Structure/Chiroptics Relationships of Planar Chiral and Helical Molecules

Stefan Grimme*[a], Jörg Harren[b], Adam Sobanski[b], and Fritz Vögtle*[b]

Institut für Physikalische und Theoretische Chemie der Universität Bonn,[a]
Wegelerstr. 12, D-53115 Bonn
Fax: (internat.) + 49(0)228/739066
E-mail: grimme@rs3.thch.uni-bonn.de

Kekulé-Unstitut für Organische Chemie und Biochemie der Universität Bonn,[b]
Gerhard-Domagk-Str. 1, D-53121 Bonn
Fax: (internat.) +49(0)228/735662
E-mail voegtle@uni-bonn.de

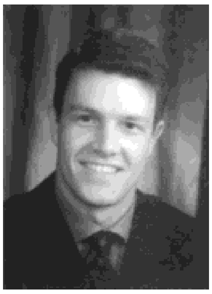
Received April 8, 1998

Keywords: Chirality / Circular dichroism / Cyclophanes / Theoretical calculations / Strained molecules

The chiroptical properties of planar-chiral and helical molecules without stereogenic centres and with well-defined structure, strain, electronic properties and chirality are investigated by experimental and theoretical circular dichroism spectroscopy. We report on the synthetic and theoretical achievements made during the past 10 years in the field of rigid [2.2]metacyclophane propellers, as well as in the area of [*n*]para- and [*n*]metacyclophanes containing aliphatic parts like adamantane or unsaturated bridges. Results for carbo and hetero helicenes and helicene-related molecules like twisted phenanthrenes are presented. It is demonstrated how reliable theoretical calculations using configuration interaction and time-dependent methods in combination with density functional theory today are and how useful the interplay between theory and experiment stimulates the development of chiral molecules optimized for this purpose. Even for large molecules it is routinely possible to assign Cotton effects to electronic transitions, to evaluate chromophore contributions, to determine absolute configurations and conformational equilibria, and to discover intramolecular charge transfer effects.

Fritz Vögtle (left, top), born in 1939 in Ehingen/Donau, Germany, studied chemistry on Freiburg as well as chemistry and medicine in Heidelberg. There he received his Ph. D. for research with H. A. Staab on the valence isomerization of double Schiff bases. After his habilitation on steric interactions inside cyclic compounds, he was H2/H3 professor in Würzburg from 1969 to 1975. He then accepted a position as full professor and director of the Institut für Organische Chemie und Biochemie in Bonn. He obtained a "literature award" for his book "Supramolekulare Chemie" (translated in English, Japanese, Chinese) and the Israeli Lise Meitner-Alexander von Humboldt award. He is interested in the field of supramolecular chemistry and dendrimers and after working on topics concerning crown ethers, podands and siderophores, he has concentrated on compounds with large intramolecular cavities, ligands for supramolecular photochemistry, molecular tweezers and belt- and tube-shaped molecules. His further areas of research are deformed, helical molecules (cyclophanes) and their chiroptical properties, compounds with appealing architectures and, last but not least, catenanes, rotaxanes and pretzelanes.

Stefan Grimme (right, top), born in 1963 in Braunschweig, Germany, studied chemistry in Braunschweig. There he received in 1991 in the group of H. Dresskamp his Ph. D. in Physical Chemistry on Photo-CIDNP studies of the photodissoziation of aromatic ketones. He then switched to Theoretical Chemistry and joined the research group of S. D. Peyerimhoff in Bonn. After his habilitation in 1997 on the development and application of quantum chemical methods to electronic structure problems, he became assistant professor. He is interested in the theoretical description of large organic molecules with special emphasis on excited states, photochemical reactions and chirality as well as the investigation of strained systems



Jörg Harren (right, bottom), was born 1969 in Linnich near Aachen, Germany. He studied chemistry at the University of Bonn, where he received his diploma in 1994. His research interests in his dissertation from 1994 to 1997 in Prof. F. Vögtle's group were stereochemistry of novel chiral systems and supramolecular chemistry of cyclophanes. After a one-year stay in a clinical laboratory he went to industry were he is working on polymer chemistry in R & D at Fa. Stockhausen GmbH, Krefeld.

Adam Sobanski (left, bottom), born in 1968 in Zbroslawice, Poland, studied chemistry at the University of Bonn. He obtained his diploma in 1997 with a thesis on helical chiral phenanthrenes in the group of Fritz Vögtle at the Kekule-Institut für Organische Chemie und Biochemie, University of Bonn. Now he is continuing his research on small helical chiral molecules and their structure/chiroptic relationships.

MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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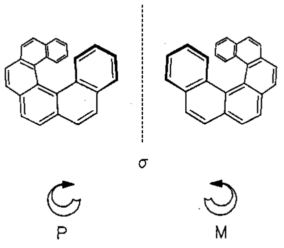
1. Introduction

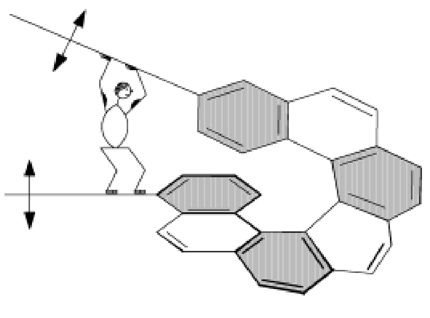
Screw-shaped objects play a dominant role in daily life and in techniques as mechanical screws, propellers etc. Helical molecules are equally important in nucleic acid, peptide, and sugar chemistry.[1][2] The different interaction of left- and right-handed screw-shaped molecules with left- and right-circularly polarized light, respectively, is a very general and fundamental process that can be studied by electronic circular dichroism (CD) measurements.[3] An advantage of smaller helical molecules is the usually rigid structure (cf. hexahelicene **1**)[4] that allows more precise calculations and conclusions compared to flexible aliphatic molecules containing stereogenic centres[5].



1 (Hexahelicene)

There has been continued interest in relationships between structure and physical and chemical properties of rigid aromatic hydrocarbons, that may additionally be strained or sterically hindered. Examples of such molecules apart from the helicenes[1a][4] are twisted alkenes[6] or propeller molecules of the biphenyl[7a][7b] and triarylmethane[7c][7d][7e][7f][7g] type (exhibiting atrop isomerism). By substitution with large groups in strategic positions a close proximity of the substitutents ("overcrowding") can be reached which results in a modified helical distortion of the aromatic system paralleled by disturbance of the π-electron system (Figure 1)[8][9]. The latter is monitored here by circular dichroism measurements that allow distinct comparisons of more or less sterically or/and electronically influenced chromophores.

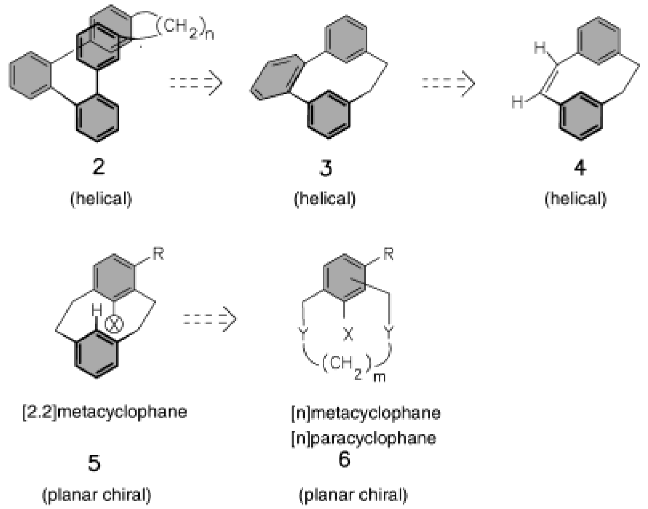
Figure 1. Manipulation of screw pitch by pressing and stretching at the ends; this can be achieved by using clamps and rigid spacers, respectively, see e.g. **2**, **3**



2. Concept

The cooperation between our synthetic and theoretical research groups aims at the design of new planar or helical chiral molecules or substance families with only small but tailored property differences. The principle is demonstrated with the cartoon in Figure 1 which shows how the pitch of heptahelicene is gradually varied by extending[9] or pressing together[10] the terminal groups of the molecule. In this sense steric and electronic effects are modified in a calculable way and extent. The spectroscopic and chiroptic examination of a number of related molecules should lead to a deeper knowledge about structure and strain on the one hand and the CD[11] and further spectroscopic (electronic) properties on the other hand.[12] Such structure-chiroptics relationships are important for the qualitative and quantitative understanding of chirality[13] and the fundamental question of interaction of circularly polarized light with chiral molecules (e.g. biomolecules like DNA or drugs).[12] The examination of model substances may also allow the prediction of (chir)optical properties and the determination of the absolute configuration.[5] As far as synthesis is concerned, such knowledge allows the design of novel helical molecules with tailored chiral properties and prevents futile synthetic efforts.

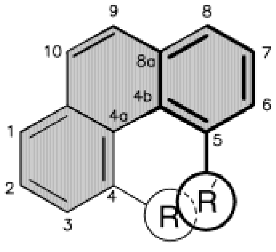
Figure 2. Evolution of more simple helical and planar-chiral molecules starting from **2** (or from heptahelicene) by continuous formal distraction of benzene rings; these molecules are chiral without having stereogenic centres



The well-known [*n*]helicenes[4] are promising candidates for structure/chiroptics correlations, but there is hitherto no easy synthetic pathway[14] to substituted, well-soluble derivatives, which would allow a gradual variation of their pitch. The range of formulae **2**–**6** (Figure 2) show our own concept to reduce the size of helicene-type molecules while preserving the propeller sense.[15] Replacing benzene rings through aliphatic bridges one finally ends up with the dinucleic *planar* chiral [2.2]metacyclophane **5** skeleton and with the mononucleic [*n*]meta- or [*n*]paracyclophanes (**6**). As one main topic of these studies we therefore used the rigid [2.2]metacyclophane **5** skeleton (Figure 2), which leads to small planar chiral compounds by suitable substitution and to small helically chiral molecules by insertion of heteroatoms into the cyclophane bridges (see **8b**, **9**–**12**, Figure 3a). The advantages of this choice are the limited number of atoms, that made a reliable calculation of the CD spectra possible for the first time, and the good solubility and the high crystallisation tendency of [2.2]metacyclophanes allowing X-ray crystallographic examination of torsion effects and absolute configurations. It should be mentioned that the molecules considered here may be regarded as small in organic chemistry but are definitly large for a quantum mechanical treatment of chiroptical properties.

