Cucurbit[7]uril host–guest complexes with cationic bis(4,5-dihydro-1*H*-imidazol-2-yl) guests in aqueous solution

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Abstract: The host–guest interactions between cucurbit[7]uril and a series of novel cationic bis(4,5-dihydro-1*H*-imidazol-2-yl)arene and 1-(4,5-dihydro-1*H*-imidazol-2-yl)- and 1,3-bis(4,5-dihydro-1*H*-imidazol-2-yl)-adamantane guests have been investigated in aqueous solution using UV–vis and NMR spectroscopy, and electrospray mass spectrometry. With the exception of the 1,3-bis(4,5-dihydro-1*H*-imidazol-2-yl)adamantane (which binds externally to the CB[7]), these guests form very stable inclusion complexes with slow exchange on the ^{1}H NMR timescale. The direction and magnitude of the complexation-induced shifts (CIS) in the proton resonances of the guests are indicative of the residence of the hydrophobic core of the guest within the CB[7] cavity and the charged 4,5-dihydro-1*H*-imidazol-2-yl units outside the cavity adjacent to the carbonyl-lined portals of the host. The CIS values and the inclusion stability constants have been correlated with the nature of the guest core and with the distance between the charges on the terminal 4,5-dihydro-1*H*-imidazol-2-yl rings.

Key words: cucurbit[7]uril, host–guest complex, dihydroimidazolyl, inclusion stability constants.

Résumé : Faisant appel aux spectroscopies UV–vis et RMN ainsi qu'à la spectrométrie de masse par électronébulisation, on a étudié les interactions hôte–invité entre le cucurbit[7]urile {CB[7]} et une série de nouveaux invités cationiques bis(4,5-dihydro-1*H*-imidazoly-2-yl)arènes et 1-(4,5-dihydro-1*H*-imidazol-2-yl)- et 1,3-bis(4,5-dihydro-1*H*-imidazol-2-yl)-adamantanes. À l'exception du 1,3-bis(4,5-dihydro-1*H*-imidazol-2-yl)adamantane qui se lie d'une façon externe avec le CB[7], ces invités forment des complexes d'inclusion très stables qui ne présentent que des échanges lents à l'échelle de temps de la RMN du ^{1}H. La direction et l'amplitude des déplacements induits par la complexation (DIC) dans les résonances des protons des invités indiquent que la portion hydrophobe de l'invité réside à l'intérieur de la cavité du CB[7] et que les unités 4,5-dihydro-1*H*-imidazol-2-yles se trouvent à l'extérieur de la cavité, adjacentes aux portails de l'hôte alignés de groupes carbonyles. On a établi une corrélation entre les valeurs des DIC ou les constantes de stabilité et la nature de la portion hydrophobe de l'invité ou la distance entre les charges qui se trouvent sur les noyaux terminaux 4,5-dihydro-1*H*-imidazol-2-yles.

Mots clés : cucurbit[7]urile, complexe hôte–invité, dihydroimidazolyle, constantes de stabilité d'inclusion.

[Traduit par la Rédaction]

Introduction

The cucurbit[*n*]urils (CB[*n*], *n* = 5–10) are a family of macrocyclic host molecules (1–5) formed in the acid-catalyzed condensation reactions of glycoluril with paraformaldehyde. While this reaction, which yields primarily CB[6], was first reported in 1905 by Behrend et al. (6), the utility of these host molecules was not fully recognized until the work of Mock and co-workers on cucurbit[6]uril in the 1980s (7–10). More recently, improvements in the synthetic yields of the other members of the cucurbituril family, primarily CB[7] and CB[8] were independently reported by the research groups of Kim et al. (11) and Day et al. (12). Since these reports, there has been considerable interest in the guest–host chemistry of CB[7] and CB[8], and the use of these host molecules as reaction vessels for photochemical isomerizations and dimerizations (13–16), stabilizers for dyes (17, 18) and other molecules (19, 20), for solubilizing ferrocene (21, 22), and in the development of molecular shuttles, switches, and sensors (23–25).

The cucurbiturils CB[6], CB[7], and CB[8] have similarly sized hydrophobic cavities as the more well-studied α-, β-, and γ-cyclodextrins (CD), respectively, but differ in the nature and size of the portals to the cavities (4, 5). Nevertheless, a number of studies have dealt with the comparisons between the binding of guests to cucurbiturils and cyclodextrins and their respective effects on the chemistries of the guest molecules (22, 26, 27). The portals of the CB[*n*] cavities are lined with ureido carbonyl groups and provide a more restrictive entry to guest molecules than the corresponding CD hosts. The polar nature of the carbonyls, however, makes them attractive to cationic guest molecules, from simple metal ions (3) to protonated α,ω-diaminoalkanes (8). The CB[7] host (Scheme 1) has been shown to form very

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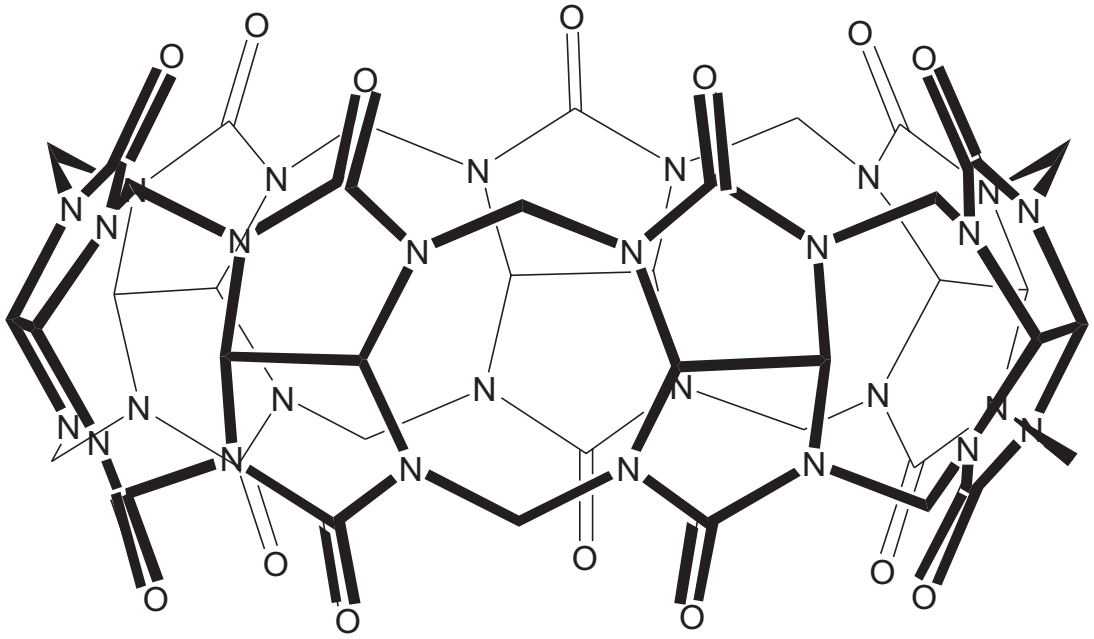
Scheme 1. Structure of cucurbit[7]uril (CB[7]).



stable inclusion complexes with guests containing a diverse set of central units, including metalloferrocenes (21, 22), carboranes (28), aromatic rings (29–32), and adamantanes (32), particularly if these groups contain cationic substituents that can be aligned with the carbonyl-lined portals upon guest inclusion.

