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THE DOUBLY HINDERED 7,11-DICIS, 7,9,11-TRICIS, 7,11,13-TRICIS AND ALL-CIS ISOMERS OF RETINONITRILE AND RETINAL#

Achla Trehan, Taraneh Mirzadegan and R. S. H. Liu*

Department of Chemistry, 2545 The Mall
University of Hawaii, Honolulu, Hawaii 96822

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Abstract

Reaction of a modified C-5 phosphonate with 7-*cis*-C_{15}-aldehyde provided the doubly hindered 7-*cis*,11-*cis*-retinal and a smaller amount of the hitherto unknown 7-*cis*,11-*cis*,13-*cis*-retinal which readily rearranged to the 7,13-dicis isomer. Properties of these and the 7,9,11-tricis and the all-cis isomers are reported. Molecular mechanics calculation was used to verify possible application of the proposed consecutive 6e electrocyclization mechanism for rearrangement of 7-*cis*,11-*cis*,13-*cis*- and all-*cis*-retinals.

Introduction

Geometric isomers of retinal have been used extensively for studies of stereoselectivity of the binding site of retinal binding proteins, in particular that of visual pigments.[1,2] Of the sixteen possible isomers of retinal, fourteen were known.[3] Recently in a preliminary paper[4] the preparation of all-*cis*-retinal was reported leaving 7-*cis*,11-*cis*,13-*cis*-retinal the only remaining unknown isomer. Preparation of the latter compound along with properties of the doubly hindered (7,11-dicis) isomers of retinal are the subject of this paper.

Experimental

Methods. All uv-vis spectra were recorded on a Perkin-Elmer λ-5 spectrometer, and ^{1}H-nmr spectra on a GE QE-300 spectrometer. A Hewlett-Packard 1040A diode array detector was used for on line recording of uv spectra of hplc fractions. An Oxford C28009A cryo-tip cell was used for recording low temperature uv/vis absorption spectra.

For studies of isomerization of all-*cis*-retinal or 7-*cis*,11-*cis*,13-*cis*-retinal by nmr, the sample tube was warmed in a constant temperature bath and its H-nmr spectra recorded at regular intervals (probe temperature, 20°C). When followed by uv, a temperature controlled cell holder of the spectrometer was used to heat the sample as well as for monitoring progress of the reaction. The relative amount of the unstable isomer and its rearranged product during the course of the thermal reaction was calculated from the ratio of their absorbance at two wavelengthes relative to the corresponding values for the two isolated isomers. In the case of the all-*cis*-retinal, the absorbance ratio at 287 and 346 nm was used (corresponding to the absorption maxima of the two isomers). For all-*cis*-retinal,

A_{287}/A_{346} = 2.98; and for 7-*cis*,9-*cis*,13-*cis* retinal, A_{346}/A_{287} = 3.49. In the case of 7-*cis*,11-*cis*,13-*cis*-retinal, the corresponding values at the absorption maxima are: A_{289}/A_{357} = 1.82 for 7,11,13-tricis; and A_{357}/A_{289} = 4.18 for 7,13-dicis.

Materials.

Bis-(trifluoroethyl)-2-methyl-3-cyano-2-propenyl phosphonate, 1. Method 1. To a stirred slurry of chloroacetone (29.61 g, 0.32 mol) and diethyl cyanomethylphosphonate (66 g, 0.372 mol) in 100 ml of ether, a solution of NaOH (14.9 g, 0.372 mol) in 100 ml of water was added slowly (4 h) which brought the ethereal mixture to a gentle reflux. The color of the solution changed to orange. The reaction mixture was stirred for one additional hour. Extraction of the aqueous layer by ether, drying the organic layer over Na_2SO_4 and evaporation of the solvent led to 37 g of a light orange colored oil. Distillation (95-100°C at 0.4 torr) gave 15.9 g of 4-chloro-3-methyl-acrylonitrile (colorless oil, trans:cis = 65.35). The mixture was used as such for subsequent reactions.

A mixture of tris-(trifluoroethyl)phosphite (2.974 g, 9.06 mmol) and 4-chloro-3-methyl-acrylonitrile (1.514 g, 1 mmol) was heated to 115-125°C for 48 h. Distillation (130-140°C at 1 torr) gave 2.1 g of the phosphonate 1 (71% yield, trans:cis = 55:45).

^{1}H-NMR: ($CDCl_3$) (cis) δ 5.39 (m, 1H), 4.43 (m, 4H), 3.14 (d, J = 24.6 Hz, 2H), 2.10 (m, 3H) ppm; (trans) δ 5.34 (m, 1H), 4.43, (m, 4H), 2.91 (d, J = 24.6 Hz), 2.22 (m, 3H) ppm.

