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Photochemistry of Structural Analogues of Previtamin D_3: Generality of the Wavelength-Dependent Triene Photocyclization

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Two structural previtamin D_3 analogues ($R = H, CH_3$) cyclized photochemically with a 1.4−1.8-fold increase in quantum yields over a 3-nm change in excitation wavelength. The sudden increase in quantum yields is due to the participation and mixing of both 2A and 1B excited states. At $\lambda \leq$ 306 nm, the 1B state is initially excited and then (a) partitions between isomerization to the corresponding trans triene isomers, (b) decays to the 2A state to give the corresponding cyclohexadienes, and (c) decays to the ground state. At $\lambda \geq$ 309 nm, the 2A state is directly excited to give the corresponding cyclohexadienes and the relaxation path from 1B state to the ground state or isomerization in the 1B state is diminished.

Introduction

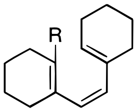
The photochemistry of previtamin D_3 (pre D_3) has been intensively studied (Scheme 1).[1] The quantum yields of the photoproducts from previtamin D_3 (pre D_3) have been measured at different wavelengths with monochromatic light between 285 and 325 nm.[2] While the quantum yields for the cis−trans isomerization decrease with increasing wavelength in the 285−325 nm range, the quantum yields for formation of ring-closed products increase, dramatically, in the same wavelength range.[3a] This increasing photocyclization yield with decreasing photoenergy has been attributed to the involvement of both the 1B and 2A excited states of pre D_3. This hypothesis is supported by measurements of the pre D_3 fluorescence specturm, fluorescence lifetime, wavelength dependence of the fluorescence quantum yield, and temperature dependence of fluorescence intensity. All these data have been integrated into a potential energy surface diagram that is consistent with both the photochemical and spectroscopic behavior.[3]

Since the postulation of the above-mentioned potential energy surface diagram, much effort has been directed toward obtaining detailed knowledge, by calculation, of the potential energy surfaces of both excited- and ground-state surfaces of pre D_3 models.[4] However, few chemical experimental studies have been performed to test the utility of the calculated surfaces and their interactions.

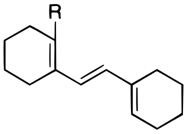
With the foregoing information at hand, it is of interest to search for wavelength effects in other conjugated triene systems. We report in this manuscript a photochemical study of simple conjugated triene systems mimicking the pre D_3 system.

Results and Discussion

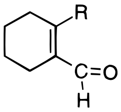
Synthesis of Pre D_3 Structural Analogues 1 and 2. Trienes **1** and **2** were obtained by convergent synthesis. A mixture of *cis*- and *trans*-1,2-di(1-cyclohexenyl)ethene were obtained in the reaction of 1-cyclohexenylcarbox-aldehyde[5a] (**3a**) with triphenyl(1-cyclohexenylmethyl)phosphonium bromide[6] in the presence of ^nBuLi. The pure cis isomer **1a** was obtained either by column chromatography of the mixture of cis and trans isomers or by photochemical sensitization[7] of trans isomer **1b** with 9-fluorenone. Similarly, **2a** was also obtained from the reaction of 2-methyl-1-cyclohexenecarboxaldehyde[5,6] (**3b**) with **4**.



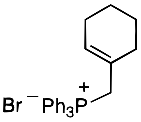
1a) R = H
2a) R = CH_3



1b) R = H
2b) R = CH_3



3 **a**) R = H
b) R = CH_3



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Photochemical Reactions of Conjugated Triene Chromphore. The cis triene at a concentration of 5×10^{-3} to 1×10^{-2} M in THF was purged with nitrogen in a quartz tube sealed with a septum and irradiated with a Rayonet apparatus at 300 nm. The same photochemical reactions as those found for pro D_3 have been observed with model trienes **1a** and **2a** upon irradiation, cis−trans isomerization around the central double bond, and the

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[†] Dedicated with love and appreciation to Professor William G. Dauben, deceased.

