Through-space Interaction and Chromophore Shape: the Chiral 13-*cis*-Retinal Schiff's Base Dimer

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The hydrogen-bridged dimer of a chiral 13-*cis*-retinal Schiff's base has been prepared and characterised by UV and circular dichroism (CD) spectroscopy; the CD spectrum is almost enantiomeric to that of the corresponding all-*trans*-retinal Schiff's base dimer pointing to the importance of chromophore shape to through-space interaction.

Of the different retinals known the all-*trans*-, 11-*cis*- and 13-*cis*-isomers merit, and have received, special attention because of their role as specialized molecular tools in basic biochemical processes: 11-*cis*- and all-*trans*-retinal as the photoreceptor and primary photoproduct, respectively, of the visual process in the vertebrate visual pigment rhodopsin; 13-*cis*- and all-*trans*-retinal both as components of the dark-adapted form of the proton-pumping pigment bacteriorhodopsin in the purple membrane of *Halobacterium halobium*. Molecular shapes and their changes during and after electronic excitation, probably play a most important role in bringing these processes about.[1]

Information regarding the conformational flexibility, or rigidity, of these molecules comes from many different sources. The picture that emerges from these studies is generally consistent with the result of force-field or quantum-mechanical calculations, *viz.* that of a polyene chain preferring a planar arrangement of the conjugated double bonds, significant deviations from this geometry being caused only by severe steric interactions. Thus, all retinals and retinal Schiff's bases are twisted about the C(6)–C(7) bond, and only the 11-*cis*-isomer has another highly twisted bond, C(12)–C(13), resulting in the existence of two conformational isomers, *viz.* the 12-s-*cis* and the 12-s-*trans* form.

We have studied the chiral dimers formed from chiral all-*trans*-[2] and 11-*cis*-retinal Schiff's bases[3] using UV and CD spectroscopy and found the results consistent with a structure in which the two retinal moieties are projecting out from a rather rigid ten-membered ring system held together by two hydrogen bonds. We now report on the aggregation behaviour of the chiral 13-*cis*-retinal Schiff's base **1**.

We also present the results of a theoretical analysis which confirms the experimental finding that the chromophores in the dimer formed from **1**, due to the *cis*-configurated double bond, have a close to mirror-image like relationship to the one formed from the homochiral all-*trans* retinal Schiff's base.

Compound **1** was prepared by condensing 13-*cis*-retinal and *R*-(−)2-aminobutanol (optical purity > 98%) in the dark under an inert atmosphere as described in an earlier paper.[4] Spectra were taken immediately after purification *via* HPLC. The CD spectra of **1** obtained in a non-polar solvent are strongly temperature-dependent (Fig. 1): at room temperature the spectrum is featureless, but upon lowering the temperature an exciton couplet develops with positive and negative extremes at 380 and 340 nm, respectively. The maximum values reached at −110°, ±40 ε-units, are somewhat larger than those found for the corresponding 11-*cis*-retinal dimers and about half of what is found in the case of all-*trans*-retinal. There are two more CD absorptions developing at shorter wavelengths, one negative (at 280 nm), the other positive (215 nm). In polar solvents, no CD absorption is observed.

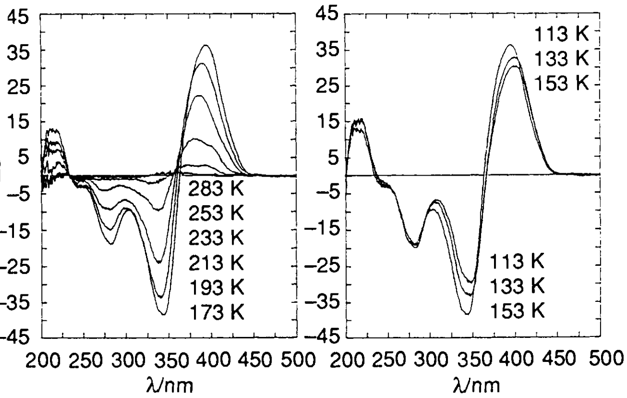


Fig. 1 Temperature dependent CD spectra of **1** in Rigisolve (2,2-dimethylbutane–pentane, 8:3). All spectra are corrected for volume contraction; the concentration is 4.8 × 10^{-5} mol dm^{-3}.