The CDs have two sets of protons on the internal surface of the cavity and changes in the chemical shifts of these provide evidence of inclusions of the guest molecules. The complexation-induced shifts (CISs) of the guest proton resonances, however, tend to be relatively small (33). While the cucurbiturils lack any protons inside the cavity, the CIS values for the guest protons located in the cavity tend to be quite large (upfield) and opposite in sign to those for protons located near the carbonyl portals. Mock and Shih (8) carried out a systematic study of the CISs of the methylene proton resonances of $H_3N(CH_2)_nNH_3^{2+}$ (n = 4–8) guests upon inclusion in CB[6]. There has not, however, been a similar study conducted on a series of related guests in complexes with CB[7]. In connection with their improved synthesis of CB[7], Kim's group (11) used the dicationic 2,6-bis(4,5-dihydro-1*H*-imidazol-2-yl)naphthalene guest to demonstrate the formation of guest–host inclusion complexes between aromatic guests and the larger CB[7], but did not report an inclusion stability constant. This guest has subsequently been employed in ab initio calculations of the energy-minimized structures of the 1:1 and 2:1 guest–host complexes with CB[7] (34) and CB[8] (35), respectively. These studies have indicated that the guest–host complexes are stabilized by hydrophobic interactions between the naphthalene group and the inside of the CB[*n*] cavity, and by ion–dipole and hydrogen bonding interactions between the dihydroimidazolyl rings and the carbonyl-rimmed portals of the CB[*n*] host molecule.

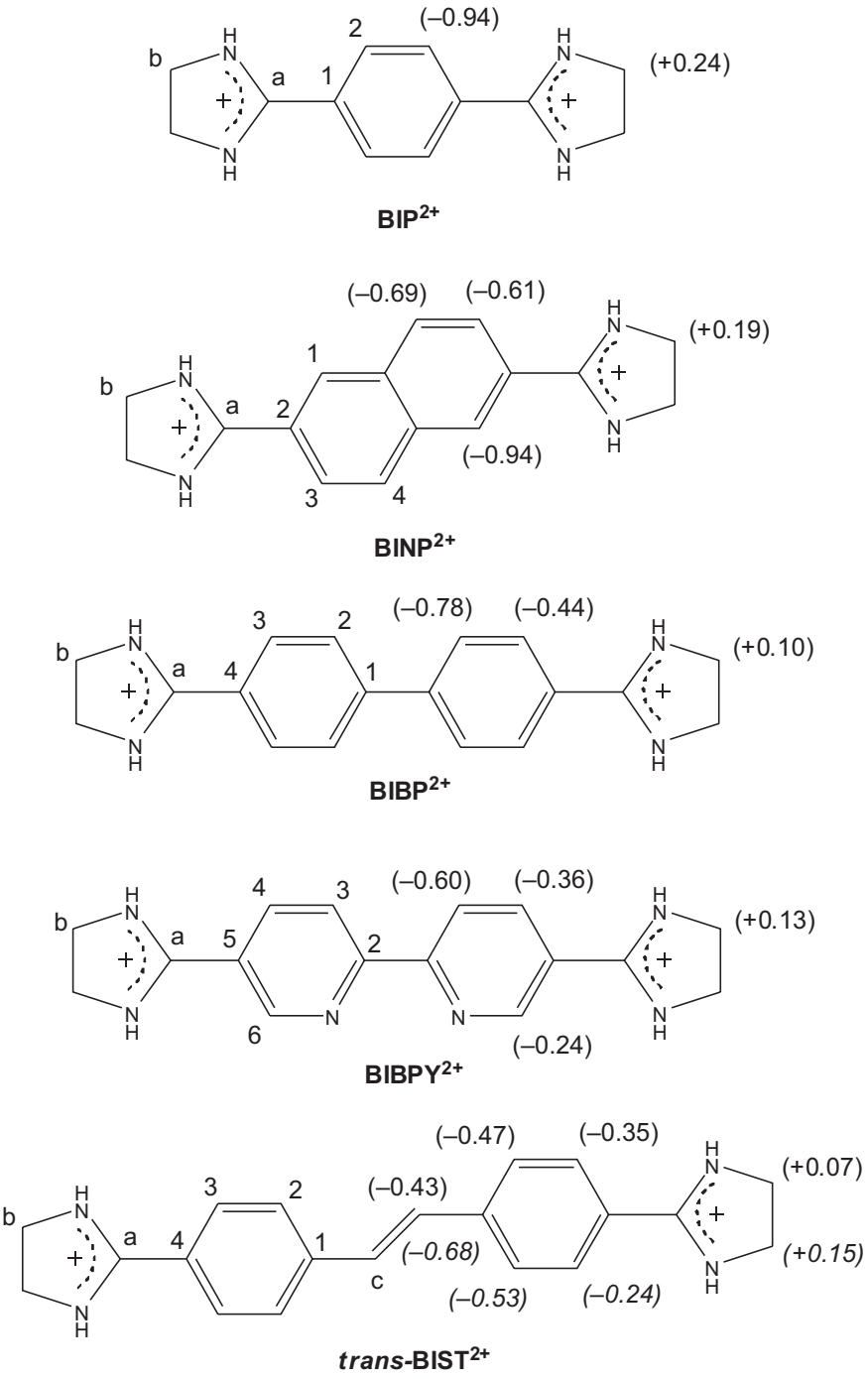
As the CB[7] cavity has a strong affinity for aromatic and adamantyl guests (32), we synthesized and characterized a series of novel cationic aromatic (Scheme 2) and adamantyl (Scheme 3) guests using the protonated (4,5-dihydro-1*H*-imidazol-2-yl) end groups. The advantage of these terminal groups is that the ethylene portion of the imidazole ring affords four equivalent protons to probe the environment of the ends of the guest molecule, in addition to the aromatic core. The guest–host inclusion stability constants with CB[7] were determined by using ^{1}H NMR chemical shift titrations and competitive binding experiments. The stability constants and CISs in the ^{1}H NMR resonances of the guests were correlated with the length of the guest (distance between positive charges) and the nature of the aromatic or aliphatic core.

