Tetrahedron Letters, Vol.22, No.26, pp 2463 - 2466, 1981
Printed in Great Britain

0040-4039/81/262463-04$02.00/0

PHOTOISOMERIZATION OF THE C_{15}-ALDEHYDE AND THE C_{18}-KETONE IN THE VITAMIN A SERIES. SOLVENT EFFECT ON PHOTOISOMERIZATION OF COMPOUNDS RELATED TO RETINAL[1]

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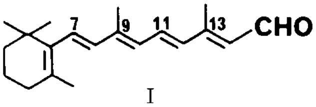
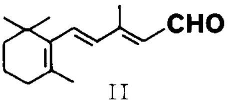
ABSTRACT: The directions of photoisomerization of polyenals and polyenones are believed to be controlled by the relative ordering of the n,π* and π,π* states.

The dependence of composition of photoisomers on solvent in direct irradiation of retinal (I) has been recognized for many years.[3] That the 11-cis isomer is formed in alcoholic solvents and not in non-polar solvents has been employed as a convenient entry to this visually important isomer.[4] Recently, the use of aprotic solvents further enhancing the formation of the hindered isomers, including the previously not detected 7-cis isomer of retinal was also reported.[5,6] It was pointed out[5,7] that the trend of solvent dependence of the direction of photoisomerization was consistent with the relative stability of the zwitterionic intermediates advanced by Salem and others.[8] We have now carried out additional studies of the photoisomerization reaction using the lower members of the retinal series. The current results are not consistent with the rationalization offered earlier. A different explanation is offered.

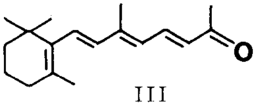
Photoisomerization of the C_{15}-aldehyde (II) was found to lead to the formation of all four known isomers.[9] They were well separated by high pressure liquid chromatography (hplc) using silica gel based columns. Irradiation of the all-*trans*-C_{18}-ketone (III) in a variety of solvents was found to give five isomers (7-cis; 9-cis; 11-cis; 7-cis,9-cis; 9-cis,11-cis). The four 11-trans isomers were well separated by hplc; however, the two 11-cis isomers were separable only with solvent of lower polarity (<5% ether in hexane). All isomers were isolated; their ^{1}H-nmr spectra agreed with those of the authentic samples.[10] In an earlier study of photoisomerization of the ketone,[10c] only the four 7-trans isomers were reported.



I



II



III

The photoisomerization reaction is accompanied by slow degradative processes. However, the geometric isomerization was sufficiently rapid to allow establishment of photostationary states before significant disappearance of the trienals or the tetraene ketones. Such mixtures have been generated by starting with all four isomers of II and the four most available isomers of III (all-trans; 7-cis; 9-cis; 7-cis,9-cis).[10] The averaged numbers are listed in Tables 1 and 2. The initial product ratios obtained by irradiating all-*trans*-retinal were reported

Table 1. Photostationary State Compositions of the C_{15}-aldehyde II by Direct Irradiation[a]

		Percentages of Isomers in Photostationary States[b]			
Solvent	ε[c]	all-trans	7-cis	7-cis,9-cis	9-cis
Hexane	1.88	22.6 ± .3	36.6 ± .4	24.7 ± 2.4	15.9 ± .2
Cyclohexane	2.02[d]	22.4 ± .4	36.1 ± 1.7	24.1 ± 1.9	17.3 ± .3
Dioxane	2.21	23.3 ± .2	37.0 ± .4	21.9 ± .7	17.7 ± .2
Benzene	2.28	22.7 ± .3	35.2 ± 1.2	24.1 ± 1.0	18.1 ± .5
Chloroform	4.81[d]	24.0 ± .4	33.0 ± 1.4	24.5 ± 1.6	17.6 ± .6
Methanol	32.70	23.0 ± .4	36.3 ± 1.2	25.6 ± .5	14.9 ± .2
Acetonitrile	37.5[d]	22.6 ± .5	37.1 ± 1.3	22.8 ± 1.3	17.4 ± 1.5
DMSO	46.68	24.0 ± .4	37.8 ± 1.4	21.9 ± 1.6	16.4 ± .6

a. Hanovia medium pressure 200W mercury lamps with Corning 3-74 cut-off filter. Analyses by hplc with 340nm detecting beam. Data corrected for different absorptivities of isomers at the wavelength. b. Average of individual runs starting from pure isomers. c. Dielectric constants determined at 25°C, unless otherwise noted. From Techniques of Chemistry, A. Weissberger, Ed., II, Wiley, N.Y., 1970. d. 20°C.