Another way to small helically deformed condensed aromatic systems is opened up by the substitution of the phenanthrene skeleton in position 4 and 5 (cf. **7**). The choice of the substituents (steric demand, electronic properties) allows a convenient tailoring of helicity.[16]

Scheme 1



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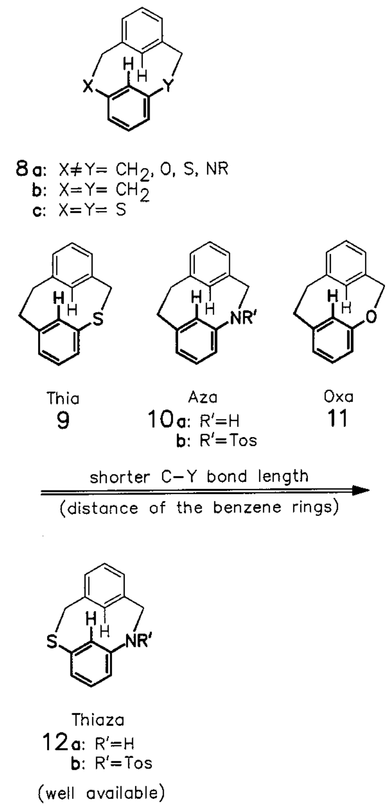
The introduction of heteroatoms into the [2.2]metacyclophane bridges (Figure 3a) allows a controlled increase of the twisting of the connected benzene rings against each other. Furthermore the internal deformation of the two-bladed propellers should be the more pronounced the closer the two benzene rings are pressed together by short cyclophane bridges $-CH_2-X-$ and $-CH_2-Y-$ in **8** (Figure 3a). During the past 20 years we synthesized a large number of monohetera- and dihetera[2.2]metacyclophanes[1a][17] in which the carbon−heteroatom distance determines the molecular strain. Figure 3a shows [2.2]metacyclophanes **9−11** in order of increasing strain. The C−X bond length decreases from X = S to X = O, so that the 1-oxa[2.2]metacyclophane **11**[18] is the sterically most strained monohetera [2.2]metacyclophane with the highest boat-shaped deformation in the benzene rings (cf. angles α, α' in Figure 3b). The tilting angle δ (Figure 3b), however, may be largest if the difference between the C−X and C−Y bond lengths is largest (i.e. for X = O and X = S).

The thiazacyclophanes of type **12** are comparatively easy to synthesize in one (cyclisation) step[1a][17] (Figure 4), so that we were able to prepare a range of differently substituted derivatives to study the influence of intraannular substituents R on the CD and other properties.[19]

3. Syntheses

As we want predominantly to direct the attention to results on structure/chiroptics relationships and especially (experimental and theoretical) circular dichroism spectra we present here only short general synthetic procedures which give an impression of the type of (macro)cyclization reactions, the problems regarding yield reductions arising from medium ring closure and the steric hindrance involved. For preparative details we refer to the literature references given below and comment only on selected compounds.

Figure 3a. Two-wing propeller molecules



a) Hetera[2.2]metacyclophanes

The chirality-inducing step is the formal substitution of one or more carbon atoms in the bridge of the [2.2]metacyclophane hydrocarbon **8b** to yield the heterocycles **8a** ($X \neq Y$; Figure 3a). The length of the bridges and consequently helicity and strain can be influenced within far limits. The first synthesized member of the [2.2]metacyclophane family in history was the hydrocarbon **8b** itself.[20] The first molecule with heteroatoms in the bridge was 1,10-dithia[2.2]metacyclophane (**8c**).[21] 1-Thia- (**9**) and 1-oxa[2.2]metacyclophane (**11**) were prepared many years later[18] by intramolecular ring closure methods. Considering that these cyclophanes are ring-strained compounds, the syntheses of **8c** and **12** and most cyclophanes mentioned in the following section were carried out under high-dilution conditions (dilution apparatus),[22] by the use of selected bases and by taking advantage of the cesium effect[23] (Figure 4).

All chiral representatives (**9−12**) could be separated into the enantiomers (see below). As described in Section 4b, the comparison of experimental and theoretical CD spectra allowed the assignment of the absolute configuration of **9** and **12**.[5][24]

A slight shortening of the cyclophane bridges was also achieved by the synthesis of the *N*-tosylazacyclophane **10b**,[25] following the same preparative principle. In this case

Figure 3b. Molecular angles indicating distortion

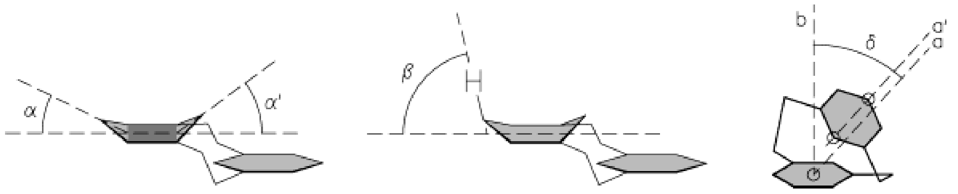
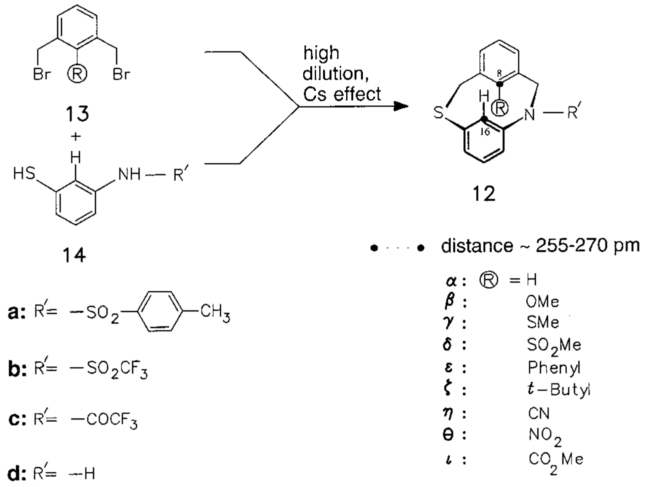


Figure 4. Synthesis of thiaza[2.2]metacyclophanes and indication of C8−C16 distances depending on intraanular substituents R



the tosyl group affected the chiroptical studies adversely, caused by the additional (tosyl) chromophore. A subsequent removal of the tosyl group in order to yield the free amine **10a** failed because of special reactivity due to the clamped molecule's geometry and strain. This problem was circumvented by using another protection-group strategy. The introduction of the *N*-activating trifluoroacetyl group allowed cyclisation and subsequent cleavage of the activating group to yield the free amine **10a** in satisfactory yield.[24][26]

Very recently the strong *N*-activating effect of the trifluoroacetyl group has enabled for the first time successful two-component cyclizations of suitable building blocks yielding 1,10-diazacyclophanes **15**[27] and 1-thia-10-aza[2.2]metacyclophanes **12bα−ι;** with varying *N*-substitution respectively.[17k] The 1,10-diazacyclophane **15b** is, according to calculations[28] and NMR studies, one of the most strained compounds in the [2.2]metacyclophane series. The close proximity of the arene rings is indicated by an extremely highfield-shifted inner proton signal [$\delta(H_i)$ = 3.81] compared to the [2.2]metacyclophane hydrocarbon **8b** [$\delta(H_i)$ = 4.25].[27]

Figure 5. Hetera[2.2]metacyclophanes

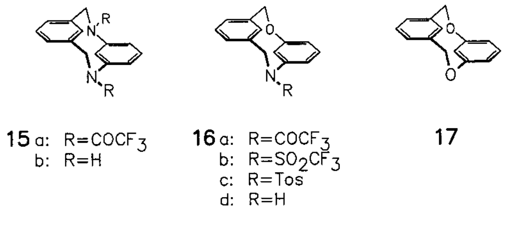
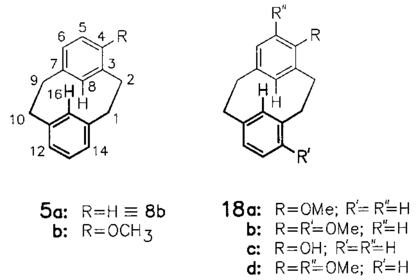


Figure 6. Planar-chiral [2.2]metacyclophanes



The even higher strained (due to the shorter C−O compared to the C−N bond length) 1-oxa-10-aza[2.2]metacyclophane **16a** was detected by mass spectrometry several times after comparable synthetic procedures as shown in Figure 4.[29] In our current research we are trying to improve the synthetic processes for such highly strained molecules (repulsive steric interactions between the intraannular positions 8 and 16, see Figure 6) combined with new *N*-activating group strategies. Nevertheless, all efforts to synthesize the highest strained 1,10-dioxa-[2.2]metacyclophane **17** failed so far.[30]

b) Planar-Chiral [2.2]Metacyclophanes

[2.2]Metacyclophanes **5**, substituted in one or more of the positions 4, 14 or 6, 12 are planar-chiral and served Lehner, Schlögl, Ugi, Ruch, and Derflinger[31] for fundamental studies towards quantitative correlations with regard to chirality functions. Thus, **18b** should exhibit a double Cotton effect intensity compared to **5b**, equal R provided. Some spectroscopic and theoretical results are discussed in the theoretical paragraph 4b.[32]

The diaza[2.2]metacyclophanes **15** were synthesized according to the scheme shown in Figure 7. Attemps to introduce substituents into its carbon skeleton to render it chiral were unsuccessful. Because of the higher steric strain the yields are lower than for **12a**.[27]

c) Planar-Chiral [*n*]Paracyclophanes and [*n*]Metacyclophanes

In addition to the existing 1,ω-dioxa- and carboxyclic [*n*]paracyclophanes[33] we synthesized a number of dithia-bridged paracyclophanes[34] with aliphatic and partly unsaturated bridges. These were obtained under dilution conditions by the use of suitably functionalised cyclisation substrates (dibromides,[35] dithiols[36]). The introduction of unsaturated elements (**a**, **b** in Figure 8) enabled the examination of the influence of etheno and ethyno bridges[37] towards the deformation of the aromatic parts and chiroptical properties. NMR and X-ray-crystallographic studies re-

Figure 7. 1,10-Dihetera[2.2]metacyclophanes **8c** and **15** and **15a** and **b**

