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EFFECTS OF WAVELENGTH AND CONFORMATION ON THE PHOTOCHEMISTRY OF VITAMIN D AND RELATED CONJUGATED TRIENES[1]

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Abstract: Irradiation experiments under various conditions establish that the photoreactions of conjugated trienes are governed by the ground state conformational equilibrium and the NEER principle, as well as by the wavelength dependent relaxation behaviour of the excited species.

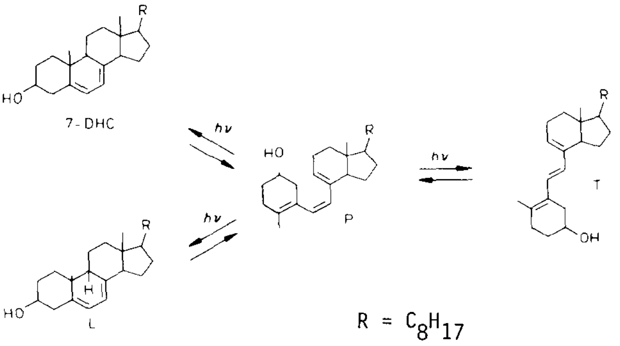
In an earlier paper[2] we reported a study of the effect of wavelength on the photoreactions of (*E*)- and (*Z*)-2,5-dimethyl-1,3,5-hexatriene, that enabled us to demonstrate the validity of the NEER principle[3], and hence to denote the difference of the absorption spectra of the various ground state conformers as a cause of the wavelength dependence of photoproduct formation. We suggested that next to this cause also higher or hot excited state reactivity may be involved, one and the same conformer yielding different products upon excitation by light quanta of different energy. In order to investigate further these possibilities we have examined the effect of wavelength in the reactions of the polysubstituted trienes previtamin D and vitamin D, the first being conformationally flexible and the second having only one form (c*Z*t) of the triene chromophore. The many more modes of vibration in these steroidal trienes, as compared to the simple model trienes in our previous study, may facilitate thermal dissipation of excess vibrational energy and therefore favour photoreactions from vibrationally relaxed molecules. We report here in brief the results of our studies[4] which lead us to conclude that wavelength dependent relaxation patterns indeed play a role in triene photochemistry. Furthermore, evidence of conformational control of the photoreaction pathway exerted by the helicity of the triene chromophore in vitamin D is presented.

For previtamin D_3 (P) the effect of wavelength was investigated by measuring the quantum yields[5,6] of formation of tachysterol$_3$ (T), lumisterol$_3$ (L) and 7-dehydrocholesterol (7-DHC) at λ 302.5 and 254 nm. In addition, the quantum yields of formation of P from L and 7-DHC were

Table 1. Quantum yields of formation at 302.5 and 254 nm.

	302.5	254
P ⟶ T	0.29	0.41
P ⟶ L	0.09	0.040
P → 7-DHC	0.02	0.014
L ⟶ P	0.49[a]	0.50
7-DHC → P	0.34	0.34

[a] Measured at 313 nm



measured. Quantitative analysis of the mixtures irradiated to only low degrees of conversion (5 % or less) was carried out using the HPLC assay method recently reported by De Vries *et al.*[7] The results corrected for the absorption by the photoproducts and for the decrease of starting material are collected in Table 1. Discrepancies with earlier values and other points of interest will be commented upon elsewhere.[4] In the present context we note that the reactions starting from P clearly exhibit wavelength dependence: the *cis/trans* isomerization to T is more efficient at 254 nm than at 302.5 nm; the reverse holds for the ring closure reactions to L and 7-DHC, the ratio of the two processes changing from 2.5:1 at 302.5 nm to 7.5:1 at 254 nm. Significantly, for this heavily substituted triene the effect of wavelength is much smaller than for the model triene (Z)-dimethylhexatriene where a change from 1:6 to 10:1 was found.[2,4a] The ring opening reactions of 7-DHC and L do not exhibit any effect of wavelength. These data indeed suggest increased ease of dissipation of excess vibrational energy with increased alkyl substitution of the chromophore. However, part of the difference in wavelength dependency between P and the model triene unquestionably arises from different compositions of the conformational equilibria and different absorption ratios of the conformers at the wavelengths employed. Since for both compounds pertinent data are lacking, it is not yet possible to quantitatively assess the separate contributions of the ground state and the excited state properties to the wavelength effects observed.

Before examining the effect of conformation and wavelength on the photoreactions of vitamin D we reinvestigated the question of its possible transformation into *trans*-vitamin D by direct irradiation, and found[4] that interconversion of *cis*- and *trans*-vitamin D_3 indeed occurs albeit with low quantum yields. Furthermore, it became apparent[4] that the cyclobutene-suprasterols SV and SVI found upon irradiation of vitamin D_3 originate mainly, if not exclusively, from *trans*-vitamin D_3. The photoreactions of D and *trans*-D are summarized in the scheme below.

