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Solid-State Studies of Some Retinal Iminium Salts and Related Compounds: Evidence for a 6-s-Trans Conformation

Ronald F. Childs,* Gary S. Shaw, and Roderick E. Wasylishen

Contribution from the Departments of Chemistry, McMaster University, Hamilton, Ontario, L8S 4M1 Canada, and Dalhousie University, Halifax, Nova Scotia, B3H 4J3 Canada.

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Abstract: The solution and solid-state ^{13}C NMR spectra of some retinylidene iminium salts have been examined. In the solid state, the interaction between cation and anion is much stronger and this is reflected by change in the chemical shift of the carbons nearest the iminium function. This interaction has been further investigated by solid-state UV techniques where a resulting blue shift from the solution spectrum occurs. In at least one case, the *tert*-butylretinylideneiminium perchlorate salt **5**, significant downfield shifts of C2 and C5 in the solid state were observed, consistent with a conformational change from predominantly 6-s-cis in solution to planar 6-s-trans in the solid. This conformational change is associated with a large red shift in the absorption maximum of **5** in the solid state.

The visual pigment rhodopsin is comprised of a chromophore, 11-*cis*-retinal, and a large apoprotein, opsin.[1] It is generally accepted that the two are linked together via a protonated Schiff base.[2] During the visual cycle a photon is absorbed by the chromophore which sets off a series of events that ultimately result in a cis/trans isomerization and bleaching of the pigment. A structurally similar pigment, bacteriorhodopsin, contains a protonated Schiff base linkage.[3] There has been considerable work and discussion surrounding the origin of the absorption spectrum of the natural pigments.[4] Simple retinal Schiff bases with an alkyl substituent on the nitrogen have an absorption at 370 nm while their protonated counterparts exhibit a red-shifted band with a maximum at approximately 450 nm.[5] In comparison, the absorption maximum for bovine rhodopsin is approximately 506 nm and that for bacteriorhodopsin 570 nm.[6] Thus while protonation accounts for some of the red shift in rhodopsin and bacteriorhodopsin, the absorption maximum is still 50–120-nm short of that in the natural pigments. In order to account for this difference several mechanisms whereby the protein could modify the electronic properties of the chromophore have been proposed.

Early studies by Blatz[5] suggested that the absorption maximum of a retinylidene iminium salt can be modified by alteration of the distance between the positively charged nitrogen of the Schiff base and the counterion. An increase in the distance between the nitrogen atom and the counterion was suggested to result in a red shift of the absorption band to a limiting value of 620 nm when the anion was completely removed. This effect can be thought of in terms of a destabilization of the relative energy of the ground state as the anion is removed, resulting in a longer wavelength absorption. However, in the compact environment of the protein binding site it is unlikely that the anion could be any further than 4 Å from the nitrogen, and this suggestion of a simple distance effect has been discounted.

The specific placement of a second "point" charge along the chain of the chromophore can also induce a modification of the absorption maximum.[7] Thus, Honig and Nakanishi and coworkers[7a] showed by calculation that the placement of two anions, one 3 Å from the nitrogen and the other 3 Å from C12 and C14 of the polyene portion of rhodopsin, could reproduce the absorption spectrum of the natural pigment. Studies with model systems containing "built-in" point charges confirmed the conclusions reached on the basis of calculations.[8] A similar study was carried out with bacteriorhodopsin analogues, and it was found that placement of a second "point" charge near C(5) could reproduce the absorption maximum of the natural pigment.[7b]

A further proposal by Honig[9] is that the conformation of the chromophore is important in determining the position of the absorption maxima of rhodopsin and bacteriorhodopsin. In particular, the conformation of the C6,C7 formal single bond is thought to be important with the longest wavelength absorption being obtained with the planar 6-s-trans conformation.