^{19}F-NMR: ($CDCl_3$, 75.3 MHz) δ -75.7 (t, J = 3.9 Hz).

Method 2. A mixture of triethylphosphite (23 g, 0.138 mol) and 4-chloro-3-methyl-acrylonitrile (15.9 g, 0.138 mol) was first heated to 125-135°C and finally to 145°C until the completion of evolution of chloroethane. The crude mixture was distilled (135-145°C at 0.6 torr) to give 27 g of the C-5 phosphonate (90% yield, trans:cis = 55:45).

The phosphonate (3.03 g, 14 mmol) was cooled to 0°C and stirred while PCl_5 (7.28 g, 35 mmol) was added. An exothermic reaction took place and EtCl was evolved. The mixture was stirred at 25°C for 1 h and then at 75°C for 3 h. Distillation removed the byproduct $POCl_3$, and yielded 3.1 g of a tarry mixture containing 2-methyl-3-cyano-2-propenylphosphonoyl dichloride. The crude dichloride was dissolved in 20 ml of benzene and treated at 0°C with a solution of trifluoroethanol (2.8 g, 28 mmol) and triethylamine (2.83 g, 28 mmol) in 30 ml of benzene, and at 25°C for 1 h. Usual work up yielded 0.85 g (24% overall yield) of phosphonate 1.

Reaction of 7-*cis*,9-*cis*-β-ionylideneacetyldehyde with phosphonate 1

A solution of the phosphonate (328 mg, 1 mmol), 18-crown-6 (1.320 g, 5 mmol; recrystallized CH_3CN complex)[5] in 20 ml of anhydrous THF was cooled to -78°C under nitrogen and treated with 1 mmol of $KN(TMS)_2$ (0.5 M in toluene). The aldehyde (218 mg, 1 mmol) was then added and the resulting mixture was stirred at -78°C for 1 h. Saturated NH_4Cl was added and the product was extracted in ether. The ether extracts were dried (Na_2SO_4), solvent evaporated, and the product isolated by flash chromatography over silica

gel (2% ether in hexane). A mixture of four isomers of retinonitriles was obtained (totally 128 mg, 46%). These isomers were separated by hplc (Lichrosorb Si column, 2% ether in hexane): order of elution of four isomers of retinonitrile; 7,9,13-tricis, 7,9,11-tricis, 7,9-dicis and all-cis. The proton magnetic resonances of the last three isomers are in agreement with those in the literature.[6] Chemical shift correlation maps (CSCM) were obtained for 7-*cis*,9-*cis*,11-*cis*-retinonitrile and all-*cis*-retinonitrile, facilitating assignment of their ^{13}C-signals.

7-*Cis*,9-*cis*,11-*cis*-retinonitrile:

^{13}C-NMR: ($CDCl_3$, 75 MHz), Table 1.

All-*cis*-retinonitrile:

^{1}H-NMR: ($CDCl_3$, 300 MHz) δ 1.05 (s, 16-CH_3, 17-CH_3), 1.46 (s, 18-CH_3), 1.88 (s, 19-CH_3), 2.19 (s, 20-CH_3), 5.13 (s, 14-H), 6.15 (d, 7-H), 6.28 (d, 12-H), 6.34 (d, 10-H), 6.54 (d, 8-H), 6.72 (dd, 11-H) ppm; $J_{7,8}$ = 12.7 Hz), $J_{10,11}$ = 12.4 Hz, $J_{11,12}$ = 12.0 Hz.

^{13}C-NMR: ($CDCl_3$, 75 MHz), Table 1.

UV-vis: λ_{max} (hexane) = 333 nm.

Table 1. ^{13}C-NMR data of doubly hindered isomers of retinonitrile. Assignments based on CSCM experiments.[a]

Isomer	Chemical Shift, ppm									
	C_1	C_2	C_3	C_4	C_5	C_6	$C_{16,17}$	C_{18}	C_{19}	C_{20}
7,11-dicis	34.6	39.1	19.1	32.1	129.3	136.3	28.7	21.5	14.8	21.5
7,9,11-tricis	34.5	39.4	19.2	32.5	130.5	136.7	29.0	21.7	22.2	21.5
7,11,13-tricis	34.6	39.2	19.2	32.1	129.6	136.4	28.7	21.6	14.6	24.0
all-cis	34.4	39.2	19.2	32.4	130.6	136.6	29.0	21.8	22.5	24.0
	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}	C_{13}	C_{14}	C_{15}	
7,11-dicis	130.8	134.2	142.7	125.8	131.1	127.3	157.7	98.3	117.8	
7,9,11-tricis	132.1	127.4	142.7	124.8	130.6	126.5	157.6	98.5	117.5	
7,11,13-tricis	130.8	134.4	142.7	124.7	131.8	126.3	157.8	97.5	117.1	
all-cis	132.3	127.2	143.0	125.0	131.4	123.8	157.0	97.5	117.2	

a. In $CDCl_3$.

