gel; 1:4 ethyl acetate–redistilled light petroleum (bp 60–80 °C)], afforded *N*-(acetoxymethyl)-4-chlorobenzamide (**2b**) (80 mg; 12%) with physical properties identical with those of the sample described above.

Reaction of *N*-(4-Chlorobenzoyl)-2-hydroxyglycine (11) with Lead(IV) Acetate. Glyoxylic acid adduct **11** (500 mg, 2.2 mmol) was treated with $Pb(OAc)_4$ (1.8 g, 4.06 mmol) according to the general method for the preparation of **2b** and **3b** above to furnish 4-chloro-*N*-formylbenzamide (**3b**) (110 g, 27%) with physical properties identical with those of the sample described above.

Acknowledgment. This work was supported generously by the Cancer Research Campaign of Great Britain.

Mechanistic Studies by Deuterium Labeling and Related Kinetic Investigations of the [1,5]-Sigmatropic Hydrogen Shift of Vitamin D Type Vinylallenes[1]

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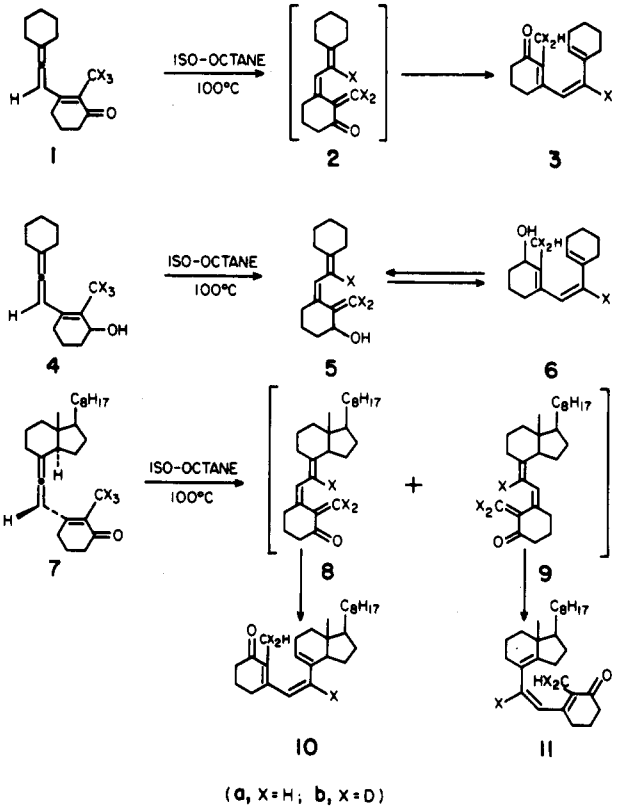
Kinetic investigations of the thermal [1,5]-sigmatropic hydrogen shift of deuterated and nondeuterated vinylallenes **1**, **4**, and **7** afforded primary kinetic deuterium isotope effects in the range 6.3–7.6 at 98.4 °C. This information together with Arrhenius data for the vinylallenone **1a** suggests a mechanistic similarity between the allenic and nonallenic variants of the [1,5]-shift process. Vinylallenes **24a** and **24b** were also studied in comparison with **1a** and **4a** in order to assess the effect of allylic substituents on reactivity. Finally, the rearrangement of **12b** and **13b** was examined in terms of the stereochemical course of the [1,5]-shift reaction.

In earlier investigations from this laboratory,[2] heating vinylallene **1a** in refluxing isooctane (ca, 100 °C) afforded the trienone **3a**[3] in quantitative yield. It was assumed that **1a** isomerized initially to **2a** via a rate-limiting [1,5]-sigmatropic shift followed by a spontaneous [1,7]-sigmatropic shift to afford the thermodynamically more stable, linearly conjugated system **3a** (Chart I). In the case of the corresponding alcohol **4a**,[3] a similar result was obtained except that the analogous alcohols **5a** and **6a** were obtained as a ~1:4 equilibrium mixture. The vinylallenone **7a**,[4] more closely related to vitamin D itself, behaves in a manner similar to **1a**[4b] except that due to the unsymmetrical moiety residing at the allene terminus, a pair of geometrically isomeric products **10a** and **11a** are obtained. The intramolecular nature of the [1,5]-sigmatropic rearrangement assures the geometry about the central double bond of the product be cis. However, the geometry at the Δ^7 double bond (exocyclic to the C ring of the steroid) is dependent upon two competing [1,5]-sigmatropic shifts. In one pathway, the desired (7*E*)-trienone **8a** is obtained. In the alternate pathway, the (7*Z*)-trienone **9a** is obtained.