There is considerable uncertainty as to the conformation about the C6,C7 bond of retinal Schiff bases and natural pigments. The energy difference between the s-cis and s-trans conformations is small. In retinal itself a twisted s-cis conformation is calculated to be more stable than the s-trans conformation by only 2.5 kcal/mol.[10] This prediction is seemingly confirmed by the reported crystal structures of *all-trans*-[11] and 11-*cis*-retinal[12] in which the C6,C7 bond is s-cis but twisted by 40° to 62°. However, it should be noted that several closely related retinoid derivatives including 13-*cis*-retinal,[13] monoclinic retinoic acid,[14] and β-ionylidene crotonoic acid[15] have been shown to have a near-planar 6-s-trans conformation by X-ray diffraction studies.

No reliable X-ray structure of a retinylidene iminium salt has yet been reported in the open literature and less direct methods have to be used to determine the conformation of these salts. Solid-state NMR studies are one such route, and using this technique Harbison et al. have shown that the C6,C7 bond of bacteriorhodopsin likely has an s-trans conformation.[16,17] In this

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* Address correspondence to this author at McMaster University.

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Table I. UV Spectra

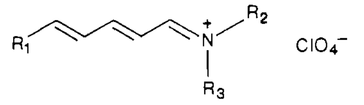
compd	λ_{max} nm (log ϵ_{max}) CH_2Cl_2	λ_{max} nm (log ϵ_{max}) solid	difference,[a] nm
1	312 (4.56)	292	−20
2	370 (4.54)	344	−26
3	320 (4.55)	312	−8
4	470 (4.59)	442	−28
5	472 (4.63)	504	+32
6	498 (4.61)	460	−38
trans-retinal	382	386	+4

[a] Difference in absorption maximum between solution and solid-state spectra.

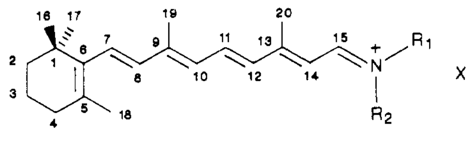
paper we report a detailed examination of the solid-state ^{13}C NMR spectra and ultraviolet absorption spectra of a series of protonated Schiff bases of retinal and related unsaturated aldehydes. The results are compared with solution studies, and it is shown that a considerable red shift of the absorption band in the UV spectrum of *tert*-butylretinylideneiminium perchlorate would seem to result from this molecule existing in an 6-s-trans conformation in the solid state.

Results

The iminium salts **1–6** were prepared with use of modified procedures of Blatz[5] and Leonard.[18] The salts are related by the presence of a linear conjugated system and similar substitutions about nitrogen. The *N*,*N*-dimethyl-substituted iminium salts **3** and **6** were prepared in order to provide examples of iminium salts that would not exhibit hydrogen bonding between the NH proton and a base in the system.



1: $R_1 = CH_3$; $R_2 = t\text{-Bu}$; $R_3 = H$
2: $R_1 = CH_3(CH{=}CH)$; $R_2 = t\text{-Bu}$, $R_3 = H$
3: $R_1 = R_2 = R_3 = CH_3$



4: $R_1 = t\text{-Bu}$; $R_2 = H$; $X = BF_4$
5: $R_1 = t\text{-Bu}$; $R_2 = H$; $X = ClO_4$
6: $R_1 = R_2 = CH_3$; $X = ClO_4$

Solution and solid-state absorption spectra of iminium salts **1–6** are reported in Table I. Solid-state spectra,[19,20] which were measured on crystalline samples on either quartz or glass plates, showed a typical Guassian shape with slightly broader bands than the corresponding solution spectrum (Figure 1). *all-trans*-Retinal, an analgous neutral compound, was found to absorb at nearly identical wavelengths in solution and as a solid.

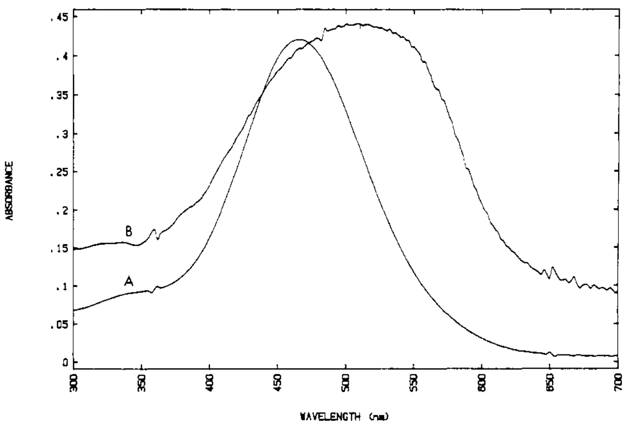


Figure 1. Absorption spectra of *tert*-butylretinylideneiminium perchlorate (**5**) in methylene chloride (A) and in the solid state (B).

