closely resemble the structures previously proposed for other tapered liquid crystalline materials.[6] However, in the present case, the macrocyclic structure is unreasonable since it would orient the polar oxo groups not assembled in the polymer inward, which generates strong repulsive forces at the column's core. Additionally, macrocyclic association would require the planes of all of the pyridine rings to be oriented along the column's axis. This organization would be highly unusual for a thermotropic liquid crystal since it does not allow for optimal dipolar interactions between neighboring aromatic rings. Thus, we propose that **1** displays the superstructure shown at the bottom of Scheme 2 with the $(\cdots Mo{=}O\cdots Mo{=}O\cdots)_n$ polymeric chain oriented along the column's axis. This organization gives rise to supermolecular dipoles along the columns axis which are frustrated by the hexagonal symmetry of the mesophase. The fluid nature should allow for a facile reorientation of these dipoles, and the electrical properties of these novel materials will be the subject of future reports.

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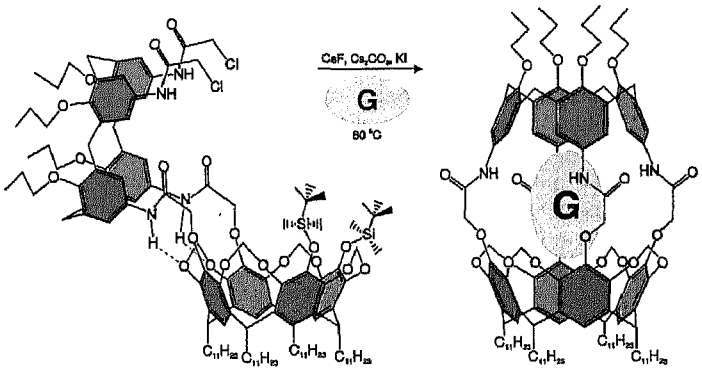
[12] The size of the mesogenic core is defined as the distance from the molybdenum center to the 4' oxygen attached to the phenyl ring. According to crystal structure data (ref. [9]) and computer modeling this distance is 13.0 Å.

A Novel Type of Stereoisomerism in Calix[4]arene-Based Carceplexes

Peter Timmerman, Willem Verboom, Frank C. J. M. van Veggel, John P. M. van Duynhoven, and David N. Reinhoudt*

Carcerands are well known for the ability to trap guest molecules in their interior.[1, 2] During synthesis they form carceplexes by capturing guest molecules from the medium that cannot leave the cavity without the rupture of at least one covalent bond of the host.[3–6]

All carcerands hitherto synthesized have D_{4h} symmetry. Different orientations of the guest molecule inside such cavities do not lead to diastereomeric structures due to the overall symmetry of the carceplex. In a previous paper we reported the first carceplex constructed from both a calix[4]arene and a resorcinol unit (**2**), which has C_{4v} symmetry.[7] This carceplex containing one molecule of *N*,*N*-dimethylformamide (DMF) inside the cavity[8] was isolated in 27% yield as a by-product in the synthesis of an organic molecule with a rigid cavity of nanometer dimensions.[7] Here we report two new carceplexes (**3** and **4**) and describe their synthesis, structure, and dynamic behavior. These carceplexes exhibit a novel type of stereoisomerism as a result of different orientations of the guest molecule inside the cavity.



When a solution of **1**, which was prepared as described previously,[7] in *N*,*N*-dimethylacetamide (DMA) was added over 8 hours to a solution of CsF, Cs_2CO_3, and KI in DMA at 80 °C, and the mixture stirred for a further 16 hours at this temperature, carceplex **3** was isolated without further purification in essentially quantitative yield. The ^{1}H NMR spectrum of **3** (Fig. 1) is consistent with C_{4v} symmetry, indicating that rotation of the guest DMA molecule about the molecular axis is fast on the ^{1}H NMR (chemical shift) time scale.[9] All guest proton signals exhibit dramatic upfield shifts as a result of the shielding effect of the aromatic rings. Similar upfield shifts of guest proton signals have been frequently observed for the "Cram" carcerands.[4, 5] The spectrum of **3** shows two broad singlets at $\delta = -1.0$ and -2.0, representing the *N*-methyl group *cis* to the carbonyl group that normally resonates at $\delta = 2.8$, and the methyl group of the acetyl unit, which resonates $\Delta\delta = 4.0$ up-

