

REGIOSELECTIVE PHOTO ISOMERISATION OF RETINOLACETATE

V. Jayathirtha Rao* and U.T. Bhalerao

Organic Division II, Indian Institute of Chemical Technology, Hyderabad 500 007, India.

Regioselective photoisomerisation of retinolacetate undergoing at tri-substituted double bonds upon singlet and triplet excitation and its ionic photodissociation process originating from singlet excited state is reported.

The photochemical behaviour of retinal and its analogues have been extensively investigated¹ because of retinals direct role as a chromophore in vision (rhodopsin) and photosynthesis (bacteriorhodopsin). Photoisomerisation of retinal and its analogues were studied with emphasis on the effect of solvent², effect of substitution³ and temperature dependence⁴. The regioselectivity noted in the photoisomerisation of retinal was rationalised in terms of substituents and medium induced barriers of rotation⁵. Intersystem crossing quantum yield⁶, estimation of triplet energy⁷, solvent dependent state ordering ($n\pi^*$ or $\pi\pi^*$)⁸ and recently resonance Raman spectroscopy has been applied to study the retinal excited states⁹. Triplet sensitised photoisomerisation¹⁰ and iodine induced thermal isomerisation¹¹ of retinal have been reported. Conversely only a very few reports¹² exists on the photochemical behaviour of retinolacetate and retinol although of their well known physiological functions¹³ and industrial importance. Recent spectroscopic studies^{12 & 14} on retinoids throws light on retinyl carbonium ion resulting from the laser flash photolysis of retinolacetate, which was postulated as "ionic photodissociation" by Ottolenghi¹⁴ and co-workers. We have been interested in the photochemistry of retinolacetate because of hitherto un explored photoisomerisation of retinolacetate, to understand and define the various governing factors involved with the photoisomerisation in polyenes and also to know and compare with the just reported retinol isomerase enzyme¹⁵. To this end, here we report on the regio selective isomerisation undergoing at trisubstituted double bonds upon triplet and singlet excitation of retinolacetate and ionic photodissociation process. Products isolated, anhydroretinol and retinyl-methylether not only proves earlier postulated ionic photodissociation process but also further reveals that this is restricted to singlet excited state of retinolacetate.

All trans retinolacetate (**1**) obtained by low temperature crystallisations was directly irradiated in various solvents using 450 W medium pressure lamp and the reaction was monitored by HPLC. In all irradiations isomerisation is very specific to the trisubstituted double bonds giving 9-cis isomer (**2**) as major and 13-cis (**3**) as minor (Table 1), further giving anhydroretinol (**4**) and retinyl methyl ether (**5**)¹⁶ (in methanol). Product distributions were determined at low per cent conversions to make sure that all-trans retinolacetate is the excited species undergoing reaction. Table 1 reveals that change in solvent polarity facilitates the formation of anhydroretinol and retinyl-methylether. Sensitisation experiment was designed such that selective excitation of sensitizer was achieved by selecting the sensitizers absorbing light in the visible region, where the retinolacetate does not have absorption. Sensitized isomerisation resulted in generating selectively 9-cis

(2) and 13-cis (3) isomers which are trisubstituted double bonds. Product distribution and photo-stationary state composition was determined for sensitisation experiments (Table 2). Sensitisation was found to be not feasible with the donor triplet energy less than 39 k cal/mol. thereby defining triplet energy of retinolacetate.

Table - 1
Photoisomerisation of Retinolacetate upon Direct Excitation^a

Solvent	Time of irradiation (min)	% Conversion	Product distribution ^b		
			9-cis	13-cis	Anhydroretinol
Hexane	10	2	2	Very little	
	30	5	4	0.5	0.5
Benzene	10	6	5	0.5	0.5
	30	12	10	1.0	1.0
CH ₂ Cl ₂	10	14	12	1.0	1.0
	30	22	18	2.0	2.0
CH ₃ CN	10	15	12	1.5	1.5
	30	24	18	3.0	3.0
MeOH ^c	10	15	10	1.5	1.5

a) Nitrogen bubbled solution of all-t retinolacetate (0.01 M) irradiated in pyrex tubes with 450 W medium pressure Hg lamp; b) analysed using amino-silica 4.6/200 mm column with hexane as eluent, 329 nm, product distribution was determined after giving correction to the absorbency at the given wavelength of detection for the corresponding isomers and products, product distributions are average of three runs; c) in methanol 2% of retinylmethylether was isolated.