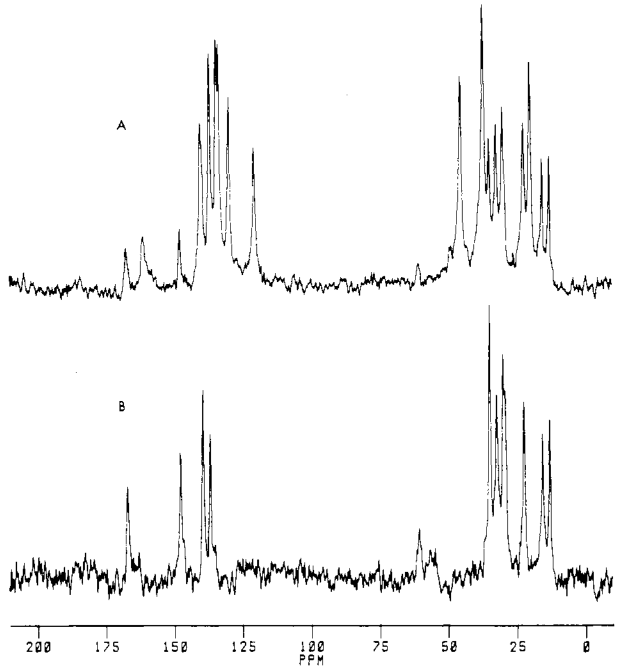
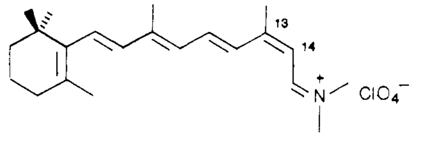


Figure 2. ^{13}C CPMAS spectra of *tert*-butylretinylideneiminium perchlorate (**5**) (A) and with a delay without decoupling pulse sequence (B).

The ^1H and ^{13}C NMR data for iminium salts **1–6** are reported in Tables II and III, respectively. Assignment of the various carbon resonances was accomplished by using *J*-modulated spin–echo sequences and comparison with literature data. No difference greater than 0.5 ppm was observed in the ^{13}C NMR spectrum of **5** when it was cooled from room temperature to −40 °C. The ^{13}C NMR solid-state spectra of **4**, **5** (Figure 2), and **6** were obtained. The assignments of various resonances were made with use of a delay without decoupling pulse sequence[21] which suppresses the CH and CH_2 resonances. The remainder of the resonances were assigned by comparison with published data.[16] In the case of **6** two sets of resonances were observed for the cation. In order to identify the second species present, a crystalline sample of **6** was dissolved in CH_2Cl_2 at −60 °C and its ^1H NMR spectrum obtained at this same temperature. The NMR spectrum showed that only one isomer was present, namely **6**, and that **7**, previously detected as a minor isomer in equilibrium with **6** at room temperature, was absent.



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Discussion

It is clear from an examination of the UV data in Table I that there are some substantial differences in the absorption maxima of these iminium salts in solution and the crystalline state. In general it can be seen that with notable exception of **5**, the absorption maxima of these salts are blue shifted in the solid state as compared to that observed in solution. In the case of **5** a very substantial red shift of the absorption maximum was observed.