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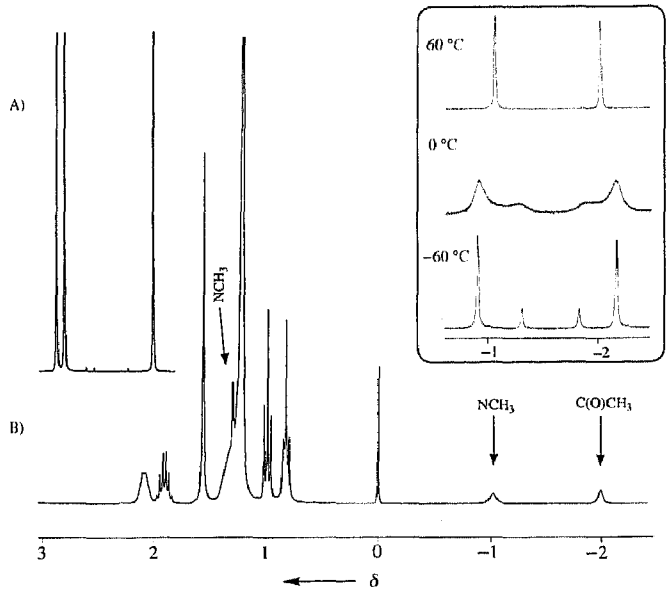
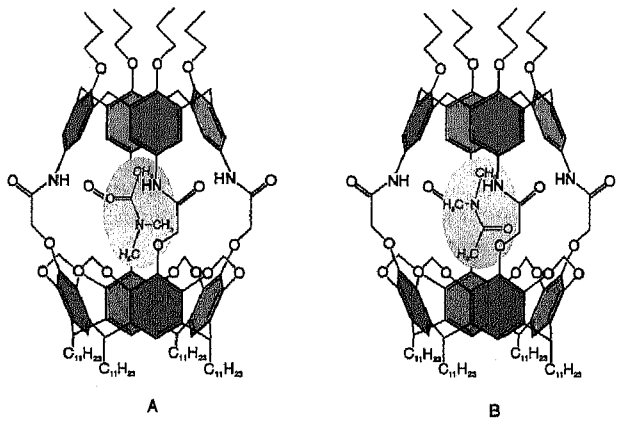


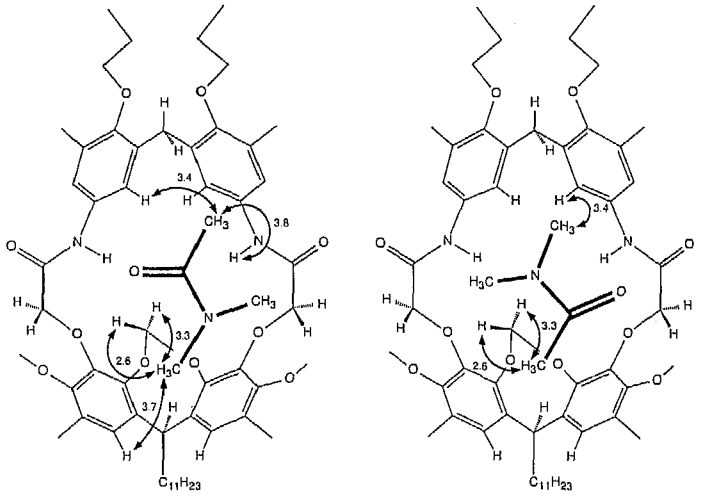
Fig. 1. ^{1}H NMR spectra (250 MHz) of DMA (A) and carceplex 3 (B) in $CDCl_3$ at room temperature; the framed inset shows sections of the ^{1}H NMR spectra (400 MHz) of 3 at different temperatures.

field from its normal position at $\delta = 2.0$, respectively.[10] The methyl group *trans* to the carbonyl resonates at $\delta \approx 1.3$ (obscured by the multiplet of the undecyl chains), which is only $\Delta\delta = 1.6$ upfield from its normal position. Apparently, it is not located close to the aromatic rings of the cavity.