All-*cis*-Retinal

To a solution of all-*cis*-retinonitrile (12 mg, 0.043 mmol) in dry hexane at -78°C was added 0.25 mmol of DIBAH (1.0 M in hexane). The reaction was complete in 5 min as shown by TLC and was quenched with NaF (42 mg, 1 mmol) and water (11 mg, 0.75 mmol). The resulting mixture was stirred at room temperature until a white solid

separated from the solution (about 1.5 h). After usual workup and passage of the crude product through a short flash column, the product was dissolved in C_6D_6 for immediate ^1H-NMR analysis. A small amount of the sample was used for the uv-vis absorption spectroscopic analysis using the diode array detector (5% ether in hexane, flow rate: 4 ml/min).

^1H-NMR: (300 MHz, C_6D_6, unstable in $CDCl_3$) δ 1.04 (s, 16-CH_3, 17-CH_3), 1.50 (s, 18-CH_3), 1.51 (s, 19-CH_3), 1.77 (s, 20-CH_3), 5.56 (d, 12-H), 5.90 (d, 14-H), 6.06 (d, 7-H), 6.13 (d, 10-H), 6.41 (d, 8-H), 6.54 (d, 11-H), 9.89 (d, 15-H), ppm; $J_{7,8}$ = 12.6 Hz, $J_{10,11}$ = 12.6 Hz, $J_{11,12}$ = 11.6 Hz, $J_{14,15}$ = 7.9 Hz.

Uv-vis: λ_{max} = 287 nm (5% ether in hexane) ε_{max} = 5,300, calculated based on ε_{max} = 36,600 for 7-*cis*,9-*cis*,13-*cis*-retinal.

Reaction of 7-*cis*-β-ionylideneacetaldehyde with phosphonate 1

A solution of phosphonate 1 (410 mg, 1.25 mmol), 18-crown-6, (1.65 g, 6.25 mmol; recrystallized CH_3CN complex[5] in 25 ml of anhydrous THF was cooled to -78°C under nitrogen and treated with 1.25 mmol of $KN(TMS)_2$ (0.5 M in toluene). The aldehyde (273 mg, 1.25 mmol) was then added and the resulting mixture stirred for 60 min at -78°C. After usual workup, a mixture of four isomers of retinonitriles was obtained (155 mg, 44%). These isomers were separated by hplc (Lichrosorb Si column, 2% ether in hexane).

7-*Cis*,11-*cis*-retinonitrile:

^1H-NMR: ($CDCl_3$, 300 MHz) δ 1.03 (s, 16-CH_3, 17-CH_3), 1.50 (s, 18-CH_3), 1.86 (s, 19-CH_3), 2.23 (s, 20-CH_3), 5.04 (s, 14-H), s-12-H), 5.91 (s, 7-H), 6.03 (8-H), 6.54 (s, 11-H), 6.58 (s, 10-H) ppm; $J_{7,8}$ = 12.5 Hz, $J_{10,11}$ = 12.0 Hz, $J_{11,12}$ = 10.0 Hz. (The chemical shift assignments of H-10 and H-11 were confirmed by computer simulation.)

^{13}C-NMR: ($CDCl_3$, 75 MHz), Table 1.

7-*Cis*,11-*cis*,13-*cis*-retinonitrile:

^1H-NMR: ($CDCl_3$, 300 MHz) δ 0.97 (s, 16,17-CH_3), 1.44 (s, 18-CH_3), 1.83 (s, 19-CH_3), 2.11 (s, 20-CH_3), 5.04 (s, 14-H), 5.91 (d, 7-H), 6.03 (d, 9-H), 6.27 (20-H), 6.51 (12-H), 6.58 (11-H) ppm; $J_{7,8}$ = 12.6 Hz, $J_{10,11}$ = 9.4 Hz, $J_{11,12}$ = 11.6 Hz. (The chemical shift assignments of H-11 and H-12 were confirmed by computer simulation.)

^{13}C-NMR: ($CDCl_3$, 75 MHz), Table 1.

