



A Configurationally Stable Pyrrolohelicene: Experimental and Theoretical Structure-Chiroptic Relationships

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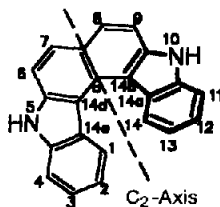
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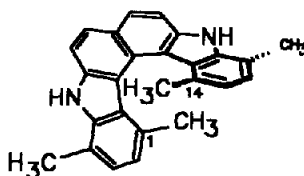
Abstract: The sterically overcrowded tetramethyldipyrrolo[6]helicene **2** was prepared by the Bucherer reaction for the first time. While the longest known hexahelicene **1** does not form stable enantiomers at room temperature, **2** could be separated into the antipodes, which is explained by the extremely different racemization barriers of the two compounds (≈ 60 kJ/mol for **1**, and ≈ 195 kJ/mol for **2**). The quantum mechanically calculated and experimentally determined geometries are in good accordance. The strongly deformed helix **2** shows a pitch enlarged by 62 pm compared to the non-substituted compound **1**. Whereas **1** forms intermolecular hydrogen bonds in the solid, the crystal structure of **2** exhibits coordination of clathrated acetone at the NH-groups. Experimental and theoretically simulated CD Spectra of **2** are compared.

INTRODUCTION

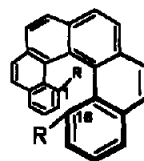
Since the hexahelicene was first prepared by M.S. Newman¹ in 1956 and photochemical syntheses were reported by Martin,² Laarhoven,³ and Wynberg⁴ later on, helicenes have attracted increasing attention⁹ as subunits in crown ethers,⁵ complexing agents, pincer molecules,⁶ cyclophanes,⁷ and proton sponge-type species.⁸ Remarkably, only a few non-photochemical syntheses of helicenes have been reported so far.^{10,11,12} In the course of our investigations on structure-chiroptic relationships¹³ we are interested in comparing the experimental with the theoretically calculated circular dichroism (CD) of helicenes.



1



2



3 (R = H)

4 (R = Me)

The longest known ² hexahelicene **1** was already described by Fuchs and Niszel ¹⁰ in 1927 and it consists of two condensed carbazol systems. Zander and Franke ¹¹ postulated in 1969 a helical structure similar to hexahelicene **3** using a space filling model. Mannschreck *et al.* finally proved this structure and therefore the chirality of this pyrrolo[6]helicene by NMR spectroscopy using electron donor-acceptor complexes with the optically active acceptor (-)-TAPA (Newman reagent). ¹⁵ Enantiomer separation and chiroptical properties of **1** have not yet been described, probably because of the low racemization barrier. Attempts to stabilize the configuration by derivatization have failed so far. ¹¹ In this work we report the first crystal structure analysis of helicene **1** and, in addition, the synthesis of the corresponding tetramethyl compound **2** that unlike **1** is configurationally stable at room temperature.

RESULTS AND DISCUSSION

Following the historical preparation pathway of **1** we reacted 2,7-dihydroxynaphthalene with the correspondingly substituted phenyl hydrazines. Double Bucherer-carbazole-synthesis^[16] afforded the strongly deformed pyrrolo[6]helicene **2** in low yield (1%). The crystal and molecular structure of this sterically strained type of helicenes could be determined as well.

