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Conformation and absolute configuration of 11,12-cyclopropyl retinal analogs – an RHF/DFT/CIS study

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Abstract Ab initio RHF and DFT/B3LYP calculations at the 6-31G** level have been performed to study possible conformations of the cyclopropyl retinal Schiff base analog **3** of known absolute configuration. In both the free base and the protonated form, the geometries are determined on the diene side by optimum conjugative interaction with the three-membered ring, on the triene side by repulsive interaction with the 9-methyl group. There are three low energy conformations, in which the seven-membered ring is either in a chair or in a twist-chair conformation. To decide between these alternatives, chiroptical parameters were calculated employing the GAUSSIAN/CIS routines and compared with the CD spectrum obtained by Nakanishi et al. Of the energy-minimized geometries only two fit the experimental data. In both, the dihedral angle C12–C13, which is indicative of the relative orientation of the two chromophores, is positive.

Keywords Retinal analogs · Retinal · Ab initio calculations · Gaussian/CIS

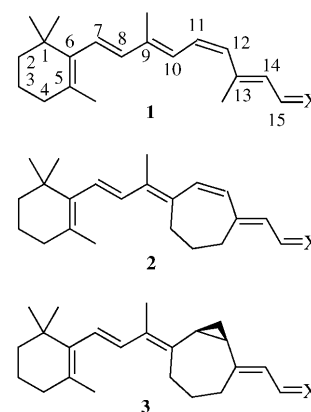
Introduction

The protonated Schiff base of 11-*cis*-retinal **1** (Fig. 1, X=NH₂⁺) is the chromophore of the visual pigment rhodopsin. Photochemical isomerization to the all-*trans* configuration is the step which initiates the process of vision in the vertebrate eye. [1] Of the many questions regarding this complex process, several have been answered by using specifically designed retinal analogs. [2] As an example, consider the retinal analog **2**, in which the 11-*cis*-bond is incorporated into a seven-membered ring. The aldehyde readily binds to opsin, showing

UV/VIS and CD spectra remarkably similar to those of the native pigment, an indication that the chemically enforced twisted 11-*cis*-geometry of **2** has features possibly similar to the geometry of **1** in the pigment. [3] That the artificial pigment prepared from **2** does not photoisomerize is not surprising considering that the conversion from 11-*cis* to all-*trans* is blocked.

Recently another 11-*cis*-locked retinal analog, the bicyclic derivative **3**, has been prepared by the Nakanishi group, and its spectroscopic properties and pigment-forming abilities have been studied. [4] Both **2** and **3** are chiral because of the non-planarity enforced by the seven-membered ring, and the chiral binding pocket of opsin should be able to discriminate between enantiomeric forms. However, in contrast to the inverting enantiomers of **2**, the absolute configuration of **3** is fixed, and the “correct” isomer should show preferential binding to the protein provided the chiral discrimination is sufficient. This effect was indeed observed: of the two mirror images of **3**, only the (11*S*, 12*R*)-enantiomer was found to form a pigment absorbing in the UV/Vis at 312 nm. The minimum energy conformation of the (11*S*, 12*R*)-**3** aldehyde obtained from force field calculations has a negative twist about the C12–C13 bond (–110°); from the preferred binding of this isomer it was deduced that the retinal chromophore in rhodopsin is also neg-

Fig. 1 11-*cis*-Retinal **1**, 11,12-*cis*-locked retinal **2**, and 11,12-cyclopropyl retinal **3**, X=O; the corresponding Schiff bases, X=NH; and the protonated Schiff bases, X=NH₂⁺



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atively twisted, a topic which is still open to debate. [5, 6]

Force field calculations have been highly successful in the calculation of molecular structures with essentially localized bonds. However, they can hardly do justice to the complicated electronic structure of a cyclopropane ring interacting with delocalized and electron-deficient π -systems. We have therefore performed quantum chemical geometry optimization on the Schiff base and protonated Schiff base of **3** and find, in addition to the structure analogous to the one reported, [4] two others with very favorable energies. Calculated chiroptical data are discussed with reference to experimental CD data.