UV-vis: λ_{max} = 343 nm (hexane)

7-*Cis*,11-*cis*,13-*cis*-retinal

To a solution of 7-*cis*,11-*cis*,13-*cis*-retinonitrile (10 mg, 0.035 mmol) in dry hexane at -78°C was added 0.2 mmol of DIBAH (1.0 M in hexane). The progress of the reaction was checked by TLC analysis. Upon completion it was quenched with NaF (33 mg, 0.8 mmol) and water (11 mg, 0.6 mmol) and the resulting mixture stirred at room temperature until a white solid separated from the solution (about 1.5 h). Extraction with ether and usual workup gave the crude product which was quickly passed through a short flash column.

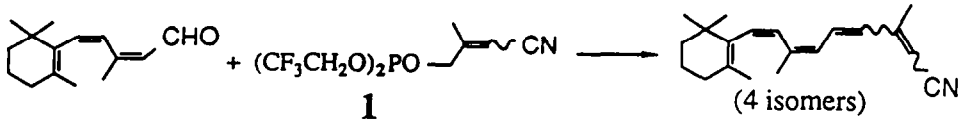
The resulting product was first dissolved in C_6D_6 for immediate ^{1}H-NMR analysis. Poor resolution necessitated the replacement of C_6D_6 by acetone-d_6.

^{1}H-NMR: (in acetone-d_6) δ 1.01 (s, 16-CH_3, 17-CH_3), 1.48 (s, 18-CH_3), 1.90 (s, 19-CH_3), 2.06 (s, 20-CH), 5.89 (d, 14-H), 5.91 (d, 7-H), 6.03 (d, 8-H), 6.22 (d, 12-H), 6.36 (d, 10-H), 6.74 (dd, 11-H), 9.63 (d, 24-H) ppm; $J_{7,8}$ = 12.5 Hz, $J_{10,11}$ = 11.7 Hz, $J_{11,12}$ = 11.4 Hz $J_{14,15}$ = 8.1 Hz.

UV-vis: λ_{max} = 289 nm (5% ether in hexane), ε estimated to be 6600 based on ε = 36,000 for 7-*cis*,13-*cis*-retinal.

Results and Discussion

Synthesis. The Still and Gennari[7] procedure for cis selective olefination has been applied to synthesis of these hindered 11-cis isomers of retinal using a similarly modified C-5 phosphonate **1** as the key reagent for the condensation reactions. With 7-*cis*,9-*cis*-C_{15}-aldehyde **1** was found to give a mixture of four geometric isomers of retinonitrile with a slight preference for the 11-cis geometry for the newly formed double bond: 7,9-dicis, 7,9,11-tricis, 7,9,13-tricis, all-cis in relative amounts of 21, 66, 7, 6. And, with the 7-*cis*-C_{15}-aldehyde the same stereoselectivity was observed; 7,11-dicis being the major product isomer followed by 7-cis and lesser amounts of 7,13-dicis, 7,11,13-tricis isomers. These isomers were readily separated by flash column chromatography. Partial reduction of the nitriles yielded the corresponding retinals. For the thermally labile 7,11,13-tricis or all-cis isomer (see below), the reduction was carried out at low temperatures (-78°C and warming up briefly to 0°C).



The isomeric nitriles were characterized by their ^{1}H- and ^{13}C-nmr, and the retinal isomers by ^{1}H-nmr and uv-vis spectra. The assignments of the ^{13}C-nmr spectra were based on their chemical shift correlation maps (CSCM). The data show that γ-shifts are applicable for the 9-cis (C_8 and C_{19}) and 13-cis (C_{20}) geometries for those hindered as well as other less hindered retinoids.[8]

While the reaction is not highly stereoselective, it represents a convenient method to the four doubly hindered 7,11-dicis isomer of retinal, particularly for the major 7,11-dicis and 7,9,11-tricis isomers. It represents a more direct route than that reported earlier to the latter two isomers. This route also afforded sufficient amounts of the previously unknown all-cis and 7,11,13-tricis isomers of retinal for studies of their properties.

Stability of the doubly hindered isomers. All retinonitriles containing the doubly hindered 7,11-dicis geometry were found to be stable at room temperature and upon extended storage at 0°C as were the 7,11-dicis and 7,9,11-tricis isomers of retinal. However, all-*cis*- or 7-*cis*,11-*cis*,13-*cis*-retinal was found to be unstable at room temperature rearranging stereospecifically to respectively 7-*cis*,9-*cis*,13-*cis*- or 7-*cis*,13-*cis*-retinal.