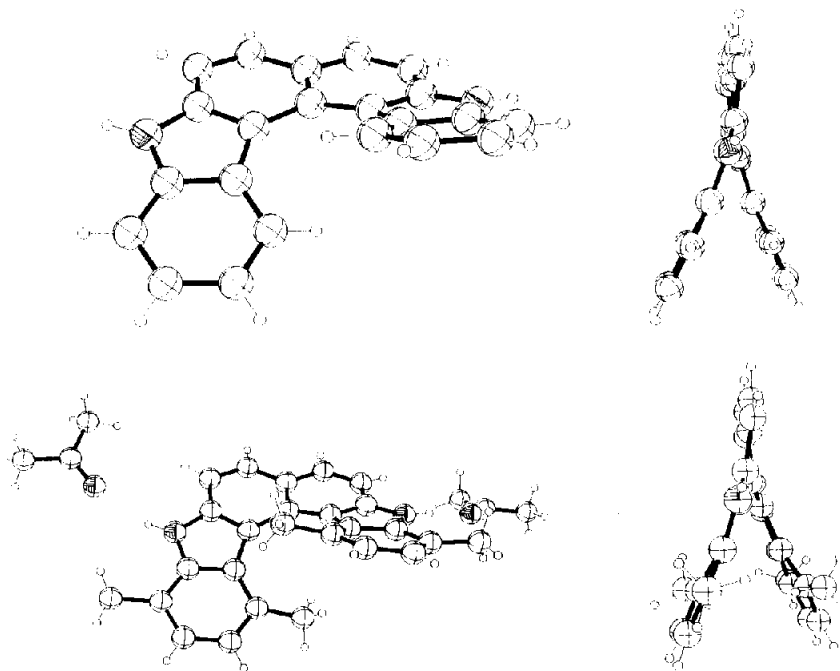


Figure 1. Crystal structure ¹⁷ of helicene **1** (top) and **2** (bottom) (view on the terminal rings left; side view right).

The non-substituted hetero[6]helicene **1** crystallizes from dimethylformamide in the space group $P\bar{1}$. Its crystal package shows remarkably short intermolecular NH...N distances of 2.38 Å (N...N = 3.24 Å) and a N-

H---N-H angle of $\approx 90^\circ$, from which the presence of hydrogen bonds can be deduced. This arrangement results in tilted stacks of molecules in which each molecule is perpendicular to a coordination partner in another stack of molecules. The total picture is a fish-bone-like structure. In contrast, the tetramethyl substituted dipyrrolo-[6]helicene **2** crystallizes from acetonitrile/acetone in the space group $Pna2_1$ with two molecules of acetone clathrating each molecule. The carbonyl oxygen of the acetone interacts with the pyrrole-NH group via a hydrogen bond. The NH---O distance is 2.07 Å (N---O = 2.88 Å) and the angle of the atom sequence N-H---O is 158° . Due to hydrogen bonding between acetone and helicene molecules there does not seem to be a polar interaction between the helicenes, but a stack-like structure is observed as well. Both compounds have C_2 symmetry within the experimental error boundaries. X-ray crystallographic data ¹⁷ (table 1) allow to determine the pitch of the inner helix and other information of the molecular geometry, e.g. dihedral angles and the distances of atoms that are not directly connected (C(1) - C(14)). Table 1 shows experimental data in comparison with the calculated ab initio geometries and with the calculated racemization barriers ¹⁸. The transition state of the racemization shows C_s symmetry similar to the carbo[n]helicenes ¹⁹ (fig. 2). In addition, we compare the hetero[6]helicenes **1** and **2** with carbo[6]helicene **3** and its dimethyl analogue **4**.

Table 1. Comparison of X-ray data (exp.) and calculated data (for **1**, **2**, **3** ab initio-SCF; for **4** AM1) of hexahelicenes 1-4.

Helicene	1	2	3	4
	exp./calc.	exp./calc.	exp./calc.	exp./calc.
pitch [pm] ^{a)}	170/172	232/230	316/314	311/329
dihedral angle Θ_1 ^{b)} [$^\circ$]	7.8/6.8	14.2/14.6	13.3/14.6	31.5/27.7
dihedral angle Θ_2 ^{b)} [$^\circ$]	22.1/20.7	24.0/24.4	30.2/28.6	23.0/27.2
shortest non-bonded C-C-distance [pm] ^{c)}	C(1)-C(14)	C(1)-C(14)	C(1)-C(16)	C(1)-C(16)
	309/311	365/367	322/320	337/357
distance Me-Me[pm]	-----	387/396	-----	494/488
racemization barrier ^{d)} [kJ/mol]	57.0-64.1/77.1	----/194.4	146.2/147.5	186.5/----

^{a)} pitch of the inner helix (triple helix model ³); ^{b)} dihedral angle over four atoms of the inner helix (e.g. Θ_1 = dihedral angle C(16)-C(16a)-C(16b)-C(16c) and Θ_2 : C(16a)-C(16b)-C(16c)-C(16d) at the [6]helicene); ^{c)} distance between the 1st and last C-atom of the inner helix; ^{d)} DFT-BLYP calculation (SVP-Basis) by using the SCF-geometries (SV-Basis). Experimental data for **3** and **4** see ref. ³.

