Sterically crowded azulene-based dication salts as novel guests: synthesis and complexation studies with crown ethers and calixarenes in solution and in the gas phase†

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The 1,4-bis(3-guaiazulenylmethylium)benzene **1** and 1,4-bis[1-(4,6,8-trimethylazulenylmethylium)]benzene **2** dication salts were synthesized *via* an acid-catalyzed condensation/dehydration protocol with guaiazulene–terephthalaldehyde (2 : 1 ratio), and 4,6,8-trimethylazulene–terephthalaldehyde (2 : 1 ratio) respectively in one-pot processes. A similar condensation reaction with the parent azulene led to an insoluble oligomer that was shown by MALDI-TOF-MS to contain 1,4-bis[(diazulenyl)methylium]benzene as a repeating unit. Dication salts **1** and **2** were fully characterized by 2D NMR and NOE techniques and by electrospray-MS (ES-MS) and MALDI-TOF-MS. NMR studies confirm that the dications are best represented as bis-tropylium species. A delicate balance of electronic (inductive stabilization) and steric influence of the alkyl groups on the seven-membered ring seems to influence the chemo-/regioselectivity of the co-condensation process. NMR titration and T_1 measurements established that, despite its highly crowded structure, dication **1** forms host–guest HG complexes with dibenzo-30-crown-10 (DB30C10) and dibenzo-24-crown-8 (DB24C8) in solution, but fails to complex with the smaller dibenzo-18-crown-6 (DB18C6). The corresponding HG cation–molecule cluster ions were also detected in the gas phase by ES-MS, showing the formation of both dication–crown 1 : 1 and 1 : 2 complexes. Similar complexation of dication salt **2** with DB30C10 was observed *via* NMR titration and T_1 measurements in solution and by ES–MS in the gas phase. Although solution complexation studies (NMR titration) did not indicate stable complex formation between **1** and *p-tert*-butyl-methoxycalix[8]arene, their $[HG]^{2+}$ and $[H_2G]^{2+}$ clusters were detectable by ES-MS. Solution decomplexation experiments ($HG^{2+} \rightarrow H + G^{2+}$) were performed on **1**–crown complex by addition of DMSO, acetone, silver tosylate, and tropylium cation salt. Complexation of **1** with DB30C10 was also studied by microcalorimetric titration.

Introduction

Onium salts have played a central role in host–guest (HG) chemistry and in molecular recognition studies over the years.[1] Ammonium,[2–11] pyridinium and bis-pyridinium salts have been widely employed as cationic guests for crown ethers, calixarenes, and cyclophanes,[12–17] and bipyridinium and 2,7-dimethyldiazapyrenium dication salts have been utilized as building blocks of different catenanes, rotaxanes and molecular shuttles.[18–20] Complexation of arenediazonium salts with a variety of synthetic receptors (crown ethers, lariat ethers, calixarenes, spherands) has been demonstrated both in solution and in the gas phase.[21–29] Among other classes of onium salts, R_3S^+–calixarene molecular complexes have been detected in the gas phase.[28] Complexation of NO_2^+ and NO^+ salts to crown ethers studied by IR provided a method for estimation and removal of $NO^+ X^-$ impurities in the nitronium salt, and NO_2^+ complexation to crown ethers provided a method to modify their reactivity and regioselectivity in model aromatic nitration reactions.[22,30,31]

In comparison, much less is known concerning the complexation of carbocation salts to host molecules and the scope and limitations of this process. Development of this area is not only useful in HG chemistry, but also in synthetic/preparative aspects involving carbocation salts, where HG complexation could lead to solubilization and to reactivity/selectivity tuning. Complexation of $PhCO^+ PF_6^-$ to a macrocyclic crown bearing a binaphthyl group was studied by Gokel and Cram many years ago.[32] ^1H NMR monitoring indicated that a complex was formed, but benzoylation of naphthalene rings accompanied complexation. Interaction of $C_7H_7^+ BF_4^-$ (tropylium tetrafluoroborate) with several benzo-crowns was studied in solution and in the gas phase by Lämsä and collaborators, and formation of an inclusion complex with dibenzo-24-crown-8 was demonstrated by X-ray analysis.[33–35] These studies pointed to the importance of cation–π interactions. Finally, Böhmer and co-workers found that $C_7H_7^+ PF_6^-$ functions as a suitable guest and template for dimerization of C_{2v}-symmetrical resorcaranes to generate 2 : 1 HG molecular capsules.[36]

In relation to our previous[28] and ongoing studies on molecule–cation HG complexes, and in connection to several recent projects in our laboratory focusing on theoretical and stable ion studies

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of carbocations and dications derived from polynuclear aromatic hydrocarbons containing the azulene moiety,[37–40] we report on HG complexation studies involving dication salts **1** and **2** (Fig. 1). This work was inspired by the report of Takekuma *et al.*[41] on synthesis of **1**. During our studies, the reported method was extended and the previously reported NMR assignment for **1** was corrected.

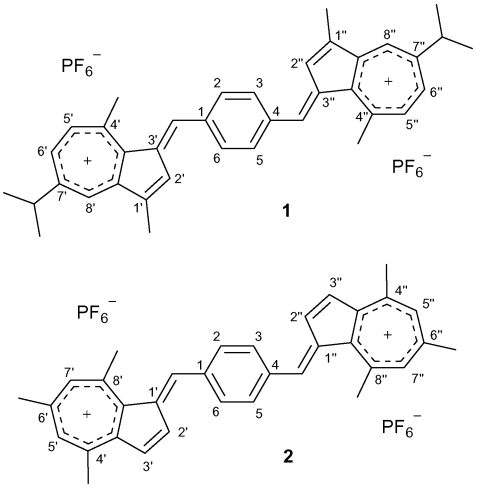


Fig. 1 Guaiazulene-based dication salts.