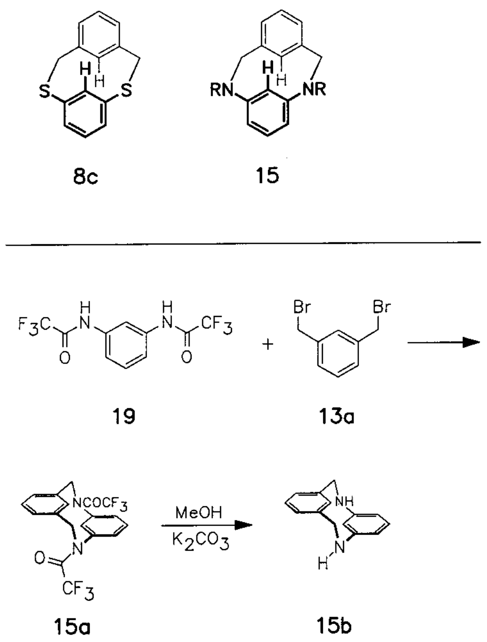


Figure 8. Synthesis of [*n*]paracyclophanes

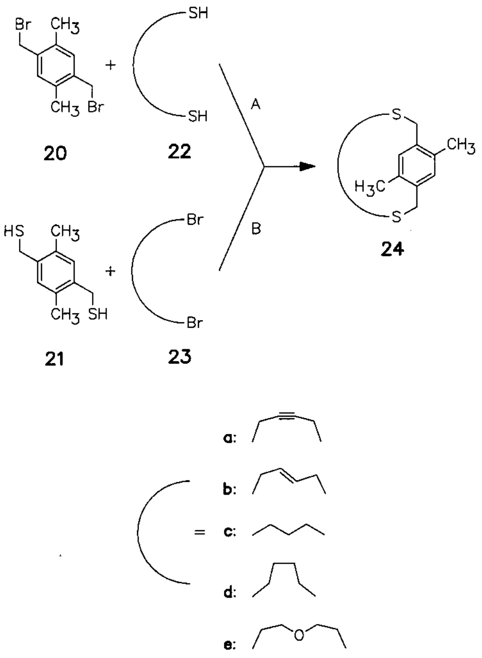
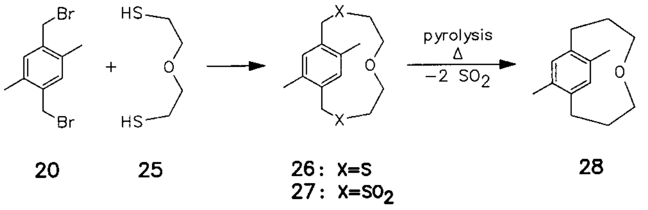
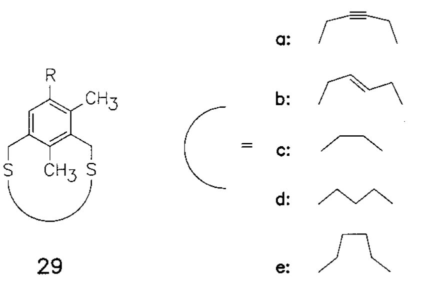


Figure 9. Synthesis of 9,12-dimethyl-5-oxa[7]paracyclophane



Scheme 2



vealed C_2 symmetry of the [8]paracyclophanes **24a**, **d** and C_1 symmetry of the [7]paracyclophanes **28** and **42** (s. b.) in solid state and solution (Figure 9).

All cyclophanes were separated into their enantiomers and showed similar CD spectra with typical Cotton effects for electron transitions of the aromatic rings with significant contributions of the sulfur atoms. According to calculations (see paragraph 4d) the first oxa[7]paracyclophane **28**[38] showed a remarkable short oxygen−benzene distance compared to the carbocyclic analogue **42**[39] which is indicated by a strong charge transfer band in the CD spectrum. The chiral cyclophane **28** was synthesised by the dithia route and sulfone pyrolysis developed by us.[40]

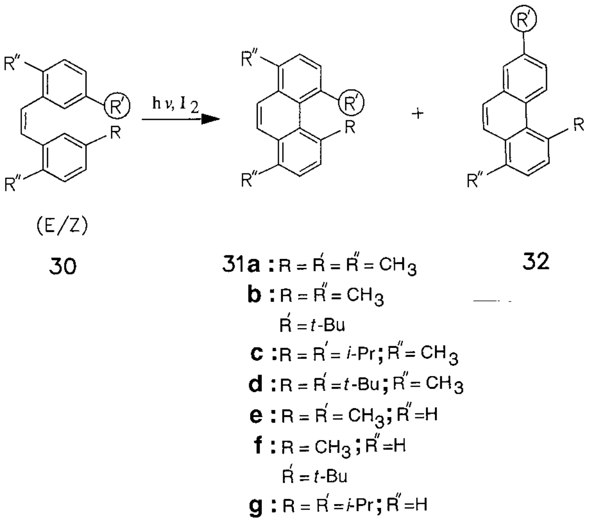
A pathway to dithia[*n*]metacyclophanes **29** by thiol/bromide cyclisations[5][41] and subsequent sulfone pyrolysis analogous to the steps shown in Figures 8 and 9 allowed the first systematic studies of the previously only poorly examined planar-chiral [*n*]metacyclophanes.[42] The motion of the cyclophane bridges was examined by dynamic NMR methods. It turned out that the cyclophane bridges undergo rather complex pseudorotation motions which can be frozen at low temperatures whereas a *flip* process[43] is prevented by the intraannular substituents. The distances between bridge and benzene ring obtained from X-ray crystal structures correlate well with the observed NMR shifts.

d) Twisted Phenanthrenes

A way to synthesize phenanthrenes − and higher helicenes − is the well-known photochemically induced dehydrocyclisation reaction from the corresponding stilbene precursor using I_2/O_2 as dehydrogenation agent.[14g] We were able to extend the known series of helically chiral phenanthrenenes[44] by the synthesis of **31b**, **c**. A steric increase of the substituents in 4,5-position (cf. **7**) should yield more strongly strained and helically distorted phenanthrenes. For **31b** we found a deformation angle of 36.6° by X-ray structure analysis which is the largest value known hitherto for a phenanthrene.[16]

The above synthesis seems to be limited to molecules that are sterically not extremely hindered. For 4,5-di-*tert*-butyl-1,8-dimethylphenanthrene (**31d**) ab initio studies revealed the largest deformation angle (45.9°) known so far.[16] Its photochemical synthesis gives very low yields, and the isolation failed. The presence of **31d** could only be determined by GC-MS analysis. Besides steric interactions, electronic effects also influence the distortion of the molecules. In decachlorophenanthrene, for example, the large number of electron-withdrawing groups, according to calculations, de-

Figure 10. Synthesis of twisted 1,10-substituted phenanthrenes **31**

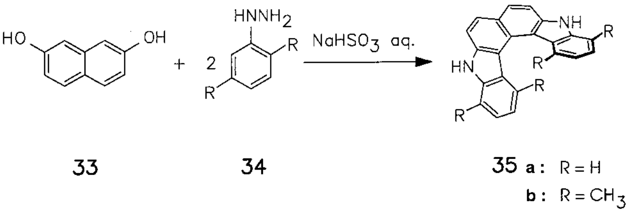


stabilizes the π-system which results in a larger helical deformation compared to the 4,5-dichloro derivative with similar interactions (vide infra)

e) Helicenes[4]

Helicenes are benzologues of phenanthrene ([3]helicene, cf. **7**) in which a regular cylindrical helix is formed through an all-*ortho* annelation of the aromatic rings. The helical structure is a consequence of the repulsive steric interactions between terminal aromatic rings or (in the case of 4,5-distubstitued phenanthrenes) substituents. In the field of helicene chemistry we are interested in non-photochemical[14a][14b][14c][14d] syntheses of helicenes and the structure-chiroptics relationships of those species. Following a historical preparation pathway we synthesised the new tetramethyl-substituted pyrrolohelicene **35b** (Figure 11).[45] Unlike the known **35a** the helix of **35b** is configurationally stable at room temperature due to the steric interactions of the inner methyl groups. This allowed us the first enantiomer separation of this heterohelicene system and recording of the CD spectra (Section 4e). X-ray crystal structure analyses of both helicenes **35** permitted to determine the pitch of the inner helix and other information of the molecular geometry. Quantum chemical calculations for the racemization barriers of helicenes (and phenanthrenes) carried out before synthesis are very helpful in order to obtain configurationally stable substances.

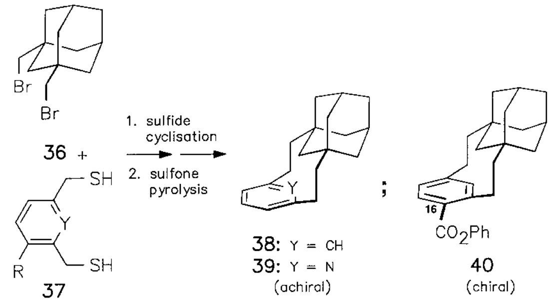
Figure 11. Synthesis of pyrrolohelicenes



f) Aliphatic Cyclophanes ("Aliphanes")[46c]

The adamantane unit, functionalised in the 1- and 3-positions is similar to the *meta*-phenylene building block − with regard to the angle between the functional groups − and opens a pathway to adamantanophane[46]-type molecules. The properties of this highly strained family of compounds regarding strain, spectroscopic effects and conformational behavior differ significantly from those of the [2.2]metacyclophane and [*n*]cyclophane systems described above. By introduction of substituents in the 16-position of the rigid [2.2]adamantanometacyclophane **38** and pyridinophane **39** we were able to synthesize planar-chiral adamantanophanes such as **40**[46] by the route of sulfide cyclisation and subsequent pyrolytic extrusion of SO_2[40] related to the syntheses shown in Figure 8 and 9. Results of experimental and theoretical CD investigations are given in ref.[46].

Figure 12. Synthesis of adamantanophanes



g) Enantiomer Separation and Circular Dichroism Measurement

Most of the enantiomer separations were carried out by HPLC on cellulose tris(3,5-dimethylphenylcarbamate[47]) columns in analytical scale, repeated several times to yield enough material for CD measurements. This successful use of Okamoto's separation resins[47] led to a base-line separation of nearly all cylophanes. For separation in preparative scale we used semipreparative columns to obtain gram amounts of pure enantiomers for further examinations like gas-phase CD measurements. Pirkle[48] and Cyclobond[49] columns were used in a few, more special cases. The CD spectra were measured with a spectropolarimeter J-720 (Fa. JASCO, Tokyo).

4. Theoretical Methods and Structure/Chiroptics Relationships

What information can we obtain from experiments and from theoretical calculations of chiral molecules? One of the most important features is the assignment of the absolute configuration by comparison of experimental and theoretical CD spectra. Furthermore, from the spectroscopic point of view we are able to give in most cases a detailed assignment of individual excited electronic states to the observed CD bands. Compared to ordinary UV absorption spectra a higher "resolution" can be obtained in CD because overlapping bands are resolved when the CD signs of the corresponding transitions are different.

In the past 5−10 years we have optimized our quantum theoretical approaches to calculate the CD even for larger molecules with high accuracy so that we also can obtain other valuable information from experimental and theoretical CD, for example about conformer equilibria. The next section contains a brief review on the theory of electronic CD and the theoretical methods employed throughout.

a) Theoretical Considerations

In electronic CD spectroscopy, one of the main quantities of interest is the rotatory strength, R, which gives the intensity of a CD band. In non-orientated media (gas phase, fluid solution),[51] the rotatory strength R for a transition between two electronic states, Ψ_0 and Ψ_f, is given by the imaginary part of the dot-product between the electronic and magnetic dipole transition moment vectors.[52]

$$R = Im\,(\langle\Psi_0|\bar{m}|\,\Psi_f\rangle\,\langle\Psi_f|\bar{\mu}|\Psi_0\rangle) \qquad (1)$$

where $\hat{\mu}$ and $\hat{m}$ are the electric and magnetic dipole moment operators (for further details the reader is referred to ref.[53]).

