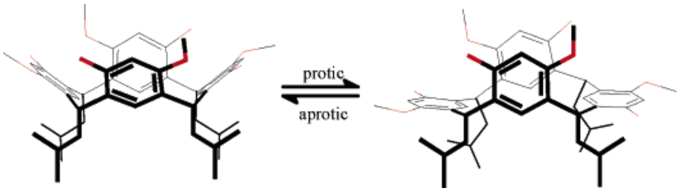
New Insights into the Geometry of Resorc[4]arenes: Solvent-Mediated Supramolecular Conformational and Chiroptical Control

Christian Schiel,[†,‡] Guy A. Hembury,[†] Victor V. Borovkov,[†] Michael Klaes,[‡] Ceno Agena,[‡]
Takehiko Wada,[§] Stefan Grimme,*[∥] Yoshihisa Inoue,*[†,§] and Jochen Mattay*[‡]

*Entropy Control Project, ICORP, JST, 4-6-3 Kamishinden, Toyonaka 560-0085, Japan,
Organische Chemie I, Fakultät für Chemie, Universität Bielefeld, Universitätsstr. 25,
33515 Bielefeld, Germany, PRESTO and Department of Molecular Chemistry, Osaka University,
2-1 Yamadaoka, Suita-shi, Osaka 565-0871, Japan, and Organisch-Chemisches Institut (Abt. Theoretische
Chemie), Universität Münster, Correnѕstr. 40, 48149 Münster, Germany*

inoue@chem.eng.osaka-u.ac.jp; mattay@uni-bielefeld.de; grimmes@uni-muenster.de



The conformations of inherently chiral resorc[4]arenes were studied by circular dichroism (CD) spectroscopy. Whereas in aprotic solvents the *crown* conformation (C_4) is preferred, protic solvents favor the *boat* conformation (C_2). As a result of electronic coupling of the lowest L_b state of the resorcinol unit in the resorc[4]arene, the CD spectra show a strong dependence on the conformation of the macrocycle. For the first time the solvent dependence of the CD spectra was qualitatively analyzed and simulated by using theoretical methods. We have thus demonstrated not only that the conformation of the calixarene is dramatically manipulated by the solvent but also that the joint use of chiroptical measurements and theoretical calculations is a powerful and versatile tool for elucidating structural variations in supramolecular chemistry.

Introduction

Chiroptical control in supramolecular chemistry is one of the most important issues in modern molecular science and technology. Since this effect is based on noncovalent interactions, there are many ways of controlling and regulating these associations by various internal and external factors,[1] of which the influence of the media may play a key role via its pronounced effect on the geometry of the whole assembly (or specific parts).[2] Hitherto various host compounds have been extensively studied, of which resorcarenes and calixarenes are particularly important classes, not only as versatile tools for rationalizing the fundamental factors that govern supramolecular chirality and chemistry but also as new molecular-based film- and layer-sensor technologies on the basis of their host−guest properties.[3] Herein we have investigated the conformation and chirality of a series of chiral resorc[4]arenes, with and without chiral appendages, but all possessing molecular chirality as a result of the unidirectional nature of the aromatic substitution pattern (see Figure 1). All compounds were synthesized according to the methods previously described.[4] The macrocycles are inherently chiral and possess a C_4 symmetry. To get enantiomerically pure resorc[4]arenes, one can, for example, attach a chiral auxiliary and separate the resulting diastereomers. After cleavage of the

---

[†] JST.

[‡] Universität Bielefeld.

[§] Osaka University.

[∥] Universität Münster.

(1) (a) Borovkov, V. V.; Hembury, G. A.; Inoue, Y. *Acc. Chem. Res.* **2004**, *37*, 449−459. (b) Aoyama, Y. *Supramolecular Chemistry*; Kluwer Academic Publishers: Netherlands, 1992; pp 17−30. (c) Tsukube, H.; Shinoda, S. *Chem. Rev.* **2002**, *102*, 2389−2403.

(2) (a) Borovkov, V. V.; Hembury, G. A.; Inoue, Y. *Angew. Chem., Int. Ed.* **2003**, *42*, 5310−5314. (b) de Loos, M.; van Esch, J.; Kellogg, R. M.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 613−616. (c) Green, M. M.; Khatri, C.; Peterson, N. C. *J. Am. Chem. Soc.* **1993**, *115*, 4941−4942. (d) Saito, S.; Nuckolls, C.; Rebek, J., Jr. *J. Am. Chem. Soc.* **2000**, *122*, 9628−9630.

(3) (a) Rickert, J.; Weiss, T.; Göpel, W. *Sensors Actuators B* **1996**, *31*, 45−50. (b) Hassan, A. K.; Ray, A. K.; Nabok, A. V.; Davis, F. *Sensors Actuators B* **2001**, *77*, 638−641. (c) Friggeri, A.;. van Veggel, F. C. J. M.; Reinhoudt, D. N. *Chem. Eur. J.* **1999**, *5*, 3595−3602.

(4) Klaes, M.; Agena, C.; Köhler, M.; Inoue, M.; Wada, T.; Inoue, Y.; Mattay, J. *Eur. J. Org. Chem.* **2003**, *8*, 1404−1409.