The data in table 1 indicates the good agreement of experimental and calculated geometrical parameters. Ab initio-SCF geometry optimizations were performed for helicene **1**, **2**, and **3** and AM1 geometry optimizations ²⁰ for the 1,16-dimethyl[6]helicene **4**. The deviation between ab initio- and crystallographic data did not exceed 0.02 Å (bond lengths) and 2 degrees (bond angles); larger differences were found in case of the AM1 geometry. The new x-ray crystallographic data allows a direct comparison of the pyrrolo[6]helicenes **1** and **2** with the analogously substituted carbo[6]helicenes. Particularly, the increase in pitch and dihedral angle going from **1** to **2** is large compared to going from **3** to **4**. In the latter case the pitch is almost constant, whereas the dihedral angles differ significantly. The different widening of the two types of helicenes can be explained by their different geometry. The helix of tetramethyldipyrrolohelicene **2** shows a total rotation angle of 270° ,

whereas dimethyl[6]helicene **4** has an angle of 330° . This creates a close proximity of the inner methyl groups in compound **2** and therefore strong steric non-bonded interactions. In contrast, the 1- and 16-methyl groups of hexahelicene **4** are located above the terminal benzene rings. The racemization energy of the non-substituted dipyrrolohellicene **1** has been determined by low-temperature NMR experiments with Newman's reagent and applying the Eyring equation²¹. A free activation enthalpy of 64.1 kJ/mol results which corresponds well with the value of 57.0 kJ/mol determined by Icli *et al.*¹⁵ Density functional calculations (BLYP functional, SV+d basis set) of the racemization barrier of dipyrrolohellicenes **1** and **2** gave 77.1 kJ/mol and 194.4 kJ/mol respectively. Prolonged heating up to 150°C did not cause any change of the CD spectrum of **2**, which corresponds well with the high calculated barrier. The large difference between the barriers of **1** and **2** are a consequence of the strong steric interactions of the methyl groups in the transition state. This is further approved by the inspection of the transition state geometries (fig. 2), which is almost planar in case of **1** but strongly folded in case of **2**.

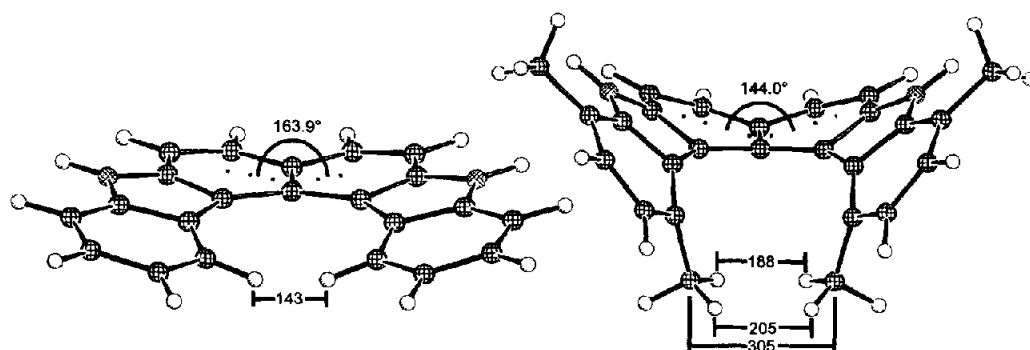


Figure 2. Calculated *ab initio*-SCF-geometries of the transition states of the racemisation for helicene **1** (left) and **2** (right). Distance of non-bonded atoms are given in pm; folding angles in the mirror plane are given in degree.