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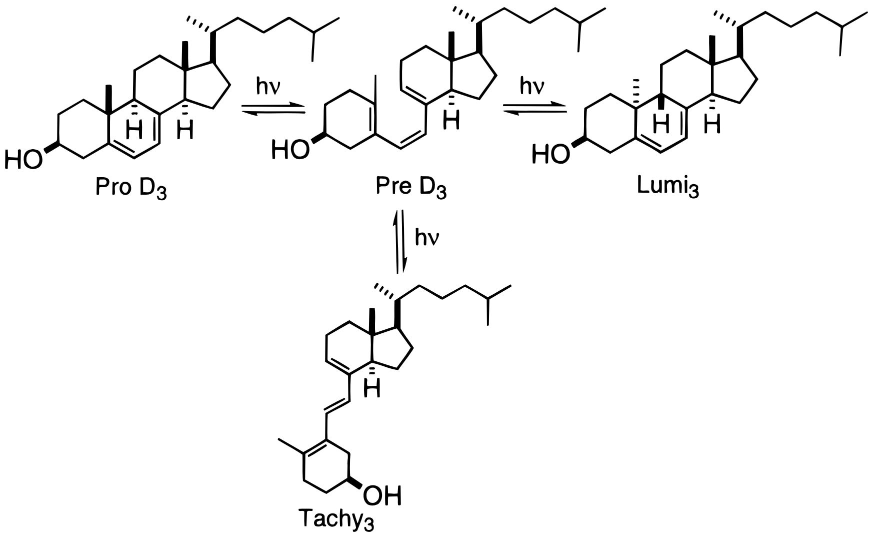
Scheme 1



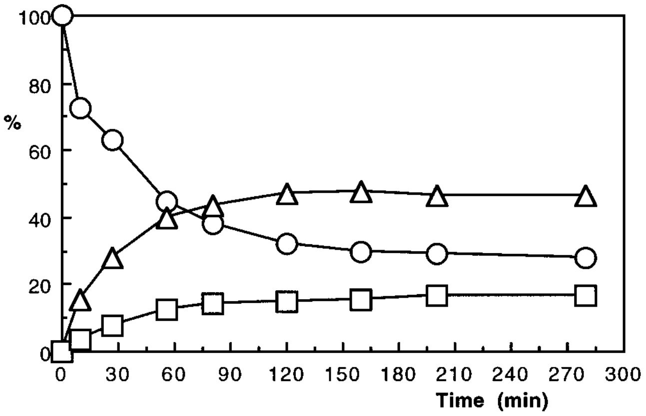
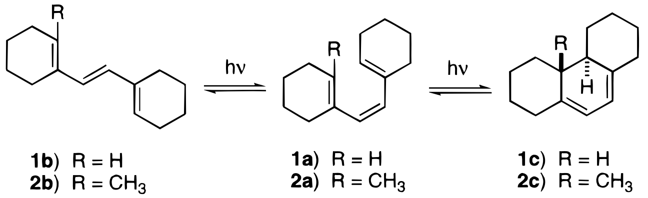


Figure 1. Plot of relative percent composition of *cis*-triene **1a** (circles), *trans*-triene **1b** (triangles), and the diene **1c** (squares) versus time upon irradiation of **1a** at 300 nm in THF.

Scheme 2



photocyclization via Woodward–Hoffmann rules (Scheme 2).[8] During the irradiation, the photoproducts experience a buildup up period and then reach a quasiphotostationary state with the reactants, which is characteristic and indicative of reversible photochemical processes.[1d,9] At the quasiphotostationary state, the ratio of **1b**:**1a**:**1c** is 3:2:1 and the ratio of **2b**:**2a**:**2c** is 2:5:1. The progress of the reaction is illustrated in Figure 1 for compound **1a** with the relative percent composition of **1a**, **1b**, and **1c** versus time upon irradiation. It is interesting to note that the reversible photochemical transformations of these simple structural analogues very closely resemble the reversible photochemical interconversions of pre D_3 series.