10.1021/jo0518654 CCC: $33.50

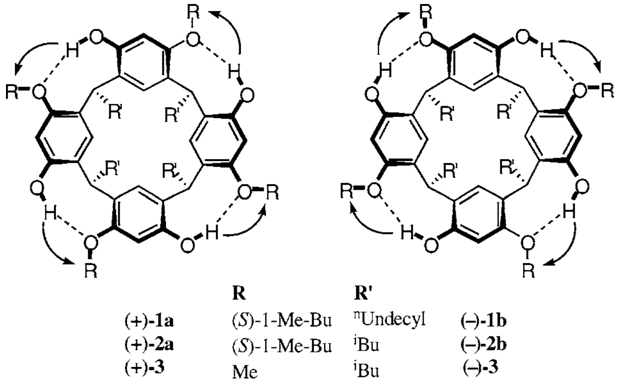
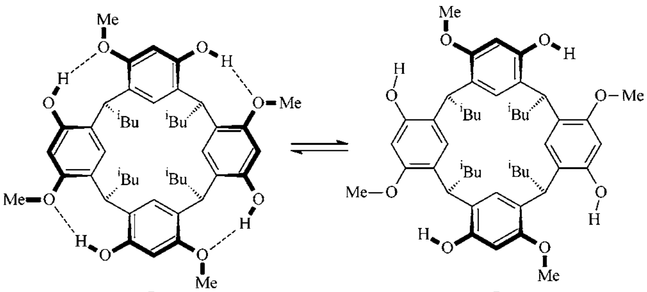


FIGURE 1. Structures of resorc[4]arenes **1**−**3**.



C_4 (*crown*) C_2 (*boat*)

FIGURE 2. *Crown* and *boat* conformations of (−)-**3**.

auxiliary the pure enantiomers are obtained. These resorc[4]arenes may exist in a number of different conformations with differing symmetries, with C_4 (*crown*) and C_2 (*boat*) being the major contributors,[5] which are crucial factors in the functioning of these molecules as supramolecular systems (Figure 2).[6] The conformational properties of resorc[4]arenes have been well-studied particularly by solution NMR and X-ray techniques,[7] and hence the potential for fast interconversion between various forms (on most spectroscopic time scales) makes the unambiguous determination of the solution-state conformation(s) difficult at best. However, the chiral nature of the compounds **1**−**3** (Figure 1) studied here affords a new and powerful tool for investigating the actual conformational states of these compounds in solution via the combined application of circular dichroism (CD) and UV−vis spectroscopies. CD spectroscopy in particular is crucial, as its spectra only arise from species that are chiral and nonracemic.

Results

The crucial feature when considering the conformations of resorc[4]arenes **1**−**3** is their 1,3-substituents (alcohols and ethers), which allow a concerted ring of four intramolecular hydrogen bonds to be formed between the alcohol and ether substituents, which locks the molecule into a C_4 *crown* conformation. Thus, competition for and disruption of these may lead to dramatic conformational changes, in particular between the C_4 *crown* and C_2 *boat* conformations (Figure 2).

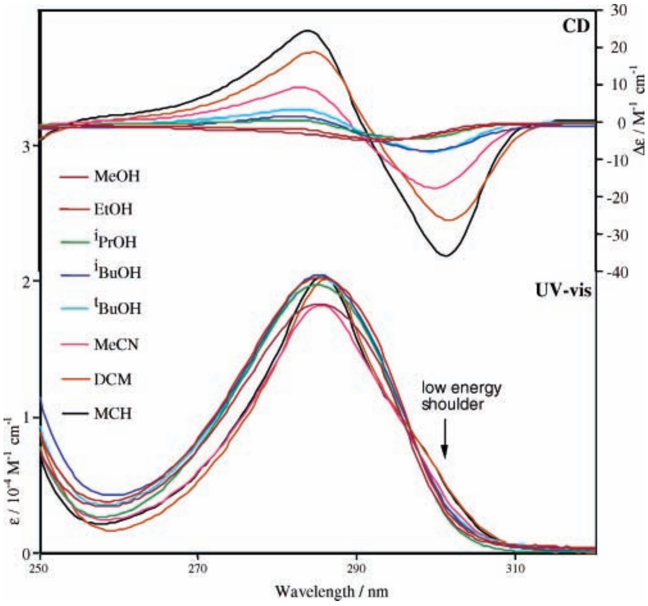


FIGURE 3. UV−vis and CD spectra of (+)-**1a** with various solvents.