Unlike **1** the new racemic and optically stable tetramethylheterohelicene **2** can be separated into its (*P*) and (*M*) enantiomers by high performance liquid chromatography with a chiral stationary phase [cellulose tris (3,5-dimethylphenylcarbamate)²²] using a base line separation with the separation parameters ($\alpha = 1.30$ and $R_s = 1.89$). The circular dichroism of the enantiomerically pure fractions were measured in hexane. The experimental and the theoretically calculated CD's of **2** are compared in figure 3.²³ The CD spectrum of **2** shows more resolved bands than that of carbohelicene **3**.⁹ Although the latter possesses an analogous, inherently chiral chromophore with an extended π -system, the π -system seems to be so much disturbed by the heteroatoms (nitrogen), that a comparison of the two spectra is not easily possible. Semiempirical CI calculations of the CD spectrum of **2**, however, result in four experimentally found CD bands with the correct sign. These are formed by 20 separate π - π^* transitions; their intensities are shown as lines in the spectra in figure 3 (right).

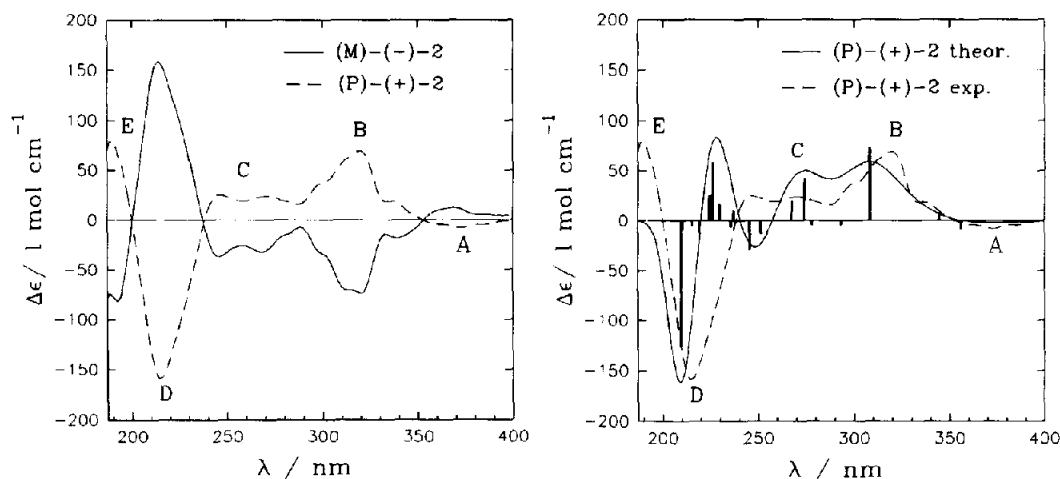


Figure 3. Experimental circular dichrograms of (P)-2 and (M)-2 solved in hexane (left). Comparison of the simulated CD spectra²³ (—) and the experimental data (----) of (P)-2. Calculated CD transitions are shown as vertical lines in the diagramm. Simulation of the circular dichrogramm is achieved by superposition of Gaussian curves for each CD transition with a constant mean half width of 0.2eV (right).

Because the experimentally determined and the calculated CD spectra correspond relatively well, the absolute helicity of the conformationally stable tetramethyl 2,5-dipyrrolohelicene **2** can be determined with high certainty. Thus, the (+)_D enantiomer has (P) helicity. This absolute configuration can be assigned by correlation to the corresponding conformer of 2,5-dipyrrolohelicene **1** which is optically unstable at room temperature. As expected, the calculated CD intensities of **1** are lower than these of **2** by the factor 0.75 due to the smaller pitch of the helix, but overall, the spectra resemble each other closely. The absolute helicity of these dipyrrolohelicenes, that have been determined for the first time, are consistent with the known absolute geometries of the carbo- and thiophenohelicenes in which so far (+)_D helicenes have always been found to show (P) helicity.

