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Carceroisomerism and twistomerism in C_{4v} tetraoxatetrathiahemicarceplexes

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Abstract

Four new C_{4v} tetraoxatetrathiahemicarceplexes were synthesized and characterized. Their carceroisomers and half-twistomers were simultaneously observed by ^{1}H NMR spectra at low temperature. The largest isomerization energy barrier of carceroisomers was 15.5 kcal mol^{-1} and the isomerization energy barriers of twistomers are significantly larger than those of carceroisomers.

Keywords: resorcin[4]arenes; carcerand; hemicarcerand; carceroisomer; half-twistomer.

New types of isomerisms in a confined carceplex or a hemicarceplex are emerging as a stimulating research field due to their potential as a molecular spin or molecular switch for data storage device and molecular electronics.[1] D_{4h} and C_{4v} container hosts composed of two resorcin[4]arene moieties could lead stable helical conformational stereoisomers, so-called twistomers,[2] stabilized by the host's constrictive binding property. In C_{4v} carcerand composed of two different hemispheres the different orientations of unsymmetrical guests through the long (C_4) axis of these hosts could also lead to different stereoisomers, which Reinhoudt et al. called carceroisomer.[3]

Usually carceroisomer interconversion, which appears to be faster than twistomer interconversion,[2] could be manipulated by the degree of confinement of interior and the secondary interactions between host and guest such as hydrogen bonding, dipole or charge interactions, whereas twistomer interconversion could be manipulated by constrictive binding property of host which mainly depends on the nature of bridges connecting two hemispheres, whose effects depending on its number or length have been reported,[1] but the effects of symmetry or heavy atom of bridge have not been explored. Here we report the synthesis and distinctions of new resorcin[4]arene-based C_{4v} tetraoxatetrathiahemicarcerands, whose carceroisomers and unprecedented half-twistomers were observed by the splitting of the guest's ^{1}H NMR spectra at low temperature.

Tetraiodide **2a** and **2b** were prepared in ~90% yields by refluxing a mixture of NaI/MEK and the corresponding tetrachlorides obtained from their tetrols[4] by treating with a mixture of

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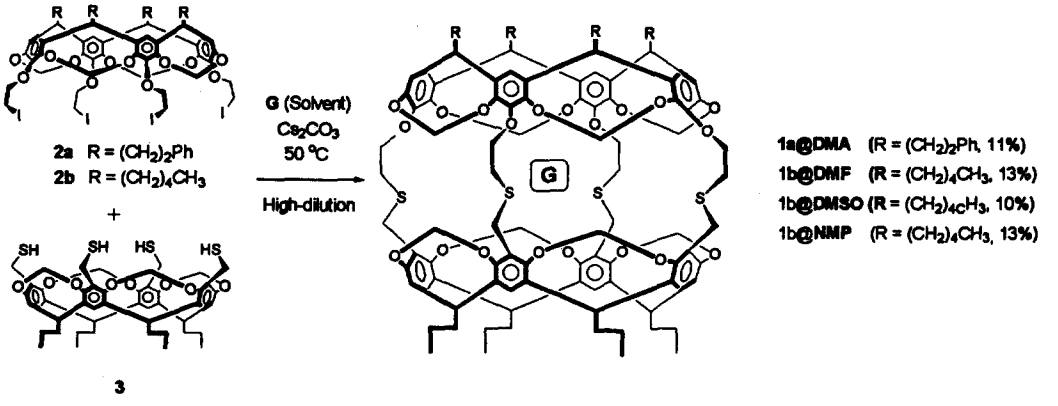
$TsO(CH_2)_2Cl/K_2CO_3/DMF$ at 50°C. Tetrathiol **3** was obtained from the corresponding tetrabromide (92%).[5] Under high dilution conditions, the shell closing reaction between tetraiodide **2a** or **2b** and tetrathiol **3** in a mixture of (G)/Cs_2CO_3 at 50°C produced tetraoxatetrathiahemicarceplexes **1a@G** or **1b@G** in 10–13% yields (Scheme 1).[6] Although large templating effects of pyrazine and 1,4-dioxane for resorcin[4]arene-based carcerands were reported,[7] pyrazine- or 1,4-dioxane-containing hemicarceplex was not detected. When acetonitrile (MeCN) was used as solvent, the free hemicarcerand **1b** was isolated in 20% yield. But the attempts to put various potential guests into the empty hemicarcerand **1b** at high temperature were unsuccessful.

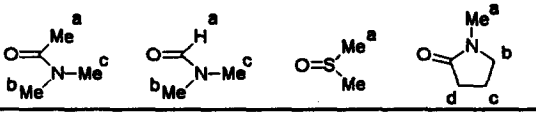


Scheme 1.