Previous studies have shown that the interaction of the solvent with parts of a molecular system may lead to geometry, chirality, and molecular function switching and can be understood in terms of specific supramolecular interactions.[1,2] Therefore, the effects of various external factors, particularly, hydrogen bonding solvents as potential competitors for the resorc[4]arenes' intramolecular hydrogen bonding network (which may affect the conformation) were investigated by UV−vis and CD spectroscopy. To this end Figure 3 shows a remarkable and strong correlation between the solvent's hydrogen bonding ability and steric bulk, with the chiroptical properties of (+)-**1a**.[8]

In the UV−vis spectra of (+)-**1a** (Figure 3), the hydrogen bonding alcohols all display broad Gaussian-shaped ^1L_b absorption bands with almost identical energy maxima of 285 nm. In contrast, the UV−vis profiles for non-hydrogen bonding solvents such as methylcyclohexane (MCH), dichloromethane (DCM), and acetonitrile (MeCN) are different, having much narrower absorptions bands and slightly red shifted maxima (by 2 nm), with a pronounced low energy shoulder at around 300 nm. It is believed that these spectral characteristics in non-hydrogen bonding solvents arise from the rigid C_4 conformation of the resorc[4]arene, which results in a more pronounced excitonic splitting of the individual electronic transitions.

From the CD spectra (Figure 3) we can clearly see that the solvents can also be grouped into two sets: first, those that result in bisignate Cotton effects, and second, those that give rise to monosignate Cotton effects. The solvents that result in monosignate Cotton effects are those that are able to compete for the intramolecular hydrogen bonding of the resorc[4]arene, such as MeOH and EtOH (which results in intermolecular solvent−resorc[4]arene hydrogen bonding), whereas aprotic solvents produce strong negative CD couplets consisting of two Cotton effects. It is noted that both polar and nonpolar aprotic solvents behave similarly, although the amplitude of the CD couplet increases with decreasing solvent polarity from MeCN to DCM

---

[5] Timmerman, P.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron* **1996**, *52*, 2663−2704.

[6] Vysotsky, M.; Schmidt, C.; Böhmer, V. *Advances in Supramolecular Chemistry*; Gokel, W., Ed.; JAI Press: Greenwich, 2000; Vol. 7, pp 139−233.

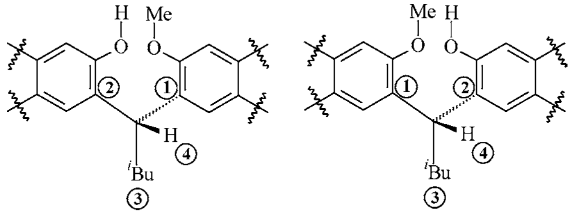
[7] (a) Tunstad, L.; M.; Tuker, J. A.; Dalcanale, E.; Wesier, J.; Byrant, J. A.; Sherman, J. C.; Helgeson, R. C.; Knobler, C. B.; Cram, D. J. *J. Org. Chem.* **1989**, *54*, 1305−1312. (b) Zahn, G.; Sieler, J.; Müller, K.; Hennig, L.; Mann, G. *Z. Kristallogr.* **1994**, *209*, 468−469.

[8] The CD Spectra of (−)-**1b** show a perfect mirror image of the one presented in Figure 3 with all solvents.

and then to MCH. Although at first sight the hydrogen bonding ^{i}BuOH and ^{t}BuOH seem to be exceptional cases, giving weak negative couplets, further investigation shows that this is due to the steric hindrance arising from the bulk of the butyl group. It is in this competition between the intramolecular and intermolecular hydrogen bonding that the reason for the bisignate CD signals of ^{i}BuOH and ^{t}BuOH resides; the bulkier BuOHs (in comparison to MeOH) are less able to compete for the hydrogen bonding sites on the resorc[4]arene due to steric clashes between the butyl group and the 1,3-substituents of the resorc[4]arene. Thus the C_4 conformation remains dominant (though less so in comparison to the MCH case).

On the basis of these results it was inferred that in the case of non-hydrogen bonding solvents the intramolecular hydrogen bonding was complete and robust, resulting in a well-defined C_4 conformation, and that the switch between mono- and bisignate CD spectra was due to the hydrogen bonding solvents competing for the resorc[4]arene's hydrogen bonding donor and acceptor sites, thus disrupting the C_4 conformation to produce another chiral conformation(s) possessing intermolecular hydrogen bonding that is monosignate in nature.

Remarkably, by considering the amplitude of the CD couplet (A value) in the region of 260−310 nm, it is found that magnitude of the A value is a direct measure of the relative ability of the solvents to compete with the intramolecular hydrogen bonding (Figure 3). For example, MCH ($A = -60.0$ cm^{-1} M^{-1}) produces the largest A value as this hydrophobic solvent enhances the stability of the intramolecular hydrogen bonding network. On moving to DCM its hydrogens are more able, electrostatically, to hydrogen bond, but the large bulk of the two chlorines prevents effective interaction, resulting in a decreased A value ($A = -45.0$ cm^{-1} M^{-1}). For MeCN this is also more able than MCH to electrostatically interact, with a lower degree of steric hindrance than DCM that allows further disruption of the intramolecular hydrogen bonding network, thus further lowing the CD amplitude ($A = -26.8$ cm^{-1} M^{-1}). On moving to ^{t}BuOH and ^{i}BuOH, with A values of −11.4 and −9.4 cm^{-1} M^{-1}, respectively, here the steric effect is quite clear; though both are alcohols the bulk of the butyl group hinders the close approach to the resorc[4]arene's rim, resulting in a continuing predominance of the C_4 conformation. However, the greater bulk of the ^{t}BuOH (compared with ^{i}BuOH) results in greater steric hindrance and thus its greater A value. ^{i}PrOH ($A = 4.9$ cm^{-1} M^{-1}) is barely bisignate, indicating that at this level of steric hindrance the solvent can effectively compete with the intramolecular hydrogen bonding of the resorc[4]arene, thus destroying the C_4 conformation. This effect is further seen when the small EtOH and MeOH are applied and only monosignate spectra are observed.



