Circular Dichroism of Isomeric 10,19-Dihydrovitamin D[1]

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Abstract: Circular dichroism (CD) spectra of all the (*E*)- and (*Z*)-10,19-dihydrovitamin D isomers were obtained. The long wavelength $\pi-\pi^*$ Cotton effects were interpreted with the aid of the "planar diene rule" for acyclic planar 1,3-dienes. The contributions made to the Cotton effect by the C and D rings were evaluated separately and then used, additively, to evaluate the contributions for the total system, the A ring plus the C,D ring.

Vitamin D, the regulator of calcium metabolism, has been the subject of active investigation.[2] However, in the past, the chromophores in these molecules have not been recognized as being chiral, and consequently chiroptical methods have not been used to elucidate any of the stereochemical problems associated with vitamin D. Only recently have Moriarty and Paaren[3] applied the homoannular cisoid "diene quadrant rule"[4] to vitamin D.

Vitamin D possesses a conjugated triene moiety, in which the central C_5–C_6 double bond is at the same time cisoidal to the C_{10}–C_{19} double bond (a homoannular system) and transoidal coplanar[5] to the C_7–C_8 double bond. Recently, four of the isomers that result from the reduction of the 10,19 double bond in (*E*)- and (*Z*)-vitamin D_2 have been fully characterized[6] (Scheme I). The reduction removes the homoannular diene system but retains the transoidal planar C_5–C_8 1,3-diene structure.[7] Our interest in understanding the chiroptical properties of acyclic transoidal 1,3-dienes led us to investigate the long wavelength $\pi-\pi^*$ Cotton effects in the CD spectra of the 10,19-dihydrovitamin D_2 derivatives.