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Table II. ^{1}H NMR Chemical Shift Data for Iminium Salts[a–c]

	compound					
position	**1**	**2**	**3**	**4**	**5**	**6**
C(1)H	8.13 dd	7.96 dd	8.38 d			
C(2)H	6.74 dd	6.84 dd	6.55 dd	1.61 t	1.50 t	1.51 t
C(3)H	7.49 dd	7.40 dd	7.63 dd	1.61 m	1.61 m	1.61 m
C(4)H	6.48 dd	6.50 dd	6.49 dd	2.06 t	2.06 t	2.09 t
C(5)H	6.65 dq	6.90 dd	6.70 dq			
C(6)H	1.99 d	6.31 dd	2.02 d			
C(7)H		6.32 dd		6.53 d	6.47 d	6.36 d
C(8)H		1.92 d		6.26 d	6.21 d	6.31 d
C(10)H				6.31 d	6.29 d	6.36 d
C(11)H				7.48 dd	7.43 dd	7.59 dd
C(12)H				6.57 d	6.58 d	6.62 d
C(14)H				6.74 d	6.65 d	6.64 d
C(15)H				8.22 dd	8.19 dd	8.56 d
C(16)H				1.05 s	1.05 s	1.08 s
C(17)H						
C(18)H				1.74 s	1.74 s	1.78 s
C(19)H				2.10 s	2.10 s	2.16 s
C(20)H				2.33 s	2.32 s	2.46 s
C(1′)H			3.49 s			3.74 s
C(1″)H			3.68 s			3.47 s
C(2′)H	1.51 s	1.51 s		1.50 m	1.51 m	
N–H	11.00 br s	11.04 br s		10.94 br s	10.82 br s	

[a] s = singlet, d = doublet, t = triplet, dd = double of doublets, dt = doublet of triplets, dq = doublet of quartets, m = multiplet, br s = broad singlet. [b] In ppm. Numbering of carbons as in text. [c] Referenced to CD_2Cl_2, 5.32 ppm. Measured at 21 °C.

Table III. ^{13}C NMR Data

				4		5		6	
carbons	**1**	**2**	**3**	solution	solid	solution	solid	solution	solid
1	166.12	164.96	171.01	34.69	34.5	34.21	34.8	34.32	34.7
2	120.46	120.90	117.53	40.16	38.8	39.44	45.2	39.82	44.1
3	160.68	160.33	163.36	19.56	19.3	19.10	19.9	19.20	19.4
4	131.25	128.35	131.54	33.76	33.6	33.32	36.7	34.41	36.2
5	151.11	150.39	152.98	132.59	129.0	132.26	136.8	133.94	137.4
6	19.11	131.73	19.94	138.02	139.1	137.45	140.1	137.63	138.6
7		143.25		133.20	132.4	132.60	134.3	132.90	130.6
8		19.26		137.32	138.7	136.94	136.8[a]	136.61	134.5
9				147.42	149.5	146.86	147.6	148.20	144.1
10				129.97	130.3	129.68	129.7	129.52	127.8
11				139.57	138.7	139.08	140.1	140.41	138.6
12				133.75	132.9	133.41	133.4[a]	133.49	133.3
13				165.53	167.1	164.98	167.2	168.30	166.7
14				119.83	118.9	119.47	120.3	116.43	117.5, 119.0
15				159.28	160(br)[b]	158.96	161.0	163.81	162.1
16,17				28.60	28.8, 29.5	28.78	29.9	28.82	28.0, 30.0
18				21.97	23.3	21.79	22.3	21.61	21.3, 23.3
19				13.44	12.9	13.16	12.8	13.22	13.4
20				14.92	14.4	14.47	15.5	14.54	16.1, 18.2
1′	65.68	60.49	41.44, 49.63	59.72	58.6	59.49	60.3	40.53, 49.90	40.7, 49.0
2′	28.40	28.43		29.16	27.9	28.15	32.2		

[a] Assignment may be reversed. [b] Broad.

As the absorption maxima of the other iminium salts with perchlorate counterions listed in Table I, **1–3** and **6**, are blue shifted in the solid state, it is clear that the difference in behavior of **5** cannot be attributed to the presence of the perchlorate anion itself. Rather the effect must derive from a change in conformation of the retinylideneiminium salt chromophore or a specific interaction of the counterion with the cation which is peculiar to **5** in the two phases.

In order to understand the changes in the absorption spectra of **5** in the two phases it is necessary to have a probe for changes in the structure and conformation of the iminium salt in solution and the solid state. Solution and solid-state ^{13}C NMR provides such a comparison and is particularly revealing in this present case.