The chemical shifts of most of the hydrogens attached to the global parts of the hosts changed upon complexation. Especially, inner OCH_2O protons of the propyl-feet hemisphere (tetrathiahemisphere, B moiety in Fig. 2) showed the large downfield shifts ranging from 0.08 to 0.25 ppm upon complexation. Table 1 records the chemical shifts in the 400 MHz ^1H NMR spectra of complexed and free guests as well as their differences ($\Delta\delta$) in host **1a** and **1b** in $CDCl_3$. Upon complexation, the ^1H NMR spectra show large upfield shifts of the guests ranging from 1.19 to 3.50 ppm due to the shielding effect of the aromatic moieties of host. As the size of guests increases, the chemical shifts of complexed guests become more upfield shifted because the larger guest approaches more closely to the shielding zone of the aromatic moieties. H_a of NMP in **1b** showed the largest upfield shift (3.50 ppm), but H_c and H_d of NMP in **1b** showed rather small changes (2.89, 2.93 ppm, respectively), which implies that due to the steric effect H_c and H_d cannot be close to the hemisphere's shielding zone. Contrary to this, H_a and H_b of DMA in **1b** showed the similar chemical shift changes (3.43, 3.34 ppm, respectively), owing to their similar steric circumstances.

As shown in Fig. 1(a), ^1H NMR chemical shifts of DMA in host **1a** appeared as two equal singlets at room temperature, which remained up to 187°C. As the temperature of **1a**@DMA in CD_2Cl_2 decreased, two singlets were broadened, and then below –90°C, the chemical shifts of incarcerated DMA were split into two new resonances at δ –0.24 (two singlets, minor) and –0.72 (singlet, major) for the *N*-methyl group *trans* to the carbonyl, and at δ –1.26 (two singlets, major) and –1.83 (singlet, minor) for the acetyl, respectively. The integration ratios of major to minor signals of guest were 3:1, which implies the presence of two normal carceroisomers in 3:1 ratio. 2D NOESY experiments of **1a**@DMA in CD_2Cl_2 at –90°C showed cross peaks between acetyl group of DMA and protons on thiahemisphere B as well as those between N–CH_3 *trans* to C=O and protons on oxahemisphere A, which confirms that the major carceroisomer is as shown in Fig. 2(a) (left). However, the interesting point is the presence of two singlets at –0.24 and –1.26 ppm for the thiahemisphere-directing *trans* *N*-methyl of minor carceroisomer and for

Table 1
^{1}H NMR spectral chemical shifts of free and complexed guests in host **1a** and **1b** in $CDCl_3$ at 25°C



Host	Guest	H	free δ	compl δ	$\Delta\delta$
1a	DMA	a	2.09	-1.33	3.42
		b	3.02	-0.31	3.33
		c	2.94	1.69	1.25
1b	DMF	a	7.99	6.23	1.76
		b	2.94	1.75	1.19
		c	2.86	-0.88	2.94
1b	DMSO	a	2.61	-0.34	2.95
1b	NMP	a	2.85	-0.65	3.50
		b	3.40	1.85	1.55
		c	2.05	-0.84	2.89
		d	2.35	-0.58	2.93

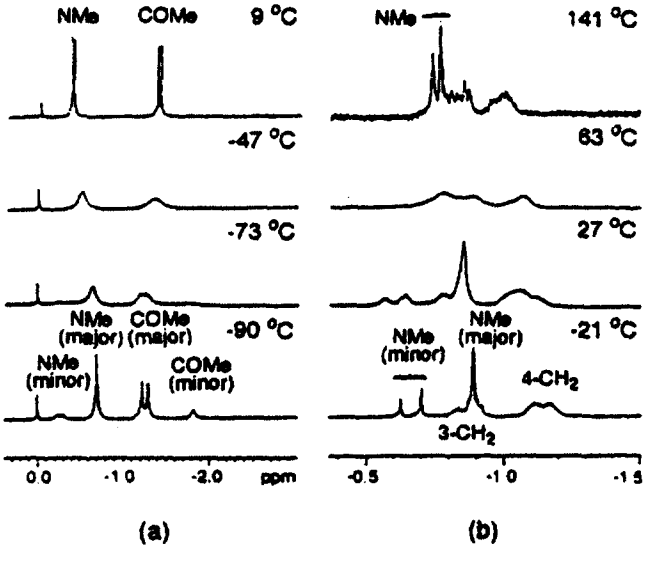


Figure 1. The partial ^{1}H NMR spectra (500 MHz) of **1a**@DMA (a) and **1b**@NMP (b) in CD_2Cl_2 at various temperatures (in $C_6D_5NO_2$ at 63°C and 141°C)

the thiahemisphere-directing acetyl group of major carceroisomers, respectively, which we assumed is due to the stable twistomerism at thiahemisphere moiety (B). These half-twistomers did not coalesce each other, but two carceroisomers coalesced each other by the rapid end-to-end rotation of DMA vertical to the C_4 axis to give two sets of two singlets at –0.31 ppm for *trans* *N*-methyl and at –1.33 ppm for acetyl at high temperature.

