Photochemistry of conjugated trienes: Vitamin D revisited

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A survey is given of various factors and conditions that affect the photoreactivity and photoproduct distribution of conjugated trienes, such as ground-state rotameric equilibrium, non-planarity of the chromophore, wavelength of irradiation, solvent and temperature. The effect of changes in ground-state conformation and geometry, caused by substitution or variation of solvent or temperature, usually appears to be more important and more easily predictable than excited state effects.

Introduction

The photochemistry and photophysics of homonuclear conjugated trienes have fascinated chemists already for many decades (1). One of the reasons for the continuing interest is the fact that – together with dienes – they are the smallest members of the group of polyenic compounds. Polyenes occur in nature in a wide variety, and their chemistry and photochemistry plays a vital role in many biological processes. They also are the basic constituents of polyacetylene which is well-known for its photoconductivity and non-linear optical properties. Conjugated dienes and trienes often serve as the simplest possible model compounds in experimental and theoretical studies of polyenes. However, they are also highly interesting in their own right. In contrast to octatetraene and many longer polyenes butadiene and hexatriene do not show fluorescence in solution. In response to electronic excitation dienes and especially trienes often give rise to a rich mixture of photoproducts that may differ essentially in composition from one triene to another, even when the substrates are seemingly very akin in structure. The singlet photochemistry, in particular, is characterized by a rich variety of photoreactions: *cis/trans*-isomerization, electrocyclizations and cycloadditions, sigmatropic shifts, fragmentations, photoreductions and –additions have all been observed. The schemes to follow serve to illustrate the variety of products resulting from these reactions. In contrast, the triplet photochemistry of conjugated trienes is limited to efficient *cis/trans*-isomerization accompanied by formation of minor amounts of dimers (1).

The wealth and variety of reactions encountered present a formidable challenge to the chemist: from the elucidation of the structures of the photoproducts and the mechanisms of the reactions in which they are produced, to the unravelling of the factors that govern the behaviour of the singlet excited triene in, its relaxation to the ground state of the product. Although considerable progress has been made the mechanisms are as yet only partly understood and it is still a precarious task to predict which of the many different relaxation pathways will be followed by a given triene and to what extent. Ultimately, this would require a detailed knowledge of the potential energy surfaces of the ground state and the relevant excited state(s), and of the geometry of the reacting species, especially at the crossings – whether avoided or not – of these states. The theoretical efforts to this goal have gained a new impetus through the recent studies of Bernardi and Robb and their coworkers on the role of conical intersections (2).

The present contribution will deal with the subject from the point of view of the experimental chemist who is in search of more or less easy to follow practical guidelines. The impact of some internal

and external factors and conditions on triene photochemistry will be discussed and illustrated with recent experimental results, mainly from work in Leiden, obtained in studying simply substituted hexatrienes as well as relatively large molecules like vitamin D and related compounds. Remarkably, the photochemical behaviour of the larger molecules sometimes turns out to be much less complex than that of the smaller ones.

Ground-state conformational equilibrium.

The oldest concept in the rationalization of triene photochemistry, and probably also the most successful in terms of predictive value, is the idea of ground-state conformational control of photoreactivity, first advanced by Havinga and Schlatmann (3) and later termed the NEER principle (Non-Equilibration of Excited Rotamers) (1a). It states that the species formed upon $\pi \to \pi^*$ excitation of the various transoid and cisoid ground-state rotamers of a triene – or a polyene in general – will not equilibrate during their short singlet excited–state lifetime because of the increased bond order of the ground-state C-C single bonds. As a result the composition of the photoproduct mixture will reflect the composition of the ground-state conformational equilibrium of the starting compound. The principle explains, for instance, the absence of a cyclohexadiene in the mixture of photoproducts from Z-hexatriene, while it is present in the mixture obtained from 2,5-dimethylhexatriene: according to the NEER principle only the curled (cZc) form can yield the cyclization product (Scheme 1). No trace of this rotamer can be found in Z-hexatriene, while in the ground-state conformational equilibrium of the dimethyl compound its presence is revealed by UV absorption and NOE measurements (4,5).