Experimental section

Materials

CB[7] was prepared by a reported method (12). CB[8] (Sigma-Aldrich) and the α-, β-, and γ-cyclodextrins (Sigma-Aldrich, Cyclolab) were used as received. The guest compounds were prepared in accordance with the literature method of Kim et al. (11) by reacting the appropriate mono- or dicarboxyclic acids (Sigma-Aldrich) with a mixture of ethylenediamine and ethylenediamine dihydrochloride under argon gas. The ethylenediamine dihydrochloride was prepared prior to the experiment by adding ice-cold concd. HCl into an ethylenediamine solution until a white precipitate formed that was filtered and oven-dried for 12 h. The monocarboxylic acid (20 mmol) or dicarboxylic acid (10 mmol), ethylenediamine (20 mmol), ethylenediamine dihydrochloride (20 mmol), *p*-toluenesulfonic acid monohydrate (0.75 mmol), and ethylene glycerol (15 mL) were placed in a 50 mL round bottom flask and heated at reflux (190 °C) for 1–10 h (depending on the carboxylic acid used) under argon gas. The precipitates, which formed on cooling and from the removal of the solvent from the filtrate, were dissolved in 50 mL of distilled water (containing

Scheme 2. Structures of the dicationic bis(4,5-dihydro-1*H*-imidazol-2-yl)arene guests with the proton labeling and the complexation induced chemical shifts changes (Δδ (ppm) in parantheses) of the ^{1}H NMR proton resonances of the guest upon formation of the 1:1 guest–host complex with cucurbit[7]uril. The Δδ values in italics for *trans*-BIST^{2+} refer to the corresponding *cis*-BIST^{2+} guest.

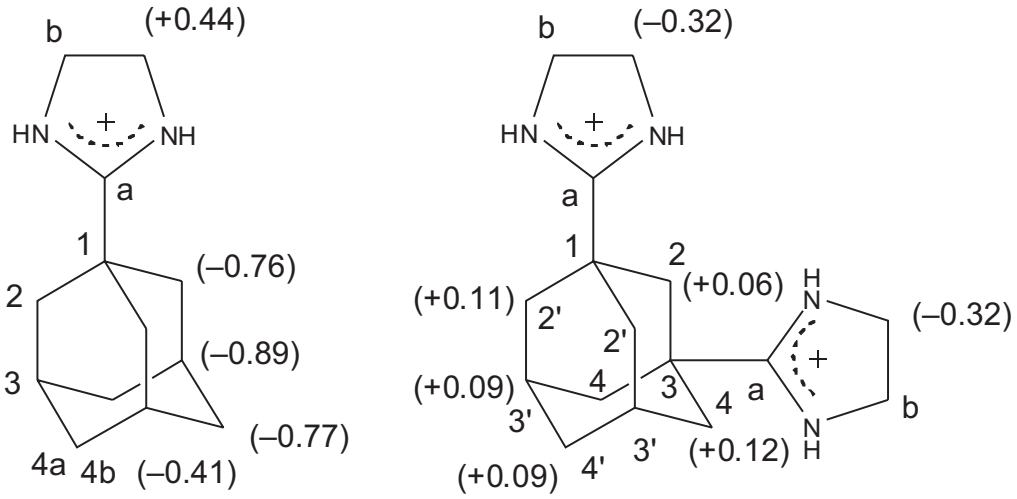


1.5 mL concd. HCl). The addition of 20 mL of 50% aq. NaOH into the mixture produced white or yellow precipitates, which were filtered, washed several times with distilled water, and dried under reduced pressure for several hours. Yields in the range of 68%–94% were obtained for the neutral guest compounds. The hydrochloride salts of the bis(dihydroimidazolyl) compounds were obtained as white or yellow solids by slowly adding a 10% HCl solution into a suspension of the product in methanol. The deposited precipitate was filtered and dried under vacuum.

*2,6-Bis(4,5-dihydro-1*H*-imidazol-2-yl)naphthalene dihydrochloride ([BINP]Cl$_2$)*

^{1}H NMR (D_2O, ppm) δ: 4.06 (s, 8H, N-CH_2), 7.83 (d, 2H, H_4, $J_{3,4}$ = 8.6 Hz), 8.18 (d, 2H, H_3), 8.45 (s, 2H, H_1 and H_5). Lit. (11) (D_2O, ppm) δ: 4.20 (s, 8H, N-CH_2), 7.94 (d, 2H,

Scheme 3. Structures of the cationic 1-(4,5-dihydro-1*H*-imidazol-2-yl)adamantane and 1,3-bis(4,5-dihydro-1*H*-imidazol-2-yl)adamantane guests with the proton labeling and the complexation-induced chemical shift changes (Δδ (ppm) in parentheses) of the ^{1}H NMR proton resonances of the guest upon formation of the inclusion complexes with CB[7].



IAD$^+$ **BIAD^{2+}**

J = 8.6 Hz), 8.31 (d, 2H, J = 8.6 Hz), 8.55 (s, 2H). ^{13}C NMR (D_2O, ppm) δ: 44.73 (C_b), 122.32 (C_1), 124.46 (C_3), 129.65 (C_4), 130.74 (C_2), 134.23 (C_c), 165.92 (C_a). Lit. (11) (D_2O, ppm) δ: 47.6, 125.3, 132.5, 133.5, 137.2, 169.0. ES-MS *m*/*z*: 266.5 $[M - H]^+$.

4,4′-Bis(4,5-dihydro-1*H*-imidazol-2-yl)biphenyl dihydrochloride ([BIBP]Cl_2·H_2O)

Melting point > 300 °C (dec). ^{1}H NMR (D_2O, ppm) δ: 4.04 (s, 8H, N-CH_2), 7.85 (d, 4H, H_2, $J_{2,3}$ = 8.6 Hz), 7.89 (d, 4H, H_3, $J_{2,3}$ = 8.6 Hz). ^{13}C NMR (D_2O, ppm) δ: 44.56 (C_b), 122.03 (C_4), 128.05 (C_2), 128.70 (C_3), 144.55 (C_1), 166.05 (C_a). ES-MS *m*/*z*: 146.0 $[M]^{2+}$. Anal. calcd. for $C_{18}H_{20}N_4Cl_2$·H_2O: C 56.70, H 5.82, N 14.69; found: C 56.31, H 5.60, N 14.32.

1,4-Bis(4,5-dihydro-1*H*-imidazol-2-yl)benzene dihydrochloride ([BIP]Cl_2·H_2O)

Melting point > 235 °C. ^{1}H NMR (D_2O, ppm) δ: 4.04 (s, 8H, N-CH_2), 7.93 (s, 4H, H_2 and H_3). ^{13}C NMR (D_2O, ppm) δ: 44.93 (C_b), 45.30 (C_2), 127.94 (C_1), 128.79 (C_3), 165.69 (C_a). ES-MS *m*/*z*: 215.7 $[M - H]^+$. Anal. calcd. for $C_{12}H_{16}N_4Cl_2$·H_2O: C 48.04, H 5.73, N 18.53; found: C 47.22, H 5.24, N 18.36.