Experimentally, one obtains R of a given CD absorption band by integrating the area under the corresponding peak. It can be shown that in cgs units

$$R = 2.297\times10^{-39}\int_{\lambda_1}^{\lambda_2}\frac{\Delta\varepsilon(\lambda)}{\lambda}d\lambda \qquad (2)$$

where $\Delta\varepsilon$ is the difference of extinction coefficients for left- and right-handed circularly polarized light and λ is the excitation wavelength. Thus, the theoretical simulation of a CD band made from one electronic transition requires the knowledge of the excitation energy ΔE (usually the center of a band) and the two transition moment vectors in Eq. 1. From actual calculations it turns out that good results for larger molecules with several close-lying states can only be obtained with wavefunctions of high quality (e.g. errors for ΔE < 0.2−0.4 eV). It is important to mention here that the relative orientation of the μ and m transition vectors determine the sign of the CD band (positive sign for angles < 90°, negative for angles > 90°). Thus, it is concluded that the calculation of the CD is not a simple task and represents really a challenge for any quantum mechanical method.

The most general theoretical approach to determine the ground- and excited-state wavefunctions and their energies is the configuration interaction method.[54] Here, Ψ_0 and Ψ_f are obtained by solving the Schrödinger equation variationally with the following linear combination ansatz

$$\Psi^{CI}_{o,f} = C_0\Phi_0 + \sum_a\sum_y C^r_a\Phi^r_a + \sum_a\sum_b\sum_r\sum_s C^{rs}_{ab}\Phi^{rs}_{ab} + \ldots \qquad (3)$$

where Φ are spin-adapted functions (CSF) made from linear combinations of Slater determinants. According to the number of electrons, which are "excited" from the occupied (in Φ_0, the closed-shell ground-state determinant) to the virtual MO space, the CSF can be classified as singles, doubles, triples and so on. For systems with more than a few electrons full CI expansions (including the CSF built from all possible excitations) become prohibitively large (more than several million terms) so that a wide range of approximations have been developed in the past.

The first is the multi-refererence singles and doubles CI (MRD-CI) method[55] which includes single and double excitations with respect to several reference CSF. Our initial approach to calculate the CD of [2.2]metacyclophanes was based on such an MRD-CI treatment.[5] However, we have not employed the exact Hamiltonian but modern semi-emprical NDDO integral approximations (AM1[56], PM3[57], NDDO/S[58]). This combination of methods was based on the idea that accurate excitation energies in larger unsaturated molecules can only be obtained by including the dynamical electron correlation between σ and π electrons. Because these effects, which are in the case of benzene larger than 1 eV for the ΔE values, are implicitely accounted for (partially) in the NDDO Hamiltonians[59] we obtained good results in several applications for molecules with benzene chromophores.[5][24][41a] However, further investigations with the NDDO/MRD-CI methods show that the applicability is quite limited and more complicated chromophores could not be described with the desired accuracy (this can be traced back mainly to the integral approximations in the Hamiltonians and the fixed minimal AO basis sets employed).

In recent years, the CASSCF/CASPT2 approach of Roos and coworkers[60] has become a valuable tool to investigate excited states of medium-sized molecules and numerous applications in UV spectroscopy have been presented. However, no investigations in the field of CD were published. This is due to the fact that the CASSCF reference function (from which the transition moments are evaluated) can not be obtained with reasonable effort and accuracy for large molecules of low symmetry.

Recently, one of us developed a combination of density functional (DF)[61] and CI approaches to attack the problem of excited-state calculations for larger molecules.[62] The basic idea behind this method is the inclusion of dynamical electron-correlation effects by using information from Kohn-Sham (KS) DF theory [the molecule orbitals (MO) and orbital energies] in a simple single CI treatment [including only singly excited CSF with respect to the closed-shell ground-state determinant, (SCI)]. The method has been proven very successful for the prediction of vertical excitation energies of a wide range of molecules (errors < 0.2−0.3 eV).[62] The first DFT/SCI investigations of CD spectra can be found in ref.[38][62][64]. Applications to EEL and XANES spectroscopy can be found in ref.[63]. We will give here a brief review of the method and describe the previously unpublished extension to the random-phase approximation (DFT/RPA).

In the DFT/SCI method empirically modified CI matrix elements for singly excited CSF (Φ'_a, a, and b represent occupied, r and s virtual MOs) are used. The CI matrix diagonal element for a singlet wavefunction (only singlet-singlet transitions are considered in this survey) is given by

$$\left\langle \Phi_a^r \middle| \hat{H} - E_0 \middle| \Phi_a^r \right\rangle = \varepsilon_r^{KS} - \varepsilon_a^{KS} - c_1 J_{ar} + 2K_{ar} + \Delta(K_{ar}, \varepsilon_a) \tag{4}$$

where ε^{KS} are the Kohn-Sham orbital energies, c_1 is a scaling factor (depending only on the exchange-correlation functional used), J and K are coulomb and exchange integrals over the KS-MO basis and $\Delta(K,\varepsilon) = c_4\varepsilon + c_2\exp(-c_3K^4)$ is an empirical shift function.[65] In order to retain the ground-state KS density all Fock matrix coupling elements are neglected, i.e. $\langle\Phi_0|F|\Phi'_a\rangle = 0$ and $\langle\Phi'_a|F|\Phi'_b\rangle = 0$ (implicit Brillouin's theorem).

The SCI off-diagonal elements are treated in analogy to Eq. 4, i.e. the coulomb term is scaled and the exchange term is kept exactly as in the HF/SCI method [(*ab rs*) represent two-electron integrals over the KS-MO basis].

$$\langle\Phi'_a|\hat{H}|\Phi'_b\rangle = -c_1(ab|rs) + 2(ar|bs) \tag{5}$$

Previous applications and the examples presented here for the first time show that the DFT/SCI approach efficiently accounts for higher excitation classes (doubles, triples, ...) and thus the most important dynamical electron-correlation effects. An advantage of this approach over standard semiempirical methods is that (i) flexible Gaussian AO basis sets can be employed, i.e. also states with diffuse character or pure Rydberg states can be investigated and (ii) all physical interactions (e.g. exchange terms) are accounted for by the effective DFT potential.

A further improvement (especially in the field of CD) can be obtained by extension of this formalism to the random-phase approximation (RPA) which is equivalent to the time-dependent Hartree-Fock approach.[66] In a complete basis this ansatz satisfies certain sum rules and (in a finite basis) gives better transition moments than the SCI method. The RPA equations read in matrix notation

$$\begin{pmatrix} \mathbf{A} & \mathbf{B} \\ -\mathbf{B} & -\mathbf{A} \end{pmatrix} \begin{pmatrix} \mathbf{X} \\ \mathbf{Y} \end{pmatrix} = \omega \begin{pmatrix} \mathbf{X} \\ \mathbf{Y} \end{pmatrix}$$

where ω is the excitation frequency, $\boldsymbol{X}$ and $\boldsymbol{Y}$ are the solution vectors of the singly excited particle-hole amplitudes, the $\boldsymbol{A}$ matrix contains all elements of the SCI matrix (Eq. 4–5) and the elements of the $\boldsymbol{B}$ matrix are given by

$$^1B(a\rightarrow r, b\rightarrow s) = 2\,(ar|bs) - (as|br)$$

In the DFT/RPA method we employ a slightly different set of empirical parameters than in the DFT/SCI method (i.e. with the B3LYP functional: $c_1 = 0.285$, $c_2 = 0.0265$, $c_3 = +1.345\cdot10^{-7}$) for the matrix elements of the $\boldsymbol{A}$ matrix but left the terms in the $\boldsymbol{B}$ matrix unscaled.

Throughout this work we are dealing only with vertical excited states, i.e., the ground-state geometries (fully optimized at HF-SCF, DFT or semiemprical NDDO levels) are employed for the excited states also. Especially for larger molecules this represents a good approximation to the excitation energy at the band maximum. All in all with the solvation effects neglected in this study we can estimate a total uncertainty for a comparsion between theoretical and experimental band positions of 0.2–0.3 eV (this represents an error of e.g. 15–20 nm for a transition at 200 nm or 50–80 nm at 400 nm). As will be shown below nearly all DFT/SCI(RPA) data for the molecules investigated here are within these error limits. In order to allow a more realistic comparison with the experimental CD spectra, summation of Gaussian curves with a half width of 0.4–0.5 eV for each calculated transition yields the theoretical CD spectrum (the dashed line in the spectral figures, the sticks and filled dots indicate the position of the individual states).[67]

We have employed Becke's hybrid exchange-correlation functional (B3LYP)[68] and AO basis sets of at least valence double-ζ quality (C, N, O: [3s2p]; S: [4s3p]; H: [2s])[69] throughout this work. Further augmentation of these VDZ basis sets with polarization d functions or diffuse Rydberg functions (usually one sp-AO set placed in the center of charge of the lowest cation state) is indicated by adding the letters d or R to the basis set acronym.

b) [2.2]Metacyclophanes

The first calculations of CD spectra with the AM1/MRD-CI method were carried out on 1-thia- (**9**) and 1-oxa[2.2]metacyclophane (**11**).[5] The results of new DFT/RPA calculations are show in Figures 13 and 14. The spectra of both compounds are remarkably similar showing three lowest lying negative bands (A–C) followed by an intense positive peak (D at 200 nm) and a negative band around 180 nm. These experimental features of the spectra are well reproduced by the calculations. To be brief, the lowest lying bands A–C are made from coupled L_b and L_a ππ* states of both rings. The bands D result from perturbed benzene-like E_{1u} states while the high density of states below 230 nm partially results from contributions of the C–X bridging bond and lone-pair orbitals so that some of these states have no simple correspondence to the parent benzene. Excitations to Rydberg orbitals, included in test calculations, have much lower CD intensities and are usually not seen in condensed-phase measurements.

As expected from a consideration of the molecular geometries (see Figure 15) the thia compound **9** shows a higher calculated CD intensity (by a factor of two; the theoretical intensities in Figure 13 have been scaled by a factor of 0.5) than the oxa compound **11** due to the stronger deviation of the geometry from C_{2h} symmetry (elongation of one bridging bond results in a larger tilt angle between the two rings, cf. Figure 3b). However, this is not found in the experiments. The reason for this deviation is not completely clear at present although an error of ± (30–50)% in the experimental determination of $\Delta\varepsilon$ is not unusual. In most cases studied the absolute $\Delta\varepsilon$ values from DFT/RPA theory deviate by less than 30% from the experimental data and larger differences suggest experimental problems (e.g. incomplete enantiomer separation; see also the case of [5]helicene, section 4e).