Scheme 1
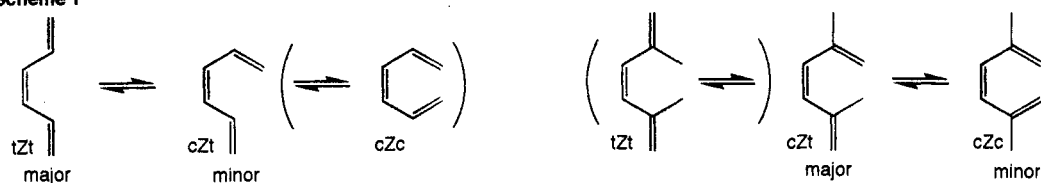
A nice illustration of the operation of the NEER principle is provided by low-temperature irradiation of previtamin D (Scheme 2) (6). Previtamin D (P) in the ground state is a very flexible molecule, probably best represented as a mixture of cZc and tZc rotamers that are highly twisted around the formally single C(5)–C(6) and C(7)–C(8) bonds. Upon irradiation at 92 K in MIP 1 : 5 these rotamers are converted into non-equilibrating excited cZt-P* and cZc-P* species that relax in part via rotation around the 6–7 bond (Z/E-isomerization) each giving rise to a single ground state rotamer of tachysterol (T), cEc and tEc, respectively. The UV absorption and circular dichroism spectra of the mixture of rotamers (Fig. 1) clearly reflect the dominant presence of the cEc rotamer. Upon standing in MIP in the dark at 92 K the UV and CD spectra gradually change to eventually take on the appearance of the spectra of the equilibrium mixture of conformers, in which the more stable tEc rotamer predominates. From the rate of change the energy barrier separating the rotamers in the ground state is calculated to be 27 kJ/mol (6.5 kcal/mol). Since this value includes a medium-dependent part imposed by the viscosity of the solvent it represents an upper limit to the intrinsic barrier to twisting.

The NEER principle, of course, is the counterpart of the Curtin-Hammett principle for ground state reactions (7). Its applicability requires a favourable ratio of the rate of photoreaction to that of interconversion of the excited rotamers. Analogous to the Curtin-Hammett principle one may expect the NEER principle to hold if the rate of photoreaction is larger by a factor of 10 or more than the rate of rotameric interconversion. Conversely, non-NEER conditions apply when the rates are in the ratio of 1/10 or smaller. For reactions at room temperature in the first excited singlet state (mean lifetime 10^{-8} s or shorter) rotation barriers of about 7 or 8 kcal/mol (~30 kJ/mol) are sufficient to ensure the applicability of
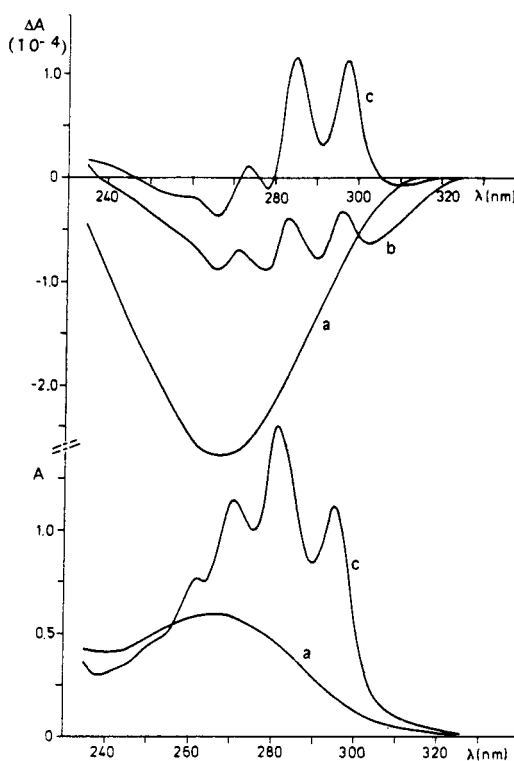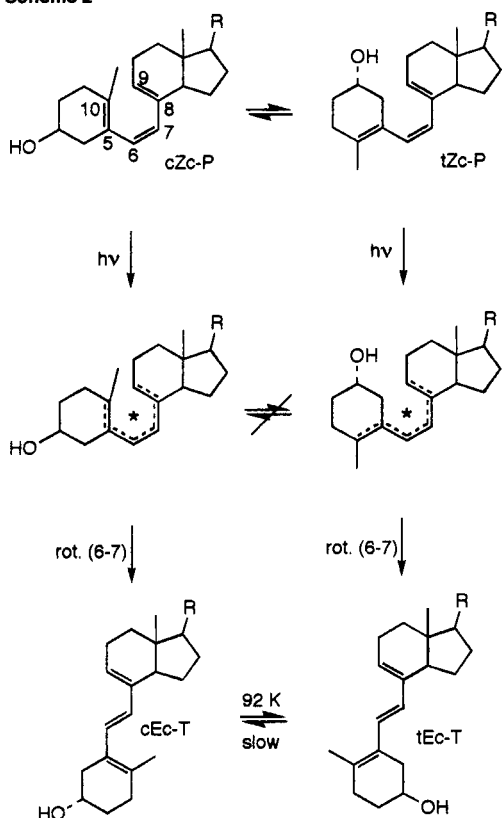
Scheme 2