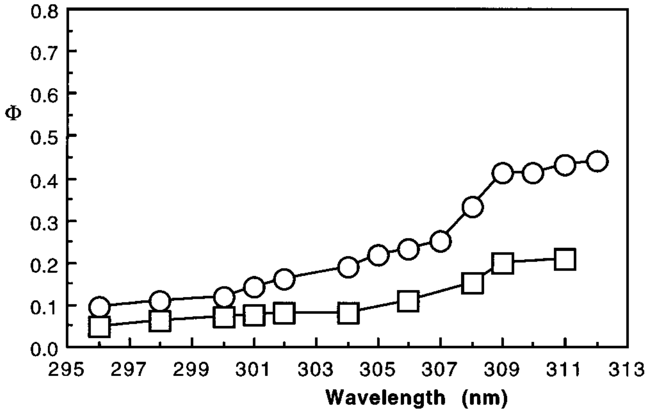


Figure 2. Wavelength–Φ profiles for the formation of **1c** from **1a** (squares) and **2c** from **2a** (circles) in ether.

Wavelength Dependence of Photochemical Quantum Yields. The quantum yields were measured by an electronic quantacount apparatus and a pulsed UV dye laser, which provide a narrow-band tunable excitation source with reasonable intensity.[3] The quantum yields of ring closure (**1a** → **b1c** and **2a** → **2c**) and cis–trans isomerization (**1a** → **1b** and **2a** → **2b**) were measured in both diethyl ether and hexane. The numerical results of Φ(**1a** → **1c**), Φ(**2a** → **2c**),Φ(**1a** → **1b**) and Φ(**2a** → **2b**) are reported in the Supporting Information, and a typical plot of quantum yield versus wavelength of **1a** and **2a** in diethyl ether is shown in Figure 2.

The quantum yields over a wavelength of 296–312 nm for the cis–trans isomerization, i.e., **1a** → **1b** and **2a** → **2b**, are more efficient than the ring closure reaction, i.e., **1a** → **1c** and **2a** → **2c**. The quantum yield ranges from Φ 0.42 to 0.51 for **1a** and Φ 0.35 to 0.46 for **2a** in cis–trans isomerization about the central double bond, and the quantum yield for ring-closure ranges from Φ 0.05 to 0.2 for **1a** and Φ 0.10 to 0.44 for **2a** in ether as the solvent. The data show that, within experimental error (±10%), the quantum yields for cis–trans isomerization about the central double bond is independent of wavelengths (296–312 nm). The ring-closure quantum yields for **1a** and **2a** increase slowly from 296 to 306 nm and then jump sharply from 306 to 309 nm with a 1.4-fold to1.8-fold increase.

Mechanism of Ring Closure. The quantum yields for ring closure from pre D_3 to pro D_3 increase slowly from

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285 to 325 nm (Φ 0.01 to 0.08) with a sudden 2-fold increase (Φ 0.02 to 0.04) from 302 to 306 nm. With evidence from the previtamin D_3 fluorescence spectrum, fluorescence lifetime, wavelength dependence of the fluorescence quantum yield, and temperature dependence of fluorescence intensity studies, the 2-fold increase in quantum yields from pre D_3 to pro D_3 has been interpreted as the participation of both 2A (S_1) and 1B (S_2) excited states in the phototransformation.[3,10] The two structural analogues **1a** and **2a** bearing the same triene chromophore display a similar wavelength−quantum yield profile for the photochemical ring closure (see Figure 2) as the pre D_3 to pro D_3, including a 1.4−1.8-fold increase in the quantum yields for the conversion of **1a** → **1c** and **2a** → **2c** between the excitation wavelengths of 306 and 309 nm. This finding points to the fact that in the ring-closure process **1a** and **2a** also react photochemically by the participation of both the low-lying 2A (S_1) and 1B (S_2) excited states. Schematically, the potential surfaces of 2A and 1B states along the conrotatory coordinate of compounds **1a** and **2a** are similar to that of the pre D_3 potential surface model.[3] With the wavelength shorter than 306 nm, excitation occurs at the higher energy 1B (S_2) allowed state[11e] and eventually partitions between (a) cis−trans isomerization such as (**1a** → **1b**) or (**2a** → **2b**), (b) decay to the 2A surface giving ring-closure products, or (c) decay to the starting ground state. Above 306 nm, the mixing[3,11] of 2A and 1B states intensifies the extinction coefficient for absorption to the 2A state and allows the molecules, preferentially, to be excited to the 2A surface at the red edge of the absorption band and so the quantum yield for ring-closure slowly increases from 296 to 306 nm. At wavelengths longer than 309 nm, the 2A state is directly exicited to give ring closure product **1c** and **2c** in high yield, and the relaxation path from the 1B (S_2) state to the ground state or isomerization to **1b** or **2b** in the 1B (S_2) state is diminished.