Cooling the sample causes the ^{1}H NMR signals to decoalesce at 0 °C (Fig. 1). At temperatures below −30 °C the broad signals are split into two sets, one of two small, equally intense singlets at $\delta = -1.3$ and -1.8, flanked by the larger singlets of the other at $\delta = -0.9$ and -2.2 also with equal intensity. 2D EXSY experiments revealed that the large singlet at $\delta = -0.9$ shows exchange with the small singlet at $\delta = -1.3$, while the other large singlet at $\delta = -2.2$ exchanges with the small singlet at $\delta = -1.8$. Apparently, calix[4]arene-carceplex 3 switches between two isomeric states **A** and **B** in which the DMA molecule



occupies different orientations inside the cavity of 3. The structures of **A** and **B** were determined by NOESY experiments (see Fig. 2). The acetyl group's methyl protons in isomer **A** (large singlet at $\delta = -2.2$) exclusively show NOE connectivities with protons that are located in the upper region of 3, such as the NH protons and the aromatic protons of the calixarene *ortho* to these amide groups (Scheme 1, left), while the protons of the *N*-methyl *cis* to the carbonyl group (large singlet at $\delta = -0.9$) show NOEs with protons located in the lower region of 3, like the protons of the methylenedioxy bridge pointing inwards or outwards and the aromatic protons of the resorcinol moiety close to the undecyl chains. The set of small singlets of **B** at $\delta = -1.3$ and -1.8 shows opposite NOEs (Scheme 1, right). The protons giving rise to the singlet at $\delta = -1.8$ exclusively show NOE connectivities with protons located at the lower regions of 3, and those assigned to the singlet at $\delta = -1.3$ with protons located in the upper part of 3. The relevant intermolecular distances in the two isomers were determined semiquantitatively[11, 12] by using the initial rate approximation.[13]



Scheme 1. Orientation of the guest DMA in the major isomer A (left) and in the minor isomer B (right) of 3. The arrows link protons that give rise to NOEs; the numbers give the intermolecular distances.

The type of stereoisomerism observed here, which is very similar to that observed in certain rotaxanes,[14] is novel, because it is based on different orientations of two molecular components that are *not* covalently attached. Since no official nomenclature exists for this type of stereoisomerism, we tentatively propose the name *carceroisomerism* (referring to the hindered rotation of a molecule inside the cavity of a carcerand).

The two isomers (carceromers) **A** and **B**, which are not equally abundant ($\Delta G = 0.7$ kcal mol^{-1} at −60 °C in $CDCl_3$),[15a] show fast exchange on the ^{1}H NMR time scale above room temperature, but give rise to separate signals below −30 °C. The activation enthalpy ($\Delta H^{\neq}$) for isomerization was calculated to be 13 ± 1 kcal mol^{-1} from ^{1}H NMR line shape analysis.[16a]

Another important point is evident from the NOESY spectrum of carceplex 3: protons belonging to the host give rise to distinctly different resonances in the two isomers. This is most clear for the protons of the methylenedioxy bridges that point into the cavity. These protons resonate at $\delta = 4.0$ in the major isomer **A** and have an NOE with the large singlet of the methyl group *cis* to the carbonyl group ($\delta = -0.9$). In the minor isomer the resonance for these methylene protons is slightly shifted downfield to $\delta = 4.1$. This signal gives an NOE exclusively with the small singlet of the acetyl's methyl group at $\delta = -1.8$, which unambiguously proves that this resonance belongs to the minor isomer **B**.