Fig. 1. UV and CD spectra upon irradiation of P (MIP, 92 K);
a: before irradiation; b: after irradiation for 1 min.;
c: = b after 15 min. in the dark at 92 K.

the NEER principle; clearly barriers in this order of magnitude easily obtain in singlet excited conjugated trienes. On the other hand, breakdown of the NEER conditions will occur when the barrier is ~5 kcal (~20 kJ) or lower.
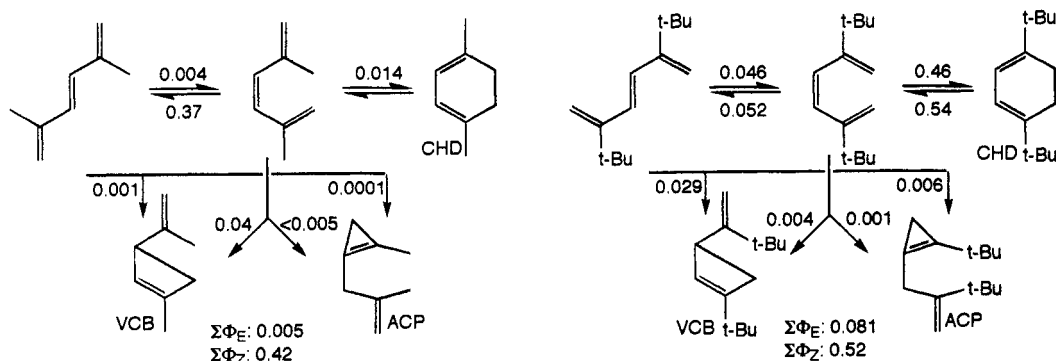
While the NEER principle was originally introduced for the S_1 state of 1,3,5-hexatrienes, later studies involving time-resolved T_1 resonance Raman spectra of the E- and Z-isomers of hexatriene and various methyl substituted derivatives (8) have demonstrated that the NEER principle can be extended to excited triplet states. The lifetimes of the triplet excited species were determined to be in the order of 100 to 200 nanoseconds from which a lower limit of ~9.5 kcal/mol (40 kJ/mol) for the rotational barrier is deduced.

Geometry and photoreactivity

The NEER principle allows us to identify the ground state conformations that are required for production of certain photoproducts, and thus provides a tool for predicting conformationally feasible reactions. However, it cannot predict to what extent a certain conformationally allowed reaction will actually occur. We have studied the photorearrangements of variously substituted alkylhexatrienes assuming that alkyl groups will affect the photochemical behaviour essentially only by conformational changes and not by differences in electronic effects. Representative examples of the effect of the conformation of the trienes in the ground state on the efficiency of their photoreactions are provided by comparison of the quantum yield data of 2,5-dimethyl- and 2,5-di-*t*-butylhexatrienes (Scheme 3) (9). The trienes are presented in their most stable ground state conformation as indicated by UV absorption and NMR measurements (5). E-dimethylhexatriene exists predominantly as the tEt form, while its Z-isomer has been shown to exist as an equilibrium of cZt and cZc rotamers, the former being predominant. The bulky *t*-butyl groups force the E/Z-isomeric di-*tert*-butylhexatrienes to adopt the cEc and cZc form, respectively.