The course of rearrangement for these two isomers was followed by their uv/vis (Figures 1, 2) and ^{1}H-nmr (aldehyde signals) spectra (Figure 3). The rate constants for the reaction calculated from the uv data are listed in Table 2. From these data, the activation energies for the reaction were found to be 21.7 +/- 0.3 and 22.0 +/- 0.3 kcal/mole for all-*cis*- and 7-*cis*,11-*cis*,13-*cis*-retinals. They are similar to those reported for the 9,11,13-tricis isomer,[11] suggesting a common mechanism for these rearrangement reactions.

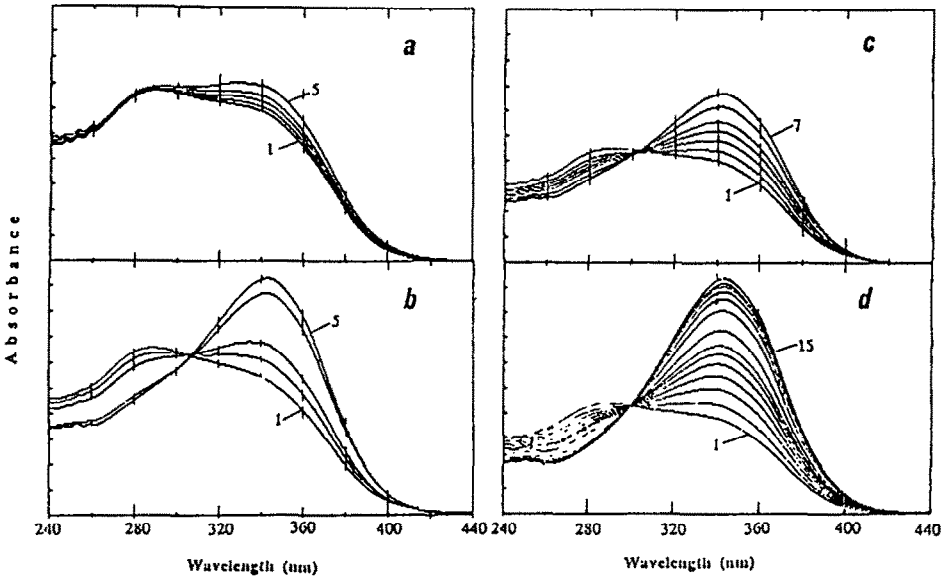


Figure 1. Conversion of 7-cis,11-cis,13-cis-retinal to 7-cis,13-cis-retinal in hexane as followed by uv/vis absorption spectra a. at 10°C, spectra recorded at the following interval 0 (spectrum 1), 1080, 2750 m (no. 3) b. at 20°C at 0 (no. 1), 30, 60, 90, 120, 150, 210, 450, 1170 m (no. 9) c. at 30°C, 0 (no. 1), 15, 30, 45, 60, 90, 120, 150, 180, 210, 240, 300, 360, 420, 480, 1380 m (no. 16) d. at 40°C, 0 (no. 1), 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210, 240, 300, 360, 540 m (no. 16).

Mechanism for the rearrangement reaction. Based on a study of simple dienones and dienals, Lillya and Kluge[11] postulated the following consecutive 6e electrocyclization for isomerization of some of the dicis isomers and suggested its possible application to the reported thermal isomerization of 11-*cis*,13-*cis*-retinal.[13] The observation that of the