When **1b** and **2b** were irradiated in the presence of 9-fluorenone as a triplet sensitizer, a mixture of cis and trans isomers was obtained and there was no sign of any ring-closure product being observed. This points to the fact that the triplet state is only limited to cis/trans isomerization and the photochemical ring closure reaction for **1a** → **1c** and **2a** → **2c** occurs in the singlet excited state.[1b,c] The sudden increase in quantum yields in the ring-closure closure reaction within 306−309 nm could not be due to the ground-state conformational effect because the molar extinction coefficient of **1a** and **2a** decreased by 36% for **1a** and by 29% for **2a** within that narrow range.[3a]

Conclusions

The 1.4−1.8-fold increase in quantum yields of photochemical cyclization of two structural pre D_3 analogues, **1a** and **2a**, over a 3-nm change in excitation wavelength is due to the participation and mixing of both 2A and 1B excited states. At $\lambda \leq 306$ nm, the 1B state is initially excited and then (a) partitions between isomerization to **1b** and **2b**, (b) decays to the 2A state to give **1c** and *2c*, and (c) decays to the ground state. At $\lambda \geq 309$ nm, the 2A state is directly excited to give **1c** and **2c**, and the relaxation path from 1B state to the ground state or isomerization in the 1B state is diminished.

Experimental Section

General Methods. ^1H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were measured in $CDCl_3$ solutions calibrated with $MeSi_4$. Et_2O and THF were distilled from sodium and benzophenone. UV spectra were run in hexane unless otherwise stated. Solvents used in irradiation were spectroscopic grade. Unless otherwise stated, other solvents and reagents were reagent-grade commercial materials used as supplied. Flash chromatography was done on 230−400 mesh silica gel. Irradiation mixtures were separated by using preparative TLC silica plates (20 × 20, 1000 microns). Analytical GLC was performed on a carbowax capillary column (30 m × 0.25 mm). Solvent evaporation after extraction was carried out under reduced pressure using a Rotovap apparatus.

***trans*-1,2-Di(1-cyclohexenyl)ethene (1b).** 1-Cyclohexenylcarboxaldehyde[5a] (**3a**) (3.0 g, 27 mmol) was added to a solution of triphenyl(1-cyclohexenylmethyl)phosphonium bromide[6] (**4**) (9.0 g, 21 mmol), *n*-butyllithium (11 mL, 2.3 M in hexane, 25 mmol), and THF (40 mL) with stirring at 0 °C. The reaction mixture was refluxed for 3 h, and then water was added. The reaction mixture was extracted with petroleum ether. The organic portion was separated and dried ($MgSO_4$). The solvent was evaporated, and the crude residue was then chromatographed with petroleum ether to give a pale yellow oil consisting of *trans*-1,2-di(1-cyclohexenyl)ethene (2.0 g, 52%) and *cis*-1,2-di(1-cyclohexenyl)ethene (0.2 g, 5%). Trans isomer: IR ν_{max} 2950, 1644, 1459, 1448, 1141, 962 cm^{-1}; ^1H NMR δ 1.62 (m, 8H), 2.14 (m, 8H), 5.73 (m, 2H), 6.13 (s, 2H); ^{13}C NMR δ 22.6, 22.7, 24.6, 26.0, 128.6, 128.8, 136.0, MS *m/z* 188, 145 (base), 117,105, 91, 77; UV λ_{max} (ϵ) 259 (20 570), 268 (24 900), 280 (20 000).