Computational methods

For the standard ab initio molecular orbital calculations of **3** and its partial structures we used the GAUSSIAN98 program package. [7] Starting geometries were taken from lower level RHF calculations and from MM2 force field calculations. Geometry optimizations were performed at the 6-31G** level using both the restricted Hartree-Fock (RHF) method and the hybrid density functional method B3LYP (where the computational method has not been indicated it is RHF/6-31G**); in addition MP2 calculations at the FC level have been performed for several crucial structures to include the effects of correlation at the RHF level. Second derivatives have been calculated to characterize structures as minimum energy conformations. All energies are in kJ mol^{-1} . Oscillator and rotatory strengths were calculated using the CIS routine of GAUSSIAN. Rotatory strengths are calculated in atomic units au. The conversion factors are $1 \text{ au} = 5.083 \text{ DBM} = 470 \times 10^{-40} \text{ cgs units}$.

Results

It is well known that a double bond system can interact in a conjugative manner with an adjacent cyclopropane ring provided the conformation is favorable to sideways or π -type overlap with the cyclopropane bent bonds. [8] This geometry corresponds to dihedral angles of $\Theta = 0$ and 180° (“*anti*” and “*syn*”, respectively) between the plane of the chromophore and the plane bisecting the three-membered ring. These so-called bisected conformations are separated by two perpendicular conformations ($\Theta = 90^\circ$ or 270°), in which the relative orientation is least suited to conjugative interaction. [9]

An appropriate basis for the following discussion is Fig. 2, which shows how the energy of a cyclopropyl-substituted diene changes as a function of the dihedral angle Θ and the nature of the substituent X. The strongest conjugative stabilization is observed in the case of the electron-deficient chromophore, $X = \text{NH}_2^+$. The energy difference between the *anti* and the perpendicular

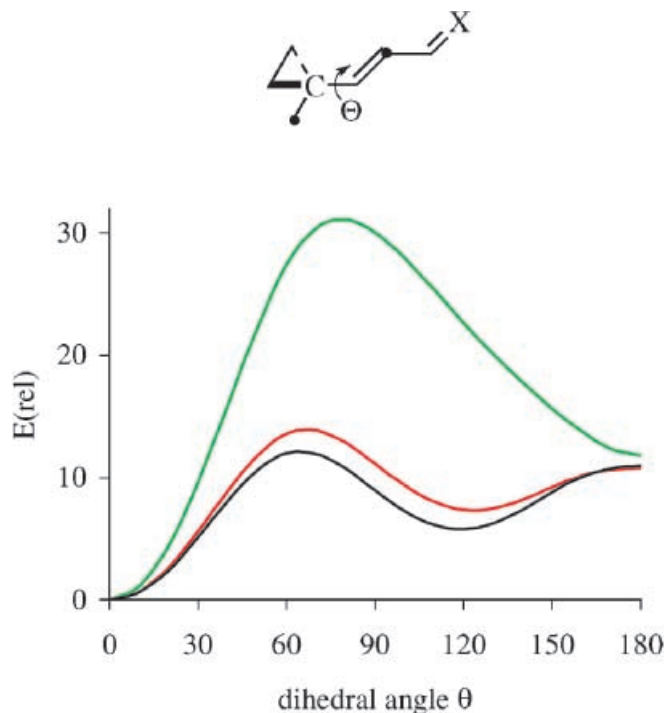
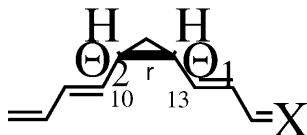


Fig. 2 RHF/6-31G** calculated energy changes (kJ mol^{-1}) of cyclo- $\text{C}_3\text{H}_5\text{-CH=CH-CH=X}$ as a function of the dihedral angle Θ . *green*: $X = \text{NH}_2^+$, *red*: $X = \text{NH}$, *black*: $X = \text{CH}_2$

conformation is more than 30 kJ mol^{-1} . For steric reasons, the *syn* conformation is less stable than the *anti* form by about 12 kJ mol^{-1} . The geometry dependence of the energy is much less pronounced when the chromophore is neutral ($X = \text{NH}$ or CH_2) when, in addition to electronic effects, steric considerations come into play. The *anti* conformation is still the energy minimum. However, superimposed on the energy curve leading to the *syn* conformation is the effect of steric interaction between the three-membered ring and the double bond system. Thus, the maximum at $\Theta = 60^\circ$ and the minimum at $\Theta = 120^\circ$ correspond, respectively, to the eclipsed and the staggered (*gauche*) conformations if the double bond is pictured in the form of two bent bonds. Note, also, that the energy difference between the two bisected conformations is almost identical in all three cases, which indicates that the destabilization of the *syn* relative to the *anti* conformer is purely steric in nature.