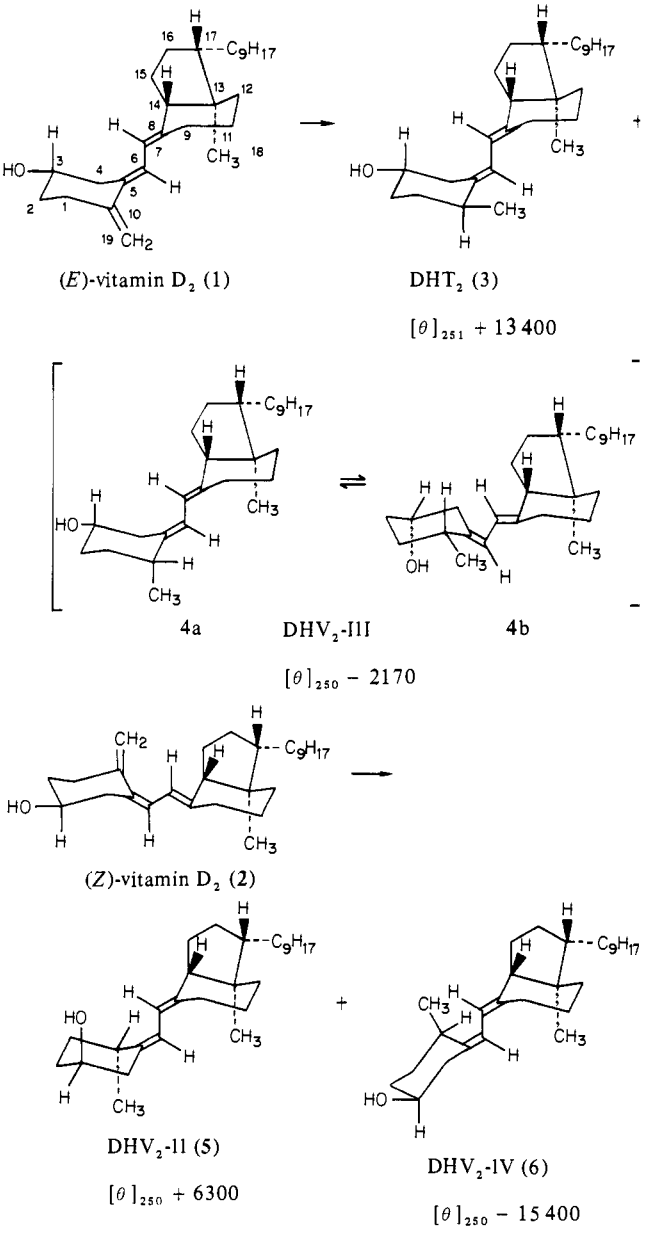
Results and Discussion

The four isomers studied, DHT_2, DHV_2-II, DHV_2-III, and DHV_2-IV (Scheme I)[10], all have a transoid 1,3-diene chromophore that is coplanar as indicated by their intense UV spectra. The C and D rings are conformationally rigid whereas the A ring is in a dynamic equilibrium between two chair conformations.[6-8] The Cotton effect would therefore be expected to reflect the conformational changes of the A ring.[9] The contribution to the Cotton effect from the C and D rings would be constant for all the isomers and is predicted to be negative by the "planar diene rule" since C_{13} and its substituents fall into the negative sector.

In order to experimentally determine the contribution from the C and D rings we desired either an achiral A ring attached to the 1,3-diene structure, which contains the C and D rings or no A ring at all. For this purpose we synthesized compounds **9**, **13**, and **14** (Scheme II).

Vitamin D_3 was ozonized to obtain ketone **8**.[12] Following the procedure of Lythgoe,[13] **8** was condensed with (cyclo-

Scheme I. Hydrogenation Products of (*E*) and (*Z*)-Vitamin D_2



(1) We gratefully acknowledge the support of this work by a grant from the National Science Foundation.

(2) A. W. Norman, "The Calcium Homeostatic Steroid Hormone", Academic Press, New York, 1979; N. F. DeLuca, "Vitamin-D: Metabolism and Function", Springer-Verlag, Berlin, 1979.

(3) R. M. Moriarty and H. E. Paaren, *J. Org. Chem.*, **46**, 970 (1981).

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(5) D. Crowfoot and J. D. Dunitz, *Nature (London)*, **162**, 608 (1948).

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(8) (a) M. Sheves, E. Berman, D. Freeman, and Y. Mazur, *J. Chem. Soc., Chem. Commun.*, 643 (1975); (b) M. Sheves and Y. Mazur, *ibid.*, 21 (1977); (c) E. Berman, Z. Luz, Y. Mazur, and M. Sheves, *J. Org. Chem.*, **42**, 3325 (1977).

(9) Okamura and Norman[7a] have proposed that vitamin D metabolites having their 1α-OH relatively more equatorial than axial should be more biologically active. The geometry about the 5,6 double bond and the conformation of the A ring are threfore important factors in understanding structure function relationships.

(10) These are the acronym designations used by Okamura.[6]

(11) See preceding paper.

(12) S. Schutz, D. Kampe, and G.F. Domagk, *Chem. Ber.*, **90**, 664 (1957).

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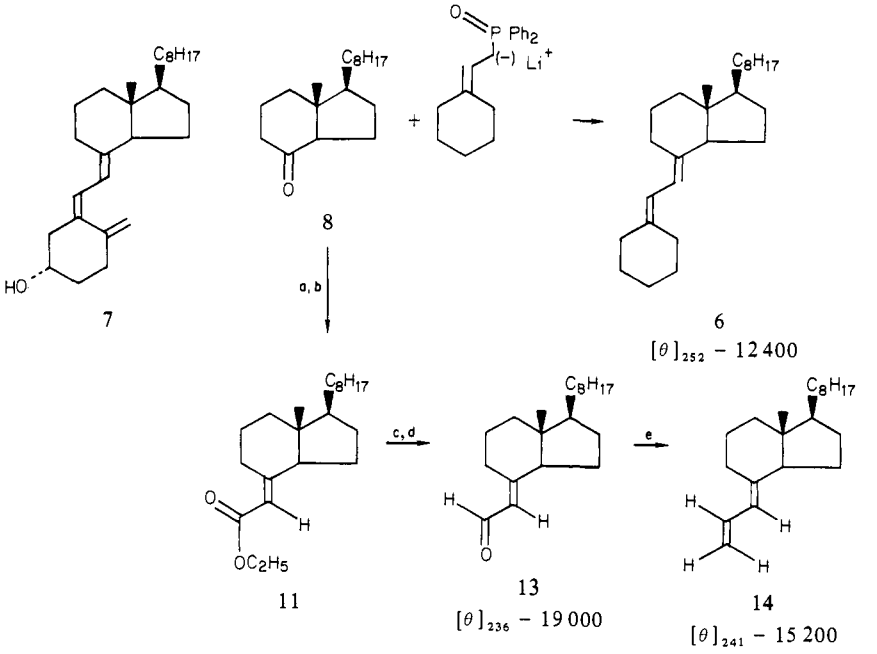
Scheme II. Syntheses of Vitamin D Analogues[a]