***cis*-1,2-Di(1-cyclohexenyl)ethene (1a).** A solution of *trans*-1,2-di(1-cyclohexenyl)ethene (0.2 g, 1.1 mmol), 9-fluorenone (0.58 g, 3.2 mmol), hexane (150 mL), and benzene (25 mL) contained in a Pyrex tube was sealed with a rubber septum at 0 °C and purged with N_2. The solution was irradiated in a Rayonet apparatus equipped with 350 nm lamps through a Uranium glass filter for 3 h (N_2 purging). The solvent was evaporated, and the crude residue was chromatographed with petroleum ether to give a pale yellow oil of *cis*-1,2-di(1-cyclohexenyl)ethene (0.08 g, 40%) and *trans*-1,2-di(1-cyclohexenyl)ethene (0.07 g, 35%). The spectral data for **1b** were same as above. Cis isomer (**1a**): IR ν_{max} 2952, 1643, 1459, 1447, 1138, 922 cm^{-1}; ^1H NMR δ 1.57, (m, 8H), 2.09 (m, 8H), 5.60 (m, 2H), 5.70 (s, 2H); ^{13}C NMR δ 22.2, 22.9, 25.6, 28.4, 127.6, 130.7, 136.4; MS *m/z* 188, 145 (base), 131, 117, 105, 91, 77; UV λ_{max} (ϵ) 246 (12 840).

***trans*-2-(1-Cyclohexenyl)-1-(2-methyl-1-cyclohexenyl)ethene (2b).[6]** The reaction procedure was as described above. 2-Methyl-1-cyclohexene carboxaldehyde[5b] (**3b**) (0.9 g, 7.3 mmol) was allowed to react with (1-cyclohexenylmethylidene)triphenylphosphorane to give *trans*-2-(1-cyclohexenyl)-1-(2-methyl-1-cyclohexenyl)ethene (0.8 g, 55%): IR ν_{max} 2950, 1643, 1468, 1459, 1144, 961 cm^{-1}; ^1H NMR δ 1.63 (m, 8H), 1.77 (s, 3H), 2.14 (m, 8H), 5.76 (m, 1H), 6.19, 6.61 (AB quartet, 2H, $J = 16$ Hz); ^{13}C NMR δ 19.4, 22.6, 22.7, 22.9, 23.0, 24.6, 25.5, 26.1, 33.1, 123.6, 127.9, 128.6, 129.0, 132.7, 136.4; MS *m/z* 202, 187, 159, 145 (base), 131, 117, 91, 77; UV λ_{max} (ϵ) 268 (34 310), 278 (42 100), 289 (31 750).

***cis*-2-(1-Cyclohexenyl)-1-(2-methyl-1-cyclohexenyl)ethene (2a).** The sensitized photochemical isomerization procedure was as described above. *trans*-2-(1-cyclohexenyl)-1-(2-methyl-1-cyclohexenyl)ethene (**2b**) (0.25 g, 1.2 mmol) was

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(10) Alternatively, Fuss, Olivucci, and Robb (Fuss, W.; Lochbrunner, S. *J. Photochem*., submitted) have studied the reaction route that occurs once the excited reactant is on the lower lying excited state (2A, S_1 state) and have suggested the conical intersection mechanism to explain the wavelength dependence of the quantum yields of pre D_3. The excited pre D_3 enters two different conical intersection points where ring closure to pro D_3 competed with the double bond isomerization to $Tachy_3$ that are of different barriers (Bernardi, F.; Olivucci, M.; Robb, M. *Isr. J. Chem*. **1993**, *33*, 265).