When the reaction of 1 with CsF, Cs_2CO_3, and KI was carried out in 1-methyl-2-pyrrolidinone (NMP) under the same conditions as used for DMA, carceplex 4 was isolated in 50% yield.

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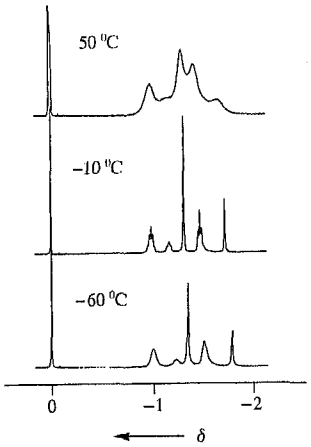
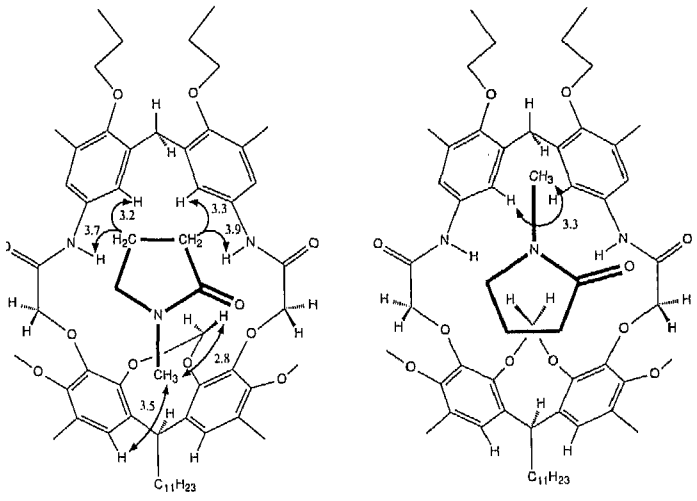


Fig. 2. Sections of the ^{1}H NMR spectra of carceplex **4** at different temperatures.

The presence of unequal amounts of two isomers can be most clearly observed at $-10\,^{\circ}C$ (see Fig. 2). The two singlets at $\delta = -1.3$ and -1.7 represent the methyl groups of incarcerated NMP in the major and minor isomer, respectively ($\Delta G = 0.4$ kcal mol^{-1} at $-60\,^{\circ}C$ in $CDCl_3$).[15b] DQ-COSY and NOESY experiments revealed that the multiplet at $\delta = -1.0$ arises from the 4-CH_2 group of NMP in the major isomer. The corresponding chemical shift for the minor isomer is -1.5 and is obscured by the triplet of the 3-CH_2 group of NMP in the major isomer. The small triplet at $\delta = -1.2$ is assigned to the 3-CH_2 group of NMP in the minor isomer. The 5-CH_2 groups of NMP in both isomers resonate at much lower field ($\delta \approx 1.4$ and 1.5), since they are not located close to the aromatic rings of the cavity.

From a systematic evaluation of the NOEs between host and guest protons, the structure of both isomers could be easily determined (Scheme 2).[17] The *N*-methyl group of NMP in the major isomer is located in the lower part of carceplex **4** as it shows strong NOE connectivities only with the protons of the methylenedioxy bridges and the aromatic protons of the resorcinol moiety close to the undecyl chains. In the minor isomer this methyl group is located in the upper part of the cavity, since it exclusively exhibits NOEs with NH and with the aromatic protons of the calixarene ortho to the amide groups. The 3- and 4-CH_2 groups both give strong NOEs with NH and the protons of the calixarene ortho to the amide groups in the major isomer, whereas these protons in the minor isomer give NOEs exclusively with the protons of the methylenedioxy bridges and with the aromatic protons of the resorcinol moiety close to the undecyl chains. All relevant intermolecular distances between host and guest protons in the two isomers were determined semiquantitatively[11, 17] with the initial rate approximation.[13]



Scheme 2. Orientation of the guest NMP in the major isomer (left) and in the minor isomer (right) of **4**. The arrows link protons that give rise to NOEs; the numbers give the intermolecular distances.