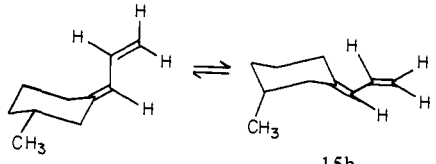


[a] a = $LiC{\equiv}COC_2H_5$, b = H^+, c = $LiAlH_4$, d = MnO_2, e = $Ph_3P{=}CH_2$

hexylideneethyl)diphenylphosphine oxide to yield the diene **9** in 55% yield. ^{13}C NMR of **9** established the expected trans geometry as well as the homogeneity of the sample. The D_2 analogue of **9** is known.[13]

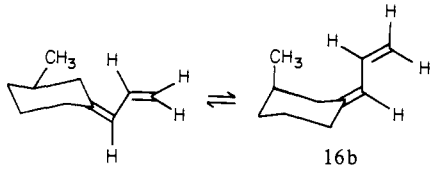
To synthesize des-A-vitamin D_3 (**14**), the ketone **8** was condensed with lithium ethoxyacetylide to obtain the acetylenic alcohol **10**, which when treated with acid rearranged to geometrically pure ester **11** in quantitative yield. Reduction of **11** with lithium aluminum hydride produced the allylic alcohol **12**, which was oxidized with manganese dioxide to the α,β-unsaturated aldehyde **13**[14] in 87% yield. Condensation of methylenetriphenylphosphorane with **13** gave the diene **14** in 60% yield. ^{13}C NMR showed that samples **13** and **14** are homogeneous.

The long wavelength π–π^* Cotton effects in dienes **9** and **14** are negative, as predicted by the "planar diene rule". The intensities at the center peak are $[\theta]_{252}$ −12 400 and $[\theta]_{241}$ −15 200, respectively. These data combined with the intensities observed for the Cotton effects in (*E*,3*R*)-(3-methylcyclohexylidene)propene (**15**), $[\theta]_{239}$ +8860) and (*Z*,3*R*)-(3-methylcyclohexylidene)propene



15a $[\theta]_{239}$ + 8860 15b

(*E*,3*R*)-(3-methylcyclohexylidene)propene



16a $[\theta]_{239}$ - 17 700 16b

(*Z*,3*R*)-(3-methylcyclohexylidene)propene

(**16**, $[\theta]_{239}$ −17 700) offer some qualitative predictive values for the A and C,D rings in the dihydrovitamin D's.

Conformational analysis[6] has shown that the A ring of dihydrotachysterol (DHT_2) (**3**) exists almost exclusively in a chair conformation in which the 3-hydroxyl and the 10-methyl group are both equatorial (Scheme I). In applying the "planar diene rule" to the A ring one finds that C_1, C_2, and C_3 with its hydroxyl group ring are in the positive space. This is analogous to (*Z*,3*R*)-(3-methylcyclohexylidene)propene (**16**). The predicted contribution from the A ring would therefore be very strong and positive. After correcting for the negative contribution from the C,D ring, the net Cotton effect in DHT_2 (**3**) is predicted as being positive. The observed Cotton effect is indeed positive and the intensity at the center peak of absorption is $[\theta]_{251}$ +13 400. The observed intensity is slightly higher than expected.

The C_{10} epimer of DHT_2 labeled as DHV_2-III by Okamura et al.[6] has been found to exist in two A-ring conformations of roughly equal population[6] (Scheme I). The "planar diene rule" analysis of the A ring in conformer **4a** shows that the 3-OH and the ring methylene (C_1,C_2) are in positive space and the axial methyl group[15] at C_{10} is in negative space. The net contribution from the A ring of **4a** is weakly positive. Upon analysis of the A ring in the conformer **4b**, one finds the ring methylenes (C_1,C_2) and C_3 with its hydroxyl group in negative space. Assuming in equal population of **4a** and **4b** then, the overall contribution from the A ring would be very small. The C and D rings would be expected to make the major contribution to the Cotton effect, with $[\theta]$ approximately −12 000. The observed Cotton effect was found to be $[\theta]_{250}$ −2170 at the center peak of absorption. Although the sign of the Cotton effect is predicted correctly, again the magnitude is lower than expected.