EXPERIMENTAL SECTION

1,4,11,14-Tetramethyl-5,10-dihydro-carbazolo[3.4-c]carbazole 2: A mixture of 2.50 g (16 mmol) 2,7-dihydroxynaphthaline, 5.50 g (32 mmol) 2,5-dimethylphenylhydrazine-hydrochloride in 40 ml of 36% sodium hydrogensulfite solution was heated under reflux for 50 hours. After 25 hours 1.65 g (10 mmol) 2,5-dimethylphenylhydrazine-hydrochloride was added. The resinous product was extracted with ether, the ethereal solution was distilled, the residue was treated with 3% potassium hydroxide and water at room temperature, then it was heated with 10% hydrochloric acid, filtered, washed with water, and dried. Work-up by liquid chromatography (SiO₂: 63-100 μm, dichlormethane; *R_f* = 0.76), and crystallisation from acetone or ethanol yields 30 mg (0.5%) of compound **2**: mp >250°C. Single crystals were yielded from an acetone/acetonitril solution by slowly evaporation. ¹H NMR (250 MHz, DMF): δ = 1.87 (s, 6H, 1,14-CH₃), 2.63 (s, 6H, 4,11-

CH₃), 6.68 (d, ³J = 7.3 Hz, 2H, H-2), 7.05 (dt, ³J = 7.3 Hz, 2H, H-3), 7.70 (d, ³J = 8.5 Hz, 2H, H-6), 7.95 (d, ³J = 8.5 Hz, 2H, H-7), 11.55 (s, 2H, NH); ¹³C NMR (62.89 MHz, CDCl₃): δ = 16.97 (1,14-CH₃), 21.43 (4,11-CH₃), 109.83 (2 C), 117.59 (2 C), 117.70 (2 C), 121.44 (2 C), 125.04 (2 C), 125.31 (2 C), 126.29 (2 C), 127.38 (2 C), 127.38 (2 C), 127.50 (2 C), 131.58 (2 C), 138.72 (2 C), 140.68 (2 C). MS(EI) *m/z* = 362 (*M*⁺ [C₂₆H₂₂N₂], 100%), 347 (*M*⁺-CH₃, 34%), 333 (347-CH₂, 63%), 318 (333-CH₃, 62%), 166 ([333-H]²⁺, 33%), DC (SiO₂): *R*_f = 0.76 (dichlormethane); C₂₆H₂₂N₂ (362.48). Enantiomeric Separation by HPLC. Column: Cellulose-tris (3,5-dimethylphenylcarbamate) (CDMPC), 500 × 4.6 mm. Eluent: *n*-hexane/isopropanol 9:1, 0.5 mL min⁻¹. Pressure: 3 bar. Temperature 25°C. Detection: UV, λ = 254 nm; *t*_r [(*-*)_D-2] = 72 min; *t*_r [(*+*)_D-2] = 90 min; *k'* [(*-*)_D-2] = 4.54; *k'* [(*+*)_D-2] = 5.92; α - 1.30; R - 1.89. [α]₅₇₈²⁰ [(*P*)-2] = +588 (c=0.02, CHCl₃) Polarimeter Perkin-Elmer 241. CD-Measurement: JASCO-Spectropolarimeter J 700, 0.015 mmol/l solution in *n*-hexane, 0.02mm cell.

