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Retinal Schiff bases with aromatic and aliphatic amino acids — the extremely different nature of the intramolecular hydrogen bond between the two types of compounds*

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Abstract

We studied the intramolecular hydrogen bonds in four Schiff bases of all-trans retinal with aliphatic aminocarboxylic acids, as well as four with aromatic aminocarboxylic acids. Osmometric, FT-IR, UV and ^{1}H NMR measurements were performed. The intramolecular hydrogen bonds formed in the aliphatic compounds always have the proton localized at the N-atom of the Schiff base, i.e. the structure $O^- \cdots H^+ N$ exists; conversely, with the aromatic compounds the proton is always localized at the carboxylic acid group, i.e. the structure $OH \cdots N$ is the only existing one. This result is explained by the fact that the aromatic compounds have a much higher degree of electron delocalization than the aliphatic compounds, and thus the N-atoms of the Schiff base are more positively charged for the former.

INTRODUCTION

In the active centre of the bacteriorhodopsin molecule, the proton of the protonated Schiff base shifts to Asp 85 and the Schiff base is reprotonated by Asp 96 [1–4]. These processes may only be performed by proton transfer processes within hydrogen bonds.

The nature of the intermolecular $N^+H \cdots O^- \rightleftharpoons N \cdots HO$ bonds formed between carboxylic acids and retinal Schiff bases have already been studied with the following result [5]: these are hydrogen bonds with large proton

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* Dedicated to Professor N.D. Sokolov on the occasion of his 80th birthday.

polarizability, as indicated by IR continua. Thus, they are very sensitive to environmental influences.

We have already studied inter- as well as intramolecular hydrogen bonds between phenols and retinal Schiff bases [6–8]. These studies have shown that the $OH \cdots N \rightleftharpoons O^- \cdots H^+ N$ equilibria are shifted by the substituents in the para position of the phenolic groups. The observed IR continua indicate the large proton polarizability of these hydrogen bonds [9].

In this paper two types of molecules with intramolecular carboxylic acid–retinal Schiff base hydrogen bonds are compared.

EXPERIMENTAL

The preparation of Schiff bases of retinal with aliphatic amino acids

To a stirred suspension of 0.00175 moles of the amino acid in 10 cm^3 of anhydrous methanol a solution of 0.5 g (0.00175 moles) of all-trans retinal in 2 cm^3 of dry methanol was added. After 3 h of stirring at room temperature the methanol was removed under reduced pressure at room temperature. The residue was dissolved in 10 cm^3 of dichloromethane, filtered, and the solvent removed from the filtrate under reduced pressure. Then 2 cm^3 of *n*-hexane was added to the solution. The precipitate obtained was filtered and washed with three portions of *n*-hexane (2 cm^3 each). Yields, melting points and analytical data of the Schiff bases with aliphatic amino acids are given in Table 1.

TABLE 1

Melting points, yields, elemental analyses, and osmotic coefficients of Schiff bases of all-trans retinal with aliphatic aminoacids (**1–4**) and 2-amino-R-benzoic acids (**5–8**)

Compound	M.p. (°C)	Yield (%)	Elemental analysis (%)			Osmotic coefficient ϕ
			Found		Calculated	
			C	H	N	
1	137	61	73.95 (73.95)	8.86 (8.90)	3.71 (3.75)	0.99
2	140	85	74.35 (74.37)	9.09 (9.10)	3.65 (3.61)	0.98
3	135	62	75.15 (75.13)	9.49 (9.46)	3.35 (3.37)	0.96
4	120	77	75.76 (75.79)	9.79 (9.77)	3.19 (3.06)	0.98
5	121	82	80.49 (80.57)	8.41 (8.45)	3.35 (3.35)	0.95
6	123	83	67.03 (67.21)	6.59 (6.69)	2.95 (2.90)	0.89
7	147	78	74.15 (74.03)	7.40 (7.36)	3.06 (3.19)	1.00
8	170	89	72.16 (72.29)	7.11 (7.19)	6.25 (6.24)	0.98

The preparation of Schiff bases of retinal with 2-amino-R-benzoic acids

To a stirred solution of 0.00175 moles of 2-amino-R-benzoic acid in 5 cm^3 of anhydrous methanol a solution of 0.5 g (0.00175 moles) of all-trans retinal in 2 cm^3 of dichloromethane was added. After 2 h of stirring at room temperature the solvents were removed under reduced pressure and then 5 cm^3 of *n*-hexane added. The precipitate was filtered and washed with three portions (each 2 cm^3) of *n*-hexane. Yields, melting points and analytical data of the obtained Schiff bases are given in Table 1.