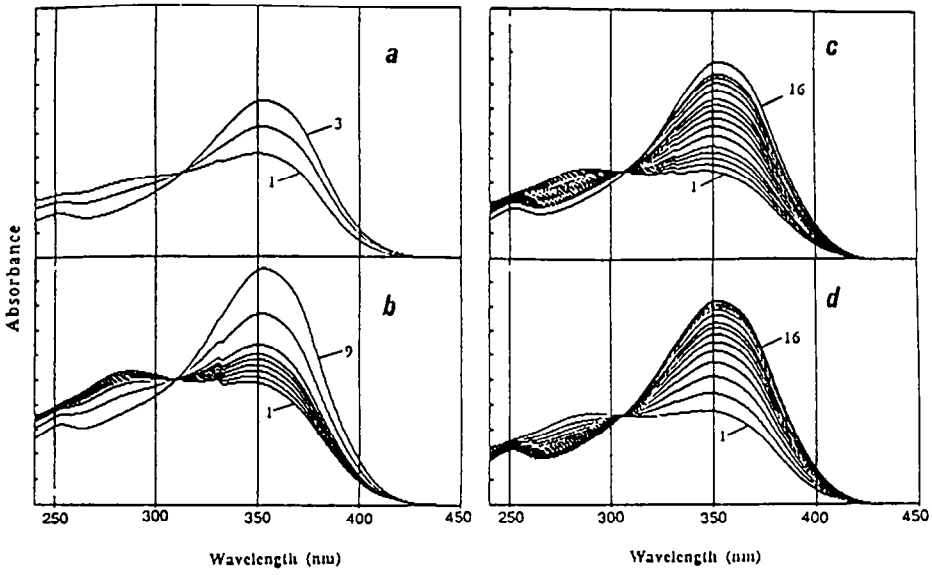


Figure 2. Conversion of all-cis-retinal in hexane to 7-cis,9-cis,13-cis-retinal as followed by uv/vis absorption spectra a. at 10°C, 0 (spectrum 1), 50, 124, 187, 378 m (no. 5) b. at 20°C, 0 (no. 1), 96, 146, 631, 777 m (no. 5) c. at 30°C, 0 (no. 1), 30, 60, 90, 120, 180, 240 m (no. 7) d. at 40°C, 0 (no. 1), 15, 30, 45, 60, 75, 90, 120, 180, 240, 300, 360, 415, 535, 576 m (no. 15).

Table 2. Rates of Isomerization of all-cis-Retinal and 7-cis,11-cis,13-cis-Retinal at Different Temperature[a]

	all-cis	7,11,13-tricis
T(0°C)	Rate, m^{-1}	Rate, m^{-1}
10	1.46×10^{-4}	1.46×10^{-4}
20	1.64×10^{-3}	9.96×10^{-4}
30	2.99×10^{-3}	2.41×10^{-3}
40[a]	6.99×10^{-3}	6.94×10^{-3}

a. Based on uv data with hexane as solvent.

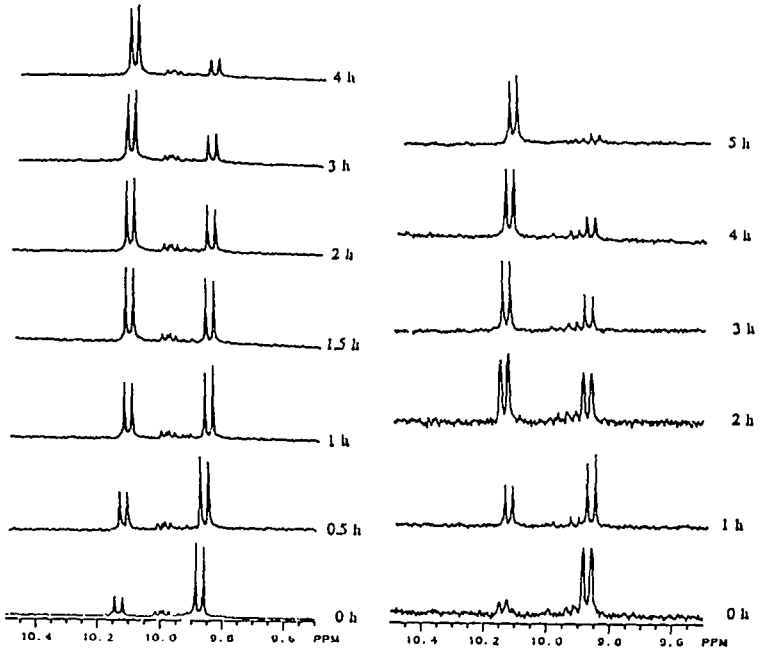


Figure 3. Conversion of 7-cis,11-cis,13-cis-retinal (left) and all-cis-retinal in C_6D_6 to respectively 7-cis,13-cis-retinal and 7-cis,9-cis,13-cis-retinal at 40°C as followed by ^{1}H-nmr (only the aldehyde region is shown).

sixteen possible retinal isomers only those containing the 11,13-dicis geometry undergo ready thermal rearrangement seems to support the postulated mechanism. However, several retinal analogs containing such a dicis geometry are known to be stable. For example, stable 11,13-dicis and 9,11,13-tricis isomers of 13-demethylretinal[14] and other retinal analogs (10-methyl, 5-butyl, 9,11-ethano) have been isolated.[15] Therefore, for the purpose of providing a better insight into the proposed mechanism, we have calculated the

