_6$]$_2$**. The formation of complexes was also confirmed by the ESI/MS with characteristic *m*/*z* values of 1067.9 (**[1][PF6]·C[4]P**)$^+$ and 1038.9 (**[2][PF6]·C[4]P**)$^+$.

Globally, the same cross peaks were observed for the **C[4]P** with **[1][PF$_6$]$_2$** and **[2][PF$_6$]$_2$** in a mixture of $CDCl_3/CD_3CN$ (80/20 V/V) (Figures 5c and 6c). The interactions occur principally between the aromatic protons of the phenyl or benzyl residues of the diimidazolium cations and the aromatic protons of **C[4]P**.

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Interestingly, intense cross peaks are also observed between H_4 and H_5 of the imidazolium residue and the aromatic protons of the **C[4]P**, and other less intense cross peaks are observed between H_2 and H_3 of **C[4]P** with H_7 of **[1][PF$_6$]$_2$** and also between H_1 of **C[4]P** with H_6 of **[1][PF$_6$]$_2$**. This observation can be interpreted as a spatial proximity of the aromatic cavity with the imidazolium residue, but the aromatic groups are positioned probably in the cavity of **C[4]P**.

For both diimidazolium salts, the stoichiometries of the complexes are 1:1. **C[4]P** forms inclusion complexes with the aromatic rings, and there are stabilizing interactions with the imidazolium cations; however, it seems that this macrocycle is too bulky to allow the formation of 1:2 complexes. The values of association constants were estimated at 7500 ± 60 M^{-1} for **[1][PF$_6$]$_2$** and 17000 ± 100 M^{-1} **[2][PF$_6$]$_2$** at 25 °C. Interaction of the **[1][PF$_6$]$_2$** or **[2][PF$_6$]$_2$** with **C[4]P** allowed the formation of the most stable complexes, as shown by the interaction energy obtained by PM3. This is reasonable because the interaction of the phenyl rings in a distance of 3.6 Å is very favorable. Molecular modeling did not allow interpretation of the particular stoichiometry obtained for **[2][PF$_6$]$_2$** with **CB[7]**, but it is reasonable to think that there is little repulsion between the two **CB[7]** molecules around the diimidazolium cation.

4. Methylenediimidazolium Cation/Dibenzo-24-crown-8 Ether Complexes. The complexes formed with **DB24C8** have lower association constants, but they can be observed very easily by ^{1}H NMR. The noncovalent interactions involved are the ion−dipole interactions with the crown ether oxygen atoms, acidic CH protons for C*H*···O hydrogen bonding and electron-poor imidazolium rings for π-interactions with the aryl groups of **DB24C8**. The rate of complexation is slow relative to the NMR scale, and the complexed components can be quantified by simple integration of the signals in the ^{1}H NMR spectrum. The **[1][PF$_6$]$_2$·DB24C8** complex shows very sharp and well-defined peaks. The chemical shifts of the complexed peaks are consistent with the formation of a complex in solution. The resonances due to the acidic NC*H*N proton on the imidazolium and NCH_2N protons on the linker are shifted downfield relative to the free imidazolium, consistent with C*H*···O hydrogen bonding. The NC*HCH*N protons on the imidazolium rings are shifted on opposite sides of the spectrum relative to the free **[1][PF$_6$]$_2$**, suggesting that one of the protons is engaged in C*H*···O hydrogen bonding while the other is pointing away from the crown ether. In the case of **[2][PF$_6$]$_2$**, the ^{1}H NMR spectrum is different from the **[1][PF$_6$]$_2$·DB24C8** complex: all the complexed and uncomplexed peaks are broad, suggesting a more rapid rate of association/dissociation or multiple possible geometries for this complex.