DHV_2-II (**5**) is the geometric isomer (5,6 double bond) of DHT_2 (**3**). To avoid $A^{1,3}$ steric repulsion[16] between the equatorial methy group at C_{10} and the C_7 methyne, the molecule assumes a chair conformation, which places the 3-OH and 10-methyl in an axial orientation. This conformer has been estimated[6] to be present to the extent of 95% at equlibrium. "Planar diene rule" analysis shows that C_1, C_2 and C_3 CHOH fall into positive space with the hydroxyl axially oriented. This results in a strong positive contribution for the A ring. The net Cotton effect in DHV_2-II (**5**)

(13) (a) B. Lythgoe, T. A. Moran, M. E. N. Nambudiry, and S. Ruston, *J. Chem. Soc., Perkin Trans. 1*, 2386 (1976); (b) B. Lythgoe, T. A. Moran, M. E. N. Nambudiry, J. Tideswell, and P. W. Wright, *ibid.*, 590 (1978).
(14) H. H. Inhoffen, *Angew. Chem.*, **70**, 576 (1958).
(15) Refer to preceding paper of a discussion regarding the relative importance of the ring methylene vs. the allylic axial methyl.
(16) F. Johnson, *Chem. Rev.*, **68**, 375 (1968).

is therefore predicted and found ($[\theta]_{250}$ +6300) to be weakly positive.

The C_{10} epimer of DHV_2-II labeled[6] as DHV_2-IV (**6**) also exists in a single chair conformation (95%) in which the 10-methyl is axial and the 3-OH is equatorial.[6] "Planar diene rule" analysis shows the C_1, C_2 and C_3 ring CHOH in negative space and hence the contribution of ring A will be negative. Reinforced by the negative Cotton effect from the C and D rings, the predicted effect is a strong negative. In agreement with the prediction is the observed negative Cotton effect, $[\theta]_{250}$ −15 400.

Experimental Section

Melting points were determined with a Mel-Temp apparatus and are uncorrected. Infrared (IR) spectra were measured with Perkin-Elmer Model 257 grating spectrophotometer. Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL C-60 or a Brucker 270 MHz spectrometer. Deuteriochloroform as solvent and tetramethylsilane (Me_4Si) as internal standard were used. The microanalyses were performed by Beller Laboratories, Gottingen, Germany.

Optical rotations were measured at either the 546.1-nm mercury line or the 589.3-nm sodium line by using a Bendix-Ericson Model 987 ETL/NPL polarimeter equipped with a Bendix Model DR-1 digital display. The cell length was 0.4 dm and all solvents used were spectrometric grades. An error limit of ±0.002° was applied to the observed rotations.

Ultraviolet (UV) spectra were recorded with a Cary 219 spectrophotometer and the peak maxima are reported in nm. Circular dichroism (CD) spectra were recorded with JASCO Model J-500C spectrophotometer. The cell path lengths used in UV and CD measurements were 1 cm and 0.1 cm, respectively.

Ozonolysis of Vitamin D_3 (7). Ozone was bubbled through a solution of 0.5 g of vitamin D_3 in 50 mL of methanol at −78 °C until the uptake of ozone was complete. Excess of dimethyl sulfide was added, and the reaction vessel was allowed to remain at room temperature overnight. The solution was poured into water and extracted with hexane, the hexane solution was evaporated, and the crude product was chromatographed on silica gel, eluting with 5% ether in hexane. Fractions corresponding to the ketone **8**[12] were collected to yield 0.32 g (93%) of an oil; $[\alpha]^{27}_{Hg}$ +22.2 ± 0.67° (*c* 0.75, CH_3OH); 2,4-dinitrophenylhydrazone: mp 105–106°; $[\alpha]^{27}_{D}$ +73.21 ± 0.78° (*c* 0.64, C_6H_6); CD (*c* 2.84 × 10^{-2} M, CH_3OH); $[\theta]_{288}$ +10 600.