Moreover, whereas tEt-dimethylhexatriene has an essentially planar triene chromophore, steric crowding forces all other forms to deviate considerably from planarity.

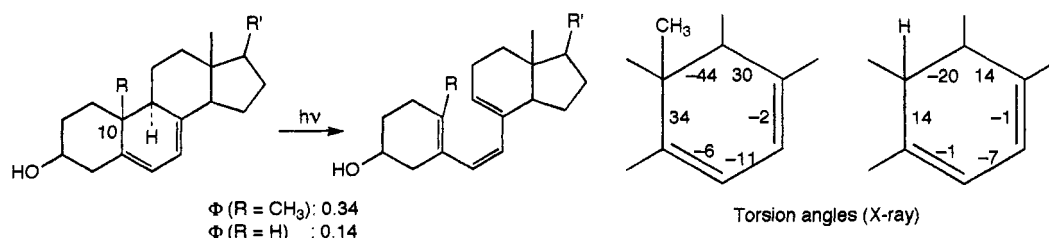**Scheme 3: Quantum yields (254 nm, cyclohexane)**

(Scheme with quantum yields: left system — 0.004 / 0.37, 0.014; 0.001, 0.04, <0.005, 0.0001; VCB, ACP; $\Sigma\Phi_E$: 0.005, $\Sigma\Phi_Z$: 0.42; CHD. Right system (t-Bu substituted) — 0.046 / 0.052, 0.46 / 0.54; 0.029, 0.004, 0.001, 0.006; VCB t-Bu, ACP; $\Sigma\Phi_E$: 0.081, $\Sigma\Phi_Z$: 0.52; CHD t-Bu.)

When comparing the efficiencies of the same reactions in the two systems the dramatic difference between the quantum yields for 4π ring closure of the E-trienes to vinylcyclobutenes (VCB) is readily explained in the context of the NEER principle. One s-*cis* linkage is clearly required for the electrocyclic process. Only small amounts of cisoid rotamers are present in the mixture of conformers of the dimethyl compound, whereas the di-*tert*-butyl derivative exists predominantly in the cEc conformation. Similar considerations apply to the 6π electrocyclization of the Z-trienes to form derivatives of cyclohexadiene (CHD). Interestingly, the efficiency of VCB formation is smaller in Z-di-*t*-butylhexatriene (having two s-*cis* linkages) than in the dimethyl analogue (predominantly cZt). Clearly, the geometry of the cZc structure (probably helical) is eminently suited for fast C–C bond formation between the terminal carbon atoms. with concomitant reduction of the efficiency of other processes.

E/Z-isomerization and allylcyclopropene (ACP) formation are geometrically feasible reactions irrespective of the ground state conformation. As is evident from the data of the E-isomers the ground state conformation nevertheless greatly influences the efficiencies of these reactions. Both reactions are significantly enhanced by the presence of s-*cis* linkages. This phenomenon is far more general (10) than appears from the examples in Scheme 3: For E- as well as for Z-trienes the reactivity increases with an increasing proportion of non-planar cisoid rotamers in the ground state equilibrium. Owing to the *cis*-configuration of the central double bond Z-trienes upon substitution are more readily distorted from planarity than their E-isomers. which explains why in a pair of E/Z-isomers the Z-triene is generally the more reactive one. The increased reactivity of non-planar trienes has tentatively been related (9) to the availability of out-of-plane motions to the non-planar excited state. The steric strain present in the ground state is relieved after excitation by twisting of the weakened central double bond, which in an early state involves nothing more than a hydrogen o.o.p. motion. Deuterium isotope effects on the E/Z-isomerization strongly support this view (11).