(+)-3
all-*R*

(−)-3
all-*S*

FIGURE 4. Absolute configuration of the enantiomers (±)-**3**.

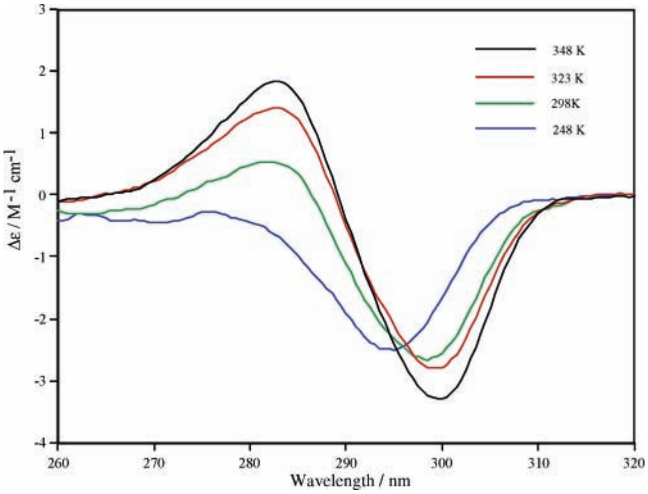


FIGURE 5. Variable temperature CD spectra of (+)-**2a** in ^{i}BuOH.

The same effects on the CD spectra, and thus the resorc[4]arene's conformations can also be seen in (+)-**2a** and (−)-**2b** (which differ from (+)-**1a** and (−)-**1b** only in the length of the alkyl side chain at the aromatic ring connecting methylene position). The macrocycles (+)-**3** and (−)-**3** have no chiral side chains at the *upper rim* and are inherently chiral as a result of the unidirectional substitution pattern of the methoxy groups (Figures 1 and 4). The absolute configuration of these resorcarenes have been determined by the combination of X-ray and NMR data.[9] The CD spectra for these resorc[4]arenes show bisignate signals with non-hydrogen bonding solvents and bulky alcohols and monosignate signals in effective hydrogen bonding solvents such as MeOH.

This consideration of the relationship between the structure of the solvent, the nature of the CD spectra, and the conformation of the resorc[4]arene strongly indicates that it is the strength with which the solvent can bind the hydrogen bond donor and acceptor sites of the resorcarene that governs its conformations and chiroptical properties. To further test this supposition a series of variable temperature CD experiments were performed with (+)-**2a** and (−)-**2b** and solvents of differing interacting abilities: MCH, MeOH, and ^{i}BuOH. The purpose of this is to vary the binding strength of the solvent−resorc[4]arene interaction, i.e., at higher temperatures the binding should be weaker and at lower temperatures stronger.

In the case of MCH there is little change in the shape or intensity, as this solvent has no interacting group and so is bisignate (see Supporting Information). For MeOH the spectra are also essentially unchanged, remaining monosignate over the entire temperature range, which is expected as it was shown that the MeOH is already able to completely disrupt the C_4 conformation at 298 K and the decrease in temperature will only further increase the binding strength (see Supporting Information). The results for ^{i}BuOH (Figure 5), however, give an important insight into the nature of the driving force of the conformation conversion. Clearly at 348 K the CD spectrum is bisignate, indicating that at this temperature the ^{i}BuOH is not able to interact sufficiently to disrupt the intramolecular hydrogen bonding network and the C_4 structure predominates. However, as the temperature is reduced and the binding is correspondingly enhanced, the A value decreases in a stepwise manner as the higher percentage of bound solvent decreases the C_4 population, until at 248 K the enhanced binding

---

(9) Klaes, M.; Neumann, B.; Stammler, H.-G.; Mattay, J. *Eur. J. Org. Chem.* **2005**, *10*, 864−868.

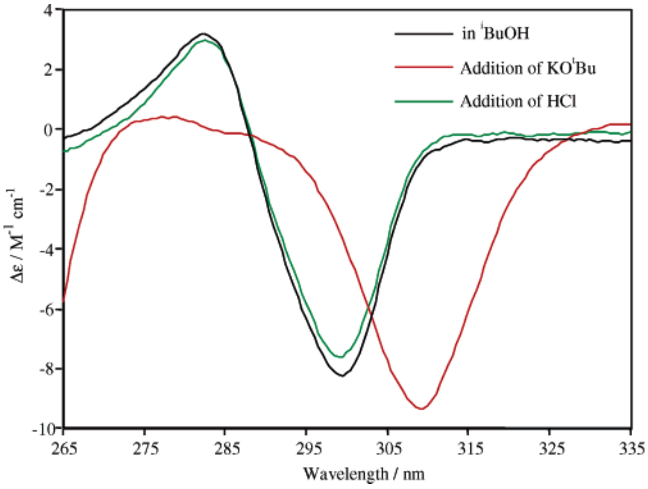


FIGURE 6. CD spectra of (+)-**1a** in ^{i}BuOH on treatment with KO^{t}Bu and subsequent treatment with HCl.