4,4′-Bis(4,5-dihydro-1*H*-imidazol-2-yl)stilbene dihydrochloride ([BIST]Cl_2·3H_2O)

Melting point > 280 °C (dec). ^{1}H NMR (D_2O, ppm) δ: 4.02 (s, 8H, NH-CH_2), 7.39 (s, 2H, HC=CH), 7.77 (s, 8H, H_2 and H_3). ^{13}C NMR (D_2O, ppm) δ: 44.46 (C_b), 127.2 (C_c), 127.5 (C_2), 128.51 (C_3), 129.6 (C_4), 139.8(C_1), 157.4 (C_a). ES-MS *m*/*z*: 159.5 $[M]^{2+}$. Anal. calcd. for $C_{20}H_{22}N_4Cl_2$·H_2O: C 54.18, H 6.37, N 12.64; found: C 54.77, H 6.04, N 12.67.

5,5′-Bis(4,5-dihydro-1*H*-imidazol-2-yl)-2,2′-bipyridine tetrahydrochloride ([BIBPY]Cl_4)

Melting point > 250 °C (dec). ^{1}H NMR (D_2O, ppm) δ: 4.05 (s, 8H, NH-CH_2), 8.38 (d, 2H, H_3, $J_{3,4}$ = 8 Hz), 8.42 (d, 2H, H_4, $J_{3,4}$ = 8 Hz), 9.04 (s, 2H, H_6). ^{13}C NMR (D_2O, ppm) δ: 44.9 (C_b), 120.3 (C_5), 123.0 (C_3), 138.2 (C_4), 148.5 (C_6), 158.4 (C_2), 164.2 (C_a). ES-MS *m*/*z*: 293.1 $[M - 3H]^+$. Anal. calcd. for $C_{16}H_{20}N_6Cl_4$: C 43.86, H 4.60, N 19.18; found: C 43.80, H 4.25, N 19.13.

1-(4,5-Dihydro-1*H*-imidazol-2-yl)adamantane hydrochloride ([IAD]Cl)

Melting point 152–154 °C (dec). ^{1}H NMR (D_2O, ppm) δ: 1.65 (d, 3H, H_{4b}, $J_{4a,4b}$ = 12.7 Hz), 1.71 (d, 3H, H_{4a}), 1.78 (d, 6H, H_2, $J_{2,3}$ < 0.5 Hz), 1.97 (s, 3H, H_3), 3.53 (s, 4H, NH-CH_2). ^{13}C NMR (D_2O, ppm) δ: 27.7 (C_3), 35.1 (C_1), 35.8 (C_2), 39.0 (C_4), 46.5 (C_b), 170.4 (C_a). ES-MS *m*/*z*: 205.4 $[M]^+$. Anal. calcd. for $C_{13}H_{21}N_2Cl$: C 64.85, H 8.79, N 11.63; found: C 64.46, H 7.75, N 11.53.

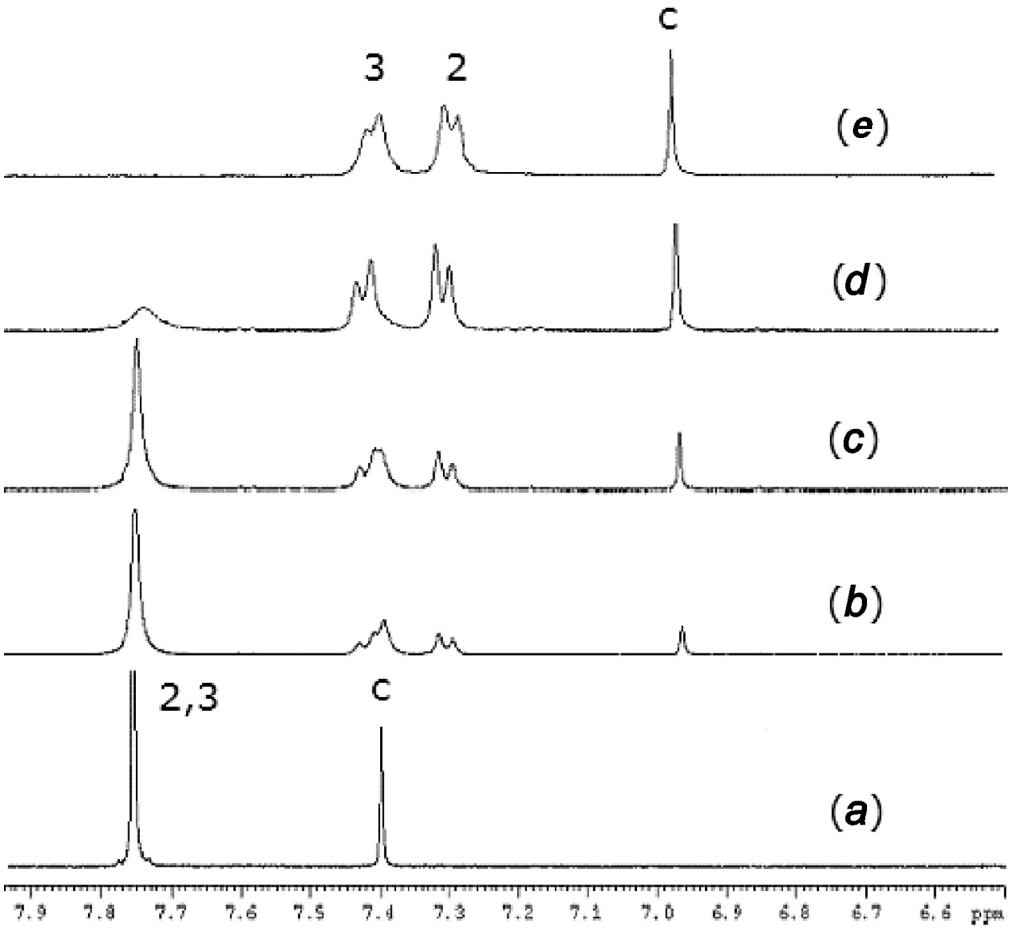
1,3-Bis(4,5-dihydro-1*H*-imidazol-2-yl)adamantane dihydrochloride ([BIAD]Cl_2·3H_2O)

Melting point > 280 °C (dec). ^{1}H NMR (D_2O, ppm) δ: 1.72 (s, 2H, $H_{4'}$), 1.87 (m, 8H, $H_{2'}$ and H_4), 2.01 (s, 2H, H_2), 2.25 (s, 2H, $H_{3'}$), 3.85 (s, 8H, NH-CH_2). ^{13}C NMR (D_2O, ppm) δ: 26.96 (C_4), 33.46 (C_5), 34.96 (C_1), 36.81 (C_3), 38.91 (C_2), 44.02 (C_b), 175.55 (C_a). ES-MS *m*/*z*: 273.4 $[M - H]^+$. Anal. calcd. for $C_{16}H_{26}N_4Cl_2$·3H_2O: C 48.12, H 8.08, N14.03; found: C 47.39, H 7.56, N 13.64.

