Induced Circular Dichroism Detection of Chiral Ammonium Guests through Inclusion in Calix[*n*]arene Cavities

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p-Sulfonatocalix[*n*]arenes include chiral quaternary ammonium guests in water and give the induced circular dichroism (ICD) spectra specific to the guest chirality and shape; the ICD bands arise from guest-induced asymmetric deformation of the benzene array in calix[*n*]arenes.

Cavity-shaped host molecules, calix[*n*]arenes are frequently compared with cyclodextrins. Although these two macrocyclic systems have several merits and demerits as host molecules,[1,2] the largest differences are (i) in the UV region calix[*n*]arenes have a π–π* absorption band of benzene chromophores whereas cyclodextrins are transparent and (ii) calix[*n*]arenes are achiral whereas cyclodextrins are chiral.[1,2] To compensate demerit (ii) of calix[*n*]arenes we previously synthesised several chiral calix[*n*]arenes by introducing either chiral substituents[3] or molecular asymmetries.[4–7] We found that these chiral calix[*n*]arenes show clear exciton coupling bands in circular dichroism (CD) spectroscopy.[3–5] It was later confirmed that the CD activity is basically ascribed to the chiral orientation of a diphenylmethane unit combined in calix[*n*]arenes.[6,7] In these systems the sign of the exciton coupling helps us to predict how the phenyl rings are arranged by chiral substituents or molecular asymmetries. Hence, demerit (i) rather serves as a merit in CD studies.

Here, it occurred to us that when chiral guest molecules are included in achiral calix[*n*]arene cavities, the benzene ring array may be arranged in an asymmetric manner and the absolute configuration of the guest may be 'read out' by induced circular dichroism (ICD) of calix[*n*]arenes. It is known that trimethylammonium ions are included in the cavities of water-soluble calix[*n*]arenes $\mathbf{1}_n$ with the aid of the cation-π interaction.[8–10] This specific binding mode may be useful to induce the chiral deformation of the benzene ring array. With these objects in mind we measured CD spectra of $\mathbf{1}_n$ in the presence of various chiral trimethylammonium ions (**2**–**5**).

The CD and NMR spectra were measured at 25 °C with a JASCO J-720 spectropolarimeter and a Bruker ARX-300 NMR apparatus, respectively. The solution pH was controlled by HCl and NaOH because addition of buffer species (*e.g.* sodium phosphate) weakened the intensity of the CD bands.

Fig. 1 shows ICD spectra of $\mathbf{1}_4$ in the presence of **3**. The CD spectra arising from **3** are offset using a memory system in the apparatus. It is clearly seen that included (*R*)-**3** induces the negative exciton coupling with the negative first Cotton effect and the positive second Cotton effect, indicating that the benzene array is deformed to (*S*)-chirality, whereas included (*S*)-**3** induces the symmetrical spectrum to (*R*)-**3**, indicating that the benzene array is deformed to (*R*)-chirality. Similar ICD spectra were also observed for several combinations of $\mathbf{1}_n$ and **2**–**5**. The spectral parameters are summarised in Table 1.

Examination of Table 1 brings us to question why some

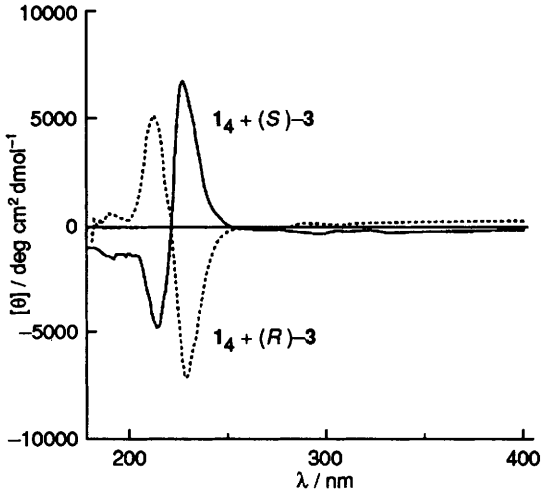


Fig. 1 ICD spectra of $\mathbf{1}_4$ (0.10 mmol dm^{-3}) in the presence of (*R*)- and (*S*)-**3** (0.10 mmol dm^{-3}) at 25 °C and pH 7.0