The shape of the energy curves agrees with what is known experimentally [10] and theoretically [11] about the conformational preference of vinylcyclopropane for the *anti* and the *gauche* forms (predominance of steric effects) and the comparable energies of the *anti* and the *syn* forms separated by a large barrier of cyclopropane-carboxaldehyde [12, 13] (predominance of conjugation effects). Also, bond length changes are observed which result from p-electron migration from the Walsh-type HOMO of the cyclopropane moiety into the LUMO of the chromophore [14] as the *anti* and *syn* geometries are approached.

Fig. 3 Partial structure 1



Interaction between cyclopropane and two chromophores

To study the interaction of the cyclopropane ring with two unsaturated systems, we consider the partial structure **1** depicted in Fig. 3, with $X=\text{NH}$ and NH_2^+ . A complete geometry search in the space of the two dihedrals Θ_1 and Θ_2 in increments of a couple of degrees is feasible; however, the fact that the four-carbon chain from C10 to C13 will eventually become part of a seven-membered ring restricts the conformational space available; e.g. the *syn* conformation is ruled out on both sides. Thus, only structures with either *anti* or *gauche* orientations of the chromophores were considered and optimized. The results are shown in Table 1. In the unprotonated case, all four combinations are realized. As expected the conformation with two *anti* orientations is most stable and that with two *gauche* orientations the least stable. In contrast, the protonated species is stable only when the electron-deficient chromophore is *anti* with respect to the cyclopropane ring. Despite the fact that the conjugation is strongest when the second chromophore is *anti* the *anti/gauche* combination is favored, probably for steric reasons.

Conformational analysis of [5.1.0] bicyclooctane

With its fused ring system the [5.1.0] geometry is considerably less flexible than either cycloheptane or cyclooctane, from which the structure can formally be derived. Using force field calculations we found five minimum energy structures that were then reoptimized at the RHF/6-31G** level. Frequency calculations for all structures have been performed at the same level to make sure the structures correspond to energy minima. The non-existence of other minima can of course not be concluded from this study. The structures are shown in Fig. 4. Relative energies and a structural parameter are given in Table 2 in order to allow a comparison between the force field and the quantum mechanical calculations.

The most stable conformation is the C_s symmetric chair-1. Ring-flip of the C3 methylene group gives a boat conformation, which is 17.3 kJ mol⁻¹ higher in energy (the corresponding MM2 value is 12.1 kJ mol⁻¹). This structure is not pursued further since the geometry around the cyclopropyl ring is almost unaffected by the flip, and thus the conformer of **3** derived from this conformation is rather high in energy (relative energy of partial structure **4** with $X=\text{NH}_2^+$, seven-membered ring in boat conformation: 24.2 kJ mol⁻¹). Inversion of the seven-membered ring gives the conformation chair-2 (also C_s symmetric) which is less stable than chair-1 because

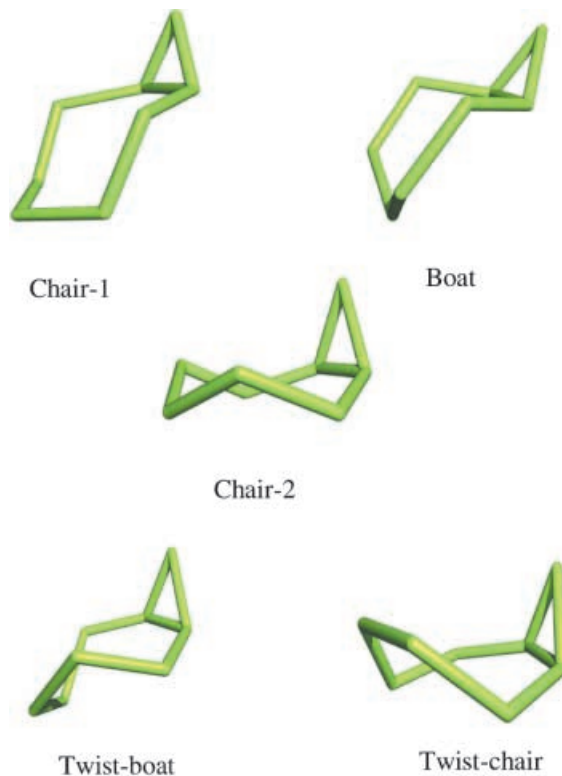


Fig. 4 RHF/6-31G** calculated minimum energy geometries of bicyclo[5.1.0]octane

Table 1 Relative energies (kJ mol⁻¹), dihedral angles (deg) and proximal bond lengths (pm) of disubstituted cyclopropanes (Fig. 2)