We reasoned that although the more reactive carbocations may undergo nucleophilic attack by the host receptor leading to covalent adducts, judicious combination of increased carbocation stability (extensive charge delocalization) and appropriate steric protection can provide the correct mix to prevent/minimize covalent adduct formation.

Results and discussion

Synthesis of the dication salts

The guaiazulene-derived dication salt **1** (Fig. 1) was readily obtained by reaction of terephthalaldehyde and guaiazulene in HCl/HOAc followed by counterion exchange with HPF_6 (as described in ref. 41). A similar reaction with 4,6,8-trimethylazulene furnished the dication salt **2**. The dication salts were studied by NMR and ES-MS, as detailed later.

By contrast, reaction of the parent azulene produced an oligomer (a green powder), insoluble in regular organic solvents (or water). It was therefore examined initially by solid state NMR (CPMAS), showing aromatic resonances (between 110 and 130 ppm; unresolved) and a small envelope of aliphatic resonances (centered at 35.1 ppm). Subsequent study by MALDI-TOF-MS established regular losses of m/z 355 and m/z 127 fragments, and m/z values as high as 1673 (Fig. S1†), pointing to an oligomeric structure of the type shown in Fig. 2. Formation of 1,4-bis[di(3-methyl-1-azulenyl)methyl]benzene by condensation of 1-methylazulene with terephthalaldehyde, and its dication salt by hydride abstraction was reported some years ago by Asao and co-workers.[42]

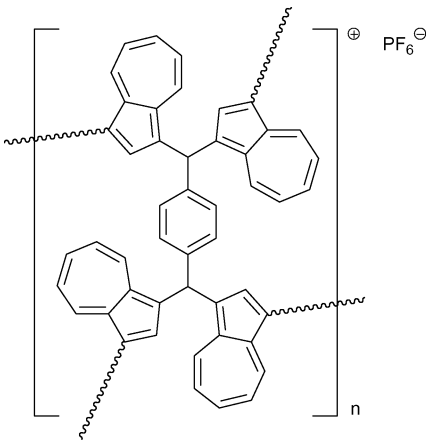
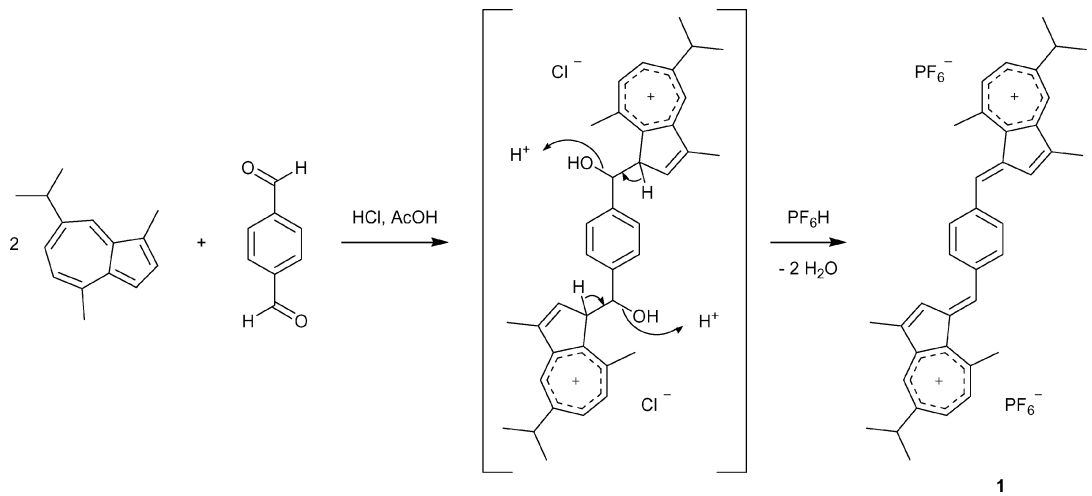


Fig. 2 Oligomer derived from parent azulene.

Whereas a conventional acid-catalyzed condensation process (highlighted in Scheme 1) could rationalize the formation of the dication salts, presence of a methyl group at C_1 and/or appropriate stabilizing groups on the seven-membered ring, ensuring the tropylium ion character, appear to be crucial in preventing further condensation with azulene.



Scheme 1 Suggested mechanism for the acid catalyzed condensation.

NMR data on 1 and 2. Complete assignments of the proton and carbon resonances were achieved by using 2D NMR and NOE. The data are sketched in Fig. 3. NMR assignments for **1** are at variance with the earlier reported values in several instances: reported proton assignments for proton $H_{5'}/H_{5''}$ and $H_{6'}/H_{6''}$ (in the seven-membered ring) were switched; phenyl ring protons ($H_2/H_3/H_5/H_6$) and the vinyl protons were specifically assigned (previously reported at the same chemical shifts as a "broad singlet"); reported assignments of $H_{2'}/H_{2''}$ and the vinyl protons were also switched. In addition, the coupling constants were refined. The following changes in the reported ^{13}C data were made: $C_{5'}/C_{5''}$ and $C_{6'}/C_{6''}$ were interchanged and $C_{2'}/C_{2''}$ and the olefinic *C*Hs were interchanged.