Another example proves the efficiency and accuracy of our calculations. The 1-thia-10-aza[2.2]metacyclophane (**12a**) was obtained in enantiomerically pure form due to spontaneous enantiomorphous crystallisation.[17g] Anomal-

Figure 13. Comparison of experimental (solid line) and theoretical (dashed line) (VDZd AO basis, HF-SCF/VDZd geometry) CD spectra of 1-thia[2.2]metacyclophane (**9**); the theoretical CD intensity has been scaled by a factor of 0.5

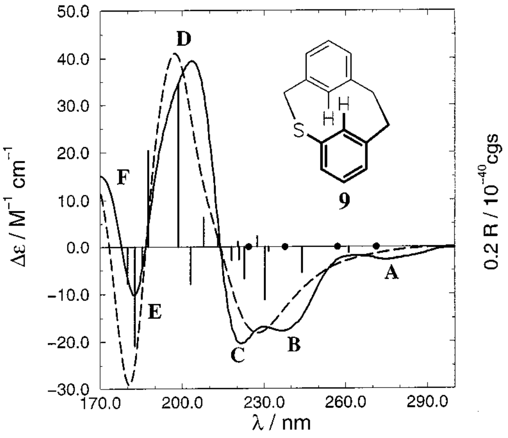
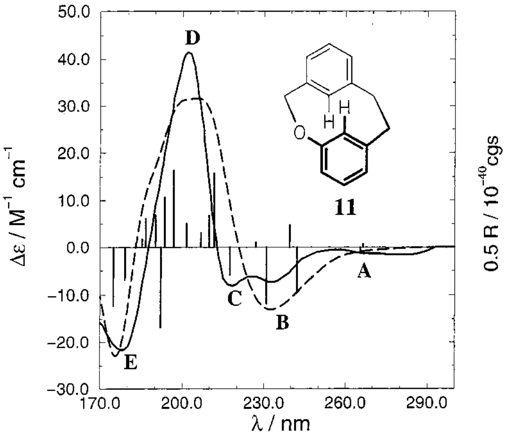


Figure 14. Comparison of experimental (solid line) and theoretical (dashed line) (VDZd AO basis, HF-SCF/VDZd geometry) CD spectra of 1-oxa[2.2]metacyclophane (**11**)



ous X-ray diffraction reavealed the sample as (*M*) enantiomer. A CD spectrum taken from this crystal corresponded reasonably well in the higher energy region with AM1/MRD-CI calculations[24] carried out beforehand. This allowed the determination of the absolute configuration of all 1-thia-10-aza[2.2]metacyclophanes synthesised until then.[17k] The absolute Δε values of **12a** range (as expected) from +90 to $-90 \cdot 10^{-40}$ cgs (i.e. twice as much than for the thia compound **11**) which indeed indicates experimental uncertainities in the case of **11**. The 1-thia-10-aza[2.2]metacyclophane was the first case studied where two energetically close-lying conformers, which are distinguished by an inversion at the nitrogen atom (see Figure 16), have to be considered.

At AM1, DFT, and HF-SCF theoretical levels **12aB** is found to be more stable by 0.5−1.3 kcal/mol and also X-ray diffraction found this structure in the crystal. However, in previous CD calculations a better agreement with the experimental spectrum was obtained for the conformer **12aA**.[24]

Figure 15. Optimized geometries of **9** and **11** at the HF-SCF/VDZd level of theory; bond lengths and non-bonded C−C distances are given in A

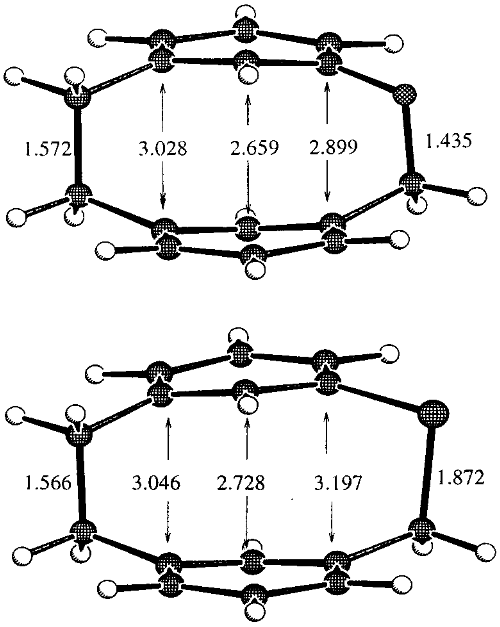
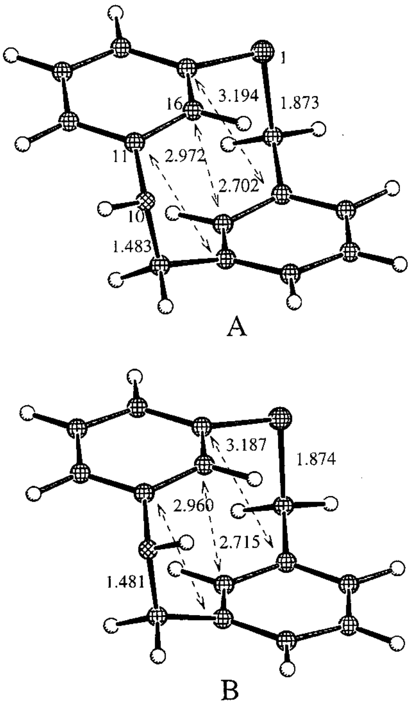
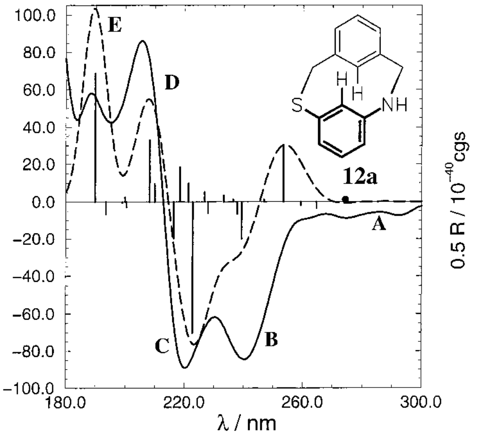


Figure 16. Optimized geometries of the two conformers of (**12a**) at the HF-SCF/VDZd level of theory; bond lengths and non-bonded C−C distances are given in A



The results of the new DFT/RPA computations (see Figure 17) employing the structure **12aA** show not a complete agreement with experiment but larger deviations for the bands B, D, and E in the case of conformer **12aB** are observed. Thus, we may conclude that confomer **12aA** is in solution (trifluoroethanol in this case) the dominating species. This can be explained with the larger dipole moment of

Figure 17. Comparison of experimental (solid line) and theoretical (dashed line) (VDZd+diff. sp-functions on the S atom AO basis, HF-SCF/VDZd geometry) CD spectra of 1-thia-10-aza[2.2]metacyclophane (**12a**); the theoretical data refer to conformer A



12aA (3.0 Debye) compared to that calculated for structure **12aB** (1.9 Debye) which causes a higher solvation energy and thus a preference in solution.

In the field of the well-examined [2.2]metacyclophane series **18** where the (planar) chirality is induced by substituents at the arene rings we added some interesting aspects. Our examinations of pure enantiomers revealed that a quantitative understanding of chiroptical properties cannot be gained through simple additive ligand parameters. Towards a complete calculation of chiroptical properties, especially for the CD spectra, different conformers have also to be taken into account. In the case of methoxy or hydroxy substituents attached to a benzene ring it is well known that the in-plane arrangement of the −OR group is energetically only slightly favoured (for anisole by ca. 2−3 kcal/mol[70]) with respect to a perpendicular structure. The combination of experimental and theoretical CD spectroscopy is able to show that the in-plane orientation of the −OMe group in the monosubstituted [2.2]metacyclophane **18a** is preferred in solution (Figure 18).

The CD spectrum of **18a** shows a very rich structure with five separated bands (A−E, see Figure 19) and alternating CD signs. The $\Delta\varepsilon$ value of the most intense band E is similar in magnitude compared to the bridge-substituted compounds **9** and **11**, suggesting that the chiral induction by the attached substituent is also quite large. Theoretically, we have tested several geometries with different orientations of the −OMe group with respect to the ring. The best agreement between theory and experiment is found for the HF-SCF/VDZ optimized structure (see Figure 18) with a nearly in-plane arrangement of the −OMe group (the dihedral angle Θ is 3°). Although bands A and C are predicted too weak and band E is found to be too intense all bands have the correct CD sign and energetic position. The difference between theory and experiment may be attributed to a quite broad distribution of the vibrational wavefunction over the Θ range.[71] CD calculations with model structures (Θ = 45 and 90°) do not yield the resolved positive band C and deviate also in the other regions more strongly from experiment. Thus, it is concluded that this comformer is the most stable in solution. The good agreement also allows us to assign the absolute configuration: the $(+)_D$ enantiomer has the (R_p) configuration.

Figure 18. Optimized geometry of 4-methoxy[2.2]metacyclophane (**18a**) at the HF-SCF/VDZ level of theory; bond lengths and nonbonded C−C distances are given in A

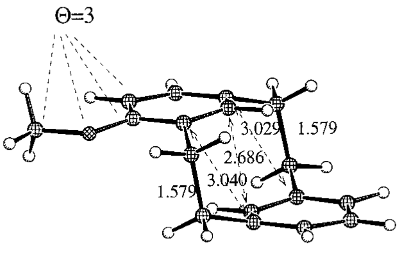
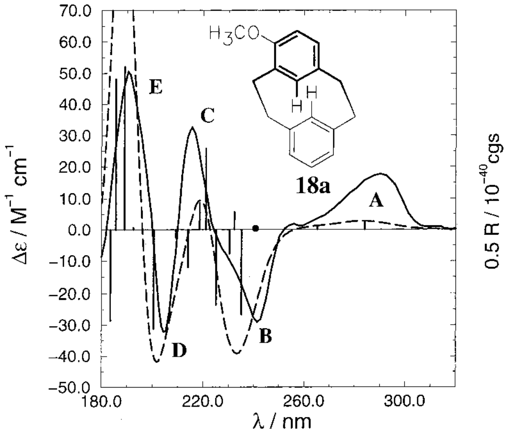


Figure 19. Comparison of experimental (solid line) and theoretical (dashed line) (VDZd AO basis, HF-SCF/VDZ geometry) CD spectra of 4-methoxy[2.2]metacyclophane (**18a**)



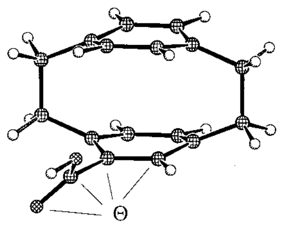
Comparision of the monosubstituted **18a** and the homodisubstituted [2.2]metacyclophane **18b** show distinct differences from the expected doubling of the CD bands (cf. chirality functions[70]). Additional substitution in the "achiral" 5-position (**18d**) changes the CD spectrum completely due to electronic effects of the neighboured electron-pushing substituents. Furthermore, steric interactions between the two methoxy groups in the 4- and 5-position change the potential-energy curves for methoxy group rotation. A very complicated situation with several conformers results which is not suitable for a theoretical analysis.

c) [2.2]Paracyclophanes

Due to the face-to-face orientation of the two benzene units in [2.2]paracyclophanes[73] larger electronic interactions between the two rings than in [2.2]metacyclophanes are to be expected which should clearly be visible in CD spectra also. The rigid molecular framework of these compounds with D_{2h} symmetry[72] becomes chiral by substitution of one benzene ring or introduction of one substituent in the ethano bridges. In detail we have theoretically investigated the CD for the 4-carboxy[2.2]paracyclophane **41** to show that accurate calculations can resolve conformational equilibria in solution.