(2-Cyclohexylideneethyl)diphenylphosphine Oxide. To a solution of 2.8 g (15.0 mmol) of diphenylphosphine in 75 mL of dry THF at −78 °C under a nitrogen atmosphere was added 6.2 mL of 2.4 M *n*-BuLi (14.9 mmol). After the red solution was stirred for 10 min 2.17 g (15.0 mmol) of 2-cyclohexylideneethyl chloride (prepared from 2-cyclohexylideneethanol according to a procedure of Meyers[17]) was added. The red color faded instantaneously to give a light yellow solution. The reaction mixture was allowed to reach room temperature and hydrolyzed by pouring into water. The mixture was extracted with ether and the solvent removed. The residue was dissolved in chloroform and the chloroform solution was shaken three times with aqueous H_2O_2. The solution was then washed with sodium sulfite, dilute HCl, and $NaHCO_3$ solutions. The organic layer was dried over Na_2SO_4 and the solvent evaporated to obtain 4.4 g (94%) of the allylic phosphine oxide. The product was crystallized from acetone, mp 164 °C (lit.[13] mp 164–165 °C).

Diene 9. To a solution of 1.35 g (4.35 mmol) of (2-cyclohexylideneethyl)diphenylphosphine oxide in 50 mL of dry THF at 0 °C under nitrogen atmosphere was added 1.8 mL of 2.4 M *n*-BuLi (4.32 mmol) over a period of 5 min. The red solution was stirred for 15 min and cooled to −78 °C and 1.15 g (4.35 mmol) of the ketone **8** in 5 mL of dry THF was added. The red color disappeared immediately. The reaction mixture was stirred at room temperature overnight and poured into water. The aqueous solution was extracted with hexane and the hexane solution was filtered and evaporated to obtain an oil. The crude product was chromatographed on silica gel by eluting with hexane. Removal of the solvent under vacuum gave 0.85 g (55%) of the diene **9** as a solid: mp 45–47 °C; $[\alpha]^{26}_{Hg}$ +89.56 ± 0.48° (*c* 1.05, cyclohexane); IR (CCl_4) 3030 (w), 3000–2800, 1625, and 1470–850 (multiplets) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.57 (s, 3 H), 0.7–2.4 (m, 37 H), 2.75 (m, 2 H), and an AB quartet centered at 5.87 (*J* = 11 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 12.10 (q), 18.89 (q), 22.36 (t), 22.58 (q), 22.82 (q), 23.51 (t), 23.91 (t), 26.97 (t), 27.70 (t), 28.05 (d), 28.65 (t), 28.80 (t), 28.95 (t), 36.20 (d+t), 37.70 (t), 39.57 (t), 40.67 (t), 45.62 (s), 56.36 (d), 56.66 (d), 115.78 (d), 117.44 (d), 140.38 (s), and 140.45 (s); UV (*c* 3.53 × 10^{-5} M, cyclohexane) λ_{262} (ε 26 360), λ_{252} (ε 37 980), λ_{243} (ε 31 180), and λ_{236} (ε 20 410); CD (*c* 3.53 × 10^{-4} M, cyclohexane) $[\theta]_{262}$ −7300, $[\theta]_{252}$ −12 400, $[\theta]_{253}$ −10 700, and $[\theta]_{215}$ (broad) +20 200.

Anal. Calcd for $C_{26}H_{44}$: C, 87.56; H, 12.44. Found: C, 87.50; H, 12.48.

α,β-Unsaturated Ester 11. To a solution of 0.53 g (7.56 mmol) of ethoxyacetylene in 30 mL of dry ether at −78 °C maintained under a nitrogen amtosphere was added 3.15 mL of 2.4 M *n*-BuLi (7.56 mmol). After 15 min, 2.0 g (7.51 mmol) of ketone **8** in 5mL of ether was added. The reaction mixture was then allowed to reach 0 °C and was quenched with water. Extraction with hexane and evaporation of the solvent provided a quantitative yield of alcohol **10**: IR (film) 3500 and 2250 cm^{-1}.

The alcohol was treated for 1 h with a few drops of 97% H_2SO_4 in 50 mL of THF. The THF solution was poured into water and extracted with hexane. The hexane solution was evaporated to yield the α,β-unsaturated ester 11 in a quantitative yield: IR (film) 1710 and 1640 cm^{-1}.