Heating the diastereomeric vitamin D type vinylallenols **12a** or **13a**[4b] gave a result similar to that of **7a** except that the primary thermolysis products (**14a** and **16a** or **15a** and **17a**, respectively; Chart II) are rearranged to or in equilibrium with secondary and tertiary thermolysis products. Interestingly, although **8a** and **9a** are produced in equal amounts from **7a**, **12a** produces an excess of **16a** over **14a** (ca. 4:1); its epimer **13a** results in just the opposite ratio, an excess of **15a** over **17a** (ca. 4:1). This *E*/*Z* ratio (**14** or **15** to **16** or **17**) is general and results from a π-facial

Chart I



(1) This is paper 29 in the series "Studies on Vitamin D (Calciferol) and Its Analogues". For paper 28, see: Hoeger, C. A.; Okamura, W. H. *J. Am. Chem. Soc.* **1985**, *107*, 268–270.
(2) Okamura, W. H. *Acc. Chem. Res.* **1983**, *16*, 81–88.
(3) Condran, P., Jr.; Okamura, W. H. *J. Org. Chem.* **1980**, *45*, 4011–4015.
(4) (a) Hammond, M. L.; Mouriño, A.; Okamura, W. H. *J. Am. Chem. Soc.* **1978**, *100*, 4907–4908. (b) Condran, P., Jr.; Hammond, M. L.; Mouriño, A.; Okamura, W. H. *Ibid.* **1980**, *102*, 6259–6267. See also: (c) Mouriño, A.; Lewicka-Piekut, S.; Norman, A. W.; Okamura, W. H. *J. Org. Chem.* **1980**, *45*, 4015–4020. (d) Leyes, G. A.; Okamura, W. H. *J. Am. Chem. Soc.* **1982**, *104*, 6099–6105. (e) Jeganathan, S.; Johnston, A. D.; Kuenzel, E. A.; Norman, A. W.; Okamura, W. H. *J. Org. Chem.* **1984**, *49*, 2152–2158.

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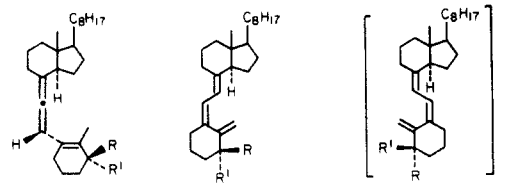
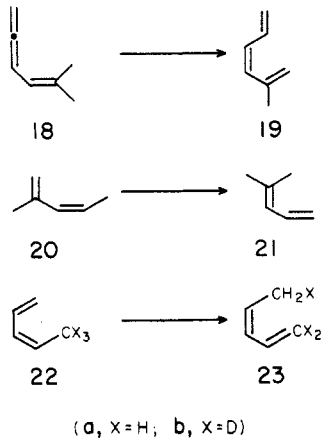
Chart II



12a, R=OH; R'=H
b, R=OTMS; R'=H
13a, R=H; R'=OH
b, R=H; R'=OTMS

14 15 16 17

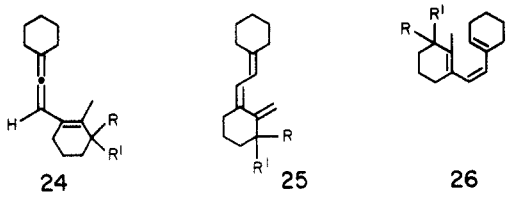
Chart III



18 19 20 21 22 23

(a, X=H; b, X=D)