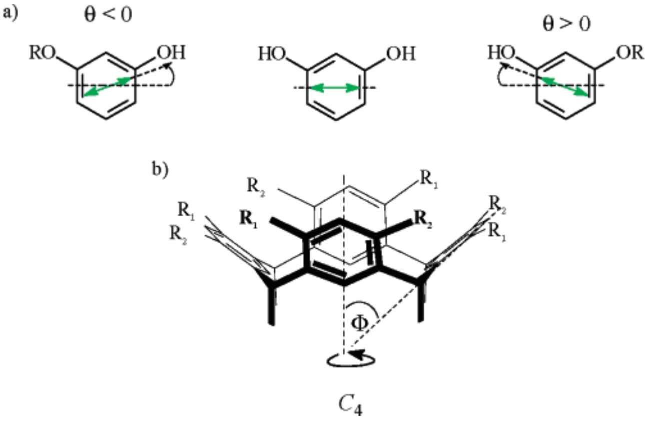


FIGURE 7. (a) Orientation of the lowest ^1L_b transitions in symmetrical and unsymmetrical substituted resorcinol. (b) The position of the resorcinol units in resorc[4]arenes determines the angle Φ.

overcomes the steric hindrance of the ^{i}Bu group and the CD spectrum becomes monosignate and the new conformations dominate.

Additionally, the critical dependence of the resorc[4]arene's conformation and chirality on the intramolecular hydrogen bonding is unequivically demonstrated by the deprotonation of the alcohol groups of (+)-**1a** in ^{i}BuOH by treatment with KO^{t}Bu and subsequent reprotonation by HCl. On addition of KO^{t}Bu the intramolecular hydrogen bonding is no longer present, precluding the formation of the C_4 *crown* (in a manner similar to that seen on the addition of ca. MeOH). As a result the CD spectrum becomes monosignate and is red shifted (309 nm) due to the increased degree of conjugation. This again confirms that the origin of the change in chiroptical properties arises from the disruption of the intramolecular hydrogen bonding network. Addition of HCl to reprotonate the resorc[4]arene's alcohol groups sees the readoption of the original UV−vis and CD spectra, showing the presence of the intramolecularly hydrogen bonded C_4 *crown* structure (see Figure 6).

Discussion and Conclusions

The new conformation formed upon disruption of the intramolecular hydrogen bonding is considered to be C_2 symmetric (in which two opposite rings are up and two "flipped-out") due to the increased flexibilty of the resorc[4]arene and subsequent minimization of internal steric clash (Figure 2). This proposed mechanism, leading to the C_4−C_2 switching was further investigated by consideration of the exciton coupling of the resorc[4]arene's aromatic electronic transitions. The orientations of the transition moments were determined using theoretical analysis and quantum chemical calculations at the DFT level (see Details of Theoretical Analysis).[10] For the analysis of the origin of the observed Cotton effects only the lowest ^1L_b state of the monomer (*meta*-di-*O*-substituted benzene) is of interest. In a model with equivalent oxygens the ^1L_b state is of B_1 symmetry in the C_{2v} point group and therefore polarized along the horizontal axis (Figure 7a). If the oxygen atoms become different (e.g., by introducing alkyl substituents), the ^1L_b moment is turned upward (counterclockwise) from the horizontal axis when the OH is located on the right-hand side or downward (clockwise) when the OH is on the left (Figure 7a).[11]

The changes in the CD spectra for the various solvents can be rationalized by consideration of the lowest energy electronic transitions of the resorc[4]arene's individual aromatic groups and how their relative orientation changes with conformational switching. In the C_4 *crown* conformation induced in non-hydrogen bonding solvents, the individual transitions are aligned in either an anticlockwise or clockwise manner (depending on the molecule's chiral spacial geometry), allowing excitonic coupling between the transitions that gives rise to the observed negative or positive CD couplets, in the case of **1**−**3** (Figures 3 and 8a). Similar observations have already been reported by Rebek et al. for nonracemic cavitands derived from resorc[4]-arenes.[2d] The authors also observed bisignate CD spectra in chloroform which diminished by adding solvents such as MeOH.