Allylic Alcohol 12. The ester 11 (7.5 mmol) was stirred with excess AlH_3 (10 mmol, prepared from LAH and $AlCl_3$) in 50 mL of dry ether for 1 h. The reaction mixture was hydrolyzed by adding 2 N NaOH solution. The precipitated salts were filtered off and the ether solution was evaporated to get an oil. The crude product was chromatographed on silica gel, eluting with hexane–ether to obtain 1.7 g (78%) of pure **12**: $[\alpha]^{27}_{Hg}$ +98.28 ± 1.23° (*c* 0.41, $CHCl_3$); IR (film) 3300 (br), 3000–2800, and 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.55 (s, 3 H), 0.77–2.75 (m, 30 H), 4.17 (d, *J* = 7 Hz, 2 H), and 5.20 (t, *J* = 7 Hz, 1 H).

Anal. Calcd for $C_{20}H_{36}O$: C, 82.12; H, 12.41. Found: C, 82.27; H, 12.30.

α,β-Unsaturated Aldehyde 13. To a solution of 1.5 g of the allylic alcohol **12** in 30 mL of pentane was added 15 g of MnO_2, and the solution was stirred until the oxidation was complete (monitored by TLC). The reaction mixture was diluted with ether and filtered. The solvent was removed under vacuum to obtain 1.3 g of the α,β-unsaturated aldehyde **13** as a low-melting solid: $[\alpha]^{26}_{Hg}$ +168.47 ± 0.99° (*c* 0.51, cyclohexane); IR (film) 3000–2800, 1670, 1630, 1470–1360 (multiplets), and 1140 (multiplets) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.59 (s, 3 H), 0.85 (d, *J* = 7 Hz, 6 H), 0.92 (d, *J* = 6 Hz, 3 H), 0.92–2.20 (m, 19 H), 3.35 (br d, *J* = 13 Hz, 1 Hz), 5.72 (d, *J* = 9 Hz, 1 H), and 10.08 (d, *J* = 9 Hz, 1 Hz); ^{13}C NMR ($CDCl_3$) δ 12.00 (q), 18.67 (q), 21.72 (t), 22.43 (q), 22.66 (q), 23.72 (t), 24.23 (t), 27.28 (t), 27.86 (d), 29.22 (t), 35.78 (t), 35.89 (d), 39.33 (t), 39.92 (t), 47.52 (s), 56.84 (d), 56.98 (d), 123.99 (dd), 167.47 (s), and 189.97 (d); UV (*c* 1.74 × 10^{-2}, 5.21 × 10^{-5} M, cyclohexane) λ_{398} (ε 2), λ_{389} (ε 10), λ_{380} (ε 26), λ_{361} (ε 51), λ_{346} (ε 67), λ_{332} (ε 68), λ_{319} (ε 65), and λ_{236} (ε 19 830); CD (*c* 1.74 × 10^{-2}, 5.21 × 10^{-4} M, cyclohexane) 19830); +2110, $[\theta]_{363}$ +5070, $[\theta]_{347}$ +5750, $[\theta]_{333}$ +4440, $[\theta]_{332}$ +2730, $[\theta]_{311}$ +1480, and $[\theta]_{236}$ −19 000.

Anal. Calcd for $C_{20}H_{34}O$: C, 82.69; H, 11.80. Found: C, 82.58; H, 11.75.

Des-A-vitamin D_3 (14). To a sitrred suspension of 0.65 g (1.8 mmol) of dry methyltriphenylphosphonium bromide in 15 mL of dry ether at −23 °C under nitrogen atmosphere was added 0.9 mL of 2.0 M *n*-BuLi (1.8 mmol). The resulting yellow solution was stirred for 10 min and 0.5 g (1.72 mmol) of the α,β-unsaturated aldehyde **13** in 2 mL of ether was added. The cooling bath was removed, and the reaction mixture allowed to reach room temperature, hydrolyzed by adding water, and then extracted with hexane. The hexane extract was evaporated and the crude product was chromatographed on silica gel, eluting with hexane. Fractions corresponding to the pure diene **14** were combined and the solvent was removed under vacuum to obtain 0.3 g: $[\alpha]^{27}_{Hg}$ +95.76 ± 0.92 (*c* 0.54, cyclohexane); IR (film) 3060, 3020, 3000–2800, 1800 (W), 1650, 1595, 1470–1330 (multiplets), 1000, and 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.57 (s, 3 H), 0.77–2.2 (m, 28 H), 2.77 (m, 1 H), 4.92 (dd, *J* = 11, 2 Hz, 1 H), 5.13 (dd, *J* = 16.5, 2 Hz, 1 H), 5.67 (d, *J* = 11 Hz, 1 H), and 6.72 (sextet, *J* = 16.5, 11, 11 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.02 (q), 18.90 (q), 22.23 (t), 22.58 (q), 22.82 (q), 23.60 (t), 23.95 (t), 27.68 (t), 28.06 (d), 29.15 (t), 36.20 (d + t), 39.58 (t), 40.57 (t), 45.88 (s), 56.06 (d), 56.74 (d), 114.21 (t), 121.34 (d), 132.72 (d), and 143.60 (s); UV (*c* 4.71 × 10^{-5} M, cyclohexane) λ_{249} (ε 19 890), λ_{241} (ε 30 600), λ_{234} (ε 28 140); CD (*c* 4.71 × 10^{-4} M, cyclohexane) $[\theta]_{249}$ −9260, $[\theta]_{241}$ −15 200, and $[\theta]_{234}$ (broad) −16 000.