The formation of complexes was confirmed by ESI/MS with characteristic *m*/*z* 923.36 (**[1][PF6]·DB24C8**)$^+$ and 937.37 (**[2][PF6]·DB24C8**)$^+$. For **[1][PF6]$_2$·DB24C8** (Figure 5d), a correlation was observed between the signals assigned to the complexed form of **[1][PF$_6$]$_2$** and the protons of the crown ether. In the spectrum of the **[2][PF$_6$]$_2$·DB24C8** complex (Figure 6d), we were surprised to see that a correlation could be observed not only between the signals assigned to the complexed form of **[2][PF$_6$]$_2$** and the crown ether but also between the signals assigned to the uncomplexed **[2][PF$_6$]$_2$** and **DB24C8**. A possible explanation for these correlation signals is a slower rate of association/dissociation for **[2][PF$_6$]$_2$·DB24C8** or the presence of different geometries for these complexes. In the case of the **DB24C8**, Job's plot experiments showed the expected 1:1 stoichiometry for both diimidazolium salts. The values of the association constants were estimated at 56 ± 10 M^{-1} for **[1][PF$_6$]$_2$** and 120 ± 20 M^{-1} for **[2][PF$_6$]$_2$** at 25 °C. The computational study confirms the location of **DB24C8** symmetrically between the two imidazolium groups. The macrocycle adopts a chairlike conformation, exactly as observed in the solid state structures of other complexes obtained by X-ray diffraction.

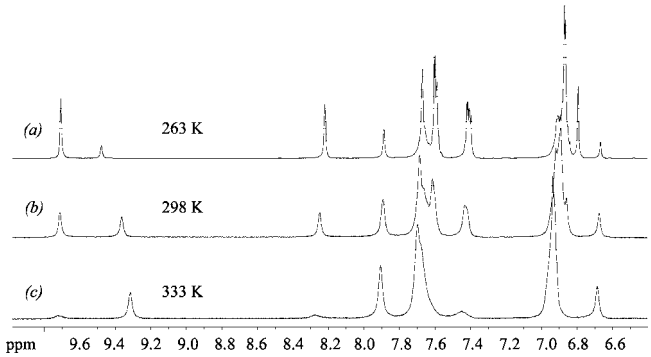

FIGURE 7. ^{1}H NMR temperature study of **DB24C8** and **[2][PF$_6$]$_2$** (25 mM) in CD_3CN.

TABLE 1. Values of the Association Constants for Various Macrocycle−Diimidazolium salts

entry	macrocycle	[X]	**[1][X]$_2$** K_{ass}/M^{-1} (host:guest)	**[2][X]$_2$** K_{ass}/M^{-1} (host:guest)
1[d]	**β-CD**	[Br]	6500 ± 20 [a] (1:1)[b]	3000 ± 10 [a] (1:1)[b]
2[d]	**CB[7]**	[Br]	4200 ± 25 [a] (1:1)[b]	2100 ± 50 [a] (2:1)[b]
3[e]	**C[4]P**	[PF_6]	7500 ± 60 [a] (1:1)[b]	17000 ± 100 [a] (1:1)[b]
4[f]	**DB24C8**	[PF_6]	56 ± 10 [c] (1:1)[b]	120 ± 20 [c] (1:1)[b]

[a] Determined by ^{1}H NMR titration. [b] Determined by the continuous variation method (Job's Plot). [c] Determined by the single point method. [d] D_2O, 25 °C (fast exchange on the NMR time scale). [e] $CDCl_3/CD_3CN$ (80/20) (fast exchange on the NMR time scale), 25 °C. [f] CD_3CN, 25 °C (slow exchange on the NMR time scale).

A supplementary ^{1}H NMR study with temperature variation was conducted for the formation of the **[2][PF$_6$]$_2$·DB24C8** complex (Figure 7). At 333 K, there are almost no complexed **[2][PF$_6$]$_2$**,whereas the complexed peaks are sharper and predominant at 263 K. The association constant is highly dependent on the temperature, and this suggests that the enthalpy plays an important role in the formation of this complex. This experiment also allowed ruling out the formation of two different 1:1 complexes in solution at the same time.

