

## Characterization of 11-*cis*-Retinal Schiff Base Dimers derived from the 12-*s-cis* and the 12-*s-trans* Conformer

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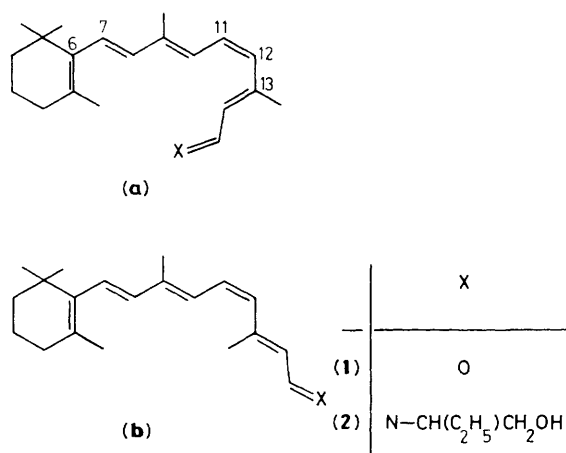
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The two conformers of 11-*cis*-retinal Schiff base, one derived from the 12-*s-cis* the other from the 12-*s-trans* geometry, are found from temperature dependent u.v. and circular dichroism spectroscopies to undergo aggregation to chiral dimers; force-field calculations reveal the surprisingly different geometries of the aggregates in agreement with the spectral data.

In addition to the distorted geometry about the C(6)–C(7) bond present in all retinal isomers as a result of steric congestion, the 11-*cis*-retinal chromophore contains a second distorted region around the C(12)–C(13) bond leading to the presence of at least two different conformers in solution, one deriving from the 12-*s-cis* (**1a**) and the other from the 12-*s-trans* configuration (**1b**) (Scheme 1). From u.v. studies of 11-*cis*-retinal Birge *et al.*<sup>1</sup> concluded that the former is intrinsically more stable while the latter is favoured by low temperatures and polar solvents. Little is known about the geometries of these conformers in solution.<sup>2</sup> We report new spectral evidence for these labile structures and their characterization by theoretical methods.

The chiral Schiff base (**2**) obtained from 11-*cis*-retinal and *R*-(–)-2-aminobutan-1-ol dimerizes in non-polar solvents in much the same way as all-*trans*-retinal derivatives.<sup>3</sup> Aggregation is seen most prominently in the temperature-dependent circular dichroism (c.d.) spectra of (**2**) in rigisolve (Figure 1)<sup>4</sup>: the development of the conservative couplet centred at 365 nm results from the interaction of the intense 350 nm B<sub>u</sub> electronic states of the two conjugated imine chromophores which are brought into close contact in the dimer. In contrast to this couplet, which increases steadily until it reaches a final amplitude, we note the passing appearance of a smaller c.d. couplet in the 250 nm region with inverse sign and maximum amplitude at 200 K. Upon further cooling, this latter couplet disappears making place for a negative band at 270 nm.

The u.v. spectra observed under identical conditions reflect this peculiar behaviour. In polar or protic media (in which no aggregation occurs) the proportion of 12-*s-cis* to 12-*s-trans* conformer decreases steadily with decreasing temperature as judged from the relative intensities of the 250 and 345 nm bands and in line with the observations on the parent aldehyde. In non-polar solvents (Figure 1) the relative intensity of the '*cis*' band at 250 nm increases with decreasing



Scheme 1

temperature, going through a maximum value around 200 K and getting smaller only as the temperature is reduced further.

To account for these spectral changes, we propose a set of coupled equilibria involving the two conformers of the 11-*cis*-retinal Schiff base and their respective dimers according to Scheme 2. Numbers in parenthesis are relative energies (in kcal/mole) of the species involved. They are obtained from MMP2 force field calculations in which we have used a parameter set recently developed<sup>5</sup> for conjugated imines.

However sceptically one may look at the individual numbers, the calculations show that the proposed equilibria are at least feasible, the comparable values of (**2a**)<sub>2</sub> and (**2b**)<sub>2</sub> leave no doubt that the dimerization of the *s-cis* conformer occurs as easily as that of the *s-trans* conformer. According to the u.v. spectra the maximum concentration of a structure containing the *s-cis* conformation and which we identify as (**2a**)<sub>2</sub> is reached at 200 K. Dominance of the equilibrium involving the *s-trans*-species is brought about only by the solvent-induced stabilization of (**2b**) relative to (**2a**) at low temperatures.