Anal. Calcd for $C_{21}H_{36}$: C, 87.42; H, 12.58. Found: C, 87.25; H, 12.59.

Dihydrotachysterol (DHT_2) (3). UV (*c* 1.20 × 10^{-5} M, CH_3OH) λ_{260} (ε 22 050), λ_{251} (ε 31 500), λ_{243} (ε 26 980), and λ_{235} (ε 18 500); CD (*c* 6.93 × 10^{-5} M, CH_3OH) $[\theta]_{260}$ +9550, $[\theta]_{251}$ +13 400, $[\theta]_{245}$ +16 400, $[\theta]_{236}$ +14 300, and $[\theta]_{227}$ +10 700.

DHV_2-III (4). UV (*c* 2.50 × 10^{-5} M, CH_3OH) λ_{259} (ε 23 900), λ_{250} (ε 34 150), λ_{242} (ε 30 730), and λ_{234} (ε 22 440); CD (*c* 8.22 × 10^{-5} M, CH_3OH) $[\theta]_{260}$ −2410, $[\theta]_{250}$ −2170, $[\theta]_{242}$ −1930, and $[\theta]_{225}$ +18 100.

(17) E. N. Collington and A. I. Meyers, *J. Org. Chem.*, **36**, 3044 (1971).

DHV_2-II (5). UV (c 2.08 × 10^{-5} M, CH_3OH) λ_{260} (ϵ 23 560), $\lambda_{250.5}$ (ϵ 35 580), $\lambda_{242.5}$ (ϵ 30 770), and λ_{235} (ϵ 21 150); CD (c 6.92 × 10^{-5} M, CH_3OH) $[\theta]_{260}$ +5440, $[\theta]_{250}$ +6300, $[\theta]_{242}$ +5440, $[\theta]_{235}$ +12300, and $[\theta]_{216}$ +32600.

DHV_2-IV (6). UV (c 1.19 × 10^{-5} M, CH_3OH) $\lambda_{259.5}$ (ϵ 23 060), λ_{250} (ϵ 34 250), λ_{242} (ϵ 29 680), and λ_{235} (ϵ 21 230); CD (c 7.31 × 10^{-5} M, CH_3OH) $[\theta]_{260}$ −10 000, $[\theta]_{250}$ −15 400, $[\theta]_{242}$ −11 900, and $[\theta]_{218}$ +12 500.

Acknowledgment. We wish to thank Professor William H. Okamura for providing us with samples of the 10,19-dihydrovitamin D isomers used in this work.

Registry No. 3, 67-96-9; **4**, 65377-91-5; **5**, 65377-86-8; **6**, 807-27-2; **7**, 67-97-0; **8**, 66251-18-1; **8** DNP, 84928-42-7; **9**, 84943-83-9; **10**, 84928-43-8; **11**, 84928-44-9; **12**, 84928-45-0; **13**, 84928-46-1; **14**, 84928-47-2; diphenylphosphine, 829-85-6; 2-cyclohexylideneethyl chloride, 61638-81-1; (2-cyclohexylideneethyl)diphenylphosphine oxide, 13303-59-8; ethoxyacetylene, 927-80-0; methyltriphenylphosphonium bromide, 1779-49-3.