	X=NH				X=NH ₂ ⁺	
	(aa)	(ag-)	(g+a)	(g+g-)	(aa)	(ag-)
E_{rel}	0	0.3	2.9	10.5	3.6	0.0
Θ_1	-2.9	1.0	119.0	120.4	-0.7	3.1
Θ_2	5.0	-116.9	0.0	-116.0	13.9	-120.9
r	152.1	151.7	151.6	151.4	155.8	154.6

Table 2 RHF- and MM2-calculated relative energies (kJ mol⁻¹) and dihedral angles (deg) of bicyclo[5.1.0]octane conformations

	RHF/6-31G**		MM2	
	E_{rel}	H-C7-C1-C2	E_{rel}	H-C7-C1-C2
Chair-1	0.0	-78.0	0.0	-74.1
Boat-1	17.3	-73.6	12.1	-71.0
Chair-2	7.7	171.7	13.3	166.6
Twist-boat	33.2	163.2/146.0	30.6	161.5/149.6
Twist-chair	19.9	-170.3/100.7 ^a	19.6	-172.7/95.1

^a Two entries correspond to the two different values of this angle due to the reduced symmetry of the conformation.

of repulsion between the axial hydrogens at C2 and C4 and the cyclopropyl endo-hydrogen which results in a flattening of the seven-membered ring. Ring-flip of the C3 methylene group of the chair-2 conformation gives an unstable boat form, which relaxes into a twist-boat conformation. Finally, by rotating carbon atoms 1 and 2 against each other from one staggered conformation into the next a twist-chair conformation is obtained that closely resembles the twist-chair conformation of cycloheptane. [15, 16]

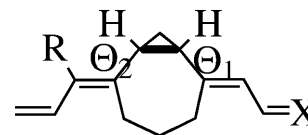
Except for the relative energies of the boat-1 and the chair-2 conformations, the energies calculated quantum mechanically and using the MM2 force field are remarkably alike. The dihedral angles, which are the most sensitive geometrical parameters, agree generally to within 3°.

[5.1.0]bicyclooctane with two chromophores

The conformations found for [5.1.0]bicyclooctane were fitted with two chromophores and energy optimized with RHF/6-31G** to give the partial structure shown in Fig. 5 (R=H). Except for the missing 9-methyl group and the β -ionone ring, this already represents the final structure 3. The relative energies and the orientation of the two chromophores with respect to the cyclopropane ring, both in the unprotonated and in the protonated form, are given in Table 3.

In both cases the twist-boat conformation becomes the least stable by a wide margin. The reason for this is

Fig. 5 Partial structure 2



the inherent destabilization of the fused rings coupled with an unfavorable constellation of the two chromophores, which can attain neither an *anti* nor a *gauche* orientation with respect to the cyclopropane ring. In the three other structures, the energy differences have become significantly smaller primarily because in the inherently favored chair-1 both chromophores assume a close to perpendicular orientation with respect to the cyclopropane ring. In the unprotonated case this is still the favored conformation, although by a considerably reduced margin. In the protonated case chair-2 is the minimum closely followed by the twist-chair.

Steric constraints due to the 9-methyl group

With a methyl group substituted in the 9-position the title compound is almost complete. The following geometry optimizations have therefore been performed using three different methodologies: (i) standard RHF/6-31G** without constraints; (ii) RHF/6-31G** with MP2 correction; (iii) density functional theory at the B3LYP/6-31G** level. A comparison of the results should enable us to assess the importance of electron correlation in these calculations. In all geometry optimizations the twist-boat conformation was found to be no longer stable; it collapsed, instead, into the twist-chair.