Table 1 CD Spectral parameters of $\mathbf{1}_n$ complexes[a]

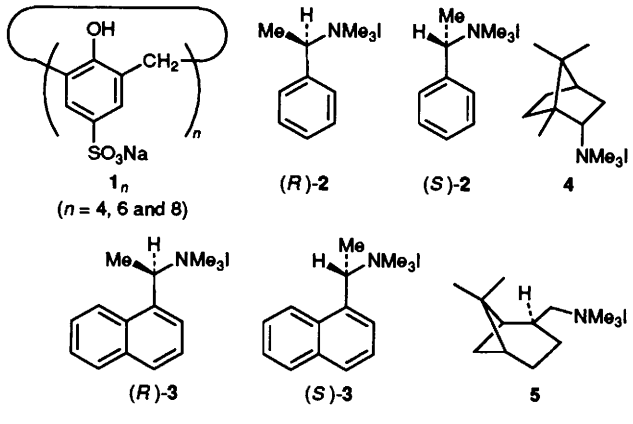
Guest	Host $\mathbf{1}_n$	Exciton type	CD (nm) $\lambda_{\theta=0}$	CD (nm) λ_{min}	CD (nm) λ_{max}	UV/nm λ_{max}
(*R*)-**2**	4	silent				
	6	+	209	203	214	210
	8	+	213	208	220	210
(*S*)-**2**	4	silent				
	6	−	208	215	203	210
	8	−	214	220	207	210
(*R*)-**3**	4	−	222	227	213	222
	6	−	203	212	196	210
	8	+	216	207	228	210
(*S*)-**3**	4	+	221	213	228	222
	6	+	204	196	214	210
	8	−	219	229	207	210
4	6	−	203	217	192	208
5	8	−	214	220	206	208

[a] [Calix[*n*]arenes] = [chiral guest] = 0.10 mmol dm^{-3} at 25 °C and pH 7.0.

Table 2 Chemical shift changes of (*R*)-**2** and (*R*)-**3** induced by the addition of $\mathbf{1}_n$[a]

	(*R*)-**2**				(*R*)-**3**			
$\mathbf{1}_n$	C*H	Me	N⁺Me	ArH	C*H	CH_3	N^+CH_3	ArH
4	1.2	1.1	1.7	0.43	1.0	1.2	1.6	0.43
6	0.72	0.59	1.1	0.22	0.48	0.47	1.1	0.13
8	0.88	0.70	0.78	0.63	0.46	0.44	0.77	0.32

[a] [$\mathbf{1}_n$] = 0.10 mol dm^{-3}, [(*R*)-**2**] = [(*R*)-**3**] = 0.010 mol dm^{-3}, at 25 °C and pD 7.0.