Warming a sample of **4** to 50 °C causes the NMP resonances to coalesce. This coalescence, which is related to isomerization of the two carceromers, takes place at a much higher temperature for **4** than for **3** (DMA carceplex). The activation enthalpy $\Delta H^{\neq}$ of 16 ± 1 kcal mol^{-1}[16b] for the rotation is 4 kcal mol^{-1} higher than for **3**.[18] This is primarily because NMP is one carbon atom larger, but the cyclic structure of NMP also renders this molecule much more rigid than DMA, which may also contribute to a higher energy barrier for carceromerization.

When the sample is cooled to $-60\,^{\circ}C$, the guest proton signals broaden markedly. This broadening is most probably related to rotation of the guest molecule about the C_4 axis of the carcerand, a process that becomes progressively slower with larger guest molecules.

The energy barriers for isomerization in carceplexes **3** and **4** is much higher than that for carceplex **2**. Even at $-60\,^{\circ}C$ an averaged ^{1}H NMR spectrum for the isomers of carceplex **2** is observed.

The type of stereoisomerism observed in carceplexes **3** and **4** constructed from calix[4]arene and resorcinol units provides a novel type of molecular switch, with potential applications in the fields of data storage and molecular electronics.[21]

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[2] For the use of hemicarcerands in stabilizing highly reactive species, like cyclobutadiene, see D. J. Cram, M. E. Tanner, R. Thomas, *Angew. Chem.* **1991**, *103*, 1048–1051; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1024–1027.
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[8] No exchange of the guest DMF for deuterated solvent DMF was observed after heating a solution of **2** in [D_7]DMF for 1 hour at 100 °C, which unambiguously proves that the guest molecule is trapped inside the cavity.
[9] The molecular axis is defined as the axis connecting the centers of the calix[4]arene and resorcinol moieties.
[10] Conclusive evidence for the identity of the methyl groups was found by heating a solution of **3** in [D_5]nitrobenzene. Above 100 °C the singlet at $\delta = -1.0$ coalesces as a result of the hindered rotation about the C–N bond, a process that is slow on the ^{1}H NMR time scale at room temperature, but fast at temperatures above 100 °C. In this way the singlet at $\delta = -2.0$ was assigned to the methyl group of the acetyl unit and the singlet at $\delta = -1.0$ to the *N*-methyl group *cis* to the carbonyl group.
[11] All intermolecular distances between protons of host and guest vary between a minimum and maximum value because of fast rotation of the guest molecule about the C_4 axis of the host. Since NOEs between two protons are inversely proportional to the sixth power of the intermolecular distance, short distances contribute much more to the NOE than large distances. For this reason the calculated distances between two protons should be interpreted as the upper limit for the minimum distance between those protons rather than an averaged distance.
[12] For the two isomers A and B of carceplex **3** the intermolecular distances in Å (± 0.2 Å) in Scheme 1 have been determined (only parts of the structures are shown for clarity).
[13] R. R. Ernst, G. Bodenhausen, A. Wokaun in *International Series of Monographs on Chemistry, Vol. 14* (Eds.: R. Breslow, J. B. Goodenough, J. Halpern, J. S. Rowlinson), Clarendon, Oxford, **1987**, Chapter 9.
[14] R. A. Bissell, E. Córdova, A. E. Kaifer, J. F. Stoddart, *Nature* **1994**, *369*, 133–137.
[15] A systematic search using Quanta/CHARMM Version 3.3 was carried out in order to find as many local minima as possible that correspond to different orientations of the guest molecule inside the cavity. The search was performed