Physical measurements

The NMR spectra were recorded on a Bruker Avance-400 instrument in D_2O (the residual solvent proton signal at 4.75 ppm served as the internal reference). Electrospray mass spectrometry measurements were obtained on a VG Quattro quadrupole mass spectrometer with an atmospheric pressure electrospray ionization source and a mass range for single-charged ions of 4000. Samples were prepared as solutions in distilled water containing the guest (2.5×10^{-3} mol/L) and CB[7] (0.015 mol/L). UV–vis spectra were recorded on a Hewlett-Packard 8452 diode array spectrome-

Fig. 1. The aromatic portion of the ^{1}H NMR spectra of *trans*-[BIST]$^{2+}$ with (*a*) 0.0, (*b*) 0.25, (*c*) 0.50, (*d*) 0.85, and (*e*) 2.0 equiv. of CB[7] in D_2O.



ter. Elemental analyses were preformed by Canadian Microanalytical Services Ltd., Delta, British Columbia.

The inclusion stability constants were determined from competitive binding studies monitored by ^{1}H NMR spectroscopy in D_2O at 25 °C, using the procedure of Isaacs and coworkers (32). The competitor primarily employed with the guests was sodium 3-(trimethylsilyl)propionate-2,2,3,3-d_4 (Sigma-Aldrich, $K_{CB[7]}$ = (1.82 ± 0.22) × 10^7 (mol/L)$^{-1}$ (32)), except for the BINP^{2+} guest, in which case (trimethylammonio)methylferrocene iodide (Sigma-Aldrich, $K_{CB[7]}$ = (3.31 ± 0.62) × 10^{11} (mol/L)$^{-1}$ (22, 32)) was used. For the weaker external binding of BIAD^{2+} to CB[7], a ^{1}H NMR chemical shift titration of the guest with CB[7] was performed in D_2O at 25 °C, with the data fit to a 1:1 binding model as described previously (33). Molecular modelling of the structures of the guest–host complexes was performed using Chem3D software (CambridgeSoft) with MM2 energy minimizations.

Results and discussion

The macrocyclic host molecule CB[7] forms very stable host–guest complexes with cationic guest molecules in aqueous solution. For organic guests, especially strong binding has been observed when the guest is comprised of a hydrophobic central core with positively charged substituents, which can be placed near the polar carbonyl groups that line the portals of the host. The dication guests formed by protonations of α,α′-diamino-*p*-xylene and 1,3-diaminoadamantane, for example, bind to CB[7] with stability constants of (1.84 ± 0.34) × 10^9 and (2.06 ± 0.33) × 10^8 (mol/L)$^{-1}$, respectively (32). The cationic guests synthesized in this study, as shown in Schemes 2 and 3, have variable hydrophobic aryl or adamantyl cores with 4,5-dihydroimidazol-2-yl end groups and would be expected to likewise form very stable inclusion complexes with CB[7].

The inclusion of the guests in the cavity of CB[7] is clearly seen by ^{1}H NMR spectroscopy (Fig. 1). The guest protons that reside within the hydrophobic cavity experience shielding and, therefore, upfield CISs in their resonances. The guest protons that are located near the ureido carbonyl groups rimming the portals are deshielded and the resonances move downfield, compared with the chemical shifts observed in the free guest. The ^{1}H NMR chemical shifts of the free guest and CB[7]-included guest protons are summarized in Table 1. The formation of 1:1 host–guest complexes is also supported by electrospray mass spectrometry. All of the complexes formed with the dicationic aromatic guests (M) exhibit peaks for the {M·CB[7]}$^{2+}$ species, while the adamantyl guests IAD$^+$ and BIAD^{2+} exhibit peaks for {M·CB[7]}$^+$ and {M·CB[7]-H}$^+$, respectively.

While Mock and Shih (8) carried out a systematic study

Table 1. ^{1}H NMR chemical shifts (in ppm) of the guest protons before and after (*in italics*) the formation of the guest–host complexes with CB[7] in D_2O (HOD at 4.75 ppm) at 25 °C, and the guest–host stability constants ($K_{CB[7]}$).

Guest	H_1	H_2	H_3	H_4	H_6	H_b	H_c	$K_{CB[7]}$ ((mol/L)$^{-1}$)
$BINP^{2+}$	8.45		8.18	7.83		4.06		$(6.0 \pm 1.0) \times 10^{10}$
	7.51		*7.57*	*7.14*		*4.25*		
$BIBP^{2+}$		7.85	7.89			4.04		$(1.7 \pm 0.2) \times 10^{8}$
		7.07	*7.45*			*4.14*		
BIP^{2+}		7.93				4.04		$(5.2 \pm 0.6) \times 10^{9}$
		6.99				*4.28*		
$BIBPY^{2+}$			8.38	8.42	9.04	4.05		$(8.9 \pm 1.1) \times 10^{7}$
			7.78	*8.06*	*8.80*	*4.18*		
trans-$BIST^{2+}$		7.77				4.02	7.39	$(5.6 \pm 0.7) \times 10^{8}$
		7.30	*7.42*			*4.09*	*6.96*	
cis-$BIST^{2+}$		7.39	7.59			3.96	6.85	
		6.86	*7.35*			*4.11*	*6.17*	
IAD^{+}		1.78	1.97	1.71, 1.65		3.53		$(1.4 \pm 0.7) \times 10^{8}$
		1.30	*1.09*	*0.94*, *1.24*		*3.97*		
$BIAD^{2+}$		1.87, 2.01	2.25	1.72, 1.87		3.85		$(1.0 \pm 0.5) \times 10^{4}$
		1.98, *2.07*	*2.34*	*1.80*, *1.98*		*3.53*		

of the complexation-induced chemical shifts of the methylene protons of $H_3N(CH_2)_nNH_3^{2+}$ guests upon inclusion in CB[6], there had not been a similar study conducted on a series of related guests in inclusion complexes with CB[7]. The upfield chemical shift changes for the ^{1}H NMR resonances of the core aryl and adamantyl protons of the guests range from –0.24 to –0.94 ppm, a similar range of shifts as observed by Mock and Shih (8) for the methylene protons (up to –1.08 ppm) of the α,ω-alkyldiammonium guests included in the cavity of CB[6]. The CISs of highest magnitude for the ligands in this study are found for the protons near the centers of the aromatic cores of the guests. Even with the guests shuttling back and forth between orientations that place one of the positively charged dihydroimidazoyl rings near one of the portals, these central protons remain in the cavity. The lower magnitude shifts in the range are observed for the protons near the ends of the aromatic cores of the longer and (or) more weakly bound guests ($BIBPY^{2+}$ and *trans*-$BIST^{2+}$), which may spend proportionately more time near the portals or outside the cavity as the guests move back and forth along the axis of the cavity.