NMR Spectra. The solution-phase ^{1}H and ^{13}C NMR spectra of iminium salts **1–5** exhibit spectra that are in each case consistent with the presence of either one conformer or a rapid interconversion between several conformers. The ^{1}H NMR spectra of iminium salts **1**, **2**, **4** and **5** in methylene chloride, Table II all display a characteristic doublet of doublets pattern for the resonance associated with the aldiminium proton (H15 in the retinylidenes) which results from coupling of this proton to the adjacent vinyl and N–H protons. The presence of the latter coupling indicates that exchange of the N–H proton is slow under the NMR conditions used. Comparison of the magnitude of this coupling, 15.4 to 16.6 Hz, with that previously reported[22] for iminium systems indicates that ions **1**, **2**, **4**, and **5** in each case have an anti configuration about the C=N bond.

Salt **6** behaved differently from compounds **1–5** in that two isomers were shown to be present in solution at room temperature. These were identified as the all-trans isomer **6** (85%) and the 13-cis isomer **7** (15%). The identity of the minor isomer was established by comparison of its NMR spectrum with that previously reported.[23]

In terms of the preferred conformation of the retinal iminium salts studied here there are two pieces of information. An NOE experiment was conducted at −60 °C on **5** in which the protons

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[23] Sheves, M.; Baasov, T. *J. Am. Chem. Soc.* **1984**, *106*, 6840.

of the C18 methyl group were irradiated. An observed 15% enhancement of the H8 resonance indicated that this cation exists to a large extent in the 6-s-cis conformation in solution.

Further evidence for the presence of a substantial amount of the 6-s-cis conformers in solution comes from the positions of the ^{13}C NMR chemical shifts of these iminium salts. Harbison et al.[16,17] have shown that the carbon chemical shift of C5 in retinoid systems is a sensitive indicator of the conformation about the C6,C7 bond. In 6-s-cis conformers, the resonance attributed to C5 is found at ca. 128 ppm whereas in the 6-s-trans conformers it was at ca. 136 ppm. This work with retinoid systems was extended to the iminium salts of retinal and bacteriorhodopsin, systems for which there is no direct structural information available, and a similar pattern of chemical shifts was found for C5 in these cases. The chemical shifts of C5 of salts **4–6**, Table III, all lie in the middle of the two extremes noted by Harbison. This would seem to indicate that both 6-s-cis and 6-s-trans conformations of these salts are present in solution in about equal proportions. This is consistent with Harbison's approximation that the 6-s-trans population is 25% in solution. The two conformers must be rapidly interconverting on the NMR time scale. In the case of **5** no change larger than 0.52 ppm was observed in the position by any carbon resonance when the solution was cooled to −40 °C. This was to be expected since the calculated energy barrier for 6-s-cis to 6-s-trans interconversion is approximately 8 kcal/mol.[10]

A comparison of the solution and solid-state spectra of **5** shows that the majority of the resonances are within 1 ppm of those measured in methylene chloride with notable exceptions of C2, C5, C6, C13, and C15. The changes in the resonance positions of the carbons near the nitrogen terminus are most likely a result of the tighter cation, anion packing in the solid state. This arises from the elimination of any solvent layers which exist between cation and anion in the solid state, resulting in a minimum cation–anion distance. The largest changes in chemical shift on going from the solution to the solid are at C2 and C5. The C5 resonance is about 4.5 ppm downfield from that in solution and exhibits a chemical shift which is exactly in the range reported for systems which have an s-trans conformation about the C6,C7 bond.[17]

The differences observed in the ^{13}C NMR spectra of **4** in the solution and solid state are quite different from those encountered with **5**. In the former case the resonance attributed to C5 does not move downfield in the solid state but shows a small upfield movement from 132.59 to 128.99 ppm. There is clearly a quantitative difference in the behavior of the two cations in the two phases, and it would seem that **5** adopts an s-trans conformation about the C6,C7 bond in the solid state whereas **4** would appear to have an s-cis conformation.