However, in spite of its non-planarity the photoreactivity of E-di-*t*-butylhexatriene is still rather low. In view of the absence of fluorescence this implies the existence of (an) efficient non-radiative return process(es) to the ground state, as is the case with the planar parent hydrocarbon. In an effort to help identify the decay channel(s) we have recently synthesized and studied 1,2-divinylcyclopentene (DVCP) (12). In this Z-triene the central double bond is incorporated in a 5-membered ring, thereby obstructing the torsional motion around this bond. Investigation of its behaviour upon irradiation revealed that the 'locked' triene is photostable, even after very long irradiation times. Moreover, DVCP was found to show fluorescence in solution, even at room temperature, the fluorescence quantum yield being 0.01 and the measured fluorescence decay time 8.5 ns. The emitting state is identified as the 2 $^1A_1$ state. This is the first observation of fluorescence of a simple hexatriene in solution.

'Scheme 4: Quantum yields (300 nm, EtOH)

HO

R'

R

10 H

hv

HO

R'

R

Φ (R = CH$_3$): 0.34
Φ (R = H)   : 0.14

CH$_3$

−44 30

34 −2

−6 −11

H

−20 14

14 −1

−1 −7

Torsion angles (X-ray)

In the vitamin D field a striking example of the effect of deviation from planarity is encountered in the efficiency of the ring opening reaction of 5,7-diene steroids (Scheme 4) (13). The presence or absence of the methyl group at C(10) has considerable effect on the puckering of the cyclohexadiene ring, as can be seen from the endocyclic torsion angles determined by X-ray analysis. The more puckered compound is considerably more reactive than the more planar one.

Wavelength effects

Variation of the wavelength of irradiation often has a dramatic effect on the composition of the mixture of primary photoproducts obtained from a particular triene. In fact, the experimental observation of the effect of wavelength has played an important role in proving the validity of the NEER principle, since it excludes the possibility of interconversion of the excited rotamers to an equilibrium composition that resembles the composition of the ground state equilibrium. The occurrence of the wavelength effect is often attributed to selective excitation of ground state rotamers that differ in their electronic absorption spectrum. However, in most cases little is known about the population of rotamers in the conformational equilibrium mixtures of trienes. Moreover, the absorption properties of the individual rotamers are also not known in detail. As a result in most cases it it not possible to prove that ground state conformational control is the exclusive origin of wavelength dependent photochemistry, and additional causes of the wavelength effect have been considered, in particular the involvement of different electronic or vibronic states. For example, in studying the wavelength dependence of the photochemical reactions of previtamin D Dauben and his group (14) have observed a sudden change in the ratio of the quantum yields of ring closure and *cis/trans*-isomerization in the wavelength region from 295 to 305 nm. The authors consider it unlikely that the relative molar absorption coefficients of the cZt and cZc rotamers of previtamin D, thought to be responsible for Z–E isomerization and ring closure, respectively, would change so drastically in so small a wavelength range, and conclude that excited-state effects are involved. In a recent study Dauben and Kohler and their coworkers (15) attribute the wavelength dependent phenomena to the participation of both the 1B and 2A excited states of the triene.

On the other hand, we have been able to show (5b) that the UV absorption spectrum of Z-2,5-dimethylhexatriene can be simulated quite well by 9 : 1 combination of the spectra of Z-2-*t*-butyl- and Z-2,5-di-*t*-butylhexatriene which feature as model compounds for the pure cZt and cZc rotamers, respectively. The relative absorption of these cZt and cZc rotamers turns out to change drastically from about 290 nm upwards; the change in the ratio of absorbances (doubled every 5 nm) is large enough to completely account for the sudden change in the photoreactivity of Z-2,5-dimethylhexatriene around 290 nm. No indication is obtained for an intrinsic excitation energy dependence of the photoreactivity of the individual rotamers. It should be noted that for previtamin D the change in relative absorbance of the rotamers would have to be even more rapid if selective excitation were the only cause of the wavelength effect reported by Dauben.