Chart IV



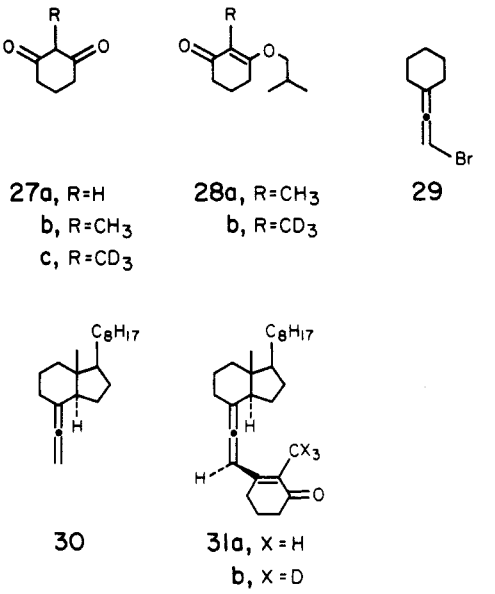
24 25 26

a, R=OTMS; R'=CN
b, R=OTMS; R'=H

anti-directing effect by the hydroxyl group.[2,4]

Nearly all of our efforts in this area have been directed toward a detailed study of these processes in terms of their synthetic applications. However, there have been only limited studies regarding a detailed mechanistic comparison of the vinylallene variant of the [1,5]-sigmatropic shift with the nonallenic variant.[5-9] Only the studies of Skattebol[9a] on the rearrangement of the vinylallene **18** to **19** have been directed toward this end (Chart III). Several studies of arylallenes have, however, been investigated by Schmid and co-workers.[9b] It is known from Skattebol's studies[9a] that the activation barrier for the vinylallene variant of the [1,5]-shift is significantly lower (ca. ~8 kcal/mol) than that for the simpler nonallenic variant **20** to **21**,[7a] and a logical rationale for this difference has been postulated.[9a] Some of the most detailed mechanistic investigations of the nonallenic acyclic variant of the [1,5]-shift process are those of Frey[7] and Roth.[8] In one study, Roth has determined that the rearrangement of **22** to **23** proceeds kinetically with a remarkably large primary deuterium isotope effect (k_H/k_D) of 12.2![8a] In order to develop a more detailed mechanistic understanding of the corresponding vinylallene variant of the [1,5]-process, it is the purpose of this paper to describe the synthesis of deuterated vinylallene ketones **1b** and **7b** and alcohol **4b** and a study of the kinetics of their rearrangement. In addition, vinylallenes **24a** and **24b** were synthesized in order to explore further how substituents effect the rate of the [1,5]-shift (Chart IV). Finally, the vitamin D type vinylallenes **12b** and **13b** were synthesized and thermolyzed in order to briefly examine the effect of substituents on the stereochemistry of the [1,5]-shift.

Chart V



27a, R=H
b, R=CH$_3$
c, R=CD$_3$
28a, R=CH$_3$
b, R=CD$_3$
29
30
31a, X=H
b, X=D

Table I. Summary of Rate Data for Rearrangement of Vinylallenes 1, 4, and 7 in Isooctane

compd	10^5k,[g] s^{-1}	k_H/k_D
1a[a,b]	9.69 ± 0.16	
		6.3 ± 0.3
1b[a]	1.55 ± 0.04	
4a[a]	12.5 ± 0.4	
		7.0 ± 0.4
4b[a]	1.79 ± 0.04	
7a[c]	5.89 ± 0.24	
		7.6 ± 0.6
7b[c]	0.780 ± 0.007	
1a[b,d]	3.68 ± 0.26	
1a[b,e]	1.34 ± 0.07	
1a[b,f]	0.496 ± 0.012	

[a] 98.40 ± 0.05 °C. [b] See Table II for activation parameters. [c] 98.8 ± 0.9 °C. [d] 88.51 ± 0.05 °C. [e] 77.52 ± 0.05 °C. [f] 68.56 ± 0.05 °C. [g] All uncertainties listed are absolute deviations from the mean.

Results and Discussion

Synthesis of Substrates. The sequence **27a** → **27b** → **28a** followed by coupling of **28a** with **29** or **30** (to afford

(5) General review: (a) Spangler, C. W. *Chem. Rev.* **1976**, *76*, 187–217. (b) Mironov, V. A.; Fedorovich, A. D.; Akhrem, A. A. *Russ. Chem. Rev.(Engl. Trasl.)* **1981**, *50*, 666–681.