Support for this suggestion comes from an examination of the resonances of the C16 and C17 methyl groups in these cations. In the 6-s-cis conformation of a retinal iminium salt it is very unlikely that the torsion angle about the C6,C7 bond can be 0° due to the steric interaction of the C18 methyl group with H8. This means that the C1 geminal methyl groups (C16,C17) will be nonequivalent in the solid state where rotation about C6,C7 would be restricted and should show different chemical shifts. On the other hand, in the s-trans conformation a torsion angle about the C6,C7 bond would be expected to be close to 0°, making the C17 and C18 methyls equivalent with respect to the polyene chairs, and thus have similar chemical shifts. In the present cases, **5** exhibits only a single resonance for these two methyl groups whereas two resonances are observed in **4**.[24]

Further support for the 6-s-trans configuration of **5** comes from the chemical shift of C2 in the solid phase. Although Harbison does not mention it, the chemical shift of C2 in all of the 6-s-trans compounds studied was downfield of the C2 resonance in the corresponding 6-s-cis conformer. An average value for this resonance in 6-s-trans conformers is 42.8 ppm. This is in excellent agreement with the value obtained in **5** of 44.5 ppm.

The solid-state ^{13}C NMR spectrum of **6** clearly indicates that there are two cations present in the crystal lattice with pairs of resonances being observed for many of the carbons along the chain (Table III). It is difficult to obtain quantitative data from the solid-state spectrum, but it would seem that these two species are present in approximately equal amounts. It was first thought that the two isomers were **6** and **7**, as is observed in solution. However, dissolution of a crystalline sample of **6** in CH_2Cl_2 at −60 °C, conditions under which **7** or other C=C conformers would be expected to be kinetically stable, showed that only **6** was present. Warming of the sample above this temperature showed the slow appearance of **7**. This means that either the second set of resonances obtained in the solid-state NMR spectrum of **6** is due to the presence of a second C–C single bond conformation of this salt present in the crystal lattice or that there are two different sites for a single conformation of the cation within the unit cell. At this point we are not certain whether **7** is converted to **6** during the crystallization process in a similar manner to that observed for C=N isomers of iminium salts[25] or whether a selective crystallization of **6** is taking place. In any event, crystallization and low-temperature dissolution of the crystalline material in a non-nucleophilic solvent allows the preparation of the single isomer **6**.

Some of the ^{13}C chemical shifts of **6** in the solid state are similar to those observed for the 6-s-cis conformer, **4**. The remaining resonances appear to signify the presence of a 6-s-trans isomer. There are resonances for C5 near 137 ppm and C2 at 44 ppm. However, the complexity of the spectrum makes it difficult to assign all the resonances unequivocally. It is possible that this salt exists in both conformations about the C6,C7 bond in the crystalline state.

Solution and Solid-State Absorption Spectra. The absorption spectra of **1**, **2**, and **4** in the solid state exhibit absorption maxima that are at substantially shorter wavelengths than in solution. The solid-state NMR results described above show that there are no major conformational differences in any of these cations in the two phases. The blue shift observed on going to the crystalline state can be understood in terms of differences in the cation/anion interactions in both phases. In solution, the hydrogen bond between the nitrogen and the perchlorate anion is quite weak. Blatz[5] and Honig[9] have calculated an anion distance–λ_{max} relationship for retinylidene iminium salts, and based on this the approximate distance for the perchlorate anion would be 3.8–4.0 Å. However, in hydrogen-bonded perchlorate crystal structures this distance can be considerably shortened to about 3.0 Å.[26] This would correspond to a stronger hydrogen bond in the solid state, a greater ground-state stabilization, and a blue-shifted absorption spectrum. A similar conclusion was reached recently in a sulfur-stabilized carbenium ion.[27] It was found to have a much stronger S–C$^+$ interaction in the solid state based on X-ray crystallographic studies. However, in a methylene chloride solution this interaction was shown to be weakened and thus the solution absorption spectrum was red shifted.

The suggestion of a strengthened hydrogen-bonding interaction being an important factor in contributing to the blue shift observed in the solid-state UV spectra of these cations is reinforced by the solution and solid-state absorption spectra of **3**. No strong hydrogen-bonding interaction is expected between **3** and the counterion. The UV spectra of **3** showed a much smaller difference in its λ_{max} on going from solution to the solid phase.