Solvent and temperature effects

Only few systematic studies on the effect of solvent on the photoreactions of conjugated trienes are known. In general the influence of the solvent seems to be of minor importance unless the triene chromophore is situated close to a polar functional group which by interaction with solvent molecules affects the geometry of the trienic part or the rotameric equilibrium. In addition the polarity or protic character of the solvent may influence the relative energy of excited states of different polarity, or facilitate the formation of polar intermediates, and thereby affect the relative importance of different pathways of relaxation (excited state effects). The latter phenomenon is particularly clear in the formation of alcohol adducts and reduction products when previtamin D is irradiated in alcoholic solvents. The mixture obtained after prolonged irradiation consists for 50% of reaction products with alcohol (1a).

Temperature dependent studies of triene photochemistry are also not numerous. Variation of temperature may influence the composition of the photoproduct mixture through its effect on the position of the ground-state rotameric equilibrium, but also by changing the rate by which the excited species can overcome thermal barriers on the pathways to products. We have recently carried out a study of solvent, temperature and wavelength dependence on vitamin D photochemistry (16). As a prerequisite the quantitative assessment of various conformational and photochemical details of vitamin D was necessary.

From X-ray measurements it is known that in the crystalline state vitamin D (D) consists of two cZt conformers which not only differ in the orientation of the 3β-hydroxyl group (axial *vs.* equatorial) but also in the sign of twist of the cisoid diene moiety of the triene chromophore: c(+)Zt *vs.* c(-)Zt (Scheme 5). Using NMR we have shown that in solution within experimental limits no cZc or tZt conformer is present. The composition of the equilibrium between the two cZt conformers was determined as a function of solvent and temperature (Table 1). The c(-)Zt conformer is the lowest in energy. The energy difference increases with the polarity of the solvent and ranges from 0.3 to 4.8 kJ/mol. The UV absorption spectrum showed only very minor differences in different solvents, indicating that the conformers have essentially the same absorption characteristics.
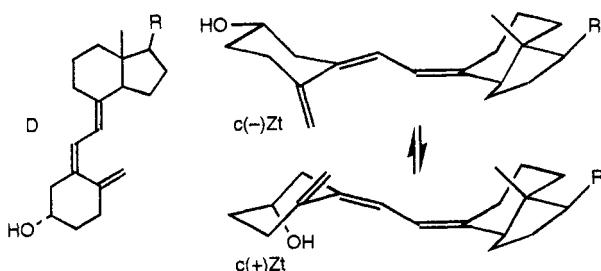
Scheme 5

TABLE 1. Ratio of the vitamin D conformers c(+)Zt / c(−)Zt in various solvents.

T (°K)	C_6D_{12}	THF-d_8	C_2D_5OD
298	47 : 53	28 : 72	13 : 87
273	47 : 53	26 : 74	11 : 89
243	46 : 54	23 : 77	9 : 91
213	46 : 54	20 : 80	6 : 94

The photoproduct formation from vitamin D and its *trans*-isomer is shown in Scheme 6 together with the quantum yields determined at 313 nm in diethyl ether. In accordance with the NEER principle the bicyclohexene and allene derivatives, the so-called suprasterols I and II, and III and IV, respectively, are formed from vitamin D only. The vinylcyclobutene compounds, suprasterols V and VI, arise exclusively from *trans*-vitamin D, although formation from the *cis*-isomer would be equally feasible. Probably, analogous to the case of the 5,7-diene steroids mentioned above, the cisoid diene moiety in *trans*-vitamin D, although far from planar, is less twisted than that in *cis*-vitamin D.

As is evident from the quantum yields, bicyclohexene formation, although not an efficient reaction, is by far the preferred photoreaction of vitamin D. In fact, after complete conversion of vitamin D and *trans*-vitamin D, the photoproduct mixture invariably contains more than 80%, and often more than 90%, of the two bicyclohexenes. It implies that vitamin D is an attractive model compound for studying the mechanism of formation of bicyclohexene and its dependence on the conditions of irradiation, such as