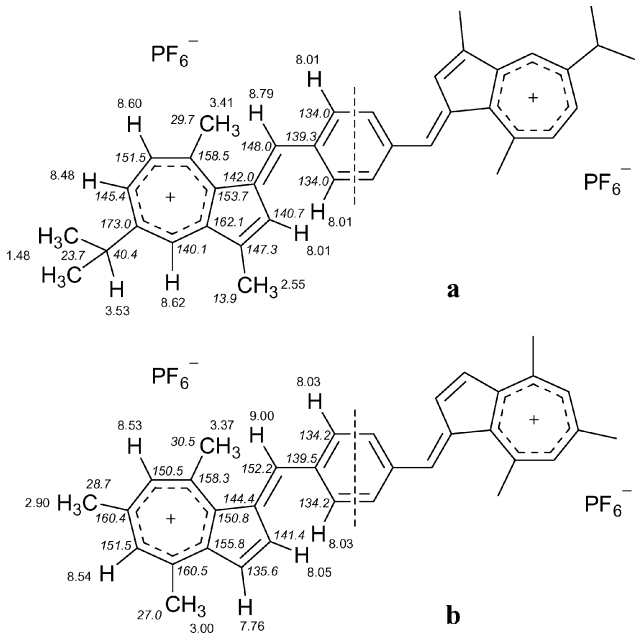


Fig. 3 Specific NMR assignments for dication salts **1** (a) and **2** (b).

For comparison, the ^{13}C NMR data and changes in charges (relative to the neutral precursor) for the guaiazulenium ion[37] are shown in Fig. 4, illustrating the predominant tropylium ion character in dications **1** and **2**.

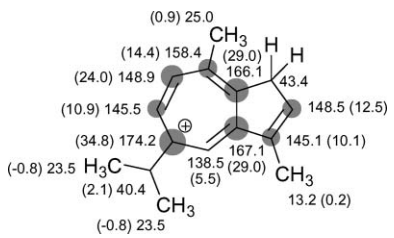


Fig. 4 NMR data mode and charge delocalization mode in guaiazulenium cation.

Complexation studies with crown ethers

NMR titration experiments were performed employing dibenzo-30-crown-10 (DB30C10), dibenzo-24-crown-8 (DB24C8), and dibenzo-18-crown-6 (DB18C6) in CD_3CN solvent. Titrations were followed by ^1H NMR from zero to three equivalents of crown, added directly into the NMR tube. Direct access to the stoichiometry of complexation (by Job's method or the mole ratio method)[43] was not possible by NMR, since addition of few drops of CD_3CN was necessary after each DB30C10 addition to allow induction of crown inside the NMR tube, and this led to a gradual decrease in the concentration of the dication salt during titration. No concentration dependency of the proton NMR chemical shifts was, however, observed in control experiments in which the concentration of the dication salt was varied in CD_3CN, thus confirming that addition of crown ether was responsible for the observed changes in chemical shifts of the dication. Complexation stoichiometry and binding constant were assessed in complimentary studies by microcalorimetric titration (see later). Fig. 5 is a stacked plot for the titration of dication **1** with DB30C10. The largest changes are for the tropylium ring protons ($H_{6'}/H_{8'}$) which gradually move upfield. The 1′-Me (methyl group in the 5-membered ring) also gradually becomes more shielded. Smaller shielding effects were observed for $H_{5'}/H_{2'}$, whereas the olefinic singlet and the benzo-ring protons ($H_2/H_3/H_5/H_6$) exhibited a deshielding trend.

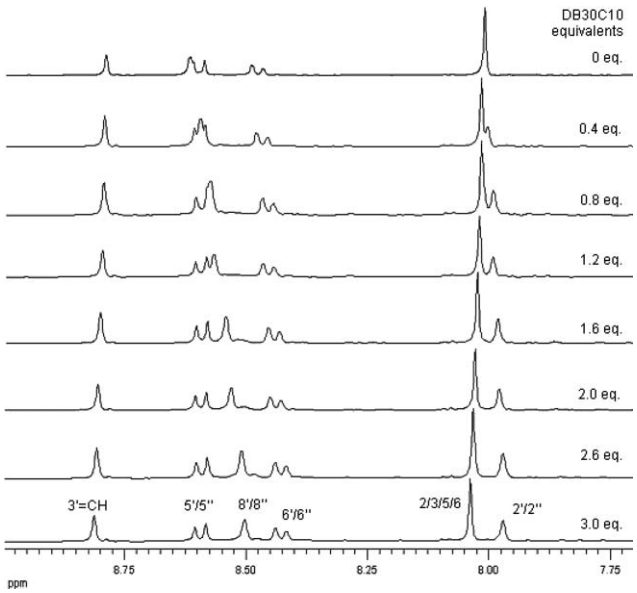


Fig. 5 NMR titration experiment (dication salt **1** with DB30C10).

The following additional change in the NMR spectra is also noteworthy. Whereas in the dication salt, itself the $H_{2'}$ proton has the same chemical shift as the benzo-ring protons ($H_2/H_3/H_5/H_6$), upon addition of the crown ether these signals split up into two groups (with $H_{2',2''}$ moving upfield and $H_{2,3,5,6}$ moving downfield).

T_1 NMR relaxation times were measured for the exocyclic vinyl proton and for $H_{5'}$, $H_{6'}$ and $H_{8'}$ in the tropylium moiety in CD_3CN for the dication salt alone, and in the presence of 1.2 and 3.0 equivalents of DB30C10. Changes in T_1 values are summarized in Table 1. Consistent with complexation, there is a gradual decrease in proton relaxation times with increasing host equivalents.