The dimethyliminium salt **6** has a solid absorption maximum at 460 nm which is in agreement with a tighter cation/anion pair. However, a comparison of the solution and solid-state absorption spectra of this compound is awkward. In the first place the

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(24) This observation would be expected on the basis of a symmetry argument since a mirror plane would pass through the β-ionone ring and polyene chain if the 6-s-trans conformer were planar. However, the six-membered ring will not be planar and there could be lattice packing effects or inequality of retinal molecules in the unit cell. Thus the presence of a singlet for the two methyls may be a sufficient but it is not a necessary requirement for the presence of the 6-s-trans conformer.

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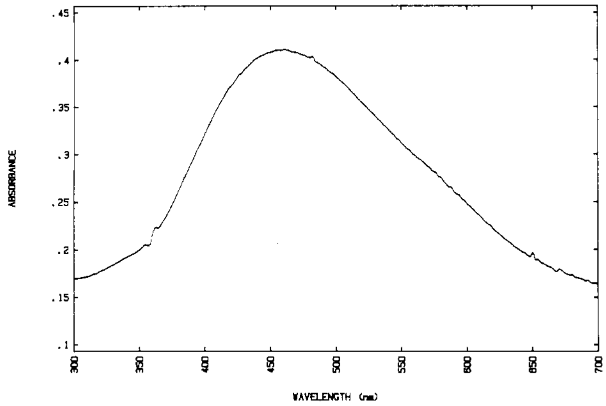

Figure 3. Solid-state UV spectrum of dimethylretinylideneiminium perchlorate (**6**).

difference in composition of this salt in solution and in the solid state makes analysis difficult. Indeed, examination of the solid-state UV spectrum (Figure 3) indicates that the spectrum is not a simple Guassian curve. At higher wavelength the peak tails off consistent with a second isomer or conformer being present. Secondly, **6** exhibits a concentration dependence of the position of the absorption maximum. At higher concentrations the absorption maximum is blue shifted by more than 20 nm. It has been suggested that this arises from changes in the relative dissociations of the salt.[28] At high concentrations the cation and anion are less dissociated thus causing a blue shift. The salt **3** exhibited a comparable concentration dependence of its UV spectrum in solution.

The retinylideneiminium salt **5** exhibits an entirely different behavior in the solid state than all the other salts examined in this work. In **5** the solid-state spectrum is red shifted by 32 nm from that in methylene chloride. This is opposite to the expected absorption shift from a tighter cation/anion pair which was observed in all of the other iminium salts. Although this interaction will still be occurring it must be overshadowed by a much larger structural change which causes the increase in the absorption maximum. The NMR results discussed above clearly indicated that **5** exists in a 6-s-trans conformation in the solid state but largely in the 6-s-cis conformation in solution. The dramatic change in the UV absorption position must reflect this conformational change in the two phases. It is interesting that the absorption maximum in the solid state corresponds very well with the calculated absorption maximum value for a planar 6-s-trans retinylidene chromophore.[9]

An approximation of the wavelength shift of **5** on going from the 6-s-cis to the 6-s-trans conformation can be obtained by comparing its absorption spectrum in the solid to that of **4** in the solid. Both **4** and **5** absorb at approximately the same wavelength in solution. In the solid phase, **4** is blue shifted by 28 nm (1348 cm^{-1}), while **5** is red shifted 32 nm from its solution absorption maximum. Assuming the same blue shift from cation/anion packing occurs in **5** as is observed in **4** then the contribution for a 6-s-cis to a 6-s-trans transition must be about 60 nm (2693 cm^{-1}). This value is somewhat higher than that calculated for the difference between a 60° twisted 6-s-cis conformer[9] and that suggested in the mechanism for the absorption maximum of bacteriorhodopsin.[29] However, it is quite consistent with the value obtained by Sorensen et al. for the addition of a double bond to a cationic polyene system.[30] Thus the red shift observed in **5** can be viewed as arising from the lack of conjugation of C5,C6 double bond in the 6-s-cis isomer with the remainder of the chromophore resulting from the 60° twist about C6,C7. Formation of the 6-s-trans conformer effectively conjugates the C5,C6 double bond, giving rise to its substantial red shift as seen in **5**.