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- 16 N. L. Drake, *Org. React.* **1942**, *1*, 105-128.
- 17 X-ray Structure of 1: Crystal data: $C_{22}H_{14}N_2$, MW 306.4 g mol⁻¹, colorless crystals, dimensions 0.30 x 0.55 x 0.65 mm, $\rho_{calc.} = 1.37$ g cm⁻³, triclinic, space group $P\bar{1}$ (No. 2), $a = 11.015(3)$, $b = 11.689(3)$, $c = 12.030(3)$ Å, $\alpha = 90.18(2)^\circ$, $\beta = 93.94(2)^\circ$, $\gamma = 105.21(2)^\circ$, $V = 1490.8(6)$ Å³, $Z = 4$, $F(000) = 640$. A total of 5493 reflections were recorded on a Nicolet R3m diffractometer (graphite monochromator, λ (Mo- K_{α}) = 0.71073 Å), μ (Mo- K_{α}) = 0.08 mm⁻¹, at $T = 293$ K. Of these, 5220 independent reflections were used the the structure solution (SHELXTL-Plus^[24]) and refinement (433 parameters, SHELXL-93^[25]). Non-hydrogen atoms were refined anisotropically (full-matrix least-squares refinement on F^2); H atoms were refined using a riding model, $wR2 = 0.205$ (R for $F > 4\sigma(F) = 0.077$). Largest difference peak 0.52 eÅ⁻³.
X-ray Structure of 2: Crystal data: $C_{26}H_{22}N_2 \cdot 2$ Aceton, MW 478.6 g mol⁻¹, colorless crystals, dimensions 0.17 x 0.25 x 0.28 mm, $\rho_{calc.} = 1.20$ g cm⁻³, orthorhombic, space group $Pna2_1$ (Nr. 33), $a = 17.951(1)$, $b = 7.505(1)$, $c = 19.754(1)$ Å, $V = 2661.3(4)$ Å³, $Z = 4$, $F(000) = 1024$. A total of 2177 reflections were recorded on an Enraf-Nonius CAD4 diffractometer (graphite monochromator, λ (Cu- K_{α}) = 1.54178 Å), μ (Cu- K_{α}) = 0.58 mm⁻¹ at $T = 293$ K. Of these, 2175 independent reflections were used the the structure solution (SHELXTL-Plus^[24]) and refinement (334 parameters and 49 restraints, SHELXL-93^[25]). Non-hydrogen atoms were refined anisotropically (full-matrix least-squares refinements on F^2); H atoms were refined using a riding model, $wR2 = 0.139$ (R for $F > 4\sigma(F) = 0.043$). Largest difference peak 0.14 eÅ⁻³. An extinction correction was applied.
- 18 All ab initio calculations have been carried out with the TURBOMOLE programm system (R. Ahlrichs, M. Bär, M. Häser, H. Horn, C. Kölmel; *Chem. Phys. Lett.* **1989**, *162*, 3). Geometry optimization have been performed at the Hartree-Fock-SCF-level with a Gaussian AO basis set of split-valence (SV) quality (7s4p/4s → 3s2p/2s) (A. Schäfer, H. Horn, R Ahlrichs; *J. Chem. Phys.*, **1992**, *97*, 2571) assuming C_2 (minima) and C_s (saddle point) symmetry, respectively. Single point calculations have been performed in the framework of density functional theory (DFT) with the non-local gradient-corrected exchange-correlation functional of Becke, Lee, Yang und Parr (BLYP, A. D. Becke, *Phys. Rev. A*, **1988**, *38*, 3098; C. Lee and W. Yang and R. G. Parr, *Phys. Rev. B*, **1988**, *137*, 785.) to elucidate the energy differences between the minima and the transition states (racemization barriers). The SV basis set has been augmented with polarization functions ($\alpha_d(C) = 0.8$; $\alpha_d(N) = 1.0$; $\alpha_p(H) = 0.8$) in this case.
- 19 Ab initio HF-SCF or AM1 calculations yield planar (n=4) or C_s (n=5-8) symmetric transition states for the racemization of carbo[n]helicenes. Racemization barriers as calculated with the DFT-BLYP method deviate by less the 5-8 kJ/mol from experimental activation energies which indicates a one-step reaction pathway via the C_s transtion state (S. Grimme und S. D. Peyerimhoff, *Chem. Phys.*, in Press).
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- 23 The singlet-singlet excitation energies and rotatory strengths of the twenty lowest lying states have been obtained from a full valence space single excitation configuration interaction treatment (SCI). The molecule orbitals and one- and two-electron integrals for the CI calculation have been obtained from a semiempirical PM3 calculation (J. J. P. Stewart, *J. Comp. Chem.*, **1989**, *10*, 209) in the framework of

NDDO-HF-SCF theory. The atomic parameters have been reoptimized for the description of excited states of organic molecules (R. Kluck, S. Grimme, unpublished). Further examples of the performance of the NDDO CI approach for the determination of CD spectra are given in ref. [14]. All semiempirical calculations have been carried out with the MOPAC 6.0 program (J. J. P. Stewart, *QCPE Bull.*, 1985, 5, 133).

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