5. Comparison between the Different Complexes. The association constants for **β-CD**, **CB[7]**, and **C[4]P** are large (Table 1). A decreased association constant was observed for **[2][Br]$_2$·CB[7]** and **[2][Br]$_2$·β-CD** compared to the **[1][Br]$_2$** complexes, but a significant increase is observed for **[2][PF$_6$]$_2$·C[4]P** compared to **[1][PF$_6$]$_2$·C[4]P**. The geometry of the **[2][PF$_6$]$_2$** diimidazolium salts allows $\pi-\pi$ interactions and enhances the possibility of additional cation$-\pi$ interactions with an imidazolium ring placed closer to the cavity of the calixarene. In the case of **DB24C8** complexes, there is a difference in the binding mode of these two cations. The increase in the association constant is not significant, but it could be due to a higher degree of ion pair dissociation due to the electron-withdrawing effect of the phenyl group placed directly on the imidazoliums. Even if the association constants of **[1][PF$_6$]$_2$·DB24C8** and **[2][PF$_6$]$_2$·DB24C8** are not as high as the **DB24C8** complexes reported in the literature,[18] the solubility of the substituted diimidazolium bis(hexafluorophosphate) is

TABLE 2. Solubilities (mol·L^{-1}) of [1][PF$_6$]$_2$ and [2][PF$_6$]$_2$ at 25 °C, Compared to Bis(pyridinium)ethane Bis(hexafluorophosphate) Salt

component	acetonitrile	nitromethane
[1][PF$_6$]$_2$	1.08	1.21
[2][PF$_6$]$_2$	1.14	1.30
bis(pyridinium)ethane **[PF$_6$]$_2$**	6.5×10^{-2}	7.7×10^{-2}

higher than the previously reported recognition units (Table 2) in polar organic solvents. In an equimolar solution of diimidazolium salt and **DB24C8**, their initial concentration and the association constant have the same effect on the ratio of [bound imidazolium]/[unbound imidazolium].[19] The association constant of a bis(pyridinium)ethane with **DB24C8**[11] is approximately 10^3 M^{-1}, almost 10 times higher than **[2][PF$_6$]$_2$·DB24C8**, but its solubility is almost 20 times lower. Thus, the ratio of [bound imidazolium]/[unbound imidazolium] at a saturation concentration is almost equivalent (for calculations, see Supporting Information).

The only undesirable effect of this high solubility is the difficulty to obtain crystals suitable for X-ray diffraction of any of the described complexes. We are currently working on using different counterions such as perchlorates or triflates to obtain less-soluble compounds suitable for the formation of crystals.

Conclusion

N,*N*′-Disubstituted methylenediimidazolium salts with two different counterions have been used as guests to obtain novel inclusion complexes with various macrocycles, such as β-cyclodextrin, cucurbit[7]uril, tetrapropoxycalix[4]arene, and dibenzo-24-crown-8 ether. For most, 1:1 complexes were obtained, except for **CB[7]** with the **[2][Br]$_2$** salts (in which case a 2:1 complex is observed). The highest association constant is obtained in the case of **C[4]P** and **[2][PF$_6$]$_2$**. This study underlines the versatility of *N*,*N*′-disubstituted methylenediimidazolium salts to form different inclusion complexes in different solvents. Work is currently underway in our laboratory to obtain supramolecular bulky carbenes of these inclusion complexes for organometallic catalysis, as well as new ionic liquid media for organic reactions.

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(19) The ratio [bound imidazolium]/[unbound imidazolium] can be directly derived from the association constant for the formation of a 1:1 complex in the case of a slow complexation in the NMR time scale. See Supporting Information for details.