The preparation of the tetrabutylammonium salts of the Schiff bases 1–8

To the CH_2Cl_2 solution of the corresponding Schiff base an equimolar amount of a 0.1 mol dm^{-3} methanol solution of tetrabutyl-ammonium

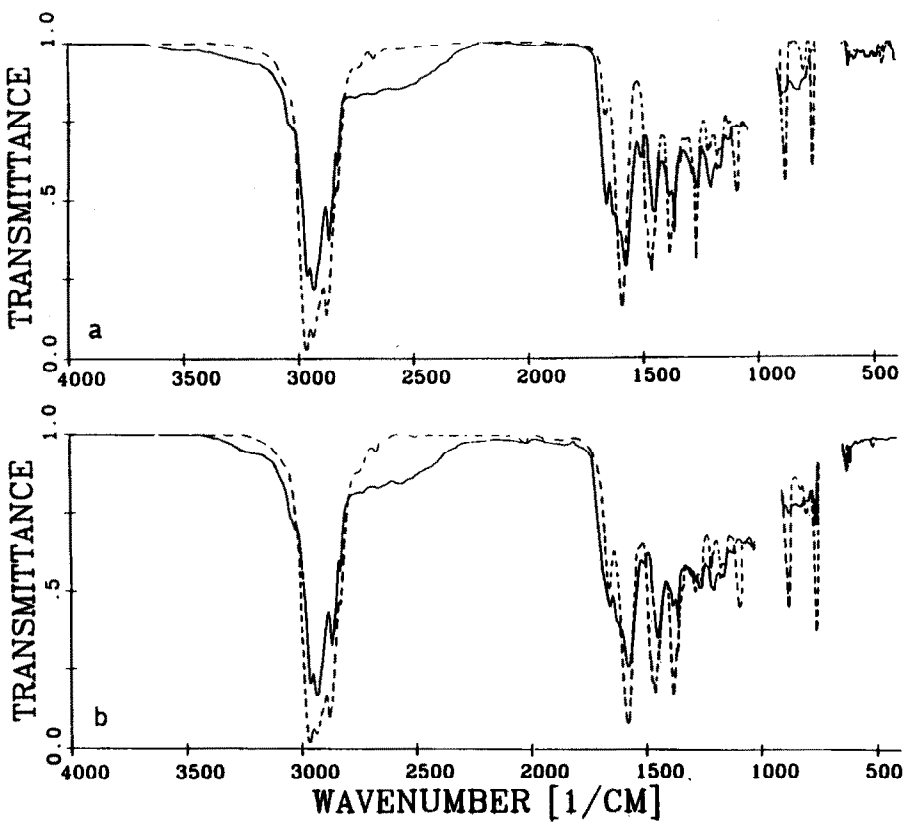


Fig. 1. FT-IR spectra of CH_2Cl_2 solutions of the Schiff base of all-trans retinal with amino-acids (——) and for comparison the tetrabutylammonium salts (– – –): (a) compound 1, (b) compound 4.

hydroxide was added. The solvents were removed under reduced pressure at room temperature and the residues were dissolved in CH_2Cl_2.

Osmometric measurements were recorded on a Knauer vapour pressure osmometer from CH_2Cl_2 solutions (0.1 mol dm^{-3}).

UV spectra of CH_2Cl_2 solutions were recorded with a Shimadzu UV-160 spectrometer at room temperature.

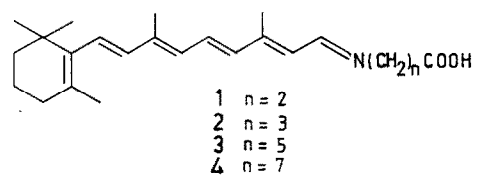
^1H NMR spectra of CD_2Cl_2 solutions were recorded at room temperature with a Jeol FX 90 Q spectrometer, using TMS as the internal standard.

The IR spectra were taken in 0.1 M CH_2Cl_2 solutions with the FT-IR spectrometer IFS 113 v (Bruker, Karlsruhe, Germany) using a cell with Si windows (sample thickness, 0.26 nm; detector, DTGS; resolution, 2 cm^{-1}; NSS, 250). CD_2Cl_2 and CH_2Cl_2 solutions of the Schiff bases were stored over 3 Å molecular sieves. All preparations and transfers for H^1 NMR and FT-IR measurements were carried out in a carefully dried glove box.