The UV spectra (not shown) are rather insensitive to changes of temperature. The intense absorption with maximum at 355 nm loses its fine structure and suffers the slight bathochromic shift which is observable also in CD. There are weak absorptions in the *cis*-peak region, at 280 and 250 nm, becoming diffuse, however, at lower temperatures.

Unlike 11-*cis*-retinal non-planarity in 13-*cis*-retinal is confined to the C(6)–C(7) bond, which can be s-*cis* or s-*trans*,[5] and to the cyclohexene ring itself. The 'fuzziness' in this region is also evident from MMP2 force field calculations. For **1** four different minimum energy conformations are obtained all within 0.35 kcal mol^{-1} (1 cal = 4.184J) and differing only in the dihedral angles along the C(1)–C(2) and the C(6)–C(7) bonds. Except for the fact that deviations from exact planarity are slightly over-estimated MMP2-calculated and experimental structures agree closely.

The monomers in their MMP2-optimized geometry with the azomethine bond confined to the more stable *anti*-configura-

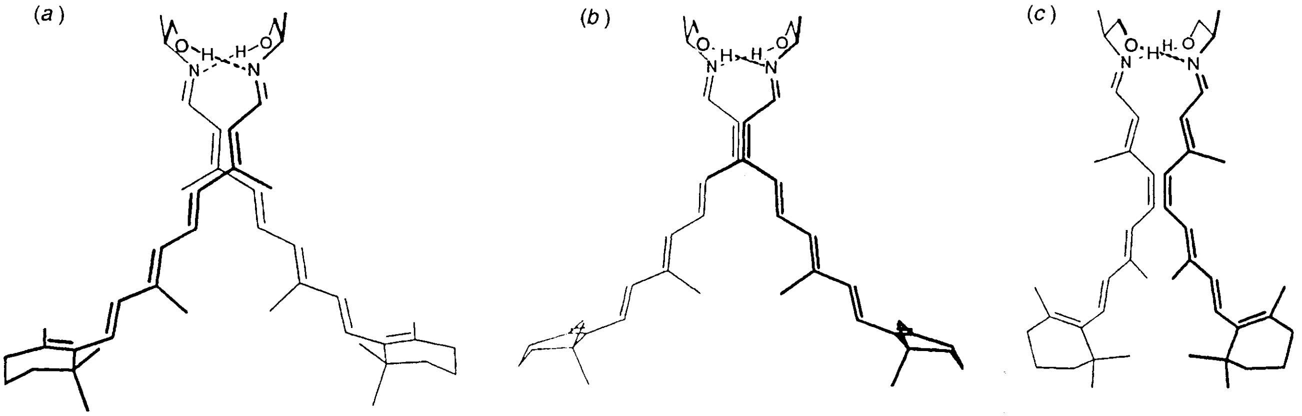


Fig. 2 MMP2 optimized geometries of (*a*) all-*trans*-, (*b*) 13-*cis*- and (*c*) 11-*cis*-retinal Schiff's base dimers. The imine part is derived in each case from *R*-2-aminopropanol. Computer generated models show heavy atoms only and bridging hydrogens.