Scheme 6: Quantum yields (313 nm, diethyl ether)
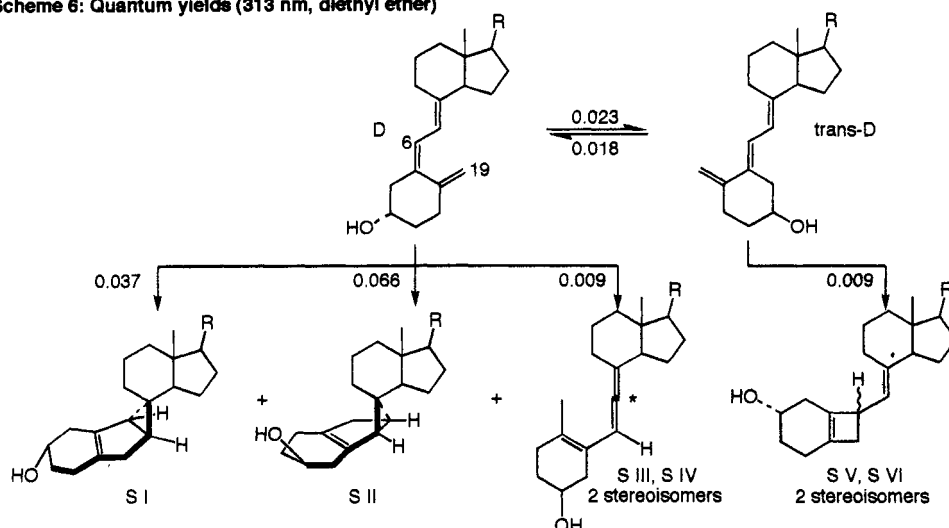
wavelength, solvent and temperature. From the stereostructures of the bicyclohexenes resulting from several suitably substituted hexatrienes Dauben and Kellogg concluded (17) that the intramolecular $[_\pi 4 + _\pi 2]$ cycloaddition leading to bicylohexene is not a concerted reaction, but proceeds in two steps, starting with conrotatory cyclopropane ring closure, and completed by non-stereospecific closure of the 5-membered ring. We have investigated this aspect by determination of the quantum yield of formation of SII from the labeled compounds vitamin D-6-d and vitamin D-19,19-d_2. C(6) is involved in the cyclopropane ring closure, C(19) in de cyclopentene closure. From these data a kinetic isotope effect of 1.19 is observed for the 6-D compound, while no effect is found in the case of substitution at C(19). This result implies that the 3- and 5-membered ring closures occur in separate steps. The kinetic data thus provide a direct proof for the non-concerted course of the cycloaddition and fully confirm the correctness of Dauben's earlier conclusions based on product analysis.

TABLE 2. Ratio of the suprasterols SI / SII upon complete conversion of vitamin D.

T (°K)	isooctane		diethyl ether		ethanol	
λ	313 nm	253 nm	313 nm	253 nm	313 nm	253 nm
298	47 : 53	51 : 49	36 : 64	24 : 76	30 : 70	22 : 78
273	46 : 54	52 : 48	33 : 67	23 : 77	28 : 72	20 : 80
243	41 : 59	53 : 47	29 : 71	19 : 81	24 : 76	17 : 83
213	30 : 70	54 : 46	25 : 75	17 : 83	20 : 80	16 : 84

In Table 2 some results of the irradiation experiments at various temperatures and wavelengths in solvents of different polarity are collected. The data reveal a complicated interplay of the effects of these factors. It is attractive to suppose that each of the two conformers of vitamin D gives rise to one of the bicyclohexenes, SI and SII. Substantiation of this idea would imply that the accordancy principle (18), formulated for cyclic dienes, is also applicable to open-chain compounds. Inspection of the data shows that the ratio of the suprasterols roughly reflects the shift in the equilibrium of c(+)Zt and c(-)Zt imposed by the changes in solvent polarity and temperature. However, there is obviously no linear relation between the ratios SI/SII and c(+)Zt/c(-)Zt, as a result of additional important effects of thermal activation and excess excitation energy. The former effect indicates that in the pathways of formation of SI and SII thermal barriers of different height are present. Bearing in mind that the UV absorption of the two conformers is essentially identical the clear effect of the wavelength of irradiation is taken to mean that the excess excitation energy enables the excited species to enter decay channels that are not or less easily accessible.

upon excitation to the lowest vibrational level of the excited state. As in the case of previtamin D the participation of both the 1B and the 2A excited state may be implicated.