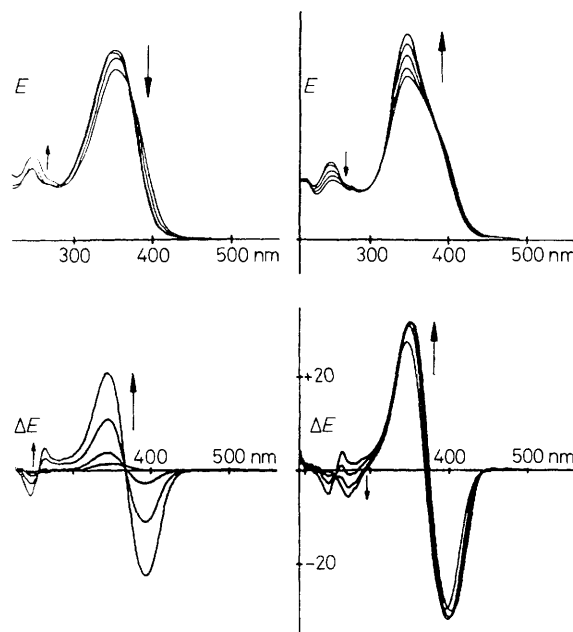
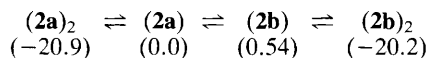
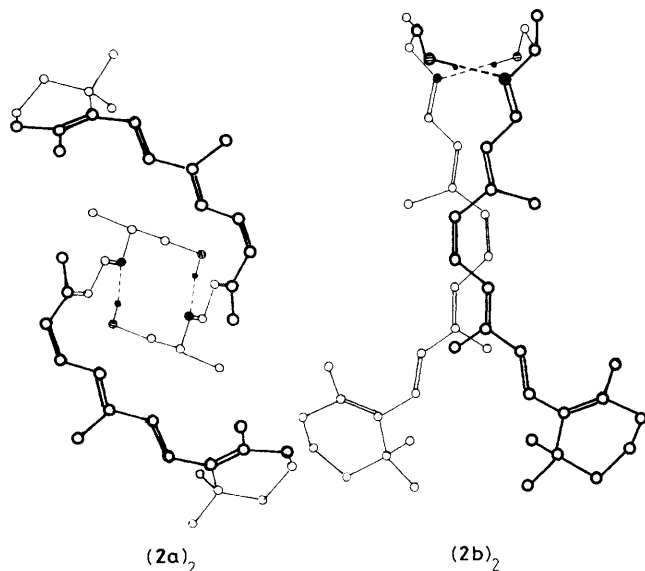


Figure 1. Temperature dependence of u.v. (top) and c.d. spectra (bottom) of (**2**) in rigisolve (2,2-dimethylbutane/*n*-pentane, 8:3). Spectra (all corrected for volume contraction) correspond to temperatures of 283, 253, 233, and 213 K (left) and 193, 173, 153, 133, and 113 K (right). The concentration is  $3.1 \times 10^{-5}$  mol/l.



Scheme 2



**Figure 2.** Minimum energy conformation of Schiff base dimer derived, respectively, from the 12-*s-cis* conformer (**2a**)<sub>2</sub> and the 12-*s-trans* conformer, (**2b**)<sub>2</sub>. Computer generated models show heavy atoms only and bridging hydrogens. Carbons are open circles, oxygens dashed, and nitrogens blackened. To simplify conditions, the ethyl group attached to the chiral carbon has been replaced by methyl.

Dimerization of  $\beta$ -hydroxyimines is effected by hydrogen-bonding and leads to a ten-membered ring structure with two =N  $\cdots$  H-O- bridges. Computer-generated molecular models of the dimers (**2a**)<sub>2</sub> and (**2b**)<sub>2</sub> are shown in Figure 2. They give an impression of the surprisingly different geometries realized in the dimers: whereas the two retinylidene moieties are in close contact over the whole length of the chromophores in the *s-trans* dimer, they extend in the *s-cis* dimer in an almost anti-parallel fashion from the central ring into space. Geometry changes of the monomers upon incorporation into the dimer are insignificant amounting to no more than 3° in the important dihedral angles which are 57 and 54° for the C(6)-C(7) bond of (**2a**)<sub>2</sub> and (**2b**)<sub>2</sub>, respectively, and 40 and 164° for the C(12)-C(13) bond.

From the very different relative orientations of the chromophores in the two dimers one would expect very different calculated spectroscopic data, and this is indeed what we find. CNDO/S calculations on the optimized geometries, which include the interaction of 200 singly excited states, reflect the strong electronic interaction of (**2b**)<sub>2</sub> compared to (**2a**)<sub>2</sub>. There is an exciton-like splitting of 4150 cm<sup>-1</sup> between the two long-wavelength absorptions in (**2b**)<sub>2</sub> compared to only 425 cm<sup>-1</sup>, or 5 nm, in (**2a**)<sub>2</sub>. Consequently, most of the rotational strength associated with two exciton states cancels in the latter and so a strong exciton couplet can be seen only in the former.† This explains why only the dimerization of the *s-trans* conformer is observed in the c.d. spectra.

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### References

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† It is interesting to note that the force field we employed gives a geometry for the *s-trans*-dimer which results in the wrong sequence of signs for the c.d. couplet. The reason is easy to understand: the transition moments of the two chromophores are almost parallel (the angle between them is less than 3°); minute geometry changes can thus reverse the absolute configuration of the whole complex.