(6) Theoretical studies: (a) Hess, B. A., Jr.; Schaad, L. J.; Pancir, J. *J. Am. Chem. Soc.* **1985**, *107*, 149–154. (b) McLennan, D. J.; Gill, P. M. W. *Ibid.* **1985**, *107*, 2971–2972. (c) Hess, B. A., Jr.; Schaad, L. J. *Ibid.* **1983**, *105*, 7185–7186. (d) Rondan, N. G.; Houk, K. N. *Tetrahedron Lett.* **1984**, *25*, 2519–2522. (e) Castenmiller, W. A. M.; Buck, H. M. *Tetrahedron* **1979**, *35*, 397–407. (f) Dewar, M. J. S.; Merz, K. M.; Stewart, J. J. P. *J. Chem. Soc., Chem. Commun.* **1985**, 166.

(7) (a) Frey, H. M.; Ellis, R. J. *J. Chem. Soc.* **1965**, 4770–4773. (b) Frey, H. M.; Pope, B. M. *J. Chem. Soc. A* **1966**, 1701–1702. (c) Frey, H. M.; Solly, R. K. *Ibid.* **1969**, 733–735. (d) O'Neal, H. E.; Frey, H. M. *Int. J. Chem. Kinet.* **1970**, 343–347. (e) Frey, H. M.; Lamont, A. M.; Walsh, R. *J. Chem. Soc. A* **1971**, 2642–2646.

(8) (a) Roth, W. R.; König, J. *Justus Liebigs Ann. Chem.* **1966**, *699*, 24–32. (b) Roth, W. R.; König, J.; Stein, K. *Chem. Ber.* **1970**, *103*, 426–439.

(9) (a) Skattebol, L. *Tetrahedron* **1969**, *25*, 4933–4938. (b) Heimgartner, H.; Zsindely, J.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 2924–2945.

Table II. Activation Parameters[a]

compd	E_a, kcal/mol	log A, s^{-1}	$\Delta G^{\ddagger}$, kcal/mol	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal/(mol K)
1a[b]	24.9 ± 0.5	10.6 ± 0.2	28.7 ± 0.5	24.2 ± 0.4	−12.3 ± 0.2
18[c]	24.6	10.3	28.9	23.9	−13.6
aryl allenes[d]	29.5 ± 0.8	10.7 ± 0.4	33.4 ± 0.7	28.8 ± 0.8	−12.3 ± 1.4
20[e]	32.7	11.2	35.6	32.0	−9.6
22a[f]	36.1	11.3	38.8	35.3	−9.0

[a] Literature data were extrapolated to 98.4 °C. [b] This study. The uncertainties indicated for this study are standard deviations. [c] Reference 9a. [d] The range for three benzo-fused cases involving (*o*-methylaryl)allenes. Reference 9b. [e] Reference 7a. [f] Reference 8a.

Table III. Substituent Effects on the Rate of the [1,5]-Shift at 98.4 °C in Isooctane

substrate	10^5k,[a] s^{-1}	relative rate
4a	12.5 ± 0.4	1.00
1a	9.69 ± 0.16	0.78
24b	10.8 ± 0.4	0.86
24a	5.32 ± 0.12	0.43
7a	5.89 ± 0.24	0.47

[a] The uncertainties listed are absolute deviations from the mean.

Table IV. Competing Rearrangement Pathways for Vitamin D Type Vinylallenes: *E*/*Z* Ratio[a]

substrate	*E*/*Z* ratio	substrate	*E*/*Z* ratio
7a	1:1[b]	**13b**	2.1:1[d]
13a	3.1:1[c]	**12b**	1:2.1[d]
12a	1:3.8[c]		

[a] At 98.4 °C. [b] Reference 4b. [c] The earlier study (ref 4b) was repeated as an analytical control, and the agreement was satisfactory. Details are presented in the Experimental Section and in the supplementary material. [d] This study. See the Experimental Section and the supplementary material for details.

1a or **7a** + **31a**, respectively has been previously reported (Chart V).[3,4b] Alkylation of **27a** with iodomethane-d_3 (99.9+% *d*) to afford **27c** followed by its conversion to the labeled substrates **1b** or **7b** + **31b** was carried out analogously. These and subsequent synthetic transformations are given in detail in the Experimental II Section and supplementary material.