Table 2. Photostationary State Compositions of the C_{18}-ketone in Various Solvents[a]

	Percentages of Isomers in Photostationary States[b]				
Solvent	All-trans	7-cis	7-cis,9-cis	9-cis	11-cis & 9-cis,11-cis
Hexane	73.7 ± 1.2	6.5 ± .5	<1	11.0 ± .8	8.4 ± .4
Cyclohexane	72.9 ± 1.2	6.7 ± .6	<1	13.0 ± .8	6.3 ± .4
Benzene	67.8 ± .3	7.3 ± .4	<1	16.0 ± .7	7.9 ± .3
Chloroform	48.3 ± 2.4	12.5 ± .9	4.0 ± .3	25.1 ± 1.3	9.9 ± .8
Methanol	44.8 ± .5	15.2 ± .5	4.6 ± .2	23.5 ± .6	9.1 ± .3
Acetonitrile	60.7 ± 7.8	9.8 ± 2.4	3.2 ± .4	20.1 ± 2.9	6.1 ± 2.0
DMSO	54.9 ± 2.4	11.0 ± .9	3.7 ± .3	23.1 ± 1.3	7.1 ± .8

a. Hanovia medium pressure 200W mercury lamp with Corning 3-74 cut-off filter. Analyses by hplc with 340nm detecting beam. Data corrected for different absorptivities at the wavelength of detection. b. Average of runs starting from all-trans, 7-cis, 7-cis,9-cis and 9-cis isomers of the C_{18}-ketone.

earlier.[5,6] The photostationary state ratios of the retinal isomers in two solvents are shown in Table 3. It is clear that the stationary state mixture of the trienals is virtually independent of the solvent employed. For the tetraene ketones the mixture shows some dependence on solvent polarity, though much less dramatic than is the case with retinal and other

Table 3. Photostationary State Compositions of Retinal[a]

	Percentages of Isomers in Photostationary States[b]								
Solvent	All-t	7-cis	9-cis	11-cis	13-cis	7,9-c	7,13-c	9,13-c	9,11-c
Hexane	40	--	5.5	3.5	51	--	--	--	--
CH_3CN	31	4.5	23	29	9.2	.2	c	.7	2.1

a. Starting from all-trans only. Irradiated with ≥380nm (Corning 0-51 filter). Hplc analyses, 360nm detecting beam. b. Another weak peak of varying intensity which has the shortest retention time is probably that of 11-cis,13-cis. c. A weak shoulder in front of 13-cis.

derivatives.[7,11] For retinal in polar solvents there is a clear tendency toward being less discriminate in product formation.

The explanation involving selective stabilization of different zwitterionic intermediates corresponding to twisting any of the four exocyclic double bonds, though successful in accounting for the results of retinal and related compounds, now fails to explain the complete lack of solvent effect for the C_{15}-aldehyde. The possibility of a dependence of relative importance of zwitterionic intermediates on chain length of a polyene is not justified on theoretical grounds.[8] Also disturbing is the fact that several recent calculations showed that the dipolar character of the excited polyene becomes evident only when well along the course of the twisting motion (the sudden polarization effect).[12] This implies that solvent stabilization of the dipolar intermediate can take place only after the molecule has committed itself to a particular twisting motion and hence is of no consequence to the geometric isomerization reaction. The validity of this explanation is in doubt.

To account for the solvent effect on the intersystem crossing efficiency of retinal, Dawson and Abrahamson[13] and Bensasson *et al.*[14] invoked an explanation involving state switching between n,π* (hexane) and π,π* (methanol) states. More recently, Das and Becker[15] argued from results of absorption and emission studies of the homologues of retinal that for the C_{15}-aldehyde and the lower member β-ionone the lowest excited state is of n,π* nature regardless of the polarity of the solvent. In the C_{18}-ketone and retinal the lowest excited state could be either n,π* or π,π* depending on the solvent polarity. We now believe that the observed photochemistry of compounds in this series is consistent with this explanation. The solvent insensitive behavior of the C_{15}-aldehyde agrees with the involvement of only the n,π* state in all solvents. The minor changing photochemical behavior for the C_{18}-ketone is due to approach of the π,π* and the n,π* states. In non-polar solvents the n,π* character dominates; and in polar solvents, the π,π* character begins to play a role. In the longer polyene retinal, there is a complete reversal of the reactive state in solvents of different polarity. The direction of isomerization can also be rationalized by the relative electron density of the pi-system for the n,π* and π,π* states. The n,π* state (non-polar solvents) involving filled bonding orbitals of the pi-system should have higher bond orders. Such an excited molecule should be quite selective in reaction thus twisting only the tri-substituted double bonds giving the 9-cis and 13-cis isomers. The π,π* state (polar solvents) on the other hand with a partially vacant bonding orbital should have lower bond orders for all formal double bonds. Twisting around the four double bonds becomes indiscriminate giving all four isomers. Consistent with this explanation is the observation that diphenyl polyenes which do not have low lying n,π^* states do not show a large solvent dependence in their photoisomerization reactions.[16] Also consistent are the directions of photoisomerization of methylated and demethylated retinals which selectively isomerize at the sterically more crowded double bonds when irradiated in hexane.[17,18]

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18. The work was supported by grants from NSF (CHE-12686) and U.S. Public Health Services (AM-17806). All-*trans*-retinal was supplied by Hoffmann-La Roche & Co.

(Received in USA 12 March 1981)