The results for the remaining three conformations are shown for the free Schiff base in Table 4 and for the protonated Schiff base in Table 5. They can be summarized as follows: in the deprotonated state the twist-chair conformation is favored, closely followed by chair-1. Chair-2 is highly disfavored according to the RHF calculations; the DFT results interconvert chair-1 and chair-2 and bring the latter closer in energy to the twist-chair form. In the protonated form, the twist-chair is clearly lowest

Table 3 Energies (kJ mol⁻¹) and geometries of partial structure shown in Fig. 5, R=H, with X=NH and (in italics) X=NH₂⁺

	X=NH (X=NH ₂ ⁺)		
	<i>E</i> _{rel}	Θ_1	Θ_2
Chair-1	0.0, 7.2	105.1, 109.5	-105.1, -107.3
Chair-2	5.5, 0	-12.0, -12.5	11.6, 8.7
Twist-chair	7.7, 1.7	5.5, 4.4	-81.6, -85.2
Twist-boat	27.8, 25.8	-16.8, -13.9	-31.0, -29.3

Table 4 RHF-, RHF/MP2- (in parentheses) and B3LYP- (in italics) calculated relative energies (kJ mol⁻¹) and geometries of partial structure shown in Fig. 5, R=CH₃, X=NH

	RHF (RHF/MP2), B3LYP		
	<i>E</i> _{rel}	Θ_1	Θ_2
Chair-1	0.1 (1.7), 4.0	105.8 (113.7), 108.6	-100.0 (-106.8), -101.8
Chair-2	11.0 (11.2), 3.1	-15.7 (-20.2), -12.8	22.7 (29.8), 19.4
Twist-chair	0 (0), 0	5.3 (1.2), 3.7	-78.0 (-82.8), -77.6

Table 5 RHF-, RHF/MP2- (in parentheses) and B3LYP- (in italics) calculated relative energies (kJ mol⁻¹) and geometries of partial structure shown in Fig. 5, R=CH₃, X=NH₂⁺

	RHF (RHF/MP2), B3LYP		
	<i>E</i> _{rel}	Θ_1	Θ_2
Chair-1	13.2 (17.5), 24.3	110.8 (127.0), 121.4	-102.1 (-112.2), -104.9
Chair-2	11.5 (11.9), 0	-14.8 (-14.6), -9.8	17.3 (18.7), 10.2
Twist-chair	0 (0), 1.9	4.2 (0.3), 2.6	-81.4 (-88.1), -84.9

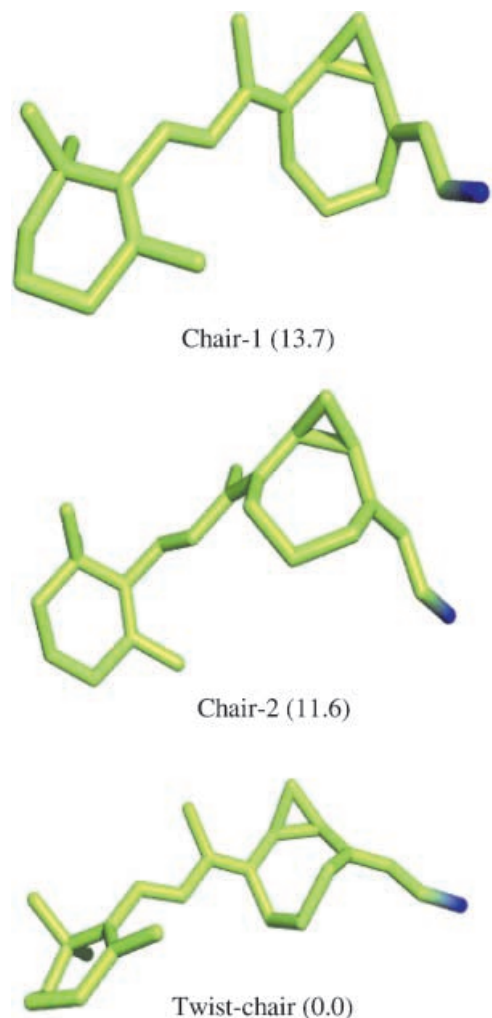


Fig. 6 Minimum energy conformations and relative energies (kJ mol^{-1}) of the protonated Schiff base **3**

in energy according to RHF. Both chair-1 and chair-2 are significantly higher. The DFT method lowers the chair-2 so that it becomes the most stable conformation, closely followed by the twist-chair. The chair-1 is highly destabilized according to this method.

We conclude that for the unprotonated Schiff base both the twist-chair and the chair-1 conformations present possible alternatives as ground-state geometries; after protonation, however, the chair-1 conformation is very high in energy and the alternative is now between the twist-chair and the chair-2 conformation. Note that we have not included the role of the solvent in these calculations!