A New 2-Azatricyclo[4.4.0.$0^{2,8}$]decenone Synthesis and Ketene Formation by Retro-Diels–Alder Reaction

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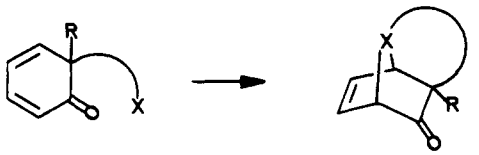
Abstract: 6-(3-Azidopropyl)-2,4-cyclohexadien-1-ones **2c** and **2d** and 6-(*o*-azidobenzyl)-2,4-cyclohexadien-1-ones **7a** and **7b** are prepared by C-alkylation of 2,4,6-trialkyl-substituted phenols. These azides provide triazolines **3a**, **3b**, **8a**, and **8b** by thermal intramolecular azide–olefin cycloaddition. Photochemical conversion of triazolines to 2-azatricyclo[4.4.0.$0^{2,8}$]dec-9-en-7-ones **4a**, **4b**, and **10a** with 366-nm light accomplished the synthetic equivalence of an intramolecular cycloaddition between a diene and a nitrene; e.g., **2** → **3** → **4**. Thermolysis of **7a** and **7b** provides triazolines **8**, aziridines **9**, and azatricyclodecenones **10**. Pyrex-filtered or 366-nm irradiation of **8a**, **9a**, and **10a** gives dienone **11** as the major reaction product. Pyrex-filtered irradiation of azatricyclodecenones in methanol results in photoinitiated retro-Diels–Alder reaction to give pyrrole ketenes (e.g., **5a** and **5b**), which undergo reaction with methanol to give pyrrole methyl esters **6a**, **6b**, **12a**, and **12b**. The preparation and photochemistry of triazolines **17a** and **17b** also are described.

There has been remarkable interest in the development of intramolecular cycloaddition processes during the past decade. Diels–Alder reactions,[1] dipolar cycloadditions,[2] and photochemical cyclobutane formation,[3] when performed intramolecularly, often display exceptional regio- and stereochemical control. The related conversion A → B (X = N) has not been exploited because nitrenes generally react with conjugated dienes to give vinylaziridines.[4]

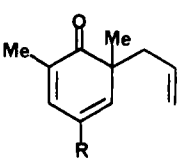


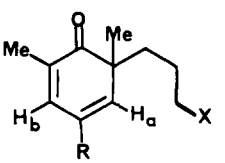
A B

We wish to report that triazolines formed by intramolecular dipolar cycloaddition of 6-(3-azidopropyl)-2,4-cyclohexadien-1-ones undergo eliminative rearrangement to 2-azatricyclo-[4.4.0.$0^{2,8}$]dec-9-en-7-ones; e.g., **2** → **3** → **4**. This two-step sequence provides a method for accomplishing the synthetic equivalence of an intramolecular cycloaddition between a diene and a nitrene. We also describe photochemical conversions of 2-azatricyclodec-9-en-7-ones **4** and **10** to pyrrolecarboxylic acid derivatives **6** and **12**, presumably via photoinitiated retro-Diels–Alder reaction of **4** and **10** to give intermediate pyrrole ketenes; e.g., **5**.

Results and Discussion

(Azidopropyl)cyclohexadienone **2c** is prepared from 2,4,6-trimethylphenol by (1) C-alkylation with allyl bromide as described by Miller[5] to give **1a**, (2) hydroboration of **1a** with disiamylborane





1a, R = Me
b, R = *t*-Bu

2a, R = Me; X = OH
b, R = Me; X = OMs
c, R = Me; X = N_3
d, R = *t*-Bu; X = N_3

in THF followed by oxidative workup with H_2O_2/NaOH to give **2a** (68% isolated yield), (3) treatment of **2a** with methanesulfonyl chloride in triethylamine/CH_2Cl_2 to give **2b** (99%), and (4) reaction of **2b** with sodium azide in DMF to give **2c** in 96% yield. In similar fashion 4-*tert*-butyl-2,6-dimethylphenol[6] is converted

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(4) Patai, S. "The Chemistry of the Azido Group"; Interscience: New York, 1971.
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(8) Ripoll, J. L.; Rouessac, A.; Rouessac, R. *Tetrahedron* **1978**, *34*, 19.
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