Electrospray-MS served as an additional technique to examine the HG cluster ions. Under the electrospray conditions, not only the crown–dication (1 : 1) HG^{2+} cluster ion (*m*/*z* 517), but also a crown–dication (2 : 1) H_2G^{2+} cluster (*m*/*z* 785) were observed.

Table 1 T_1 measurement for **1**–DB30C10 in CD_3CN

		Relaxation time, T_1/s		
Entry	Proton	0 eq.	1.2 eq.	3.0 eq.
1	$C_{3'}$=C*H*	1.11 ± 0.02	1.00 ± 0.02	0.94 ± 0.02
2	$H_{8'}$	1.18 ± 0.02	1.13 ± 0.03	1.08 ± 0.03
3	$H_{5'}$	1.28 ± 0.02	1.21 ± 0.03	1.17 ± 0.02
4	$H_{6'}$	1.46 ± 0.03	1.32 ± 0.04	1.26 ± 0.04

Consistent with their constitutions, MS/MS on *m*/*z* 517 (Fig. S2†) gave the doubly charged guest G^{2+} as the product ion (*m*/*z* 248), and the MS/MS of the *m*/*z* 785 ion (Fig. 6) produced abundant *m*/*z* 516 (HG^{2+}) ion and a less intense *m*/*z* 248 (G^{2+}) ion as products.

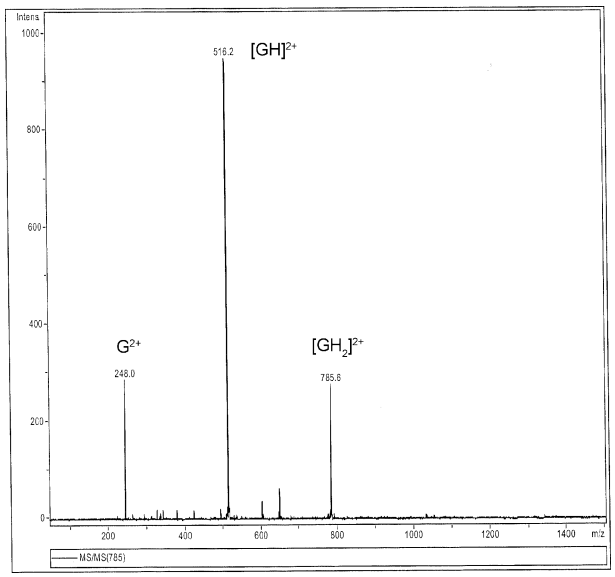


Fig. 6 MS/MS of *m*/*z* 785 ion.

NMR titration experiments between dication salt **1** and DB24C8 produced the same variation in trends but to a smaller degree. Thus $H_{8'}$ and $H_{6'}$ exhibited the largest upfield shifts and measurable upfield shift also occurred in the methyl group (on the five-membered ring), but other protons either did not shift or moved slightly downfield. Furthermore, the ring protons of the benzo-moiety exhibited no measurable changes.

Proton relaxation data for complexation of **1** with DB24C8 are summarized in Table 2. It can be seen that overall T_1 values decreased with increasing crown equivalents (except for $H_{8'}$ in entry 2), but the effect was smaller for DB24C8 than for DB30C10.

Table 2 T_1 measurement for **1**–DB24C8 in CD_3CN

		Relaxation time, T_1/s		
Entry	Proton	0 eq.	1.2 eq.	3.0 eq.
1	$C_{3'}$=C*H*	1.11 ± 0.02	1.08 ± 0.02	1.03 ± 0.01
2	$H_{8'}$	1.18 ± 0.02	—	1.19 ± 0.01
3	$H_{5'}$	1.28 ± 0.02	1.22 ± 0.02	1.11 ± 0.01
4	$H_{6'}$	1.46 ± 0.03	1.42 ± 0.02	1.33 ± 0.02

Influence of the crown cavity size/structure on the formation of the HG complex was further revealed by titrating dication salt **1** with DB18C6. In this case, no measurable changes were observed by NMR, but splitting of $H_2/H_3/H_5/H_6$ and $H_{2'}$ protons into two sets of signals still occurred.

Microcalorimetric study

In an effort to determine the stoichiometry of HG complex and to get access to the binding constant(s) and the thermodynamic parameters, complexation of dication salt **1** with DB30C10 was studied by microcalorimetric titration (for details of the procedure see the Experimental). The corresponding ITC plot is shown in Fig. 7 (for an enlarged copy of this plot, see Fig S5). The upper frame shows the raw data (with each peak corresponding to one injection). The upside-down orientation of the peaks is consistent with an exothermic process. The lower frame represents the integrated area of these peaks after subtracting the heat of dilution, and the solid line represents the best least-square fit for the obtained data. On the basis of a two binding sites model (the "one set of sites" model did not fit the data), microcalorimetric experiment provided access to the thermodynamic parameters for complexation between **1** and DB30C10 (Table S1†). Literature microcalorimetric titration studies on HG complexation[44] are mainly concerned with alkali-metal cations or neutral molecules as guests, with crown ethers, calixarenes, hemicarcerands, or cyclodextrins as typical hosts. Studies involving onium cations[45] as guests are limited, and we have not found any data on carbocations, for a direct comparison. Nevertheless, the value of log *K* (binding constant) deduced herein is comparable to binding data reported by Ungaro *et al.* for $[PhCH_2NMe_3]^+$ complexed to a calixarene receptor.[45]