After affixing the β -ionone ring to the terminus of the diene chromophore, the three conformations were reoptimized at the RHF/6-31G** level. These calculations do not change the relative energies of the three species nor their geometries. The resulting structures are shown in Fig. 6.

Calculation of spectroscopic data

The calculation of spectroscopic parameters (energies, oscillator strengths and rotatory strengths) were performed with two questions in mind: (i) Can a decision, based on the experimental spectra and the calculated structures, be made between the preferred conformation of the compound **3** and can the absolute configuration be assigned? (ii) Is the observed CD spectrum manifest of an inherently chiral chromophore or is it the result of excitonic interaction between the partial chromophores? If the first alternative applies, the chromophores should be viewed as interacting by conjugation, including the cyclopropyl ring. For excitonic interaction, on the other hand, conjugation is excluded by definition.

The geometry optimizations have shown that substitution of the C11–C12 double bond of retinal by a cyclopropyl group renders the whole chromophore intermediate between conjugated and isolated. The strongly preferred bisected orientation of the eniminium system and the increased C11–C12 bond length indicate conjugative interaction with the three-membered ring; the orientation of the triene on the other side, which is the result of steric effects, interrupts the conjugation.

From a computational view the calculation of the cyclopropyl retinal excited states presents a challenging problem. We have recently shown that the CASSCF-method is able to describe the UV/Vis and CD spectra of retinal protonated Schiff bases in the visible region in a consistent manner. [17] In this method orbitals assumed to be important for the excitation process are selected into an active space and a complete configuration interaction calculation is carried out within this active space. Because of their higher excitation energies the partial chromophores of the cyclopropyl retinal analog **3** can more easily interact with the saturated groups of the molecule than the through-conjugated retinal chromophore. This in addition to the highly twisted geometry has the consequence that all π -orbitals contain significant σ -contributions. This leads to enormous difficulties in identifying a limited set of “important” chromophore orbitals, and this is probably the reason why all our attempts to perform CASSCF calculations on this system failed. It was not possible to define a window with active orbitals that would lead to convergent results.

CIS is a set of routines of the GAUSSIAN98 program package in which the CI calculation is restricted to singly excited states and does not require orbital selection. We show in the following that this method gives coherent results, which, moreover, allow the interpretation in the simple physical picture of exciton theory. We first present the results for a simple model system and then for the complete structures obtained in the preceding section.

GAUSSIAN98/CIS and exciton chirality calculations on a simple model system

The model system consists of the cyclopropyl ring with two partial chromophores attached, leaving out the sev-