However, on the disruption of the intramolecular hydrogen bonded structure in polar solvents the individual rings are able to move more freely and adopt a C_2 conformation. Crucially the resorc[4]arene does not adopt just a single C_2 conformation but is in a fast dynamic equilibrium between two C_2 conformations: one where two opposite rings (P1 and P3) are up, and the other two opposite rings (P2 and P4) are flipped out and the opposite conformation with P1 and P3 flipped-out and P2 and P4 up, referred to as C_{2a} and C_{2b}, respectively (see Figures 8b and 8c). With these two C_2 conformations in mind the reason for the monosignate CD spectra can be understood on consid-

---

[10] All quantum chemical calculations have been performed with the TURBOMOLE suite of programs. The structures have been fully optimized at the density functional (DFT) level employing the BP86 functional, a Gaussian AO basis of valence-triple-ζ quality including polarization functions (TZVP) and the RI-approximation for the two-electron integrals. The structures have been used in subsequent calculations of the CD spectra, which have been performed in the framework of time-dependent DFT employing the B3LYP density functional and the TZVP basis set. (a) *TURBOMOLE*, Version 5.3; Ahlrichs, R.; Bär, M.; Baron, H.-P.; Bauernschmitt, R.; Böcker, S.; Ehrig, M.; Eichkorn, K.; Elliott, S.; Furche, F., Haase, F.; Häser, M.; Horn, H.; Huber, C.; Huniar, U.; Kattannek, M.; Kölmel, C.; Kollwitz, M.; May, K.; Ochsenfeld, C.; Öhm, H.; Schäfer, A.; Schneider, U.; Treutler, O.; von Arnim, M.; Weigend, F.; Weis, P.; Weiss, H. Universität Karlsruhe: Karlsruhe, 2000. (b) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098−3100. Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822−8824. (c) Schäfer, A.; Horn, H.; Ahlrichs, R. *J. Chem. Phys.* **1992**, *97*, 2571−2577. (d) Eichkorn, K.; Treutler, O.; Öhm, H.; Häser, M.; Ahlrichs, R. *Chem. Phys. Lett.* **1995**, *240*, 283−289. (e) Bauernschmitt, R.; Ahlrichs, R. *Chem. Phys. Lett.* **1996**, *256*, 454−464. (f) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652. Stephens, P. J.; Devlin, F. J.; Chablowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623−11627.

[11] Canceill, J.; Collet, A.; Garbard, J.; Gottarelli, G.; Spada, G. P. *J. Am. Chem. Soc.* **1985**, *107*, 1299−1308.

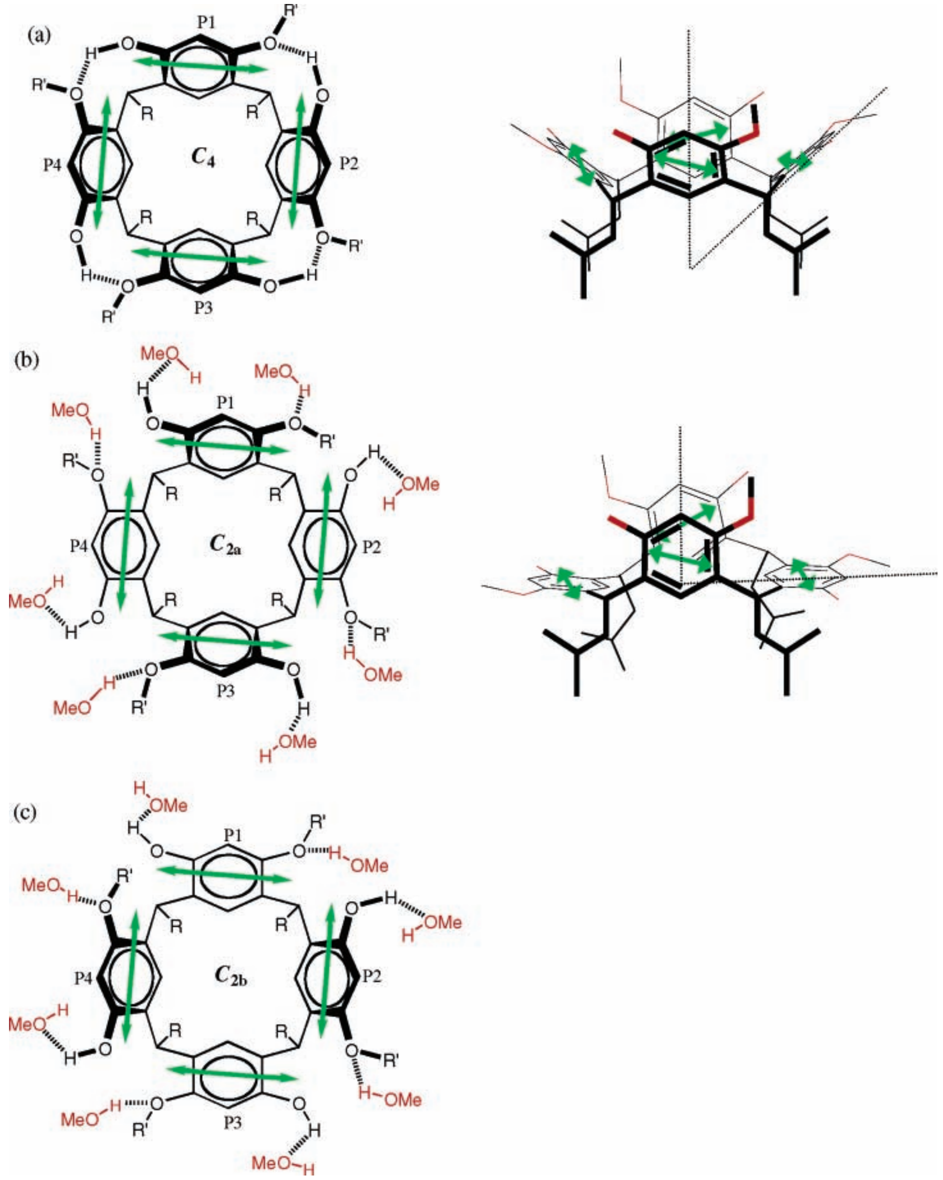


FIGURE 8. Schematic representation of conformations C_4, C_{2a} and C_{2b} with their associated ^1L_b electronic transitions (green arrows): (left) top view, (right) side view.