The ground state conformational equilibrium of vitamin D essentially consists of only two conformers, both having the cZt form of the triene chromophore and differing in the chair conformation of ring A. The latter has its bearing on the triene geometry by fixing the sign of the torsion angle Φ(6-5-10-19) between the double bonds in the cisoid diene moiety, and probably also in the transoid part, Φ(5-6-7-8).[4] This results in cZt forms of opposite chirality conveniently designated by the symbols c(-)Zt(+) and c(+)Zt(-).[8] When irradiating[10] vitamin D_3 at λ 313 nm in solvents of different polarity till complete conversion of both *cis*- and *trans*-

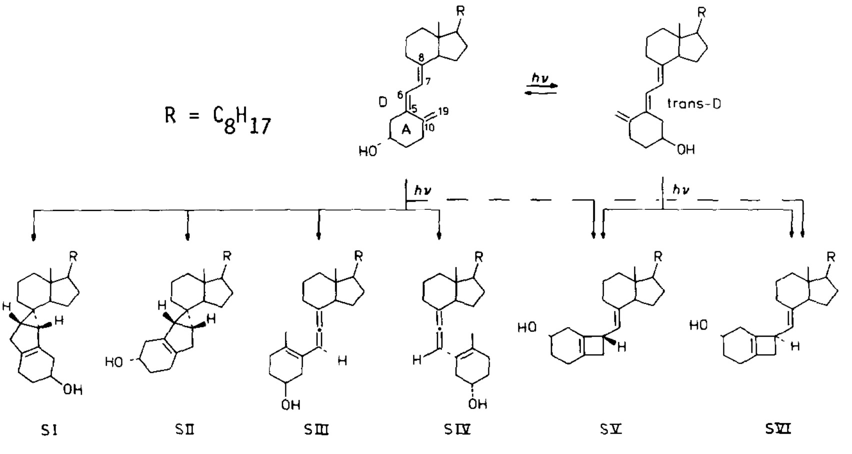


Table 2. Conformational equilibrium of vitamin D_3 and photoproduct ratio SI/SII (λ_{irr} 313 nm) in solvents of different polarity.

Solvent	c(+)*Z*t(-) :	c(-)*Z*t(+)	SI :	SII	Solvent
cyclohexane-d_{12}	44	56	48	52	isooctane
tetrahydrofuran-d_8	25	75	31	69	diethyl ether
methanol-d_4	23	77	26	74	ethanol

vitamin D, we found a close correspondence (Table 2) between the ratio of the photoproducts SI and SII (irreversibly formed from the *cis*-isomer alone in 83-89 % combined yield) and that of the two c*Z*t conformers[11] in solvents of similar polarity. Assuming that a shift in equilibrium composition may also be induced by a change in temperature, we irradiated vitamin D_3 at various temperatures. The SI/SII ratios of the mixtures obtained (combined yield of SI and SII 87-94 %) are listed in Table 3. A plot of ln SII/SI *vs* $(RT)^{-1}$ suggests a value of 0.95 kcal/mole (4.0 kJ/mole) for the difference in energy between the two conformers in isooctane, that with the equatorial hydroxyl group, c(-)*Z*t(+), being the more stable. Similarly, replacement of the hydroxyl group at C-3 in vitamin D by other substituents changed the SI/SII ratio parallel to the expected shift in conformational equilibrium.[4]

Table 3. Ratio of photoproducts SI and SII from vitamin D_3 at various temperatures (λ_{irr} 313 nm, isooctane).

Temp. in °C	SI :	SII
23	48	52
0	47	53
- 40	42	58
- 60	35	65
- 80	28	72

These results strongly indicate a one-to-one relationship between conformer helicity and suprasterol I or II formation: SI originates from the c(+)*Z*t(-) conformer, SII from the c(-)*Z*t(+) form.[13] Inspection of the geometries of precursor and product shows that the mode of cycloaddition followed in the formation of the bicylohexene-suprasterols accords with the ground state helicity of the triene chromophore. To our knowledge this represents the first example of the operation of the accordancy and least motion principles[14,15] in the photoreactions of an open-chain polyene.

The vitamin D experiments described above pertain to irradiations at 313 nm, *i.e.* at the extreme low-energy side of the absorption band (λ_{max} 263 nm). In investigating the effect of wavelength we determined the composition of the mixtures obtained after complete conversion by irradiation at 313 and 254 nm (Table 4). The effect of excess excitation energy is evident from the increased proportion of the cyclobutene-suprasterols SV and SVI - probably to be

Table 4. Wavelength effect on the composition (in %) of vitamin D_3 irradiation mixtures (isooctane, 0° C).

λ_{irr} (nm)	SI	SII	SIII+SIV	SV+SVI	Unidentified products
313	41	46	4	6	3
254	39	33	3	14	11

ascribed to enhanced ease of *cis/trans* isomerization of vitamin D at lower wavelengths - and from the decreased combined yield of the bicyclohexene-suprasterols SI and SII. The ratio of bicyclohexene to cyclobutene products changes from 15:1 to 5:1. Moreover, the ratio SI/SII changes from 0.9 to 1.2, and at λ 254 nm no longer parallels the composition of the conformational equilibrium. Since in separate experiments we demonstrated[4] that the UV absorption spectrum of vitamin D_3 does not change upon varying the conformer ratio, the wavelength effects observed in this case cannot be ascribed to ground state factors but have to be explained by a wavelength dependent relaxation pattern of the excited species.

We conclude that generally with conjugated trienes wavelength dependence of photoproduct formation arises as a result of two factors:

1) Different absorption spectra of the various conformers combined with non-equilibration of the excited rotamers (NEER);
2) One and the same conformer showing different photochemistry depending on the vibronic level reached upon the absorption of a light quantum.

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Notes and References

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