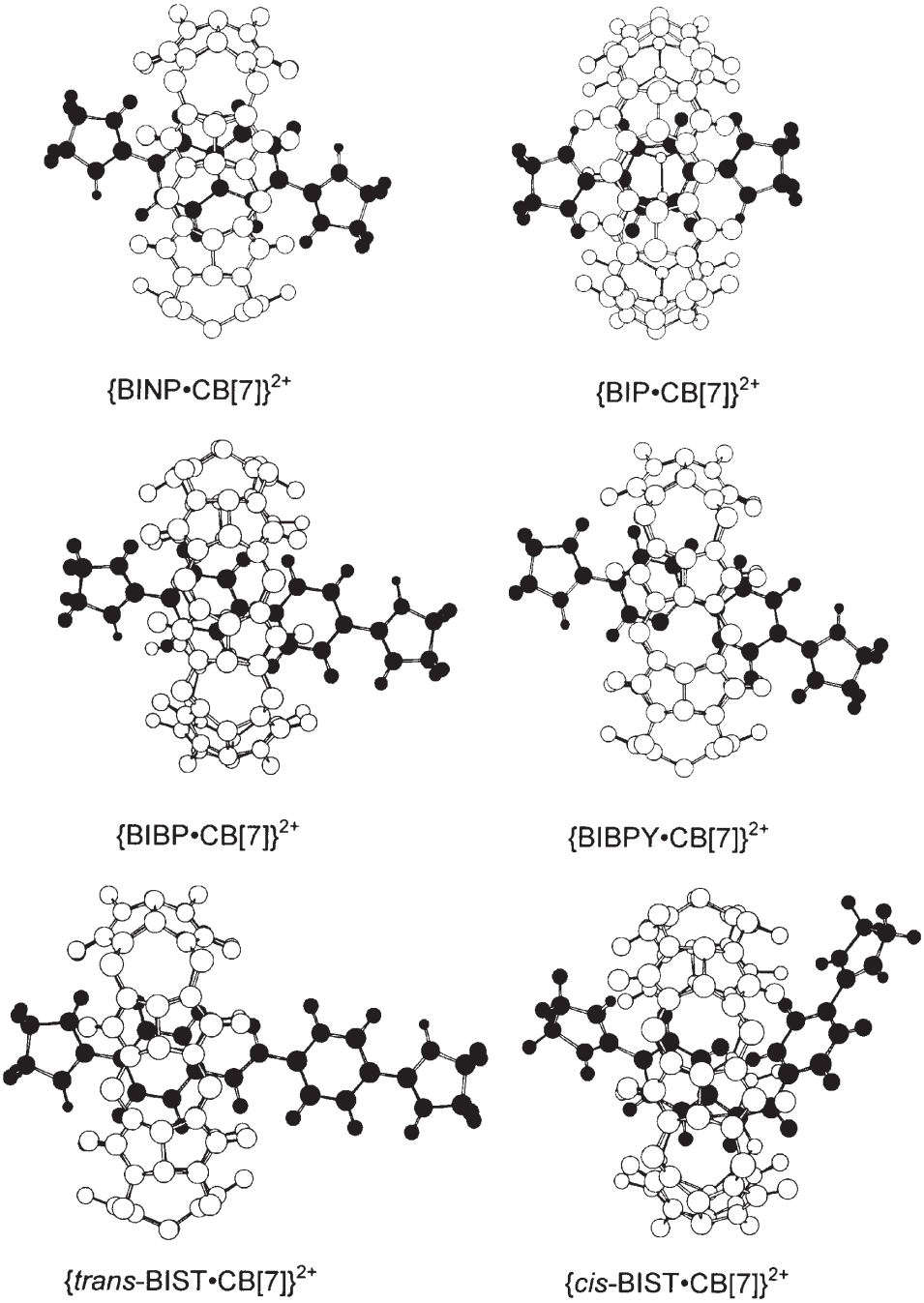
The further away that the cationic dihydroimidazolyl rings are from the portal carbonyl groups, on average, the less deshielding will be felt by the ethylene H_b protons on the ring. The largest CIS values for the H_b protons are observed for the shorter BIP^{2+} and $BINP^{2+}$ guests, while a much smaller value is exhibited by the more extended *trans*-$BIST^{2+}$. Using the distances between the C_a carbons on the rings as a measure of the extension of the guests (determined using Chem3D MM2 energy minimizations, see Fig. 2), a good correlation between the lengths of the guests (distances between the positive charges) and the CIS values for the H_b protons is established (see Fig. 3).

The inclusion of the dicationic guests in the cavity of CB[7] resulted in bathochromic shifts in the λ_{max}, with a lowering of the molar absorptivity coefficient for the π–π* transitions in the UV–vis spectra compared with the free guests (Table 2). This behaviour has also been observed with other dicationic guest molecules, such as methyl viologen (29, 30), 2,7-dimethyldiazapyrenium (31), and protonated 2-aminoanthracene (24). The bathochromic shifts are consistent with the solvatochromic behaviour of the aromatic guests within the CB[7] cavity, which has a less polar environment than the bulk aqueous solution (18, 36).

The stability constants for the host–guest inclusion complexes formed between CB[7] and the dicationic guests in this study (with the exception of the external binding of $BIAD^{2+}$, discussed later) are too large (>10^7 (mol/L)$^{-1}$) to be measured by conventional UV–vis spectrophotometric or ^{1}H NMR chemical shift titrations. The stability constants for the host–guest complexes formed between CB[7] and the cationic guests were thus determined by performing competitive binding studies, monitored by ^{1}H NMR spectroscopy, using guests whose stability constants with CB[7] had been reported previously (32). The 3-(trimethylsilyl)propionic acid-2,2,3,3-d_4 ($K_{CB[7]} = (1.82 \pm 0.22) \times 10^7$ (mol/L)$^{-1}$ (32)) was employed as the competitor for the BIP^{2+}, $BIBP^{2+}$, $BIBPY^{2+}$, *trans*-$BIST^{2+}$, and IAD^+ guests, while (trimethylammonio)methylferrocene iodide ($K_{CB[7]} = (3.31 \pm 0.62) \times 10^{11}$ (mol/L)$^{-1}$ (22, 32)) was used for the $BINP^{2+}$ guest.

The stability constants (Table 1) for the aromatic guests decrease in the order $BINP^{2+}$ > BIP^{2+} > *trans*-$BIST^{2+}$ > $BIBP^{2+}$ > $BIBPY^{2+}$. The trend is likely the result of several factors, including (*i*) the length of the aromatic core (distance between the positive charges), (*ii*) the fit of the aromatic core to the interior of the CB[7] cavity, and (*iii*) the hydrophobicity of the aromatic core. The highest stability constant is observed for the guest with the naphthyl core, suggesting that this guest optimizes the fit of the aromatic core with the CB[7] cavity and the cation–dipole and hydrogen bonding interactions between the dihydroimidazoyl groups and the portal carbonyl groups. The lowest stability constant among this set of guests is observed for $BIBPY^{2+}$. This is not unexpected as the introduction of the N hetero-

Fig. 2. Energy-minimized structures of the CB[7] host–guest complexes with $BINP^{2+}$, BIP^{2+}, $BIBP^{2+}$, $BIBPY^{2+}$, and *trans*- and *cis*-$BIST^{2+}$. The hydrogen atoms on CB[7] have been removed for clarity.



atoms into the bipyridine rings would reduce the hydrophobicity of the aromatic core and the stability constant compared with the biphenyl core of the $BIBP^{2+}$ guest.