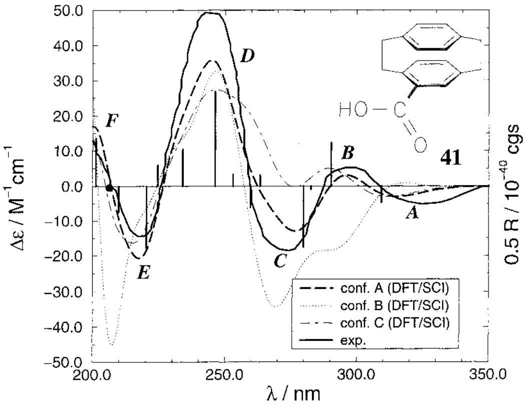
Semiempirical PM3[57] optimizations of this phane reveal the existence of at least three low-lying confomers which were considered further. The first (**41a**, see Figure 20) has a C=O group twisted by −129° with respect to the benzene ring. In confomer **41b** the C=O moiety is nearly in plane but rotated to the opposite side while conformer **41c** is obtained from **41a** by a 180° rotation around the Ar−COOH bond. Because the π conjugation between the ring and the COOH group is largest for the conformer **41b** we expect similar CD spectra for **41a** and **41c** and some differences for the spectra of **41b**. This is indeed found in the DFT/SCI calculations shown in comparison with the experimental data[74] in Figure 21.

Figure 20. Optimized geometry of 4-carboxy[2.2]paracyclophane (**41a**) at the PM3 level of theory; the dihedral angles Θ are given in°



Θ
conformer **41a**:-129.4
41b: 4.2
41c: 55.6

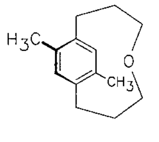
Figure 21. Comparison of experimental (solid line) and theoretical (dashed line) (VDZ AO basis, PM3 geometry) CD spectra of (−)-(*R*)-4-carboxy[2.2]paracyclophane (**41**); the geometries of the considered conformers **41a**, **41b** and **41c** are discussed in the text



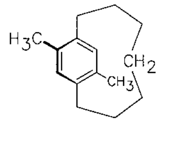
Although the simulated spectra of the conformers **41a** and **41c** are quite similar, a quantitative agreement for the band positions and CD intensities for the six resolved bands is only obtained for **41a**. Thus, we can conclude that this structure is mainly responsible for the CD in solution. It is important to mention here that the three conformers have very similar total (gas-phase) energies (within 2 kcal/mol; which is calculated to be most stable depends on the theoretical method employed) so that this conclusion can not be obtained from any quantum chemical approach which considers only the ground-state energies. The experimentally assigned absolute configuration of (−)-(*R*)[75] is confirmed by our calculations.

d) [*n*]Cyclophanes

In general, calculations for the CD spectra of [*n*]cyclophanes seem to be more difficult due to the inherent flexibility of the relatively long aliphatic chains ($n \geq 6$). However, in favourable cases the conformers which result from a chain rotation are indentical as shown below for the recently synthesized 9,12-dimethyl-4-oxa[7]paracyclophane[75] (**28**) (see Figure 22) so that only one molecule has to be considered.

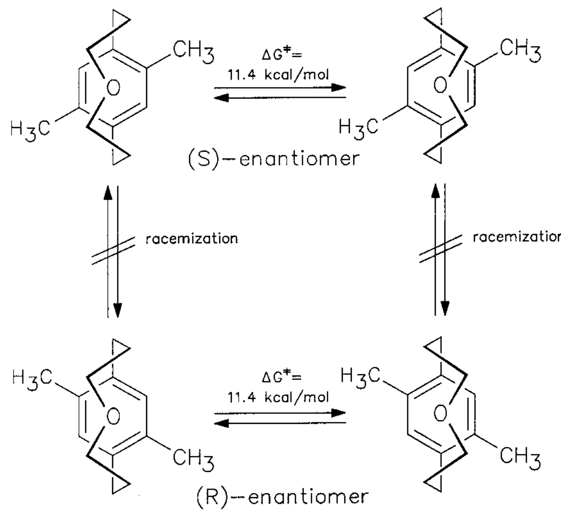


28



42

Figure 22. Schematic relations between the "no-reaction" conformers and enantiomers of **28**



Shortening of the aliphatic bridge in [*n*]paracyclophanes results in stronger deformations of the benzene ring towards a boat-shaped conformation (as measured by the boat-type deformation angles α and β in Figure 23; see also Figure 3b). Comparison of the data of **28** and the hydrocarbon analogue **42** shows that a shortening of the chain due to shrinked C3/C5−X4 bonds (1.43 vs. 1.56 A for the C−O and C−C distances, respectively) in **28** has a negligible effect on α, and β is increased by less than 1.5°. Moreover, no systematic changes of the bond angles in the chain are observed. Unexpectedly, a decrease of the C−C(chain) bond lengths in **28** compared to **42** is noticed which can partially be attributed to the inductive influence of the oxygen atom. Another effect may result from the significantly different orientations of the C3−X−C5 fragments (see Figure 23): the non-bonded interactions of the additional C−H bond with the ring charge density in the hydrocarbon prevents an optimal orientation of these three atoms (the CH_2 group is tilted upwards) which causes additional strain in the methylene bridge of **28**. This may overcompensate the effects of the shorter CO bond lengths. The distance of the O atom to the center of the benzene ring in **28** is calculated to be only 2.784 Å (the corresponding C-atom−ring distance in **42** is 3.112 Å). Thus, strong interactions of the energetically high-lying lone-pair orbital at the oxygen atom with benzene ring orbitals can be expected from these geometrical considerations.

At room temperature, both the ^{1}H- and ^{13}C-NMR spectra of **28** indicate an apparent C_2 symmetry. Thus, time-averaged signals due to the rotation of the chain (shown schematically in Figure 22) are observed under these conditions. This process can be interpreted as a "no-reaction" since the resulting conformer can be transformed into the substrate by application of a C_2 symmetry operation. Thus, although **28** contains neither the C_2 nor the C_s symmetry element both operations are inherently present and affect the structural properties of the molecule (the bridge has nearly C_s, the ring nearly C_2 symmetry).

The "no-reaction" could be frozen out by experimentally decreasing the temperature below 210 K. In low-temperature ^{1}H-NMR experiments a splitting of the aromatic proton signals was observed. Application of the Erying equation to the NMR data results in a free activation enthalpy of 11.4 kcal/mol (48 kJ/mol). This barrier is within the same range as has been found for other [*n*]paracyclophane derivatives (13−14 kcal/mol, $n = 6$).[76] The corresponding transition state has been located at the semiempirical AM1[56] level to be 10.2 kcal/mol above the minimum which is in good agreement with the experimental value.

The experimental CD spectrum of **28** in acetonitrile shows four resolved CD bands A−D (see Figure 24). The comparison of the experimental and theoretical CD data[77] is very good, i.e. all bands A−D are predicted with the correct sign and good relative intensities (bands A−C). The negative band D shows a blue-shift in the theoretical spectrum of ca. 0.5 eV which may be caused by solvation effects absent in the theoretical treatment (see below). This quantitative agreement allows the assignment of the absolute configuration of **28**: the (−) enantiomer has the (*S*) configuration. This result is in agreement with the absolute (−)-(*S*) configurations of 8-carboxy[6]paracyclophane and a [7]paracyclophane derivative derived independently.[78] Since absolute $\Delta\varepsilon$ values could not be determined accurately enough, the experimental CD intensities have been scaled to the theoretical $\Delta\varepsilon_{\max}$ of band C. However, the $\Delta\varepsilon_{\max}$ calculated here for **28** is quite similar to the corresponding values of other dithia[7]paracyclophanes with the same ring-substitution pattern.[34a]

The negative bands A and B are attributed to benzene-type L_b and L_a states. The slight underestimation of the band A intensity may result from the neglect of vibronic-coupling effects which are known to be quite important in benzene derivatives. The positive band C is composed of two intense transitions which correspond to localized benzene-type ππ* transitions (1^1E_{1u} in benzene). The first negative CD transition at 205 nm coincides with the calculated excitation energy of a $\pi\rightarrow 3p$ Rydberg state (not assignable to one of the benzene states). However, this state is probably not responsible for the measured band D since states with diffuse character are in general strongly blue-shifted or their intensities are completely quenched in condensed media.[79] We can also attribute this CD band to a valence state (S_{12}) calculated at 190 nm (the second negative transition nearby is due to a Rydberg state). In this case, excitations out of the oxygen lone-pair orbital (this MO has also some contributions from the neighbouring CH_2 groups) into the two lowest lying π-MOs are important. The occurence of such a CT transition at these relative low energies is somewhat unexpected but seems to be an inherent feature of the molecule due the close proximity of the oxygen atom and the benzene ring. The CT nature of the S_{12} state is also demonstrated by the large increase of the dipole moment relative to the ground-state value [$\mu(S_0) = 1.8$ Debye, $\mu(S_{12}) = 7.9$ Debye] which partially explains the blue-shift of the theoretical excitation energy compared to the measured band position in acetonitrile.

In the case of dithia[*n*]metacyclophanes ($n = 6, 7$, see Scheme 2)[41a] two energetically close-lying conformers for each enantiomer must be taken into account to explain the experimental CD spectra. The best AM1/MRD-CI CD data were obtained for a 70/30% mixture of two conformers of 8,12-dimethyl-2,5-dithia[6]metacyclophane (**29cA** and **29cB**, R = H). This value is in good agreement with the ratio (70 ± 5%) derived from NMR data. Because **29cA** and **29cB** are enantiomers if one of the methyl groups is absent the two contributing spectra are nearly mirror images of each other. This could be explained by the importance of the Ar−C−S−C dihedral angles in the chain (which have nearly opposite signs in both conformers) to the chirality of these molecules. Although the theoretical and experimental spectra agree quite well it was not possible to assign the absolute configuration since too small energy differences and large uncertainties in the calculated CD spectra are involved.

e) [*n*]Helicenes

In previous work we have considered theoretically mainly the ground-state properties (structures and racemization barriers)[16][45][80] of the compounds and we focus here on the CD spectra. Due to their size and the large number of excited states involved the theoretical description of the CD of these molecules represents a challenging goal for any computational method. This is indicated by a recent semiempirical CNDO/S-SCI study of [*n*]helicene CD spectra[81] where substantial disagreement between theory and experiment has been found.