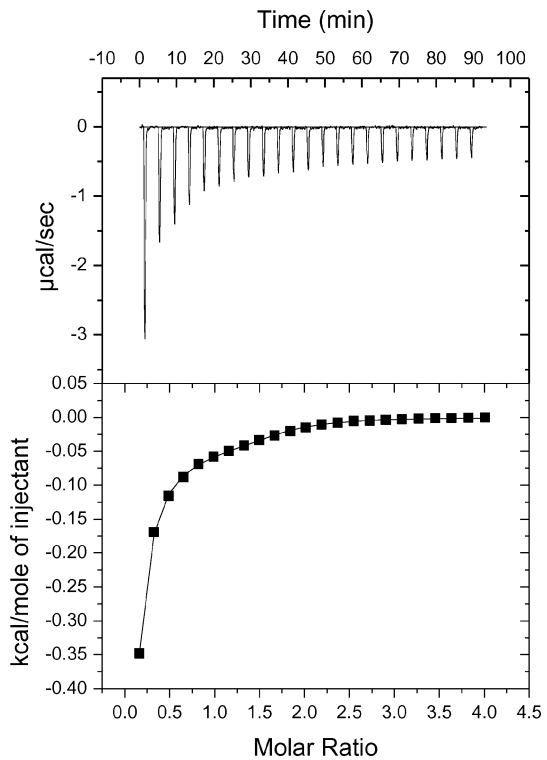


Fig. 7 Microcalorimetric study (**1**–DB30C10 in MeCN).

Complexation study with calixarenes

NMR titration experiments with *p-tert*-butyl-calix[*n*]arenes (n = 4, 6, 8) were thwarted due to solubility problems in CD_3CN which required the use of CS_2 as co-solvent. However, this led to the formation of two separate layers. With *p-tert*-butyl-methoxycalix[8]arene, it was possible to generate homogeneous solutions by using CD_3CN–$CDCl_3$ (1 : 1), but no measurable changes in the NMR chemical shifts could be observed. By contrast, ES-MS proved to be a suitable technique for detection of the cation–molecule clusters. With *p-tert*-butyl-methoxycalix[8]arene, the 1 : 1 complex $[GH]^{2+}$ (m/z 953) and a less abundant 1 : 2 complex $[GH_2]^{2+}$ (m/z 1658) were detected along with the uncomplexed G^{2+} (m/z 247) and G^{+} (m/z 494) (Fig. S3†). Confirming their constitution, MS/MS on $[GH]^{2+}$ produced G^{2+}, and MS/MS on $[GH_2]^{2+}$ gave $[GH]^{2+}$, showing in both cases the loss of one host molecule from the resulting complexes (Fig. 8 and Fig. 9, respectively).

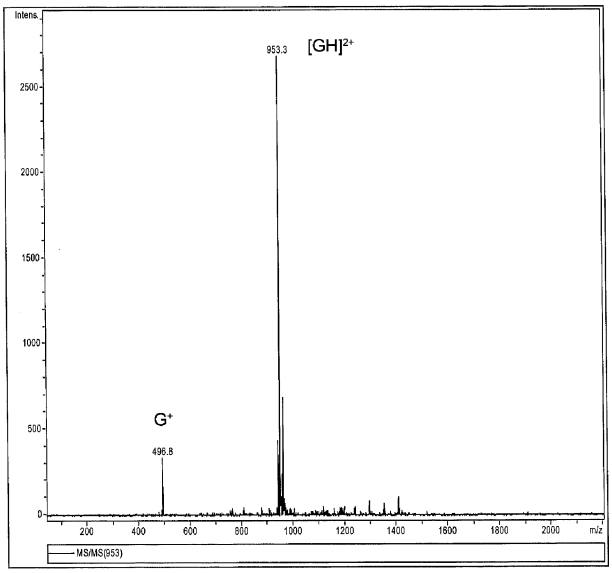


Fig. 8 MS/MS on $[GH]^{2+}$ (dication salt **1** and *p-tert*-butylmethoxycalix-[8]arene).

Decomplexation studies

Solvent effects on complexation–decomplexation processes have been exploited previously, notably by Stoddart's group[20] to examine "slipping on" and "slipping off" processes in self-assembly of rotaxanes. In the context of the present study, we sought to gain more insight into the complexation of dication salt **1** with DB30C10. Two types of approaches were considered, namely addition of a different solvent to induce decomplexation (as in eqn (1); see sections (a) and (b) below), and addition of a 2nd cationic guest (as in eqn (2); see sections (c) and (d) below).

$$[H_nG]^{2+} \xrightleftharpoons{\text{electron-rich solvent}} nH + G^{2+} \quad (1)$$

$$[H_nG]^{2+} \xrightleftharpoons{G'^{+}} [H_nG'] + G^{2+} \quad (2)$$

(a) Addition of DMSO to the HG complex. When DMSO-d_6 was added to the CD_3CN solution of **1** containing 3.0 equivalents of DB30C10, the color of the solution changed from deep-purple to deep-green (after 4 hours). NMR analysis of the sample indicated that resonances due to the dication salt had disappeared from the spectrum and only the signals of the crown ether remained (with the dibenzo-protons of DB30C10 appearing as two symmetrical multiplets). Small quantities of a white solid precipitated in the NMR tube. This was isolated, and was found to be DB30C10 based on its NMR spectrum. In a control experiment, an NMR sample of **1** alone in CD_3CN–DMSO-d_6 (2 : 1) gave broad resonances, no longer consistent with the dication salt. These experiments appear to suggest redox chemistry, induced by DMSO, possibly generating the radical cation of **1**, undetectable by NMR. This process may have the potential to serve as a complexation/decomplexation "switch", but this aspect requires further studies.