Experimental Section

General Procedure for the Synthesis of [1][X]$_2$ and [2][X]$_2$. A mixture of *N*-substituted imidazole (11 mmol, 2.2 equiv) and dibromomethane (5 mL) in a round-bottom flask was heated at 80 °C for 18 h. The white precipitate formed was filtered off and dried under high vacuum to yield **[1][Br]$_2$** or **[2][Br]$_2$**. These compounds were dissolved in a minimum amount of hot water, and ammonium hexafluorophosphate (10 mmol, 2 equiv) in water (2 mL) was added to the solution. The white precipitate formed was filtered off and washed successively with diethyl ether, ethyl acetate, and hexane and dried under high vacuum to yield **[1][PF$_6$]$_2$** or **[2][PF$_6$]$_2$**.

1,1′-Dibenzyl-3,3′-methylenediimidazolium Bis(bromide)[1][Br]$_2$: (78% yield); ^{1}H NMR (D$_2$O, 400 MHz) δ (ppm) 7.79 (d, 2H, J = 2.2 Hz), 7.61 (d, 2H, J = 2.2 Hz), 7.46−7.47 (m, 10H), 6.67 (s, 2H), 5.44 (s, 4H); ^{13}C NMR (D$_2$0, 75 MHz) δ (ppm) 137.7, 133.4, 130.5, 130.3, 129.9, 124.6, 123.1, 59.8, 54.4; HR-MS *m*/*z* found 329.17622 (M − H)$^+$, calcd 329.17661. Mp: 278−280 °C.

1,1′-Diphenyl-3,3′-methylenediimidazolium Bis(bromide)[2][Br]$_2$: (54% yield); ^{1}H NMR (D$_2$O, 400 MHz) δ (ppm) 8.02 (m, 4H), 7.64−7.70 (m, 10H), 6.96 (s, 2H); ^{13}C NMR (D$_2$O, 75 MHz) δ (ppm) 135.0, 131.6, 131.2, 124.2, 123.5, 123.3, 60.3; HR-MS *m*/*z* found 301,14386 (M − H)$^+$, calcd 301,14529. Mp: 270−272 °C.

1,1′-Dibenzyl-3,3′-methylenediimidazolium Bis(hexafluorophosphate)[1][PF$_6$]$_2$: (83% yield from **[1][Br]$_2$**); ^{1}H NMR (CD$_3$CN, 400 MHz) δ (ppm) 8.78 (s, 2H), 7.62 (t, 2H, J = 2.0 Hz), 7.48−7.52 (m, 8H), 7.28−7.47 (m, 4H), 6.34 (s, 2H), 5.39 (s, 4H); ^{13}C NMR (CD$_3$CN, 75 MHz) δ (ppm) 137.7, 133.6, 130.4, 130.2, 129.9, 124.4, 123.5, 59.7, 54.3; HR-MS *m*/*z* found 475.1481 (M − PF$_6$)$^+$, calcd 475.1498. Mp: 195−197 °C.

1,1′-Diphenyl-3,3′-methylenediimidazolium Bis(hexafluorophosphate) [2][PF$_6$]$_2$: (72% yield **[2][Br]$_2$**); ^{1}H NMR (CD$_3$CN, 400 MHz) δ (ppm) 9.26 (s, 2H), 7.92 (s, 2H), 7.89 (s, 2H), 7.64−7.75 (m, 10H), 6.62 (s, 2H); ^{13}C NMR (CD$_3$CN, 75 MHz) δ (ppm) 136.9, 135.2, 131.8, 131.3, 124.0, 123.6, 60.2; HR-MS *m*/*z* found 447.1168 (M − PF$_6$)$^+$, calcd 447.1169. Mp: 238−240 °C.

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Supporting Information Available: General experimental details, ^{1}H NMR, ^{13}C NMR, and ESI-MS of **[1][Br]$_2$**, **[2][Br]$_2$**, **[1][PF6]$_2$**, and **[2][PF6]$_2$**, ^{1}H NMR of complexes, NOESY NMR of complexes, association constants, and determination for complexes with DB24C8. This material is available free of charge via the Internet at http://pubs.acs.org.

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