It is apparent from these studies that the existence of **5** as the 6-s-trans conformer in the solid state and its likely presence as a minor component in solution make it an excellent choice as a model compound for light-adapted bacteriorhodopsin.

Experimental Section

General Methods. *all-trans*-Retinal (Aldrich) was used without further purification. Sorbaldehyde was distilled under vacuum prior to use. Octa-2,4,6-trienal was prepared by literature methods.[31,32] *tert*-Butylamine was distilled and stored at 0 °C before use. Methylene chloride was distilled from P_2O_5 and stored over 3Å molecular sieves. Diethyl ether was distilled from $LiAlH_4$. All work was carried out under a nitrogen atmosphere and in the case of retinal compounds in dim red light. Solution ^{1}H NMR spectra were obtained at 250 MHz with a Bruker WM250 spectrometer or at 500 MHz on a Bruker AM500 spectrometer. Solution ^{13}C NMR spectra were obtained at either 62.9 or 125.8 MHz. All solution spectra were obtained in CD_2Cl_2 (MSD Isotopes) which was also used as an internal standard (^{1}H 5.32, ^{13}C 53.8).

Preparation of Salts 1, 2, 4, and 5. These were prepared by the method of Blatz et al.[5] The appropriate aldehyde (1 mmol) was dissolved in approximately 15 mL of diethyl ether over 3Å molecular sieves or anhydrous K_2CO_3. *tert*-Butylamine (10 mmol) was added slowly and the solution stirred for 3 h. The reaction mixture was filtered, and ether and excess amine were removed under vacuum. Ether was added–removed twice more to ensure complete elimination of amine. Protonation was accomplished by dissolving the appropriate imine in approximately 20 mL of ethyl ether and adding an ethereal solution of the desired acid dropwise until precipitation was complete. The resulting iminium salts were recrystallized twice, below 0 °C, from methylene chloride–ether and dried under vacuum.

Preparation of Salts 3 and 6. The method of Leonard et al. was used.[18] Dimethylammonium perchlorate (1 mmol) was dissolved in a minimum amount of absolute ethanol and the desired aldehyde (2 mmol) was added dropwise. The reaction mixture was allowed to stir overnight and then cooled to 0 °C and a small amount of ether added to induce crystallization. The iminium salt was filtered and recrystallized twice from methylene chloride–ether and dried under vacuum.

Solid-State ^{13}C Spectra. Carbon-13 NMR spectra of all solid samples were obtained with magic-angle sample spinning (MAS) and cross-polarization (CP) on a Bruker MSL-200 at 50.3 MHz. Powdered samples of the iminium salts (0.5 g) were packed into cylindrical rotors made of alumina in an inert atmosphere. Samples were spun at approximately 4500 Hz with use of a broadband MAS probe with a double bearing rotor. Proton-to-carbon cross-polarization was accomplished with $\omega_H = \omega_C = 3.9 \times 10^5$ rad s^{-1} (i.e., 4 μs $\pi/2$ pulses) and a contact time of 3 ms. Acquisition times of 0.3 s were used to define the spectrum and all FID's were multiplied by an exponential decay function which corresponds to a line broadening of 15 Hz prior to Fourier transformation. The methyl and quaternary carbon resonances were assigned by using the pulse sequence of Opella and Frey[21] in which the high-power decoupler was switched off for 40 μs before data acquisition. All carbon-13 chemical shifts were referenced with respect to external adamantane, which has shifts of 29.50 ppm (*C*H) and 38.56 ppm (*C*H_2) with respect to TMS.[33] All spectra were obtained at approximately 20 °C.

UV Spectra. All solution and solid-state absorption spectra were measured on a Hewlett Packard 8451A diode array spectrophotometer. Solution spectra were 10^{-5} M in methylene chloride. Solid-state spectra were measured with use of the same general method.[20] A thin layer of freshly crystallized iminium salt was placed on the surface of a glass or quartz microscope slide. A similar slide or one containing a thin surface of KBr was used as a reference.

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