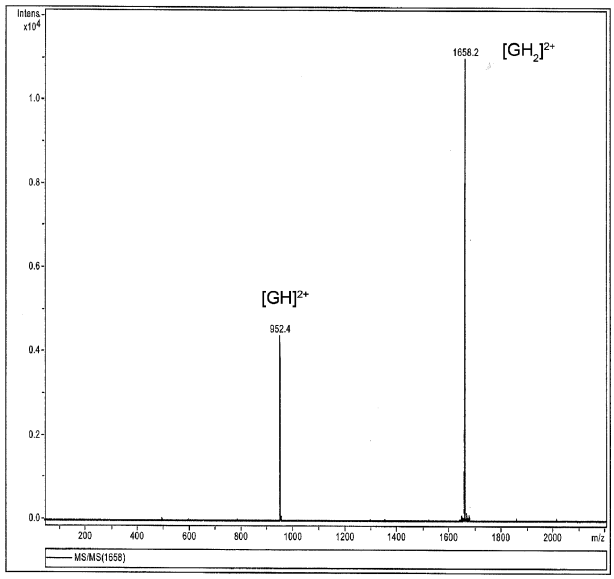


Fig. 9 MS/MS on $[GH_2]^{2+}$ (dication salt **1** and *p-tert*-butylmethoxycalix-[8]arene).

(b) Addition of acetone-d_6 to the HG complex. In a similar approach as above, acetone-d_6 was used instead of DMSO-d_6. ^{1}H NMR monitoring at various time intervals (up to 5 days) did not indicate decomplexation. However, a small solvent-induced downfield shift was measured for all protons of the guaiazulene moiety (by 0.05 ppm), except for $H_{8'}$, which was a little more deshielded (by 0.07 ppm). This presumably reflects a change in the nature of the solvation shell surrounding the HG complex, causing larger changes in the guest protons that are more intimately involved in complexation.

(c) Addition of silver salt. In an attempt to displace the guaiazulene dication–crown complex by Ag^+, 3.0 equivalents of silver tosylate was added to the NMR sample of **1**–DB24C8 (CD_3CN solvent) in portions of one equivalent. Similar observations (as in DMSO-d_6 addition) were made, *i.e.* the reaction mixture turned deep-green and some white precipitate appeared. ^{1}H NMR monitoring of the sample after adding each portion of AgOTs showed broadening of the dication salt resonances until they eventually disappeared into the baseline. Examination of the liquid phase by ES-MS did not indicate an Ag^+–crown complex; showing only an Na^+–crown complex.

(d) Addition of tropylium cation salt. Complexation of tropylium cation (Tr^+) to DB24C8 has been studied, and its X-ray structure revealed the presence of cation–π interactions.[35] In the context of the present study, $[Tr^+][PF_6^-]$ was selected to explore its effect on the **1**–DB30C10 HG complex in CD_3CN solvent. The ^1H NMR spectrum of the tropylium salt alone in CD_3CN is a singlet at 9.24 ppm. Addition of 2.0 equivalents of $[Tr^+][PF_6^-]$ to the NMR sample containing **1** and 3.0 equivalents of DB30C10 resulted in an upfield shift in the Tr^+ signal (δ 9.17 ppm), consistent with complexation, but with no concomitant changes in the NMR signals of the dication salt (still complexed). Addition of a third equivalent of $[Tr^+][PF_6^-]$ salt did not cause any further changes in the Tr^+ proton chemical shift. Considering the stoichiometries, and assuming two separate complexation equilibria involving **1**–crown and Tr^+–crown, one would expect that at that point of the titration experiment there would be a deficiency of DB30C10 relative to **1**, but nonetheless only the signals of the **1**–crown HG complex were present in the NMR (no uncomplexed **1**). These observations appear consistent with a cooperative complexation forming **1**–DB30C10–Tr^+ (a *ménage à trois*, as shown in Fig. 10).

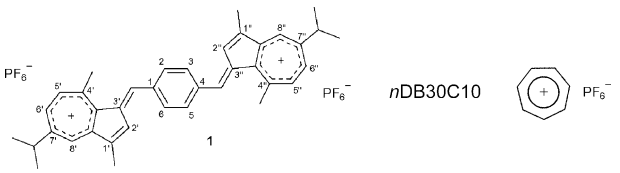


Fig. 10 Cooperative complexation involving two different carbocations.

In another experiment, a complex of Tr^+–DB24C8 was first prepared in CD_3CN by adding 4.5 equivalents of crown to 1.0 equivalent of $[Tr^+][PF_6^-]$ (as in ref. 35), which gave a Tr^+ chemical shift of 9.02 ppm. This solution was titrated with dication salt **1**.

Thus, 7.0 equivalents of **1** were gradually added in a total of 10 addition steps. Further addition of **1** was not possible, since solubility problems manifested beyond this point. NMR monitoring showed that the Tr^+ resonance gradually became deshielded (from 9.02 to 9.08 ppm), but despite the fact that at the end of the titration the crown was in default relative to Tr^+, the chemical shift of Tr^+ did not reach the value expected for uncomplexed tropylium (9.24 ppm). At the same time, throughout the titration, the resonances belonging to the guaiazulene dication were those of the complexed species, and no measurable changes occurred throughout the titration. In another experiment, 1.0 equivalent of $[Tr^+][PF_6^-]$ was added to 4.5 equivalents of DB30C10 in CD_3CN (Tr^+ signal at 9.13 ppm). The resulting complex was titrated with **1** (up to 5.0 equivalents). NMR monitoring produced essentially the same trend as that observed in the above experiment (with the smaller DB24C8), whereby the Tr^+ signal was gradually deshielded (9.13 → 9.17 ppm), without any indication for the formation of the "free", uncomplexed, guaiazulene dication.