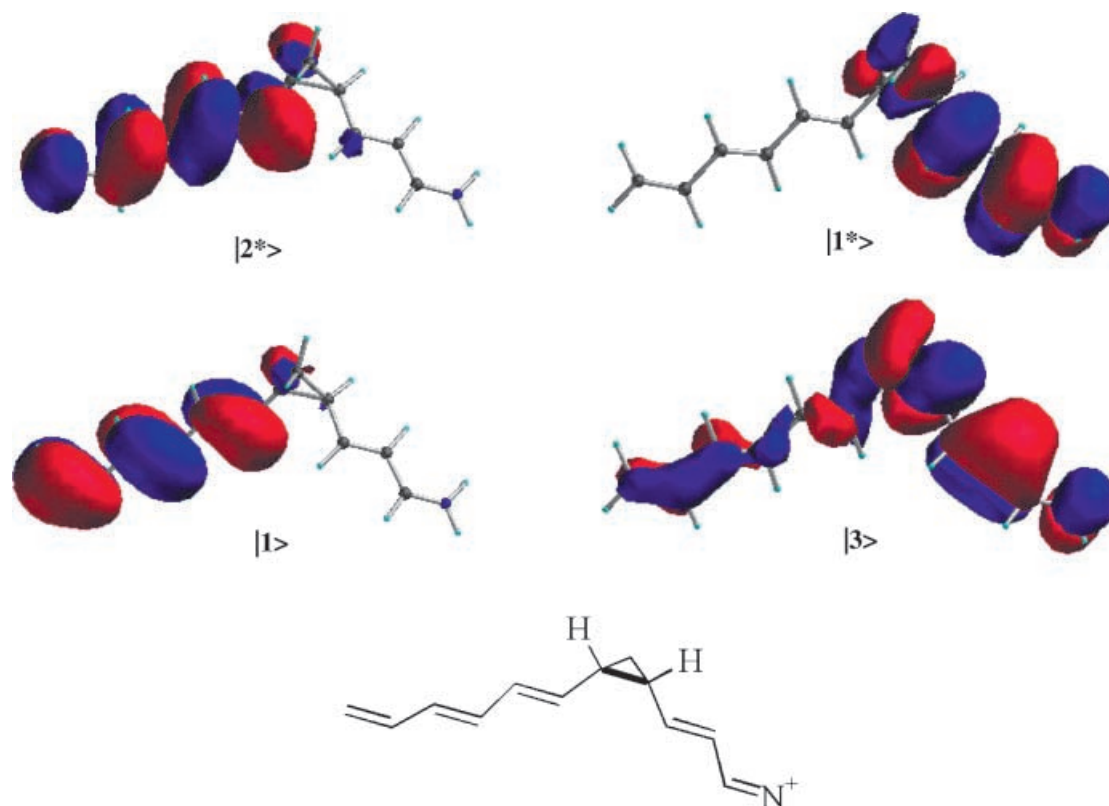


Fig. 7 The four orbitals which contribute mainly to the excited states of the cyclopropane substituted model retinal protonated Schiff base; exact weights are given in Table 6

en-membered ring, the β -ionone ring and the 9-methyl group (Fig. 7). The chromophores have a planar all-*trans* geometry, and their relative orientation is taken from the twist-chair conformation of **3**. The calculated spectral data of the three excited states of lowest energy are given in Table 6, together with the weights of the main configurations contributing to the states. These configurations are derived mainly from four molecular orbitals which are shown in Fig. 7. They correspond, respectively, to the HOMO and LUMO of the triene ($|1\rangle$ and $|2^*\rangle$) and of the diene chromophore ($|3\rangle$ and $|1^*\rangle$). (These orbitals are numbered in sequence for the whole molecule; unstarred MOs are (ground state) occupied and numbered from the HOMO downward, while starred MOs correspond to virtual orbitals and are numbered from the LUMO upward.) According to Table 6, the three spectroscopic states of the model system can be characterized as follows. The main contribution to the lowest excited state 2A is the HOMO to LUMO excitation of the whole molecule, with an electron being transferred from the triene to the diene

chromophore. The oscillator strength is low because of the small overlap between the contributing wave functions. The states 3A and 4A are mixtures of local excitations of the diene and of the triene, representing, respectively, the out-of-phase and the in-phase combination of the local HOMO–LUMO excitations. These states have large oscillator strengths and large rotatory strengths with opposite signs. Both the configurational parentage and the spectroscopic parameters indicate that the 3A and 4A states are best described as exciton states resulting from the interaction of the two chromophores affixed to the cyclopropane ring. [18]

To test whether exciton theory is applicable to this system, we have calculated the spectroscopic properties of the model system of Fig. 7 using the following assumptions: (i) The two chromophore excitations were approximated by two transition moments of lengths 1.3 (for the triene) and 1.13 (for the diene) and energies of 37 735 and 34 483 cm^{-1} , respectively. Energies were taken from the wavelengths (260 and 290 nm) of the isolated chromophores in the UV/Vis spectrum of 11,12-dihydroretinal PSB [5] and oscillator strengths from the data for ω -dimethylbutatriene and -hexatriene. [19] (ii) These dipoles were placed at the centers of the respective chro-

Table 6 CIS-calculated spectroscopic data of the model cyclopropyl retinal protonated Schiff base of Fig. 7

State	Wavelength (nm)	Oscillator strength	Rotatory strength (au)	Weight of main configuration
2A	268	0.2	0.243	$0.65\langle 1 1^*\rangle - 0.22\langle 2 2^*\rangle - 0.11\langle 3 1^*\rangle$
3A	229	2.06	0.973	$0.55\langle 3 1^*\rangle + 0.34\langle 1 2^*\rangle + 0.16\langle 1 1^*\rangle$
4A	209	0.83	-0.419	$-0.32\langle 3 1^*\rangle + 0.59\langle 1 2^*\rangle - 0.12\langle 2 1^*\rangle$

Table 7 CIS-calculated spectroscopic data (rotatory strengths in bold) of different conformations of cyclopropyl retinal protonated Schiff base **3**