Conclusions

The above survey shows that in the photochemical behaviour of conjugated trienes the impact of ground-state conformational and geometrical properties usually is more important than excited-state effects. By changes in substitution or variation of solvent or temperature the ground-state properties can be modulated. The choice of the irradiation wavelength offers an additional possibility to selectively populate the excited state. Further experimental and theoretical studies are needed to assess the role of intrinsic excited-state effects.

References

1. Reviews: a. H.J.C. Jacobs and E. Havinga, *Advances in Photochemistry* **11**, 305 (1979); b. W.G. Dauben, E.L. McInnes and D.M. Michno, in *Rearrangements in Ground and Excited States* (P. de Mayo, Ed.), Vol **3**, p. 91, Academic Press, New York (1980); c. W.H. Laarhoven, in *Organic Photochemistry* (A. Padwa, Ed.), Vol. **9**, p. 129, Marcel Dekker, New York (1987).
2. F. Bernardi, M. Olivucci and M. Robb, *Isr. J. Chem.* **33**, 265 (1993) and references cited therein.
3. E. Havinga and J.L.M.A. Schlatmann, *Tetrahedron* **16**, 146 (1961).
4. P.J. Vroegop, J. Lugtenburg and E. Havinga, *Tetrahedron* **29**, 1393 (1973).
5. a. A.M. Brouwer, *Ph.D. Thesis*, Leiden 1987; b. A.M. Brouwer, J. Cornelisse and H.J.C. Jacobs, *Tetrahedron* **43**, 435 (1987).
6. P.A. Maessen, H.J.C. Jacobs, J. Cornelisse and E. Havinga, *Angew. Chem.* **95**, 752 (1983); *Angew. Chem. Int. Ed. Engl.* **22**, 718 (1983); *Angew. Chem. Suppl.* 994 (1983).
7. J.I. Seeman, *Chem. Rev.* **83**, 83 (1983).
8. a. F.W. Langkilde, N.-H. Jensen, R. Wilbrandt, A.M. Brouwer and H.J.C. Jacobs, *J. Phys. Chem.* **91**, 1029 (1987); b. F.W. Langkilde, R. Wilbrandt, A.M. Brouwer, H.J.C. Jacobs, F. Negri and G. Orlandi, *J. Phys. Chem.* **96**, 64 (1992).
9. A.M. Brouwer, J. Cornelisse and H.J.C. Jacobs, *J. Photochem. Photobiol., A: Chem.* **42**, 117 (1988).
10. A.M. Brouwer, L. Bezemer, J. Cornelisse and H.J.C. Jacobs, *Recl. Trav. Chim. Pays-Bas* **106**, 613 (1987).
11. A.M. Brouwer, J. Cornelisse and H.J.C. Jacobs, *J. Photochem. Photobiol., A: Chem.* **42**, 313 (1988).
12. a. A. ten Wolde, H.P.J.M. Dekkers and H.J.C. Jacobs, *Tetrahedron* **49**, 6045 (1993); A. ten Wolde, *Ph.D. Thesis*, Leiden 1994.
13. R.B. Koolstra, J. Cornelisse and H.J.C. Jacobs, *Recl. Trav. Chim. Pays-Bas* **106**, 526 (1987).
14. W.G. Dauben and R.B. Phillips, *J. Am. Chem. Soc.* **104**, 5780 (1982).
15. W.G. Dauben, B. Disanayaka, D.J.H. Funhoff, B.E. Kohler, D.E. Schilke and B. Zhou, *J. Am. Chem. Soc.* **113**, 8367 (1991).
16. a. E.M. Vroom, *Ph.D. Thesis*, Leiden 1993; b. E.M. Vroom and H.J.C. Jacobs, in *Vitamin D: Gene regulation, structure-function analysis and clinical application* (A.W. Norman et al., Eds.), p. 196, W. de Gruyter, Berlin (1991).
17. W.G. Dauben and M.S. Kellogg, *J. Am. Chem. Soc.* **94**, 8951 (1972).
18. J.E. Baldwin and S.M. Krueger, *J. Am. Chem. Soc.* **91**, 6444 (1969).