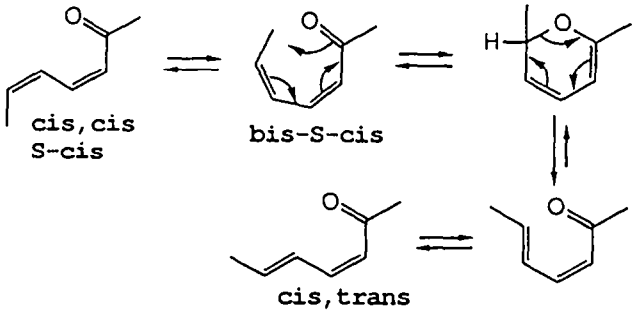


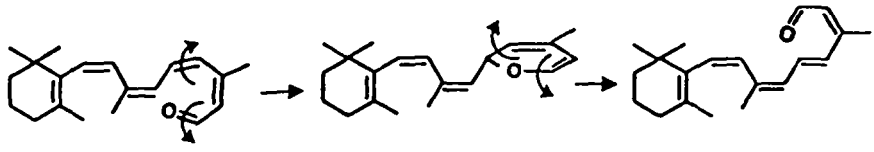
Table 3. Calculated (MMP2-85)[a] conformation and strain energy of minimized conformers of 11,13-dicis isomers of retinal (2) and 13-demethylretinal (3)

Compound	Dihedral angle					strain En	
	6,7	8,9	10,11	12,13	14,15	kcal/mole	ΔE^b
11,13-dicis-2							
12,14-bis-S-trans	-28	170	180	-169	-180	24.4	--
12-S-cis	-26	170	177	54	-179	26.0	1.6
12,14-bis-S-cis	-25	169	175	56	7	28.7	2.7
13-cis-2							
12,14-bis-S-trans	-26	171	-179	-179	-180	17.9	-6.5
11,13-dicis-3							
12,14-bis-S-trans	-28	170	-179	-180	180	18.5	--
12-S-cis	-29	172	178	53	-179	25.3	6.8
12,14-bis-S-cis	-33	165	172	57	5	28.0	9.5

a. Ref. 15. b. Obtained by subtracting its strain energy by that of the 12,14-bis-S-trans conformer.

relative strain energies of all the conformers of retinal and 13-demethylretinal believed to be involved in the reaction by using the molecular mechanics program for π systems (MMP2-85).[16] The results are summarized in Table 3.

The data confirm the suspicion that the additional methyl group at the 13-position has a significant effect on the relative stability of the conformers. Hence in the case of the 13-demethyl series, the bis-S-cis conformers are >9 kcal/mole higher in energy than the corresponding s-trans conformers, thus not expected to be involved in the reaction. In the case of the parent retinal, the higher energy of the S-trans conformers makes the bis-S-cis conformer readily accessible at room temperature. Accordingly, the rearrangement for all-*cis*-retinal can be formulated as below.



Other known stable 11,13-dicis isomers of retinal analogs can also be rationalized on similar ground. The bis-S-cis conformer is not expected to be important in the more crowded 10-methylretinal, 5-butylretinal and 9,11-ethanorethanl.[15] Geometrical constraint in other analogs, such as the presence of fused ring systems, eliminates possible existence of the bis-S-cis conformer, hence adding stability to their 11,13-dicis isomers.[17]

It is of interest to note that for retinyl imines, a similar 6e electrocyclization process leads to stable dihydropyridines.[18]

Spectroscopic properties of doubly hindered isomers. The uv/vis absorption spectra of the four doubly hindered isomers of retinal are shown in Figure 4. Those of 7,11,13-tricis and all-cis, because of their ready rearrangements to the more strongly absorbing 11-trans isomers, were recorded on a hplc diode array detector. Their extinction coefficients were estimated from those of the corresponding thermal products.

The absorption maxima of 7,11,13-tricis (in hexane 287 nm ε = 6,600) and all-cis (285 nm, ε = 5,300) isomers are much blue shifted (and with much smaller extinction coefficients) from those of other retinal isomers including the other two containing the 11,13-dicis geometry (305nm for both 11-*cis*,13-*cis*- and 9-*cis*,11-*cis*,13-*cis*-retinal).[11] As