In 4,5-distubstitued phenanthrenes (**7**) the most important geometrical effect on the CD should be the twisting between the two outer benzene units as measured by the dihedral angle C4−C4a−C4b−C5 (Θ_{ext}, see Scheme 1). As shown in Figure 25 this angle increases in general with the size (as measured by its molar volume[82]) of the two substituents indicating non-bonded interactions as the origin of the π-system deformation. Inspection of the data for the series of substituents shows an unusual low Θ_{ext} value for the diisopropyl compound. This can be attributed to the ability of this group to rotate so that only H-H interactions (as in the dimethyl compound) remain. The large defor-

Figure 23. Top: HF-SCF/VDZ optimized structure of (*S*)-9,12-dimethyl-4-oxa[7]paracyclophane (**28**); bond lengths are given in Å, bond angles (the central atom of the angle is indicated by an arrow) in°; the values written in italics refer to the HF-SCF/VDZ data of 9,12-dimethyl[7]paracyclophane (**42**) for comparison; bottom: side-view of the optimized structures (hydrogen atoms omitted) of **28** and **42**; the distances of the O4 and C4 atoms to the center of mass of the benzene ring atoms are given in Å

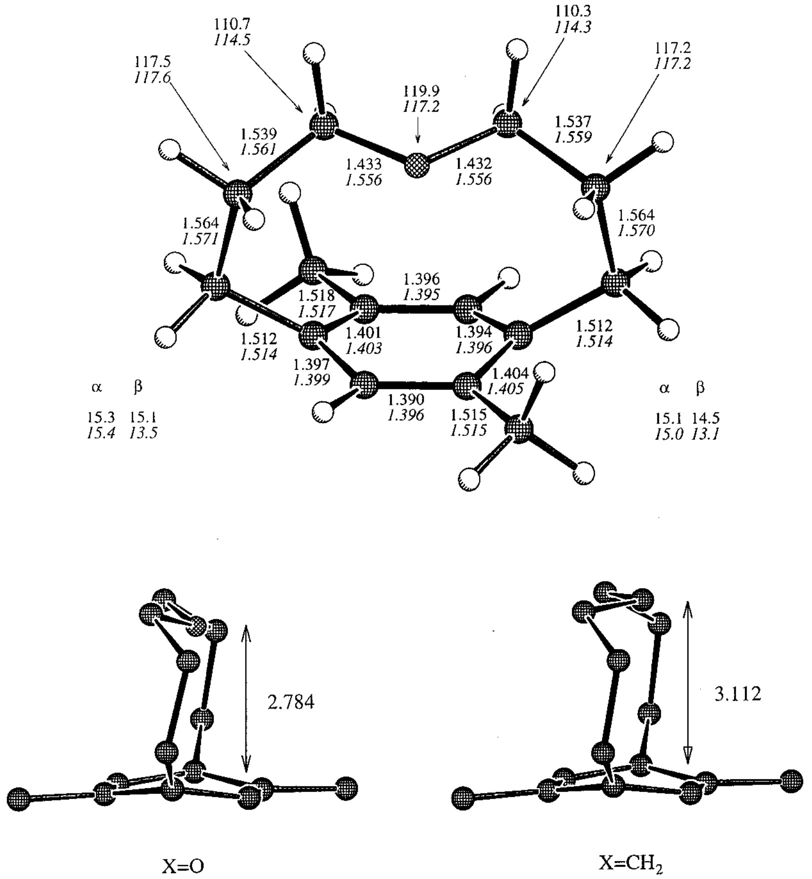
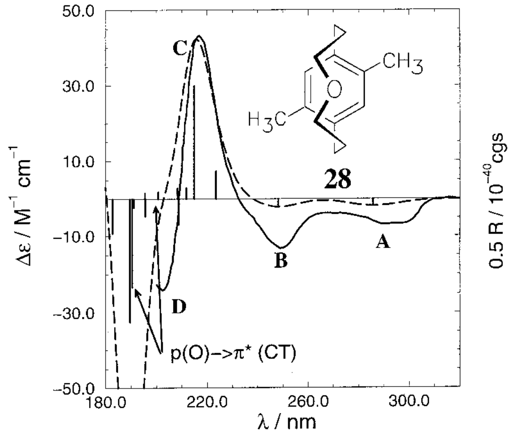


Figure 24. Comparsion of experimental (solid line) and theoretical (dashed line) (TZPR AO basis, HF-SCF/VDZ geometry) CD spectra of (*S*)-9,12-dimethyl-4-oxa[7]paracyclophane (**28**)



mation induced by two fluoro substituents can be explained semiquantitatively[83] with the additional coulomb repulsion between the negative partial charges of the fluoro atoms.

We now discuss the CD spectra of the three compounds with R = R′ = Me (**31a**), R = R′ = isopropyl (**31c**) and R = Me, R′ = *tert*-butyl (**31b**).[84] The data for **31a** are taken from the literature.[44e] The HF-SCF/VDZ optimized C_2 geometries of **31a** and **31c** with Θ_{ext} = 33.1 and 35.6°, respectively, are quite similar so that we can expect some differences to the CD spectra of **31b** which has a value of Θ_{ext} = 37.9° and no symmetry element at all. However, both theory and experiment find very similar CD spectra for all three compounds. The experimental data shown in Figure 26 reveal a quite close resemblance between **31b** and **31c**. Compared to **31a** the bands B, C and F are red-shifted (as expected for a more twisted structure[85]) but the signs of the CD bands are not changed and also the absolute and relative intensities are quite similar. Our measurements were able to resolve for the first time the CD band of the lowest L_b state around 370 nm which has not been found for **31a** due to unfavourable experimental conditions (low concentration and low temperature because of the small racemization barrier (14 kcal/mol[80] of **31a**). For the L_b band we clearly observe a further red-shift in going from **31c** to **31b**.

In general, the theoretical DFT/RPA data shown in Figure 27 compare very well with the experimental spectra. The main bands A−F are predicted with the correct sign and position for all three compounds; the relative red-shifts mentioned above are also reproduced. Although the differences between the spectra of **31c** and **31b** are slightly over-

Figure 25. Dependence of the calculated deformation angles (HF-SCF/VDZ geometries) on the calculated molar volume of the substituents for several 4,5-disubstitued phenanthrenes

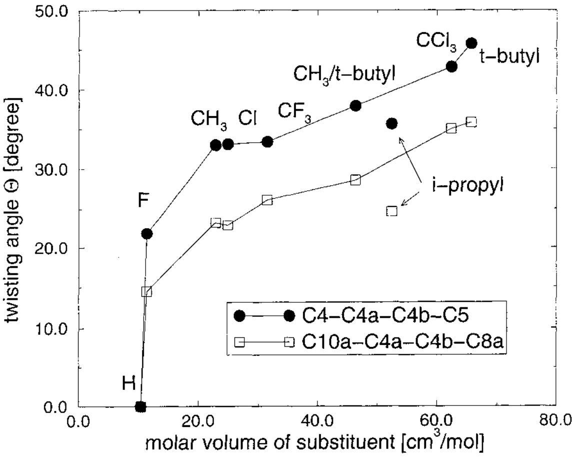


Figure 26. Comparsion of experimental CD spectra of the (*M*)-4,5-disubstitued phenanthrenes **31a**−**31c**

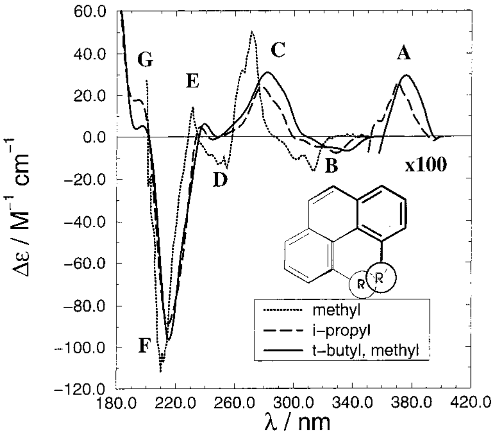
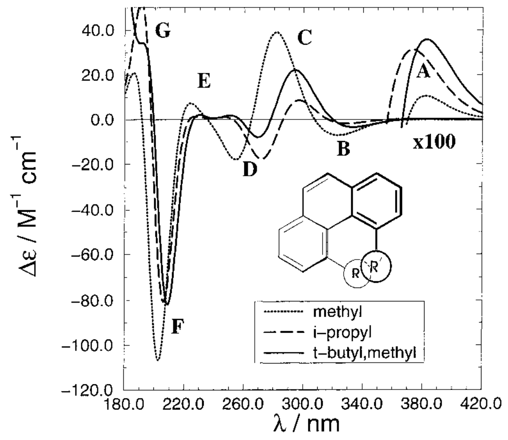
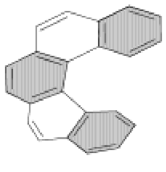
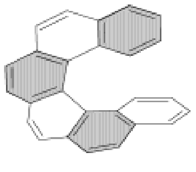


Figure 27. Comparsion of theoretical (DFT/RPA, VDZd AO basis, HF-SCF/VDZ geometries) CD spectra of the (*M*)-4,5-disubstitued phenanthrenes **31e**−**31g**



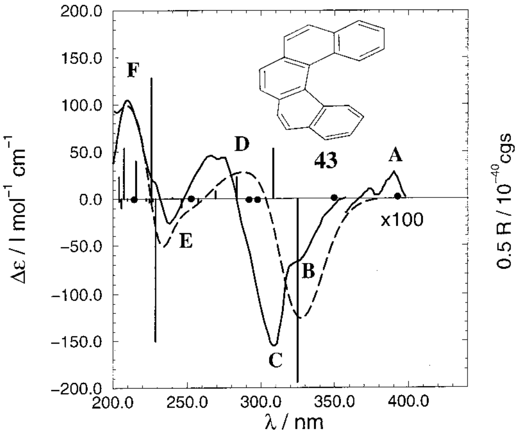


43



44

Figure 28. Comparison of experimental (solid line) and theoretical (dashed line) (VDZd AO basis, HF-SCF/VDZ geometry) CD spectra of (*M*)-[5]helicene (**43**); the experimental intensity has been scaled by a factor of 0.5



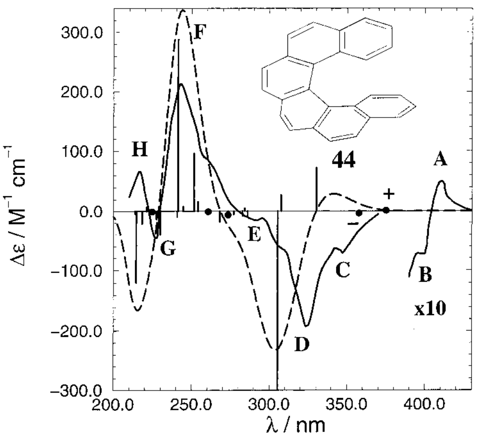
estimated in the region of bands C and D we can conclude from experiment and theory that changes in the range $\Theta_{ext} < 5°$ are too small to influence the CD significantly. With the exception of band A, the CD band intensity decreases with increasing twisting angle Θ_{ext} which is quite unexpected. In summary, it is found that the phenanthrene chromophore seems not to be very sensitive to comformational changes opposed to what is observed for the cyclophanes. In this respect the synthesis and CD investigation of the most distorted di-*tert*-butylphenanthrene with $\Theta_{ext} = 45.7°$ remains a challenging goal to obtain more conclusive answers.