Kinetic and Related Studies. The results of the kinetic measurements for the deuterated and nondeuterated vinylallenes are summarized in Table I. With the availability of vinylallenes **1b**, **4b**, and **7b**, ^1H and ^{13}C NMR analyses of the products of the thermal experiments reveal that **3b**, **5b** + **6b**, and **10b** + **11b** are the only products produced. This definitively establishes the intramolecular nature of the reaction including the fact that the hydrogen does indeed migrate from the allylic methyl in the A ring to C-7 (steroid numbering) of the product triene system. Moreover, kinetic studies reveal that the rearrangement of vinylallenes **1**, **4**, and **7** to the corresponding isomeric trienes very likely proceed in the primary step through a classical sigmatropic [1,5]-hydrogen shift completely analogous to their nonallenic variants. Our observed kinetic isotope effect data (uncorrected for secondary effects), k_H/k_D in the range of 6.3–7.6 at 98.4 °C, are large and in line with Roth's k_H/k_D value of 12.2, a value obtained by extrapolation of data obtained at 185–211 °C to 25 °C. In fact, when Roth's data obtained for the transformation **22** to **23** are extrapolated to 98.4 °C, a k_H/k_D value of 7.8 is obtained. Such large isotope effects are characteristic of highly symmetrical hydrogen-transfer processes, but the actual suprafacial trajectory for each of the systems including our own is not clear.[6]

For the case of ketone **1a**, an Arrhenius study over the temperature range 68.6–98.4 °C (Table I) afforded the activation parameters summarized in Table II. Our data are compared to those of others described in the literature. Appropriate differences are apparent, but the similarities of the log *A* and entropy of activation terms for all of the systems are noteworthy. Like the primary isotope effect result, these data also imply that the vinylallene variant of the [1,5]-sigmatropic hydrogen shift is mechanistically similar to the nonallenic variant.

A somewhat surprising result of the kinetic measurements was the relatively small change in rate in going from ketone **1** to alcohol **4**. This effect was further exemplified by other substituents such as the trimethylsilyl cyanohydrin derivative **24a** and the trimethylsilyl ether **24b**. The results are summarized in Table III.[10] Although the rate of the [1,5]-shift is not significantly affected by changes of the substituents studied at the C-1 position, as we have noted previously, there is a significant effect on stereochemistry. The data are summarized in Table IV. For ketone **7a**, the competing *E* and *Z* pathways proceed with equal abundance.[4b] In the case of the corresponding alcohols **13a** and **12a**, where the carbonyl is now replaced by OH, the *E*/*Z* ratio is 3.1/1.0 and 1.0/3.8, respectively. In new data, substitution of OH with OTMS leads to a small attenuation of the *E*/*Z* ratio to 2.1/1.0 and 1.0/2.1, respectively. We have thus far been unsuccessful in enhancing the *E*/*Z* or *Z*/*E* ratios through additional substituent modifications.[10]

Summary and Conclusions. We have thus shown that the vinylallene variant of the [1,5]-sigmatropic shift is mechanistically analogous to the corresponding non-allene variant. To the extent that [1,5]-shifts of nonallenic pentadienyl systems are considered to be concerted,[11] there is no reason to believe that vinylallene systems behave otherwise.

Experimental Section

[2′-(2″-Methyl-3″-oxocyclohex-1″-en-1″-yl)ethenylidene]cyclohexane (1a) and [2′-(2″-(Trideuteriomethyl)-3″-oxocyclohex-1″-en-1″-yl)ethenylidene]cyclohexane (1b). To a 100-mL round-bottom flask were added 1.43 mL (1.87 g, 10.0 mmol) of the bromoallene **29** and 20 mL of dry ether. The solution was cooled to −78 °C, and 6.71 mL of 1.64 M *n*-BuLi (11.0 mmol) was added dropwise. The solution was allowed to stir for 30 min, and then 2.19 g (11.9 mmol) of the isobutoxy enol ether **28a** dissolved in 10 mL of ether was added via cannula. After the mixture was stirred for 10 min at −78 °C, the cooling bath was removed, and the solution was allowed to warm to room temperature over 1 h. The reaction was quenched by addition of 20

(10) The rearrangement of alkali metal salts of **4a** was also studied by ^1H NMR. At 66.5 °C (refluxing THF), the half-life of **4a** was 32 h. In the presence of 1.2 equiv of *n*-BuLi/hexanes, the half-life was 21.5 h; in the presence of potassium hydride (1.2 equiv) and 18-crown-6 (3 equiv), the half-life was 18.5 h. For each time point, aliquots were removed, quenched, and workup up. Mixtures of reactant and products were analyzed by ^1H NMR in the same way as described in the text. Similar studies of the vitamin D vinylallenols **12a** and **13a** were precluded as a result of apparent deterioration of reactants and/or products to complex mixtures. In other studies, esters of these vinylallenols were prone to elimination.