Collectively, NMR titration experiments with DB30C10 and DB24C8 as hosts support a more complex supramolecular model involving both guaiazulene dication and Tr^+, rather than one crown molecule for each positive charge equivalent. Based on the NMR titration data, it can be surmised that whereas 3.0 equivalents of the crown is adequate to reach full complexation with guaiazaulene dication salt, 4.5 equivalents of crown is required for full complexation with Tr^+, indicating that despite significant steric crowding, the dication–crown complex may be thermodynamically more stable!

Complexation study with dication salt 2. Focusing on the relatively less crowded dication salt **2** derived from 4,6,8-trimethylazulene (see earlier), NMR titration experiments were performed with DB24C10 in a similar fashion as those described for dication salt **1**. The results indicated notable upfield shifts for $H_{3'}$ (five-membered ring), for the tropylium $H_{5'}$ and $H_{7'}$ protons, and for the 8-Me, while little or no changes were observed for the other protons. Considering the mesomeric carbocations/azulenium ion forms, and the fact that there is large net positive charge at C-1′, lack of sensitivity of $H_{1'}$ to titration by crown seems surprising, but may be rationalized in a model where the "azulenylic" CH is in close contact with the counter-ion $[PF_6^-]$. A noticeable difference between dications **1** and **2** in NMR titration with DB30C10 is gradual appearance of small new signals with increasing crown concentration in the NMR sample. But these signals remain small even after 4 days at room temperature. It is conceivable that they belong to a higher order complex (possibly 2 : 1) in a minor equilibrium, but there is no clear evidence to demonstrate this in solution, although a 2 : 1 complex is present in the electrospray-MS study (*vide infra*). The ES-MS spectrum of **2**–DB30C10 exhibits the 1 : 1 complex $[GH]^{2+}$ (*m*/*z* 489) and G^{2+} (*m*/*z* 220) (Fig. 11). A much less intense 2 : 1 complex $[GH_2]^{2+}$ (*m*/*z* 756) was also detected (Fig. S4†). Constitutions of the HG complexes were verified by MS/MS on the *m*/*z* 489 ion, which resulted in the formation of *m*/*z* 220, and by MS/MS on the $[GH_2]^{2+}$ complex, which produced both $[GH]^{2+}$ and G^{2+} along with other unknown product ions.

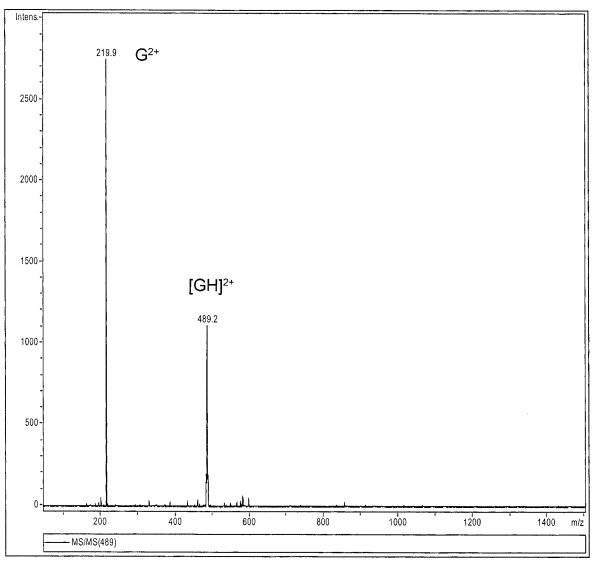


Fig. 11 ES-MS spectrum; **2**–DB30C10.

Complexation of dication salt **2** with DB30C10 was further examined by proton relaxation measurements in CD_3CN solvent. The T_1 values for $H_{3'}$ were measured for dication salt alone and in the presence of 1.6 and 3.3 equivalents of crown (Table 3). As expected, T_1 decreases with increasing equivalents of DB30C10. The ΔT_1 values are actually larger than those measured for **1**–DB30C10, which is consistent with a more favorable/stronger complexation for the less sterically crowded dication.

Table 3 T_1 measurement for **2**–DB30C8 in CD_3CN

	Relaxation time, T_1/s		
Proton	0 eq.	1.6 eq.	3.3 eq.
$H_{3'}$	1.5 ± 0.1	1.30 ± 0.06	1.02 ± 0.07

Comparative summary and conclusion

Dication salts 1,4-bis(3-guaiazulenylmethylium)benzene **1** and 1,4-bis[1-(4,6,8-trimethylazulenylmethylium)]benzene **2** are readily prepared from guaiazaulene and 4,6,8-trimethylazulene, but a similar procedure with parent azulene gave an oligomer whose structure could be inferred from MADI-TOF-MS. Unambiguous carbon and proton NMR assignments for **1** and **2** were made with the help of 2D-NMR and by NOE studies. The dications are best viewed as bis-tropylium cations, whose charge delocalization modes are analogous to protonated azulenes (azulenium cations).