	Θ_{6-7}	Wavelength (nm); Oscillator strength; Rotatory strength (au)			
Chair-1, P	61.9	273/0.03/ 0.00	227/0.72/ -1.34	211/1.05/ 1.09	204/0.04/ 0.06
Chair-1, M	-65.3	270/0.03/ 0.01	226/0.86/ -1.21	210/0.91/ 1.66	201/0.01/ -0.04
Chair-2, P	65.0	281/0.49/ 0.13	222/0.79/ 0.42	212/0.80/ -1.18	199/0.00/ 0.02
Chair-2, M	-61.7	283/0.46/ 0.13	223/0.72/ 0.60	216/0.91/ -0.84	202/0.02/ -0.03
Twist-chair, P	61.8	252/0.31/ 0.24	229/1.38/ 0.57	215/0.50/ -0.63	194/0.05/ -0.10
Twist-chair, M	-65.3	250/0.38/0.23	227/1.32/0.22	212/0.53/0.09	192/0.01/ -0.03

mophores, for the triene midway between C5 and C10 and for the diene between C13 and N⁺, with their directions coinciding with the vectors joining these points. (iii) The interaction energy was calculated using the extended dipole approximation. [20] For the B state, in which the transition moments couple in-phase, the calculated wavelength is $\lambda=292$ nm, with an oscillator strength of 0.56 and rotatory strength of 129×10^{-40} cgs. For the A-coupled state the corresponding numbers are 263 nm, 0.61 and -129×10^{-40} cgs. In agreement with the GAUSSIAN CIS calculations exciton theory predicts a positive couplet. In contrast to the quantum mechanical calculations, where significant interaction with other excited states occurs, the sum rule for the rotatory strengths is strictly obeyed in the exciton calculations.

GAUSSIAN98/CIS calculations on different conformations of **3**

CIS calculations were carried out on the geometry-optimized structures of Fig. 6. The results are shown in Table 7. Since the orientation of the β -ionone ring relative to the chromophore was not optimized, the calculations were performed on two geometries each, one in which the dihedral along the C6–C7 bond was positive (“P”), another one in which it was negative (“M”). The exact values of these angles are also shown in Table 7. The different orientations of the β -ionone ring do not change the relative energies of the three conformations. They do affect, however, the calculated spectroscopic data because of the different conformation that the triene chromophore assumes.

The three states that we identified in the calculation on the model system in the preceding section are easily recognized in all six conformers. There is the low intensity, low energy state between 250 and 283 nm, followed by two close-lying states around 225 and 215 nm, with large oscillator strengths and large and opposite rotatory strengths. The only conformation which does not adhere to this pattern is the twist-chair conformation with a negative C6–C7 dihedral for which only positive values for the rotatory strength are calculated.

The experimental CD spectrum of the aldehyde **3** [4] consists of a positive shoulder at 304 nm with positive rotatory strength followed by what looks very much like a positive exciton-split couplet, with the first maximum at 304 nm ($\Delta\epsilon=+16$) and the second at 266 nm ($\Delta\epsilon=-25$). Due the neglect of doubly excited configurations in the

CI calculations, one cannot expect a more than qualitative agreement between the calculated energies of the excited states and the experimental wavelengths in the UV/Vis and CD spectra. However, the relative energies, signs and magnitudes of the three experimental CD bands are reproduced fairly well by the two chair-2 conformations and by the twist-chair conformation with positive C6–C7 dihedral. For the chair-1 conformations the calculated high intensity CD bands are of opposite signs to those in the experimental spectrum.

Conclusions

Using different non-empirical theoretical methods we have built up a series of molecules leading to the cyclopropyl retinal protonated Schiff base **3**, which with its rigid geometry might be an important model compound for the retinal conformation inside the protein pocket of rhodopsin. In addition to the chair-1 conformation, which corresponds to the published conformation of the chromophore in the aldehyde **3** we have found two other conformations, chair-2 and twist-chair, in which the relative orientation of the two chromophores is opposite to that of chair-1. The calculated energy differences between these three conformers are probably too close to identify the most stable conformation in solution. However, chiroptical data calculated quantum mechanically agree only with the chair-2 and with the twist-chair conformation. We add finally that in the two latter conformations the C12–C13 dihedral angle is positive, in agreement with what we have proposed for the twisted 11-*cis*-retinal protonated Schiff base. [6]

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