(11) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 209–219.

mL of 1.0 M aqueous HCl. After the reaction was stirred 5 min, the aqueous layer was removed and replaced with 20 mL of fresh acid followed by stirring for an additional 30 min. The crude mixture was transferred to a separatory funnel. Workup included washing with aqueous $NaHCO_3$, water, and brine. Drying with $MgSO_4$ and rotary evaporation under reduced pressure afforded a yellow liquid, which was purified by radial chromatography (Chromatotron, 4-mm plate, 10% EtOAc/low boiling petroleum ether, 30–60 °C). The resulting vinylallenone was dissolved in a small amount of hexane and allowed to crystalize at 0 °C to afford 1.12 g (5.18 mmol, 52%) of the pure vinylallenone **1a**.

The deuterated vinylallenone **1b** (1.09 g, 50% yield) was prepared in the fashion stated above using exactly the same amounts except that the labeled enol ether **28b** (2.22 g, 12.0 mmol) was used.

Thermolysis of [2′-(2″-Methyl-3″-oxocyclohex-1″-en-1″-yl)ethenylidene]cyclohexane (1a) and Its Deuterated Analogue 1b to 3a and 3b. Vinylallenone **1a** was thermolyzed as described in the procedure below for the kinetic studies. An ampule was opened after 11 h at 98.4 °C. The starting material was shown to be completely consumed as determined by ^1H NMR, resulting in essentially quantitative conversion of vinylallenone **1a** to **3a**.

The deuterated analogue **1b** was thermolyzed in the same manner; however, approximately 10% starting material remained after refluxing for 40 h. The reaction was stopped at this time and the product **3b** separated from the starting material by HPLC (M-9 Partisil, 10/50 ODS-2 column, 83/17 (v/v) $MeOH/H_2O$, 4.0 mL/min).

[2′-(3″-Hydroxy-2″-methylcyclohex-1″-en-1″-yl)-ethenylidene]cyclohexane (4a) and [2′-(3″-Hydroxy-2″-(trideuteriomethyl)cyclohex-1″-en-1″-yl)ethenylidene]-cyclohexane (4b). A solution of 300 mg (1.39 mmol) vinylallenone **1a** and a spatula tip of $CeCl_3$ in 15 mL of absolute ethanol was prepared, and then 260 mg (6.88 mmol) of $NaBH_4$ was added. The solution was allowed to stir at room temperature. TLC examination (silica gel, 10% EtOAc/low-boiling petroleum ether, 30–60 °C) showed the reaction to be complete after 2.5 h. The excess borohydride was quenched with 1 M aqueous acetic acid. The solution was transferred to a separatory funnel with ether and aqueous Na_2CO_3 rinsings. The aqueous layer was drawn off and extracted with ether. The combined ether extracts were washed with $NaHCO_3$, H_2O, and brine. Drying over $MgSO_4$ and evaporation of solvent under reduced pressure afforded the desired vinylallenol **4a**. Purification by radial chromatography (Chromatotron, 4-mm plate, 10% EtOAc/low-boiling petroleum ether, 30–60 °C) and drying by evacuation under an oil pump yielded the pure allenol **4a** (288 mg, 1.3 mmol, in 95% yield).

The same procedure was used to prepare the deuterated vinylallenol **4b** (289 mg, 92%) starting from the deuterated vinylallenone **1b** (308 mg, 1.43 mmol).