Focusing on the HG complexation aspect, NMR titration experiments and T_1 measurements demonstrated that, despite rather severe steric crowding around the azulenium moieties, both **1** and **2** form complexes with DB30C10 and DB24C8 in solution. The resulting $[GH]^{2+}$ and $[GH_2]^{2+}$ clusters were also detected by ES-MS, and their constitutions were confirmed by MS/MS measurements. Although attempts to observe stable HG complexes of **1** or **2** with large calixarenes were unsuccessful, these complexes were detected under electrospray conditions, and studied in the gas phase by ES-MS.

Decomplexation process $[GH_2]^{2+} \rightarrow [2H] + [G]^{2+}$ and/or $[GH]^{2+} \rightarrow [H] + [G]^{2+}$ was probed by NMR by addition of DMSO-d_6 and acetone-d_6. Decomplexation *via* the "cationic guest switching" approach, $[GH]^{2+} + G_1^{+} \rightarrow G^{2+} + [G_1H]^{+}$, was also investigated by addition of AgOTs and $[Tr^{+}][PF_6^{-}]$ salts. Results with DMSO-d_6, acetone-d_6, and AgOTs were inconclusive, but indirect evidence was gathered suggesting a redox process possibly forming radical cations. With the Tr^{+} salt, the data could best be explained by cooperative (ternary) complexation. Since complexation stoichiometry was not accessible by NMR titration, a microcalorimetric titration study was undertaken. Only a two-binding-site model could provide the right fit.

Taken together, the data provide convincing evidence for the formation of HG complexes, with the H–G^{2+}–H (crown–dication–crown) 2 : 1 complex suggested to be the main species.

The present study illustrates the efficacy of utilizing stable carbocations and dications as guest molecules in supramolecular architecture. Progress in this area is clearly linked to preparative carbocation chemistry.

Experimental

Starting materials

Guaiazulene (Acros Organics), 4,6,8-trimethylazulene (AccuStandard), azulene (Acros Organics), terephthaldicarboxaldehyde (Acros Organics), crown ethers (Aldrich), and tropylium hexafluorophosphate (Aldrich) all had high purity and were used without further purification. The calixarenes used in this study were available in our laboratory from earlier studies.

NMR spectra

These were recorded on 400 and 500 MHz instruments with CD_3CN as solvent.

T_1 measurements

The T_1 relaxation time measurements were performed on a 500 MHz instrument and are reported in seconds (s). They were measured at the beginning, middle and end of titrations, on the protons of the dication salts that produced the largest chemical shift changes in NMR titration (each reported value is an average of 3 measurements).

Electrospray-MS

Spectra were acquired by direct infusion method on nanomolar concentrations of the salts in HPLC-grade acetonitrile solvent.

MALDI-TOF-MS

The method reported by Zenobi *et al.*[46] for MALDI sample preparation method from insoluble polymers was adopted. A fine powder was obtained by grinding the oligomer with a mortar and pestle. The matrix used was 2,5-dihydroxybenzoic acid. Different matrix/sample mixing ratios were tested and the optimal conditions were observed for 3 : 1 to 1 : 1 ratios (by weight). Finally, the resulting finely ground mixture was pressed into a thin pellet and placed on the MALDI probe tip with double-sided tape and introduced into the instrument.

Microcalorimetric titration

An isothermal titration calorimeter (VP-ITC) was used for microcalorimetric experiments. These were performed at atmospheric pressure and 25 °C in HPLC-grade acetonitrile. Several titrations involving **1** and DB30C10 were carried out to confirm the reproducibility of the results. A 20.8 mM solution of DB30C10 in a 0.250 mL syringe was sequentially injected with rapid stirring at 470 rpm into a 0.9 mM solution of **1** in the sample cell (1.4321 mL volume). The titration experiment was composed of 23 successive 10 μL injections, with an injection time of 24 s, and with a 240 s interval between injections. Data were analyzed by using the "Two Sets of Sites" model in Origin Microcal software for the best curve fitting.

Synthesis of dication salts 1 and 2

1,4-Bis(3-guaiazulenylmethylium)benzene bis(hexafluorophosphate) (**1**) and 1,4-bis[1-(4,6,8-trimethylazulenylmethylium)]-benzene bis(hexafluorophosphate) (**2**) were prepared according to the following procedure: to a solution of guaiazulene (12 mg, 60 μmol), or 4,6,8-trimethylazulene (10 mg, 60 μmol), dissolved in acetic acid (0.5 mL) was added a solution of terephthalaldehyde (4 mg, 30 μmol) in acetic acid (0.5 mL) and hydrochloric acid (35% aqueous solution, 45 μL). The mixture was stirred at 25 °C for 15 min under aerobic conditions. Subsequent addition of hexafluorophosphoric acid (60% aqueous solution, 100 μL) to the solution led to the precipitation of a maroon-brown solid, which was centrifuged for a couple of minutes. The solid that separated out from the crude reaction solution mixture was carefully

washed twice with cold water. After drying under vacuum, it was re-crystallized from acetone–hexane (1 : 4) to give pure compound **1** (13 mg, 53%), or **2** (19 mg, 87%).

Typical procedure for NMR titration experiments

NMR titrations were carried out directly in NMR tubes. To a solution of dication salt (1 eq.) in acetonitrile-d_3 (0.4 mL), the crown was added directly into the tube in small portions from 0.3 eq. up to 3–3.5 eq., until there was no further shift in the signals of dication salt. Addition of ~2 drops of acetonitrile-d_3 was necessary to enable the introduction of crown inside the NMR tube. The NMR sample was thoroughly mixed (vortex) after each addition and the ^{1}H NMR spectrum was recorded within 15 min after each addition.

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