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irradiated in a solution of 9-fluorenone (0.6 g, 3.3 mmol), hexane (150 mL), and benzene (25 mL) to give *cis*-2-(1-cyclohexenyl)-1-(2-methyl-1-cyclohexenyl)ethene (0.15 g, 55%): IR ν_{max} 2950, 1642, 1457, 1445, 1143, 855 cm^{-1}; ^{1}H NMR δ 1.55 (m, 11H), 2.02 (m, 8H), 5.68 (m, 2H), 5.80 (AB quartet, 1H, J = 12 Hz); ^{13}C NMR δ 20.6, 22.3, 23.0, 23.11, 23.13, 25.9, 26.8, 29.8, 31.3, 128.47, 128.52, 128.7, 129.6, 132.1, 136.8; MS m/z 202, 187, 159, 145 (base), 131, 117, 91, 77; UV λ_{max} (ϵ) 238 (14 980).

Photochemical Reaction of *cis*-1,2-Di(1-cyclohexenyl)ethene (1a). A solution of **1a** (0.2 g, 1.1 mmol) and hexane (120 mL) in a Pyrex tube purged with nitrogen was irradiated at 0 °C in a Rayonet apparatus with 300 nm lamps. The solvent was evaporated, and the crude residue was purified by using preparative TLC with petroleum ether to give an oil (0.12 g, 60%). The ^{1}H NMR spectrum showed a mixture of **1a**, **1b**, and **1c** in a ratio of 28:10:15. The spectral data of **1a** and **1b** were the same as above. 1,2,3,4,4a,4b,5,6,7,8-Decahydrophenanthrene (**1c**): ^{1}H NMR δ 1.33−2.18 (m, 18H), 5.38 (s, 2H); ^{13}C NMR δ 22.6, 28.7, 34.8, 37.2, 44.1, 115.2, 139.2; GC−MS m/z 188, 145 (base), 131, 117, 105, 91, 77 (^{1}H NMR and ^{13}C NMR corrected for the presence the triene).

Photochemical Reaction of *cis*-2-(1-Cyclohexenyl)-1-(2-methyl-1-cyclohexenyl)ethene (2a). A solution of **2a** (0.2 g, 1.0 mmol) and hexane (120 mL) was irradiated at 300 nm in a Rayonet apparatus as was described above to give an oil (0.13 g, 65%). The ^{1}H NMR spectrum showed a mixture of **2a** and **2c** in a ratio of 1:1. The spectral data of **2a** were the same as above. 1,2,3,4,4b,5,6,7,8-Nonahydro-4a-methylphenanthrene (**2c**): ^{1}H NMR δ 0.86 (s, 3H), 1.24−2.35 (m, 17H), 5.46 (m, 2H); ^{13}C NMR δ 16.1, 22.6, 22.7, 23.9, 25.0, 25.4, 26.7, 32.7, 37.6, 40.5, 48.0, 117.4, 117.5, 128.4, 139.2; GC−MS m/z 202, 187, 159, 145 (base), 131, 117, 91, 77 (^{1}H NMR and ^{13}C NMR corrected for the presence the triene).

Kinetic Irradiation. The relative concentration vs time plot was obtained by irradiating a solution of the corresponding trienes (5×10^{-3}−1×10^{-2} M), hexadecane (internal standard; 1×10^{-3} M), and THF in a Rayonet at 300 nm in a quartz tube sealed with septum. Aliquots of the samples were taken out with syringes and analyzed by GC, and the relative percentages of cis and trans triene and cyclohexadiene were ploted vs time. The quantum yields were measured by an electronic quantacount apparatus equipped with either a 1000 W HP lamp or a pulsed UV dye laser and were calibrated by potassium ferrioxalate actinometry.[3]

Acknowledgment. This research was supported by National institute of Diabetes and Digestive and Kidney Disease, PHS Grant 00709.

Supporting Information Available: UV spectra of compounds **1a** and **2a** and a table of quantum yields (Φ) of **1b** and **1c** from **1a** and **2b** and **2c** from **2a** in hexane and ether are available (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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