by rotation of the guest about the x (0–60°), y (0–330°) and z axes (0–330°) in steps of 30° each, followed by energy minimization (conjugate gradient) until the root mean square (RMS) of the gradient was less than 0.01. Visual inspection of the minimized structures revealed that they correspond to several different orientations of the guest inside the host. The lowest energy structure of each orientation was minimized further with ABNR (ABNR = adopted basis set Newton–Raphson) until the RMS of the gradient was less than 0.001. a) For carceplex **3** seven energy minima with different orientations of DMA inside the cavity were found. Molecular Dynamics Simulations at 300 K revealed that all orientations isomerize to either of the two lowest energy orientations within 100 psec. The two lowest energy orientations are structurally identical (within the experimental error of the NOE measurements) with the two isomers **A** and **B** found experimentally. The internal energy (ΔE) of the major isomer was calculated to be 1.7 kcal mol^{-1} lower than that of **B**. This energy difference [E (isomer **B**) – E (isomer **A**)] is slightly higher than the experimentally determined Gibbs free energy difference (ΔG) of 0.7 kcal mol^{-1}. b) For carceplex **4** six minima with different orientations of NMP inside the cavity were found. Also here the two lowest energy orientations were structurally identical (within the experimental error of the NOE measurements) with **A** and **B** [17]. In this case the major isomer was calculated to be 1.3 kcal mol^{-1} lower in energy. Again ΔE is higher than the experimental determined ΔG of 0.4 kcal mol^{-1}.

[16] The isomerization of **3** and **4** was studied using the computer simulation program Conjugate Peak Refinement ("TRAVEL") [19]. For a given isomerization process this program finds saddle points on the adiabatic potential energy surface. CHARMM Version 22g3 was used for the TRAVEL studies. a) In case of **3**, an activation energy for interconversion between the two lowest energy structures of 9.8 kcal mol^{-1} was calculated [20], which is 3.2 kcal mol^{-1} lower than the experimentally determined activation enthalpy. b) In case of **4**, an activation energy for interconversion between the two lowest energy structures was calculated at 12.4 kcal mol^{-1} [20], which is 3.6 kcal mol^{-1} lower than the experimentally determined value.

[17] The intermolecular distances in Å (±0.2 Å) in Scheme 2 have been determined for the two isomers of **4** (only parts of the structures are shown for clarity).

[18] Attempts to determine the activation enthalpy for interconversion using ^{1}H NMR line shape analysis were hampered by the complexity of the spectrum. The activation enthalpy was therefore determined by measuring the exchange rate by EXSY (at five different temperatures).

[19] S. Fischer, M. Karplus, *Chem. Phys. Lett.* **1992**, *194*, 252–261.

[20] A physically realistic activation energy for interconversion was only found when one (in case of **3**) or two (in case of **4**) of the higher energy structures were used as intermediates.

[21] a) J. S. Miller, *Adv. Mater.* **1990**, *2*, 98–99; b) *ibid.* **1990**, *2*, 378–379.

Corrigenda

In the communication "Spectroscopic Studies of Anhydroretinol, an Endogenous Mammalian and Insect *retro*-Retinoid" by F. Derguini, K. Nakanishi, J. Buck, U. Hämmerling, and F. Grün (*Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1837–1839) an editorial error was made in the description of the UV/VIS spectrum of the all-*trans*-anhydroretinol **4**. A weak band at $\lambda = 262$ nm was incorrectly attributed to *cis* double bonds. This absorption actually arises from bending of the conjugated system induced by sterid hindrance. Because this bending is enhanced by the *cis* double bonds of sterically hindered *cis* isomers, it is called the "*cis*-band". This term does not necessarily imply the presence of a *cis* double bond.

In the review "Otto Roelen, Pioneer in Industrial Homogeneous Catalysis" by B. Cornils, W. A. Herrmann, and M. Rasch (*Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2144–2163), the names of two of the authors were assigned to the wrong photographs. The central picture is of W. A. Herrmann and the right-hand picture is of M. Rasch.

  0570-0833/94/2222-2348 $ 10.00+.25/0