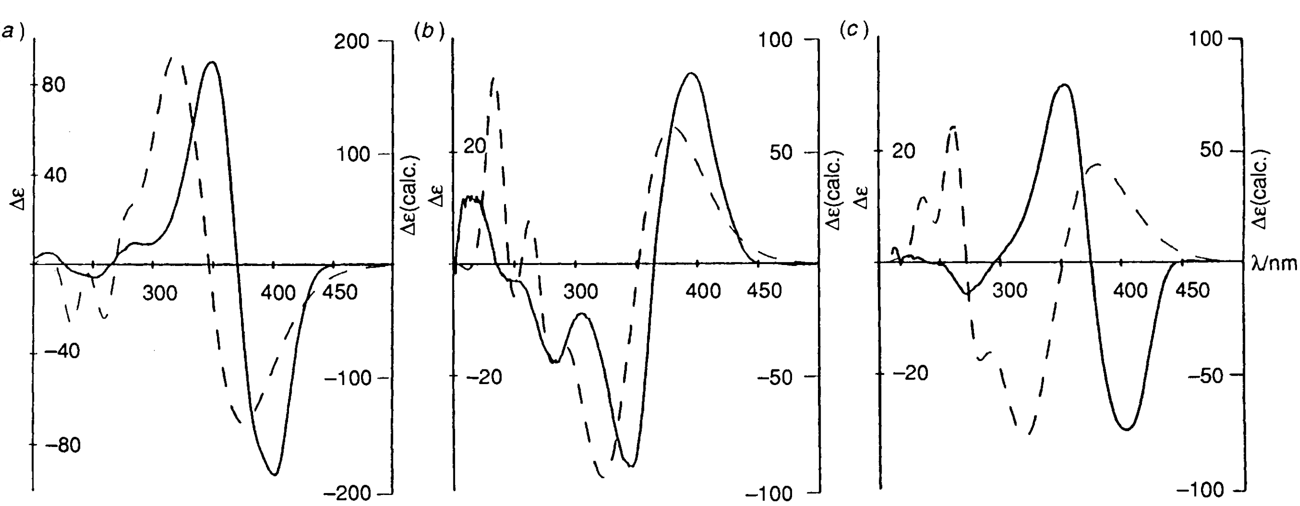
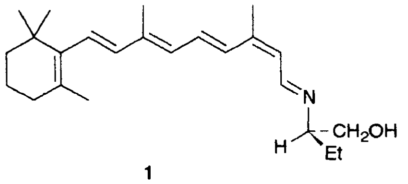


Fig. 3 Calculated (- - -) and experimental CD spectra (—) of (*a*) all-*trans*-, (*b*) 13-*cis*- and (*c*) 11-*cis*-retinal Schiff's base dimers. For the computed spectra, half widths of, respectively, 2300 and 1250 cm^{-1} were assumed for the two long wavelengths and the shorter bands. Note the uniformly reduced scale of those spectra.



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tion[6] were joined *via* two hydrogen bonds to form a ten-membered ring in a boat-like arrangement found earlier[7] to represent the minimum energy conformation. The dimer was then allowed to relax in the MMP2 force field. The geometry obtained is shown in Fig. 2, together with the structures of the all-*trans*- and 11-*cis*-retinal Schiff's base dimers calculated in a completely analogous manner. The only symmetry element of these aggregates is a C_2-axis making them dissymmetric and non-superimposable on their mirror-images. The asymmetric centre which is the carbon next to the azomethine nitrogen is identical in all three aggregates; still the over-all shapes differ widely due to the different shapes of the retinylidene chromophores. Indeed, the two dimers derived from the all-*trans*- and the 13-*cis*-retinal isomers have an almost mirror image-like relationship with respect to the chromophores (see Fig. 2). The inverse relationship of the CD spectra of these two dimers, with rotational strengths of opposite sign for the two exciton states should therefore really not come as a surprise. For additional support of the proposed structures we have calculated the spectroscopic data to be expected for the dimers by a perturbational treatment involving the energies of the seven lowest CI states obtained from CNDO/S and the Coulombic interaction between atomic charges obtained as a multipole expansion of the corresponding CI transition densities. Energies and oscillator and rotatory strengths were then obtained from the eigenstates of the diagonalized interaction matrix. The resulting CD spectra are compared in Fig. 3 with the experimental spectra. There is very good agreement for the all-*trans*- and 13-*cis*-retinal Schiff's base dimers, except for a 10 to 15 nm blue shift, of the long wavelength couplets; for 11-*cis*-retinal, however, the results completely disagree, the most probable reason being the almost parallel orientation of the transition moments which leads to sign inversion upon minute geometry changes in this dimer† and the inability of the geometry optimization procedure to account for differences as subtle as these.

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References

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5 C. J. Simmons, R. H. Liu, M. Denny and K. Seff, *Acta Crystallogr.*, *Sect. B*, 1981, **37**, 2197.
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† The geometry adopted for the 11-*cis*-retinal chromophore has both the C(6)–C(7) and C(12)–C(13) bonds twisted in the same direction (+57 and +158 °, respectively) from the planar s-*cis* conformation. There is another feasible geometry, with the C(6)–C(7) bond twisted in the opposite direction, which, however, leads to a dimer energy which is 2.2 kcal mol^{-1} higher than the one described. The CD spectrum of this second dimer is essentially unchanged with respect to the long wavelength couplet.