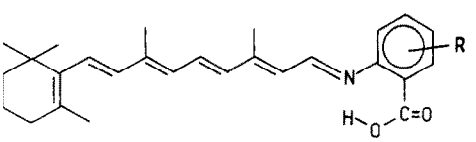
Melting points were determined on a Kofler hot-stage and are uncorrected.

RESULTS AND DISCUSSION

We studied four Schiff bases of all-trans retinal with aliphatic amino-carboxylic acids, as well as four with aromatic amino-carboxylic acids. In the cases of the Schiff bases with aromatic carboxylic acids, the π-electron system of the benzene ring and the polyene chain of the retinal are electronically conjugated.



1 n = 2
2 n = 3
3 n = 5
4 n = 7



5 R = 5-CH_3
6 R = 5-Br
7 R = 4-Cl
8 R = 4-NO_2

Osmometric measurements of all the substances listed in Table 1 prove that these molecules are present as monomers in the CD_2Cl_2 solutions. Thus, the hydrogen bonds formed by these molecules are intramolecular.

Figure 1 shows two examples of retinal Schiff bases with aliphatic amino-carboxylic acids (for comparison, the tetrabutylammonium salts of the corresponding Schiff bases are given). No ν(C=O) band, expected at about

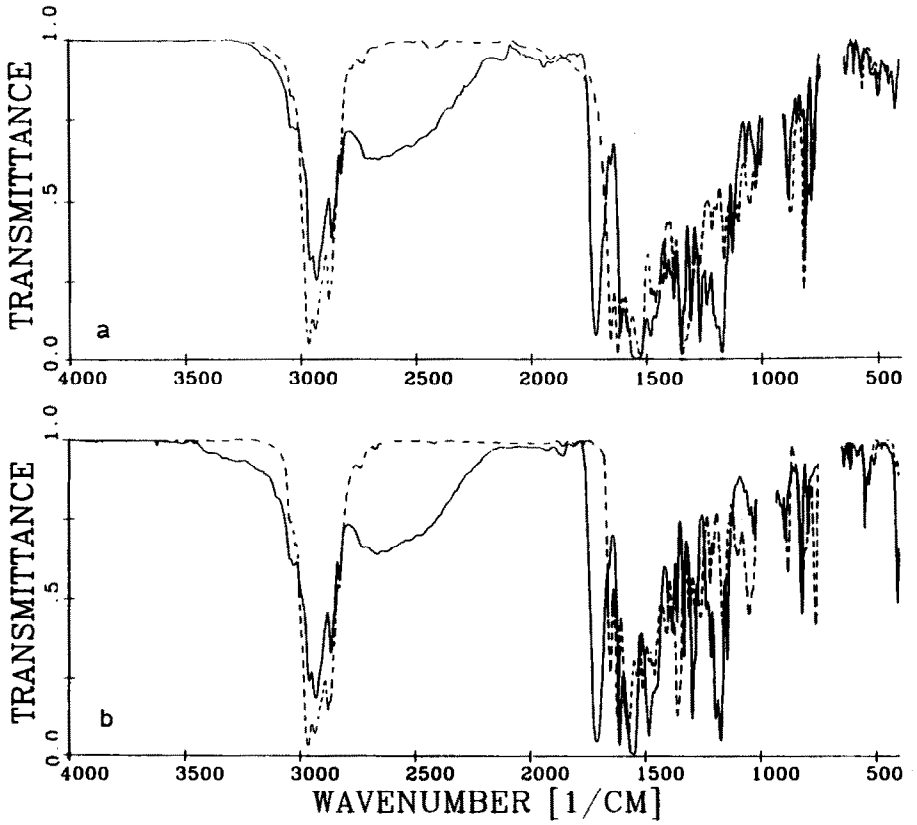


Fig. 2. FT-IR spectra of CH_2Cl_2 solutions of the Schiff bases of all-trans retinal with aminobenzoic acids (——) and for comparison the tetrabutylammonium salts (– – –): (a) compound **8**, (b) compound **5**.

1720^{-1}, of the carboxylic acid group is found in the spectra, whereas $\nu_{as}(CO_2^-)$ is observed at 1572 cm^{-1} and $\nu_s(CO_2^-)$ as a very weak band at 1392 cm^{-1}. Thus, in all the intramolecular hydrogen bonds in these compounds the proton is completely shifted to the N atom, i.e. only the polar structure $N^+H\cdots O^-$ is present. Furthermore, no continuum is observed. This result is confirmed by the band caused by the $\nu(N^+H)$ stretching vibration. This appears as a very broad band in the region 3300–2400 cm^{-1}. This spectral feature shows that the N^+H groups are strongly hydrogen bonded. But these hydrogen bonds show almost no proton polarizability [9].