The simultaneous observation of twistomers and carceroisomers of **1b**@NMP under the same condition was possible even at 27°C (Fig. 1(b)). At a temperature below –21°C, the ^{1}H NMR chemical shifts of *N*-methyl group of **1b**@NMP clearly showed that carceplex **1b**@NMP exists in major (the singlet at

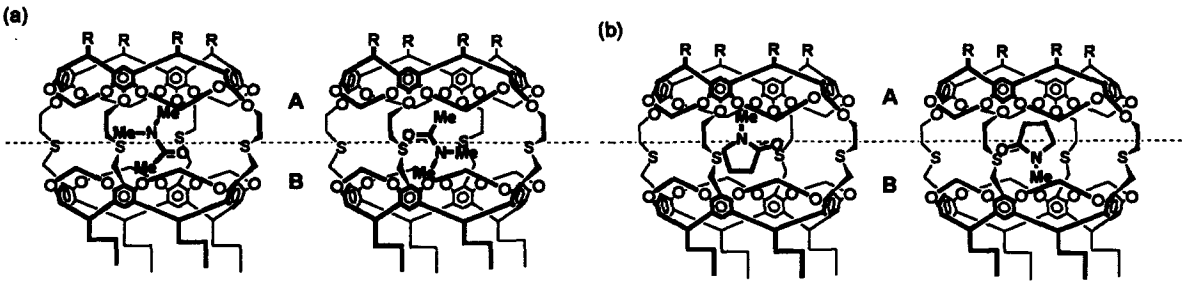


Figure 2. Suggested orientation of guests in the major (left) and minor isomer (right) of (a) **1a**@DMA (R=$(CH_2)_2Ph$) and (b) **1b**@NMP (R=$(CH_2)_4CH_3$)

Table 2
The rate constant (k), coalescence temperature (T_c), and rotational barrier ($\Delta G_c^{\neq}$) for isomerization of carceroisomers

Host	Guest	k(Hz)	T_c	$\Delta G_c^{\neq}$ (kcal mol^{-1})
1b	DMSO	-	<-116℃	-
1a	DMA	559±2	-61℃	9.6±1
1b	DMF	773	-39℃	10.5±1
1b	NMP	255	50℃	15.4±1

*Determined by variable-temperature ^{1}H NMR (500 Hz,CD_2Cl_2 or $C_6D_5NO_2$).

δ –0.89) and minor (two unequal singlets at δ –0.63 and –0.70) carceroisomers at 2:1. The two unequal singlets of minor isomer implies that the stabilities of two twistomers are different from each other due to the prochirality of NMP. Its NOESY experiments in CD_2Cl_2 at –21°C showed that *N*-methyl group of the major isomer is directing the A moiety (Fig. 2(b), left).

Table 2 records the energy barriers for carceplex isomerization on a 500 MHz ^{1}H NMR time scale. The coalescence temperature of **1b**@DMSO was below –116°C. For **1a**@DMA, four isomers coalesced to two isomers at –61°C to give the rotational barrier ($\Delta G_{212K}^{\neq}$) of 9.6±1 kcal mol^{-1}. The rotational barrier of **1a**@DMF, $\Delta G_{234K}^{\neq}$=10.5±1 kcal mol^{-1}, is slightly higher than that of **1b**@DMA. The *N*-methyl proton peaks of NMP were coalesced to two unequal singlets at 50°C to give $\Delta G_{323K}^{\neq}$=15.4±1 kcal mol^{-1}, which is the largest reported ever[2] and 5.8 kcal mol^{-1} higher than that of **1a**@DMA primarily due to the larger size and rigidity of NMP. Until 141°C in $C_6D_5NO_2$, the *N*-methyl proton peaks of **1b**@NMP remained as two unequal singlets, which confirms the stability of half-twistomers as noted for **1a**@DMA.

CPK molecular model shows that the cavity of B moiety is smaller than that of A moiety due to the inward-directing sulfur atoms. ^{1}H NMR spectra in Fig. 1 show that the guest's peaks located in the B moiety are split into the doublet, slightly downfield shifted, whereas the peaks located in the A moiety are not split and more upfield shifted. It is probable that the twistomer isomerization at A moiety is faster on a ^{1}H NMR time scale but that at B moiety is slower on a ^{1}H NMR time scale due to the large rotational barrier of thia bonds, which results in the unprecedented half-twistomerism.

When any kind of supramolecular isomerism in container molecules could be manipulable at amenable temperature and these container molecules could be applied as matrixes for guest aligning, unprecedented molecular devices utilizing molecular spin concept could be developed.

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