eration of the opposite orientations of the coupling transitions in C_{2a} and C_{2b}, resulting in the cancelation of the two couplets by each other, leaving only the monosignate CD signal due to the inherently optically active electronic transitions.

Additionally, on observation of the NMR spectra of these compounds in MeOD-d_4 at room and low temperatures only a single set of signals was observed due to the fast interconversion (on the NMR time scale) between C_{2a} and C_{2b} and not distinct signals for the two different ring conformations in C_2. It is this absence of distinct NMR signals for the proposed C_2 conformations that has led to the widely held belief that such resorc[4]-arenes are in a C_4 conformation even in hydrogen bonding solvents. However, from consideration of the above UV−vis, CD, and computational results it can be revealed that when the intramolecular hydrogen bonding network is sufficiently disrupted the C_4 conformation is replaced by the much more dynamic C_2 conformations, which are "invisible" to NMR but can be observed by consideration of the CD spectra and the associated molecular electronic transitions. This realization may then have profound effects when applied to the functioning of resorcarenes, cavitands, and other macrocycles in general as molecular hosts and sensors, due to the dramatic change in the cavity's geometry.

Details of Theoretical Analysis

To elucidate the origin of the influence of conformation on the CD spectra, a theoretical analysis and quantum chemical calculations at the DFT level[10] were carried out (for an overview about theoretical simulations of UV and CD spectra see the literature[12]).

For a qualitative analysis of the origin of the observed Cotton effects only the lowest L_b state of the monomer (*meta*-di-*O*-substituted benzene) is of interest. The L_a band lies far away at 220−230 nm and therefore we deal with a 4-state model. In a model with equivalent oxygens (Figure 9A) the L_b state is of B_1 symmetry in the C_{2v} point group and therefore polarized along the y axis. If

---

(12) (a) Grimme, S. *Rev. Comput. Chem.* **2004**, *20*, 153-218. (b) Diedrich, C.; Grimme, S. *J. Phys. Chem. A* **2003**, *107*, 2524−2539.

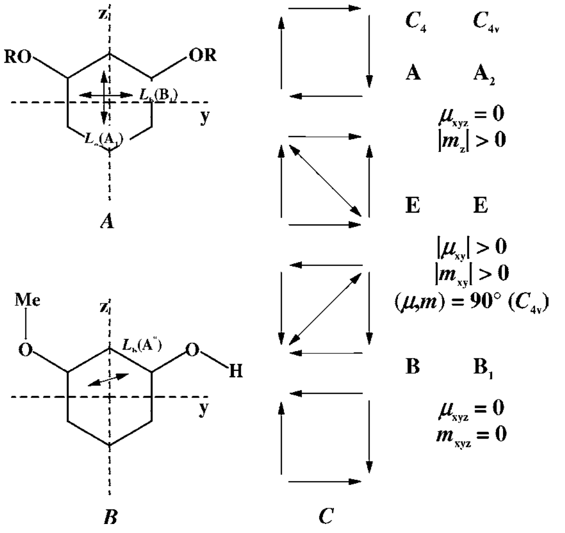


FIGURE 9. Analysis of transitions in (A) symmetrical resorcinol and (B) unsymmetrical resorcinol, and (C) coupling of four L_b transitions as in resorc[4]arene.

the oxygen atoms become different (e.g., by introducing OMe and OH), the L_b moment is turned upward (counterclockwise) from the *y* axis when the OH is located on the right-hand side as shown in Figure 9B or downward (clockwise) when the OH is on the left. Thereby the transition gets a small *z* component (up in the former case and down in the latter case), which is very important for the CD.