guests make $\mathbf{1}_n$ CD-active while some guests are ineffective. The binding modes of **2**–**5** can be specified by ^{1}H NMR spectroscopy. Particularly, we carefully examined the ^{1}H NMR spectra of the $\mathbf{1}_n$·**2** and $\mathbf{1}_n$·**3** complexes. The chemical shift changes induced by these guest molecules are summarised in Table 2. Judging from the CPK molecular models, $\mathbf{1}_4$ can include either the ammonium moiety or the phenyl moiety of **2** whereas $\mathbf{1}_6$ and $\mathbf{1}_8$ can include the whole molecule in their cavities. Similarly, $\mathbf{1}_4$ and $\mathbf{1}_6$ can include either the ammonium moiety or the naphthyl moiety of **3** whereas $\mathbf{1}_8$ can include the whole molecule in its cavity. Examination of Table 2 reveals that the prediction made on the basis of the CPK model building is well reflected by the spectral change. Although all chemical shifts move to higher magnetic field in the presence of $\mathbf{1}_n$, the shift of δ_{N+Me} (1.1–1.7) is much greater (by more than 1.0) than that of δ_{ArH} in $\mathbf{1}_4$ + **2**, $\mathbf{1}_4$ + **3** and $\mathbf{1}_6$ + **3**, supporting inclusion of the ammonium moiety, whereas the difference is relatively small (0.32–0.63) in $\mathbf{1}_6$ + **2**, $\mathbf{1}_8$ + **2** and $\mathbf{1}_8$ + **3**, supporting inclusion of the whole molecule. Comparison of Table 2 with Table 1 proves that except CD-silent $\mathbf{1}_4$ + **2**, the former group shows (*S*)-chirality and the latter group shows (*R*)-chirality for (*R*)-guest: that is, inclusion of the ammonium moiety deforms the benzene array in (*S*) whereas inclusion of the whole molecule deforms the benzene array in (*R*). It is predictable from the CPK molecular model studies that inclusion of the ammonium moiety of **2** in $\mathbf{1}_4$ with the shallow cavity does not cause the steric repulsion between the benzene rings in $\mathbf{1}_4$ and the phenyl groups in **2**, but in other systems inclusion inevitably causes some steric repulsion. This steric repulsion induces asymmetric deformation of the benzene array and becomes the origin of the CD-activity.

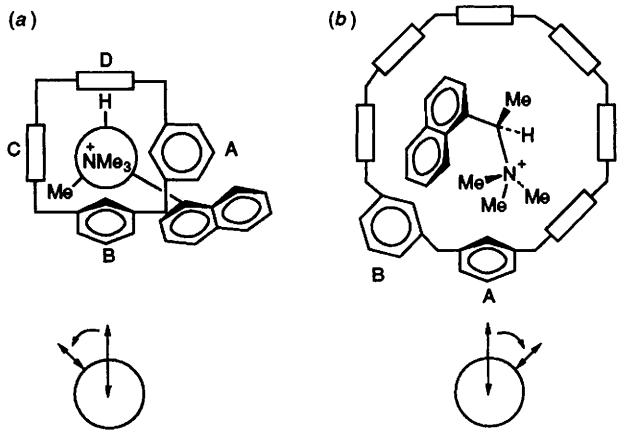


Fig. 2 (*a*) The $\mathbf{1}_4$·(*R*)-**3** complex viewed from the lower rim and (*b*) the $\mathbf{1}_8$·(*R*)-**3** complex viewed from the lower rim. The OH and SO_3^- groups in $\mathbf{1}_n$ are omitted for clarity.

How can we explain the sign of the exciton coupling? The structure in Fig. 2*a* shows a view of the $\mathbf{1}_4$·(*R*)-**3** complex from the lower rim. When the ammonium moiety is included in the cavity, naphthyl (largest) → Me → H (smallest) groups are arranged in a clockwise direction. The largest steric repulsion is generated between the naphthyl group and benzenes A and B, inducing the orientation of these benzene units whereas benzenes C and D are less immobilised because the contacting H and Me groups are sterically smaller. This suggests that the CD-activity stems from the orientation of benzenes A and B. Here, benzene A flanked by the naphthyl group and H should be more flattened into the cavity than benzene B flanked by the naphthyl group and Me. This orientation is (*S*) which gives the negative exciton coupling. On the other hand, it is difficult to image the orientation of the benzene array for inclusion of the whole molecule. Presumably, the largest steric crowding occurs at around the naphthyl group or the N^+Me_3 group. If so, benzene B close to the flat naphthyl group is more flattened and benzene A close to the spherical N^+Me_3 group stands up. This binding mode results in the (*R*) orientation which gives the positive exciton coupling (Fig. 2*b*). Hence, the sign of the exciton coupling can be explained by guest-induced deformation of the two benzene units.

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