As mentioned above, good theoretical results for the CD spectra of [*n*]helicenes in the entire energy range have not been obtained so far (see e.g.[86][82][87]). In order to demonstrate that the DFT/RPA approach is also useful for molecules with extended π-systems we want to show a comparison between theory and experiment for [5]helicene (**43**)and [6]helicene (**44**) (see Figures 28 and 29). The experimental spectra have been taken from the literature.[88][86]

For both helicenes the overall agreement between theory and experiment is satisfactory and much better than for any previously published approach (only semiempirical methods have been employed so far). For [5]helicene theory finds (as expected for a smaller chromophore) a lower intensity for the strong band C at 300 nm compared to the larger homologue, i.e. the experimental data have to be scaled by a factor of 0.5 which again indicates experimental errors. According to our calculations the shoulder at 330 nm (band B) in the [5]helicene spectrum is not due to an electronic transition but may be a vibrational progression of the intense state responsible for band C (the rotatory strength calculated for the L_a state in this area is too low).

For [6]helicene the calculated excitation energies of the two lowest L_b and L_a states and the intense 2^1B state (band

Figure 29. Comparison of experimental (solid line) and theoretical (dashed line) (VDZd AO basis, HF-SCF/VDZ geometry) CD spectra of (*M*)-[6]helicene (**44**)

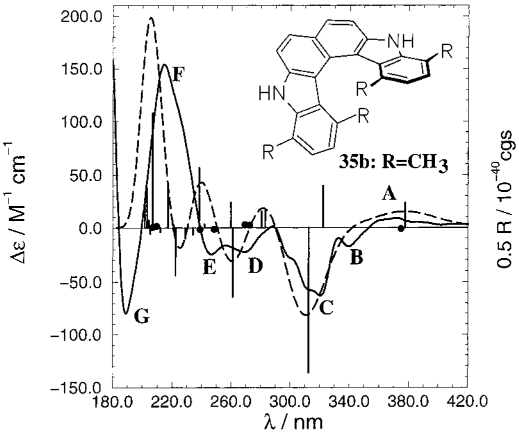


D) are in error by 0.3−0.4 eV. Furthermore, the sign of the 3^1A transition (band C) is incorrect. The remaining parts of the theoretical spectrum, however, correspond rather well with the experimental findings which shows that our theoretical methods work also in the case of extended π-systems with a large number of excited states.

Our calculations also allowed to determine the absolute configuration of the recently synthesized sterically crowded pyrrolohelicene **35b**. DFT/RPA calculations of the CD spectrum (see Figure 30) result in seven experimentally resolved CD bands made from 30 ππ* excited states. Obviously, in the calculated spectrum only the signs of bands B and E are incorrect. It should also be mentioned here that the new DFT/RPA results represent a major improvement compared to the previously published NDDOS/SCI CD data.[45] The overall shape of the spectra resembles those of the 4,5-distubstituted phenanthrenes more closely than that of [6]helicene. This can be attributed to the structural changes, i.e., although **35b** is formally a [6]helicene the pyrrolo units prevent full conjugation of two terminal with the two middle rings. Because the experimentally determined and the calculated CD spectra correspond relatively well, the absolute helicity of this pyrrolohelicene can be determined with high certainty as $(-)_D$-(*M*). This result found for the first time for pyrrolohelicenes is consistent with the known absolute configurations of carbo- and thiophenohelicenes in which so far $(-)_D$ enantiomers have always the (*M*) helicity.

However, the correlation of absolute configurations with the sign of optical rotation at the sodium-D line may be misleading. If we compare the CD signs of the two most intense bands (C/D and F) in the (*M*)-[*n*]helicene family, we see for $n = 3$ a Cotton effect pattern of +/− which changes at $n = 5$ to −/+ (see also the discussion in ref.[81]). The (*M*)-pyrrolohelicene bands show a −/+ pattern which indicates that this molecule fits also in this respect well into the data of the carbohelicenes.

Figure 30. Comparison of experimental (solid line) and theoretical (dashed line) (VDZd AO basis, HF-SCF/VDZ geometry) CD spectra of (*M*)-tetramethylpyrrolohelicene (**35b**)



5. Conclusions and Future Aspects

The above review shows that the synthesis of strained molecules lacking stereogenic centres can be accomplished. The enantiomer separation by using chiral column materials is much more efficient than a few years ago and now mostly leads to base-line separations in up to gram amounts[47a]. The circular dichroisms can be routinely recorded down to short wavelengths (180 nm) owing to excellent commercial devices and even shorter wavelengths by use of synchrotron radiation.[50] The conditions for experimental examinations of structure/chiroptic correlations are therefore nowadays much more favourable than ever before. The calculation of the electronic circular dichroism spectra even for molecules with more than 100 electrons is today also faster and more exact than in the past and allows a reliable treatment of comparably large functionalised molecules far beyond the application of octant-type rules.[89] Even for compounds with a geometry distorted by steric and electronic effects like many of the molecules mentioned above the theoretical CD spectra are in good accordance with the experimental results.

The comparison of experimental and theoretical circular dichroism allows the assignment of the absolute configuration of the molecules, without use of X-ray (Bijvoet) or exciton-chirality methods. The comparison of theoretical circular dichroisms with the experimental data enables the analysis of conformational processes. Predominant conformers of different substituted [*n*]para- and -metacyclophanes could be assigned.

In this contribution we tried to show how specially designed molecules can raise interesting questions regarding chiroptic properties on the one hand, and how successful the calculation of circular dichroisms can promote design and synthesis of new planar-chiral and helically chiral molecules on the other. The increasing efficiency concerning synthesis and enantiomer separation enables the reexamination of older, formerly not soluble but still attractive problems. One example is the pentaphenylenicenophane **45**, which we synthesised in 1979 in small quantities.[15a][b][90]

However, the enantiomer separation by chiral resins was not successful at that time. Now this topic can be taken up again, because enantiomer separation and following chiroptic examinations should not be a problem anymore with regard to the new improved chiral column materials.[47] The methods developed and used above to explain CD spectra therefore should stimulate the stereochemical design of well-defined new molecules in order to apply and even improve our understanding of the interaction of circularly polarized light with chiral matter.

In this connection the helix **46** described recently by Pascal[8] again shows the possibilities in this topical field, which inspired us also to undertake the synthesis and enantiomer separation of novel designed "Geländer"-type helices like **47**,[91] the building blocks of which are arranged perpendicularly compared to the helicene helices like **45**.

The just succeeded[92] enantiomer separations and circular dichroism measurements of the topologically chiral[93] catenane **48** and cycloenantiomeric rotaxane[92] **49** (the axle and wheel by itself are not chiral)[93] seem to be an invincible challenge in the investigation of the structure-chiroptic relationships (and in the quantification of the chirality[13]) due to the high molecular masses and the high conformational mobility of these molecules.[94] The increasing number of new chiral nano-size molecules and macromolecules like calixarenes[95] and synthetic peptides[2] shows again the relation to biomolecules and stresses the importance of dealing with structure-chiroptic relations.

This work was supported by the *Deutsche Forschungsgemeinschaft* (Sonderforschungsbereich 334: "Wechselwirkungen in Molekülen"). We would like to thank all researchers taking part in this special research project and the Bonn coworkers cited in the references. Special thanks are due to Prof. Dr. *J. Hormes* and his group of the *Department for Experimental Physics* at University of Bonn for measuring gas-phase CD. We are greatful to Prof. Dr. *S. D. Peyerimhoff* and Prof. Dr. *B. A. Hess* for their continuous interest and support of our work. We also thank *W. Boomgaarden*, *S. Busch*, *W. Mennicke*, *A. Parham*, and *D. Udelhofen* for drawing figures and formulae, and Prof. Dr. *N. Krause* for fruitful discussions.

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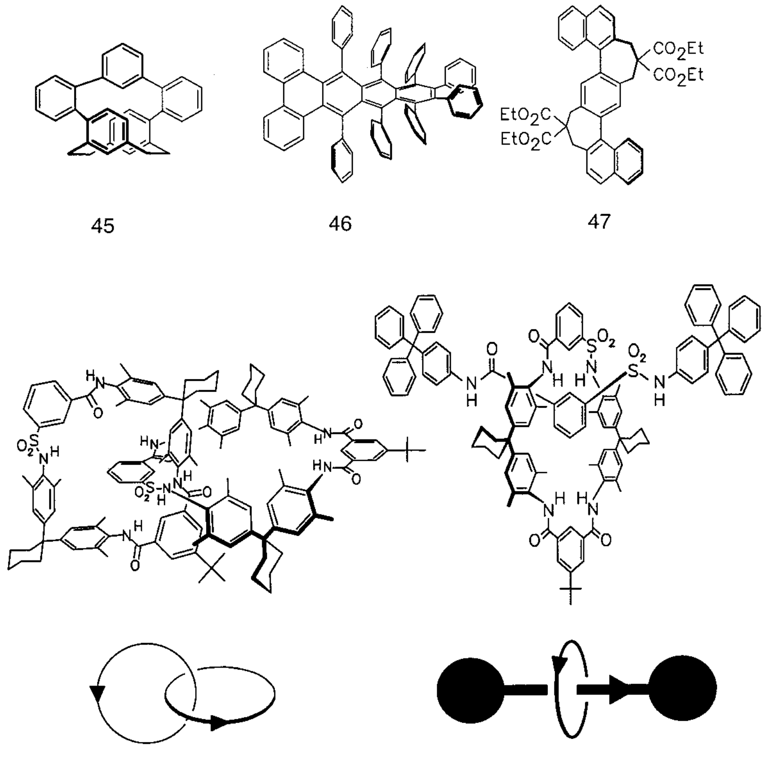
Figure 31. Larger helical molecules ("helicene-type" helix **45**, twisted molecular ribbon **46**, "Geländer"-type helix **47**), topologically chiral catenane **48** and cycloenantiomeric rotaxane **49**



45 46 47

48 49

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