The mono(IAD^{+}) and bis(dihydroimidazolyl) ($BIAD^{2+}$) substituted adamantane cations exhibit different modes of binding to CB[7] and CB[8]. For the monocation, the adamantyl portion binds tightly to the interior of CB[7] (Fig. 4), as reported previously for the protonated 1-aminoadamantane (32), with upfield shifts in the adamantyl proton resonances and a large downfield shift for the H_b protons on the dihydroimidazolyl ring. Contrary to the observation of binding of the 1,3-diaminoadamantane in the cavity of CB[7] (32), we observe that only external binding occurs with the $BIAD^{2+}$ dication. The 1,3-bis(4,5-dihydro-1*H*-imidazol-2-yl)adamantane ($BIAD^{2+}$) guest is too large to form a guest–host complex with CB[7], in which the adamantyl core is located in the cavity of the host. The H_b protons on the ring shift upfield (–0.32 ppm), while the adamantyl protons shift downfield (+0.06 to +0.12 ppm). These changes in the chemical shifts of the guest protons, upon the addition of CB[7], reveal that it is one of the dihydroimidazolyl rings that is located in the cavity, while

Fig. 3. Plot of the downfield chemical shift change ($\Delta\delta$) for the H_b protons upon inclusion of the dicationic guests in cucurbit[7]uril as a function of the distance between the C_a carbon atoms of the two dihydroimidazolyl rings. BIP^{2+} (■), $BINP^{2+}$ (●), *cis*-$BIST^{2+}$ (Δ), $BIBP^{2+}$ (▼), $BIBPY^{2+}$ (◆), and *trans*-$BIST^{2+}$ (▲).

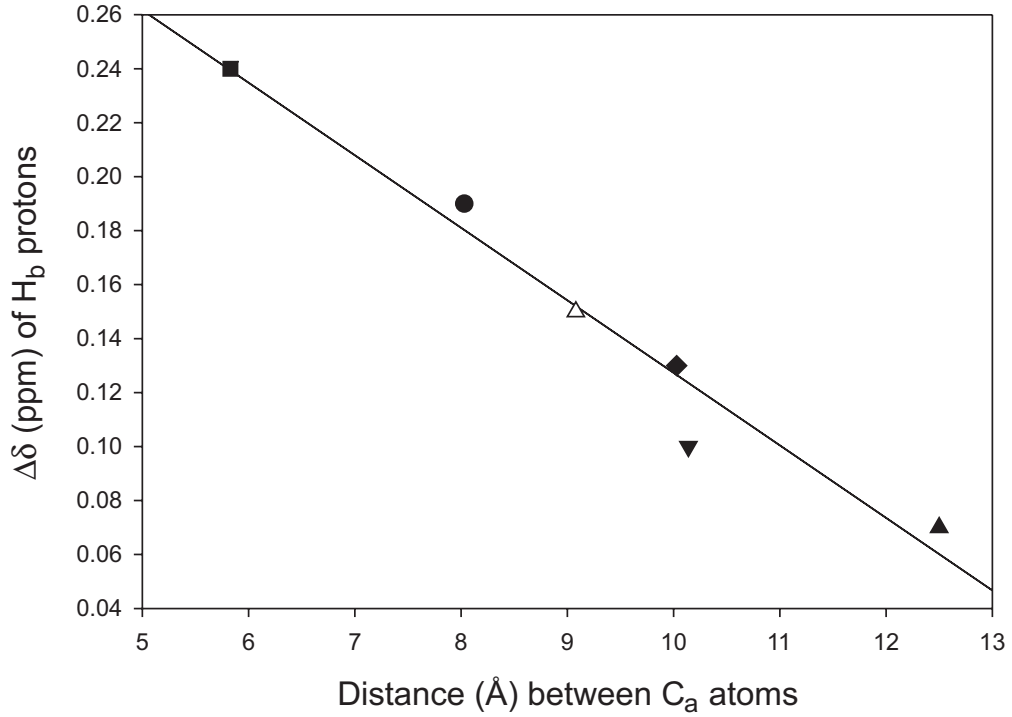


Table 2. Wavelength maxima and molar absorptivity coefficients of the bis(4,5-dihydroimidazol-2-yl) dicationic guests and the guest–host complexes with CB[7] in aqueous solution.

Guest	λ_{max} (nm)	ε ($(mol/L)^{-1}$ cm^{-1})
$[BINP]^{2+}$	246	6.41×10^4
$\{BINP\cdot CB[7]\}^{2+}$	250	4.53×10^4
$[BIP]^{2+}$	246	3.76×10^4
$\{BIP\cdot CB[7]\}^{2+}$	244	2.11×10^4
$[BIBP]^{2+}$	288	3.96×10^4
$\{BIBP\cdot CB[7]\}^{2+}$	290	2.98×10^4
$[BIBPY]^{2+}$	252	1.04×10^4
	300	1.67×10^4
$\{BIBPY\cdot CB[7]\}^{2+}$	258	8.40×10^3
	308	1.56×10^4
$[trans\text{-}BIST]^{2+}$	336	6.44×10^4
$\{trans\text{-}BIST\cdot CB[7]\}^{2+}$	344	4.29×10^4

the remainder of the guest is outside. The presence of only average resonances for the guest in the presence of a stoichiometric deficiency of CB[7] indicates that the guest is exchanging between the bound and unbound states rapidly on the NMR timescale.

A chemical shift titration and Job's plot of the $BIAD^{2+}$ with CB[7], as depicted in Fig. 5, confirms a 1:1 stoichiometry (maximum at $\chi^{BIAD} \approx 0.5$) and yields a stability constant of $(1.0 \pm 0.5) \times 10^4$ $(mol/L)^{-1}$. As indicated earlier, the protonated 1,3-diaminoadamantane guest forms a very stable complex with CB[7], in which the adamantyl core is located in the cavity. The smaller size of the ammonium group compared with the 4,5-dihydroimidazol-2-yl ring may account for the difference in the accessibility of the guest to the cavity. The addition of the larger CB[8] host to a solution of $BIAD^{2+}$, however, does result in the formation of an internal inclusion complex (Fig. 4), and the expected upfield shifts in the adamanyl proton resonances with downfield shifts in the H_b protons of the 4,5-dihydroimidazol-2-yl rings are observed.

A comparison of the binding behaviours of CB[7] with the CDs was undertaken in which the $[BIBP]^{2+}$ guest was mixed with slight stoichiometric excesses of α-, β-, and γ-CD and the ^1H NMR spectra compared to the inclusion complex formed with CB[7]. The $[BIBP]^{2+}$ guest undergoes inclusion complex formation with β- and γ-CD (but not the smaller α-CD cavity), exhibiting fast guest exchange on the NMR timescale. The larger ^1H NMR CIS values for the $[BIBP]^{2+}$ guest are observed for inclusion by β-CD, with its similar cavity size to CB[7].