The arrangement of four C_{2h} resorcinol monomers leads to a C_{4v} symmetric resorc[4]arene, whereas with alternating hydroxyl and methoxy groups at the *upper rim* the macrocycle has C_4 symmetry. In Figure 9C the four possible linear combinations of the four L_b states (transition moments) are shown. The energy increases from top to bottom. The lowest state is an A_2 (A in C_4) that has only a magnetic moment m along z due to the helical arrangement of the moments, while the electronic transition moment μ is zero. The components of the E state cause the strong UV signal. The highest B state is irrelevant, due to missing m and μ. Therefore the UV maximum should correspond with the rear part of the "couplet." The CD of the A state is generated in C_4 through the huge m_z and the small μ_z due to the unsymmetrical substitution pattern of the resorc[4]arene. If the induced m_z component points upward, the CD is positive (OH right, angles μ, $m = 0°$), and vice versa (OH left, angles μ, $m = 180°$). The analysis becomes even more complicated if the CD of the E state is considered. Twisting the L_b moment leads to a deviation of the angle between μ and m away from 90°. Both components of the E state will have the same CD sign opposite to that of the first A state. In general, the exciton chirality theory can be applied, but the observed "couplet" cannot be explained by only two transitions. To put these qualitative conclusions on a more solid basis we have performed quantum chemical calculations of the CD spectra for the "real" structures. The results of TDDFT-B3LYP/TZVP computations for the *crown* conformation of a resorcarene with all-*S* configuration at the methane bridges are shown in Figure 10.[10] This spectrum shows a positive bisignate Cotton effect like the CD spectra of (−)-**1**, (−)-**2** and (−)-**3**. The amplitude of the CD couplet ($A = 47$ cm^{-1} M^{-1}) is as high as the A values of the measured spectra in apolar solvents such as MCH or DCM, while the zero crossing is at 283 nm and very close to the observed absorption maxima but slightly shifted to shorter wavelength.

The *boat* conformation is not stable in the gas phase. Geometry optimization (with different methods) always leads to the C_4 structure. Stabilizing the *boat* conformation was possible by adding four MeOH molecules through formation of intermolecular hydrogen bonds (see Supporting Information). As can be seen in Figure 10 a remarkable change of the CD curve in comparison to the spectra of the *crown* conformer occurs. The spectra of the C_2 symmetric resorc[4]arenes have smaller amplitudes than the ones of the *crown* conformers. In addition, the sign of the CD couplet changes as well, indicating dramatic changes of the CD spectra upon rearrangement of the macrocycle. Note, however, that the computationally investigated boat structure represents only a crude and extreme model of the experimental situation in solution where many different conformations with various amounts of inter- and intramolecular hydrogen bonding can be expected. Thus, a quantitative agreement between theoretical and experimental CD spectra cannot be obtained in our simulation; unfortunately, a more realistic treatment (averaging CD spectra along a molecular dynamics trajectory including solvent) is currently not feasible.

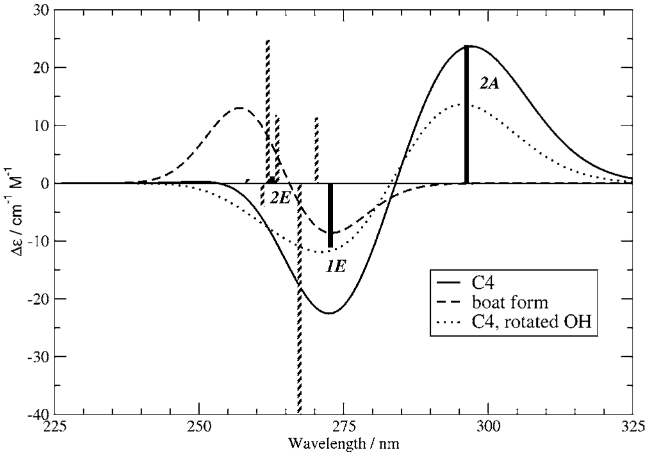


FIGURE 10. Calculated CD spectra of an inherently chiral all-*R* resorc[4]arene depending on its conformation. The bars indicate the intensity and position of the calculated transitions; the curve has been obtained by adding Gaussian curves with a width of 0.4 eV at 1/e height.

In summary, we presented CD spectra of inherently chiral resorc[4]arenes in different solvents such as MCH, DCM, MeCN and alcohols with varying alkyl chains. While the resorc[4]arene's hydrogen bond network is intact in aprotic solvents an exciton coupling of the resorcarene chromophores is observed. In alcohols such as EtOH and MeOH a conformational change leads to a disruption of the hydrogen bond network and a monosignate Cotton effect. We also presented the first calculated CD spectrum of a C_4 symmetric resorc[4]arene in *crown* conformation on the basis of TDDFT-B3LYP/TZVP computations, which shows the same exciton coupling as the resorc[4]arene in aprotic solvents. We showed that CD spectroscopy can provide further information about the conformation of chiral resorc[4]arenes in solution which is not possible by NMR spectroscopy due to the fast interconversion of the two *boat* conformations (Figure 8).

Experimental Section

CD spectra were obtained at 298 °C in a range of 400−200 nm. The bandwidth was either 0.5 or 1.0 nm, and the scanning speed was 50 nm/min. At least two spectra were accumulated. Solvents used were of spectroscopic grade. The concentrations of the solutions were in a range of 10^{-4} to 10^{-5} mol/L. The cell length was 1 cm. For the variable temperature CD spectra the spectrometer was equipped with a liquid-nitrogen cryostat.

Acknowledgment. We gratefully acknowledge financial support by the German Research Foundation (DFG), the Department of Science and Research NRW (MSWF), the Fonds der Chemischen Industrie (FCI), and the Innovations Fonds der Universität Bielefeld.

Supporting Information Available: Computational details for the *crown* conformer and the *boat* conformation stabilized with four MeOH molecules; temperature-dependent CD spectra of (+)-**1a** in MCH, ^{i}BuOH, and MeOH; and complete ref 8a. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0518654