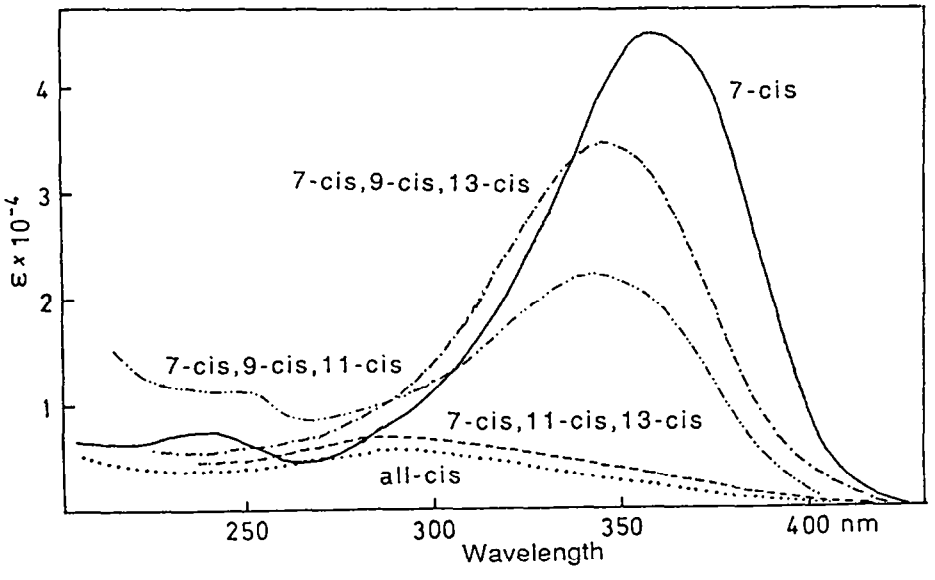


Figure 4. UV-vis absorption spectra of all-cis-retinal and 7-cis,11-cis,13-cis-retinal in hexane (5% ether) recorded on a Hewlett Packard 1070a diode array detector.

pointed out earlier, for the latter two, the large blue shift is likely due to the highly twisted conformation around the 12,13 bond.[11] The additional ~20 nm shift for the present two hindered isomers is likely due to the twisted conformation associated with the highly crowded 7-cis geometry.[19] The low extinction coefficients are consistent with a highly twisted chromophore.

The temperature dependent uv/vis absorption spectra of the hindered 11-*cis*-retinal[20] and analogs[21] are believed to be due to population inversion of conformers at different temperatures with the 12-S-trans conformer, at the expense of the 12-S-cis conformer, favored at low temperatures.[22] For the highly hindered all-*cis*-retinal, we have now recorded its spectrum at liquid nitrogen temperature (Figure 5). There was no significant increase of absorption of the main band nor concommitant decrease of absorption in the uv region as known for 11-*cis*-retinal.[20,22] Hence for all-*cis*-retinal there are probably no spectrally distinct conformers that equilibrate readily within the temperature range of investigation.

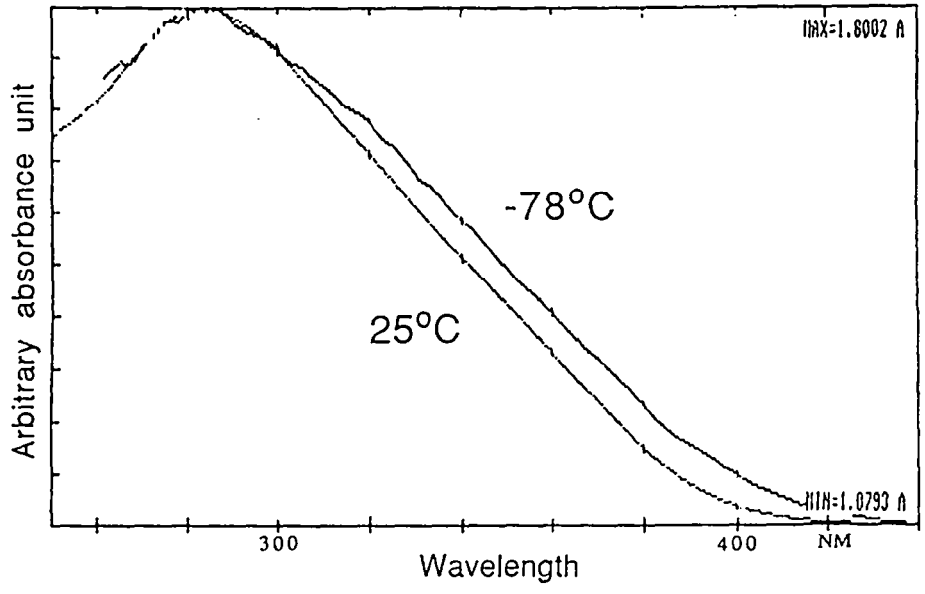


Figure 5. Uv-vis absorption spectra of all-cis-retinal in 3-methylpentane: spectrum 1, at room temperature 298K; spectrum 2, at liquid nitrogen temperature 77K.

The thermal rearrangements of both 7,11,13-tricis and all-cis isomers of retinal were too rapid to allow formation of isomeric rhodopsin analogs. In fact, by chromophore extraction experiments, it has been shown that some of the dicis isomers of retinal undergo

catalyzed isomerization to the mono-cis isomers prior to pigment formation.[23] Thus, any pigment formed from prolonged incubation of these hindered poly-cis isomers with opsin is unlikely to retain the original geometry.

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References

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