The *trans*-$BIST^{2+}$ dication undergoes a photochemical isomerization to *cis*-$BIST^{2+}$ under UV irradiation in aqueous solution.[2] Inclusion of the *trans*-$BIST^{2+}$ guest in CB[7] also facilitates photoisomerization and eliminates photohydration side products. The resulting $\{cis\text{-}BIST\ B[7]\}^{2+}$ complex exhibits similar, but somewhat larger, chemical shifts of the guest protons upon inclusion in the CB[7] cavity. This is most likely the result of a more compact guest core within the CB[7] cavity.

We are currently investigating the CB[7] inclusion of other dicationic guest molecules with 4,5-dihydroimidazol-

[2] R. Wang, L. Yuan, D.S.N. Hettiarachchi, and D.H. Macartney. Manuscript in preparation.

Fig. 4. Energy-minimized structures of the CB[7] host–guest complex with IAD^+ and the CB[8] host–guest complex with $BIAD^{2+}$. The hydrogen atoms on CB[7] have been removed for clarity.

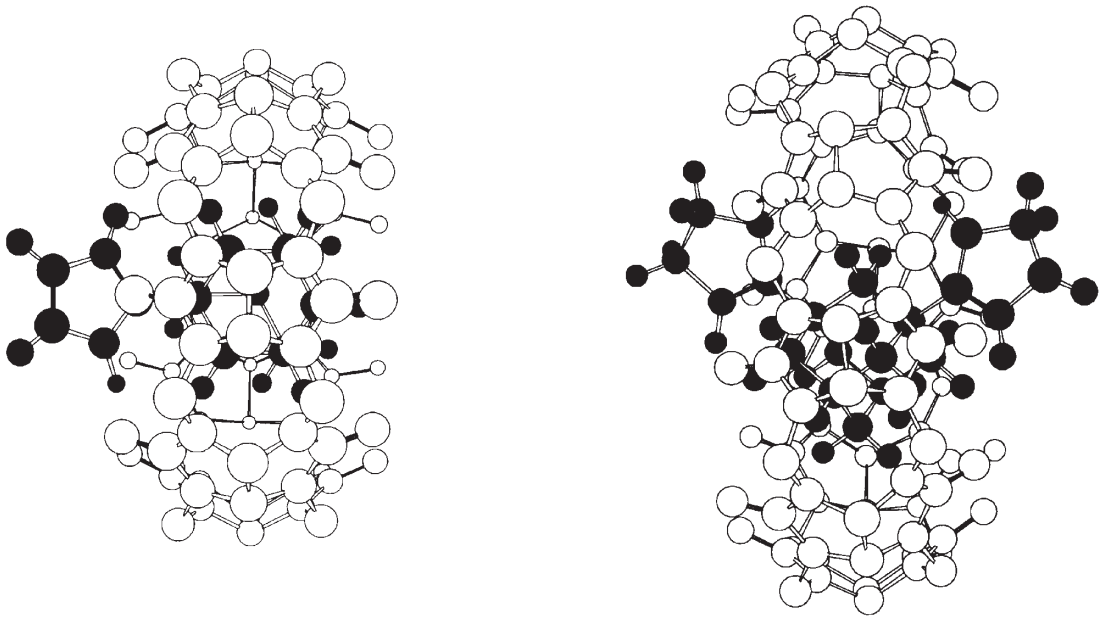
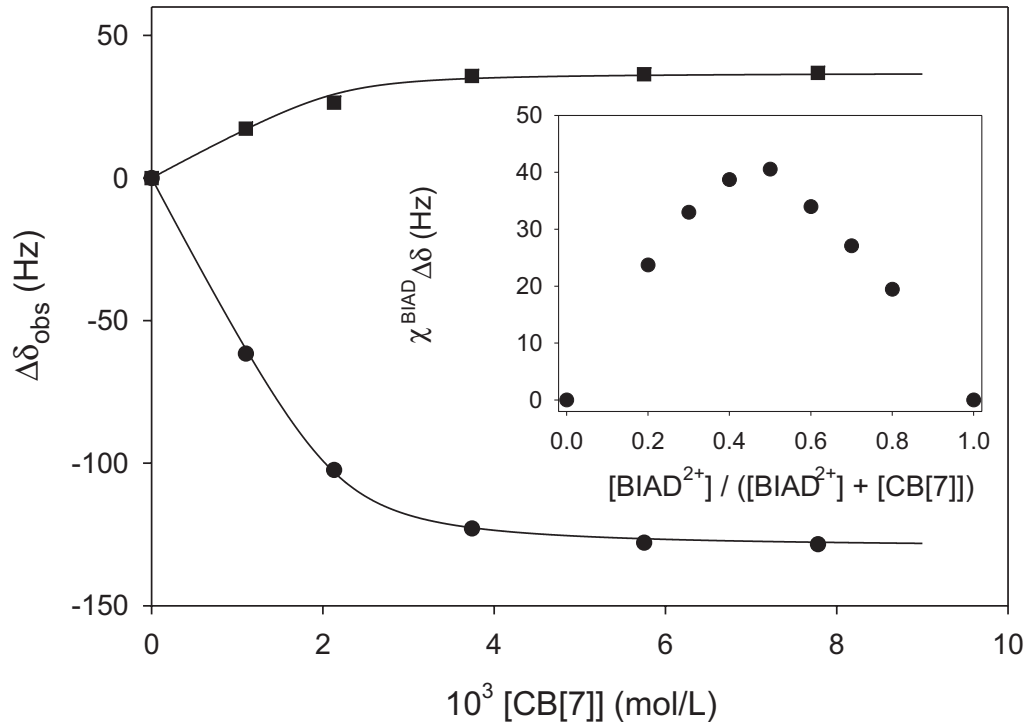


Fig. 5. A ^1H NMR chemical shift titration of $[BIAD]^{2+}$ (2.2×10^{-3} mol/L) with CB[7] in D_2O at 25 °C. The solid lines represent the fits of the H_b (●) and H_4 (■) resonances to a 1:1 binding model with a guest–host stability constant of 1.0×10^4 $(mol/L)^{-1}$. Inset: Job's plot of $\chi^{BIAD}\Delta\delta$ against $[BIAD^{2+}]$ / ($[BIAD^{2+}]$ + [CB[7]]) for the guest H_b resonance.



2-yl and related cationic end groups, including the protonated forms of the water-soluble azo radical initiators azobis[2-(4,5-dihydro-1*H*-imidazol-2-yl)propane] and azobis(2-amidinopropane). Preliminary studies indicate that these initiators bind to CB[7] with comparable strength to the guests in the present study and that inclusion in the CB[7] cavity significantly stabilizes them with respect to unimolecular decomposition to carbon-centered radicals.

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