Figure 2 shows two examples of retinal Schiff bases with aromatic aminocarboxylic acids (for comparison, the tetrabutylammonium salts of the corresponding Schiff bases are given). In these spectra a very intense $\nu(C{=}O)$ band is found at 1719 cm^{-1}. Furthermore, a very broad intense band

TABLE 2

λ_{max} and ε of Schiff bases of all-trans retinal with aliphatic aminoacids (1–4) and 2-amino-R-benzoic acids (5–8) in CH_2Cl_2 solutions

Compound	λ_{max} (nm)	ε ($dm^3 mol^{-1} cm$)
1	327.0	9.100
2	330.5	10.700
3	328.5	6.900
4	330.5	6.000
5	442.0	45.850
6	450.5	39.550
7	450.0	45.600
8	465.0	35.700

is found in the region 3200–2200 cm^{-1} and no IR continuum is observed in these spectra. These results taken together demonstrate that the protons are localized at the carboxylic acid groups and form strong hydrogen bonds with the nitrogen of the Schiff base, i.e. only the non-polar OH···N hydrogen-bond structure exists. This result is independent of the acidity of the carboxylic acid group.

The very different behaviour of the retinal Schiff bases, comparing those with aliphatic and aromatic aminocarboxylic acids, is explained as follows: with the aromatic compounds the π-electron systems of the benzene ring and those of the polyene chain of the retinal are electronically conjugated. Owing to this conjugation the negative charge becomes more delocalized and hence the nitrogen atom of the Schiff base becomes more positively charged, resulting in the fact that the carboxylic acid proton cannot transfer to this nitrogen atom.

The fact that the negative charge is more delocalized is confirmed by UV measurements. If one compares the position of the UV band of the aliphatic and the aromatic compounds in Table 2, one obtains the result that with the aromatic compounds the UV band is shifted about 100 nm towards longer wave lengths. This result demonstrates that the π-electrons are more delocalized in the aromatic compounds. This result is in good agreement with the generally known fact that the pK_a values of aromatic *N*-bases decrease with increasing aromatic character of these *N*-bases [10].

All these results are confirmed by the NMR data given in Table 3.

In the case of the aliphatic aminoacids the chemical shift of the hydrogen-bonded proton amounts to about 6.5 ppm, i.e. this shift is almost independent of the length of the methylene chains. Thus, the strength of the $O^- \cdots H^+ N$ bonds is almost the same for all aliphatic compounds.

In the case of the aromatic carboxylic acids, Table 3 shows that the chemical shift of the hydrogen-bonded proton amounts to 15.12–15.25 ppm.

TABLE 3

Chemical shift (ppm) of the COOH protons from Schiff bases of all-trans retinal with aliphatic aminoacids (1–4) and 2-amino-R-benzoic acids (5–8) in CD_2Cl_2 solution

Compound	Concentration (mol dm^{-3})		
	0.1	0.3	0.6
1	6.70	6.71	6.72
2	6.73	6.72	6.72
3	6.57	6.58	6.58
4	6.49	6.50	6.51
5	15.25	15.25	15.25
6	15.17	15.17	15.17
7	15.18	15.18	15.17
8	15.12	15.11	15.12

The chemical shift of the hydrogen-bonded proton increases slightly in the series of substituents from R = NO_2 to R = CH_3. This result demonstrates that the increase in the basicity of the N atom of the Schiff base determines the strength of the OH $\cdots$ N bonds within this series of compounds. This change in the strength of the OH $\cdots$ N bonds with different substituents is, however, very small.

CONCLUSIONS

The comparison between Schiff bases of retinal with aliphatic and aromatic aminocarboxylic acids shows that the nature of the intramolecular hydrogen bonds within these compounds is completely different. With the aliphatic compounds the proton is completely transferred to the N atom of the Schiff base, i.e. only the polar structure $O^- \cdots H^+ N$ exists. In contrast to this behaviour, in the aromatic compounds the proton is completely localized at the carboxylic acid group, i.e. only the non-polar structure OH $\cdots$ N exists. This result is explained as follows: with the aromatic compounds the electrons are much more delocalized and thus, the N-atom of the Schiff base is more positively charged than in the case of the aliphatic compounds.

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