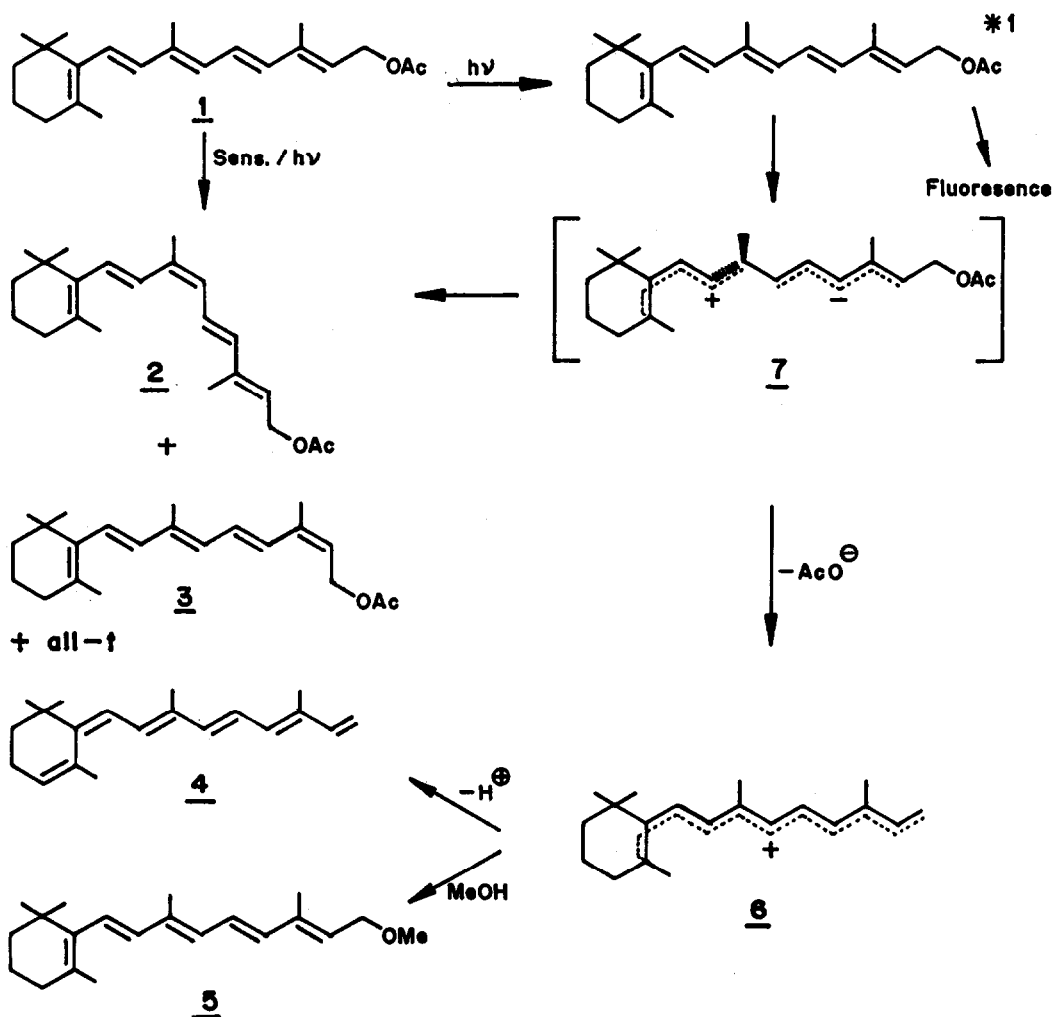
Table - 2
Sensitised Isomerisation of Retinolacetate^a

Sensitiser ^b	λ_{\max} (nm)	E _T k cal	Time of irradiation(min)	% Conversion	Product Distribution ^{d,e}		
					all-t	9-cis	13-cis
Erythrocin	515	42	30	17	83	13	4
			120	PSS ^c	70	16	14
Resebengal	550	39	30	16	84	12	4
			120	PSS	68	17	15
Methylviolet	585	37		No reaction			
Methylene blue	660	32		No reaction			

a) Nitrogen bubbled solution of retinolacetate (0.01 M) in MeOH with sens.0.0001 M was irradiated using 500 W tungstenlamp; b) triplet energies are from Advan. in Photochem. vol.5; c) PSS = photostationary state; d) amino-silica column, hexane as mobile phase, product distribution is of average of three runs; e) prolonged irradiation gives 9,13-dicis isomer.

The results are compatible with the concepts introduced earlier. Theoretical calculations (Salem)¹⁷ and experimental findings¹⁸ (Stryer) have revealed that vertically excited polyene undergoes charge migration and this is the basis in rationalising the results. Charge migrated species Z (Scheme) resulting from the excited singlet upon twisting (Sudden Polarisation) at the central most double bond is reasonable in explaining selective isomerisation at trisubstituted double bond leading to major isomer as 9-cis¹⁹. Charge migration shown in species Z (Scheme), -ve charge

towards end of acetate moiety is explicable based on the products 4 and 5-resulting from the retinylcarbonium ion 6. Formation of products 4 and 5 resulting from the retinyl carbonium ion is facilitated by polar solvents can be explained by the role played by the solvent in the relative stabilisation and ionisation of the species 7. triplet sensitisation leads only to isomerisation preferentially at trisubstituted double bonds and not leading to ionic dissociation process is reasonable based on the low energy associated with triplet state and its diradical nature. The absence of 7-cis and 11-cis (disubstituted double bonds) isomers in the direct excitation and sensitised isomerisation process makes more interesting because the behaviour of this system is different from the corresponding aldehydes, esters and nitriles²⁰.



SCHEME

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