Thermolysis of [2′-(3″-Hydroxy-2″-methylcyclohex-1″-en-1″-yl)ethenylidene]cyclohexane (4a) and Its Deuterated Analogue 4b to 5 and 6. Vinylallenol **4a** was thermolyzed as described in the procedure below for the kinetic studies. An ampule was withdrawn from the constant temperature bath (98.4 °C) after 9 h. The starting material has been essentially completely consumed. Separation of the thermolysis products was achieved by HPLC (M-9 Partisil, 20% EtOAc/Skellysolve B, 3.0 mL/min) to afford pure **5a** and the corresponding previtamin form **6a**. The deuterated analogue **4b** was thermolyzed in the same manner; however, after 7.5 h of reflux, approximately 60% of the starting material remained. The reaction was stopped at this time in order to minimize excessive scrambling of the deuterium label. The products **5b** and **6b** were separated from the starting material by HPLC using the same conditions stated above. These samples were utilized for obtaining the spectral data given in the supplementary material.

(6*R*)-9,10-Secocholesta-5(10),6,7-trien-1-one (7a) and (6*R*)-19,19,19-Trideuterio-9,10-secocholesta-5(10),6,7-trien-1-one (7b). An allenyllithium species was prepared by reacting **30** (1.3652 g, 4.95 mmol) in 40 mL of dry ether at −78 °C with 1.84 M *t*-BuLi (2.7 mL in pentane, 5.0 mmol), which was added dropwise with stirring. After 5 min, the reaction flask was transferred to a second bath maintained at −55 °C. The solution was stirred at this temperature for 40 min and then transferred to the original bath at −78 °C. Enol ether **28a** (0.9250 g, 5.00 mmol) dissolved in 25 mL of dry ether was added via cannula, and the mixture was stirred for 5 min. The cooling bath was removed, and the solution v as allowed to stir at room temperature for 1 h. Aqueous acetic acid (1 M, 20 mL) was added with vigorous stirring, and after 10 min, the aqueous layer was removed by pipet. Fresh acid (20 mL) was added and stirring continued for another 0.5 h. The crude mixture was transferred to a separatory funnel, and the workup included washing with $NaHCO_3$, H_2O, and brine. Drying over $MgSO_4$ and evaporation under reduced pressure afforded a viscous yellow oil. The oil was purified by column chromatography (silica gel, 10%, EtOAc/low-boiling petroleum ether, 30–60 °C) to give a mixture of (6*R*)- and (6*S*)-vinylallenones **7a** and **31a**, respectively (1.5126 g, 80%). The isomers were separated by HPLC (M-9 Partisil, 5% EtOAc in SSB) to give pure (6*R*)- (1.3542 g, 72% yield based on **30**) and (6*S*)-vinylallenones (0.1028 g, 5%) in a ratio of 13.2 to 1.0. The deuterated (6*R*)-vinylallenone **7b** (1.2585 g, 79% yield based on **30**) was prepared in the same manner using the labeled enol ether **28b**.

Thermolysis of (6*R*)-9,10-Secocholesta-5(10),6,7-trien-1-one (7a) and Its Deuterated Analogue 7b To Afford 10 and 11. Vinylallenone **7a** was thermolyzed in refluxing isooctane as described in the general procedure for the kinetic studies. After 20 h, the starting material was completely consumed. Separation of the thermolysis products was achieved by HPLC (M-9 Partisil, 5% EtOAc/SSB, 3.0 mL/min) to afford the *cis*-isotachysterone **11a** and the previtamin ketone **10a** in a 1:1 ratio.

The deuterated analogue was thermolyzed in the same manner; however, approximately 27% of the starting material remained after 43 h. The reaction was stopped at this time in order to avoid formation of secondary products. Separation of starting material (**7b**) and products (**11b** and **10b**) was achieved by HPLC using the same conditions as above.

(1*R*,6*R*)-9,10-Secocholesta-5(10),6,7-trien-1-yl Trimethylsilyl Ether (13b) and (1*S*,6*R*)-9,10-Secocholesta-5(10),6,7-trien-1-yl Trimethylsilyl Ether (12b). To a solution of 30 mg (0.08 mmol) of (1*R*)-vinylallenol **13a** in 10 mL of dry DMF was added 0.5 mL of (trimethylsilyl)imidazole (98%). Stirring for 10 min at room temperature resulted in complete conversion of the alcohol to the silyl ether. The crude mixture was transferred to a separatory funnel containing H_2O and then diluted with ether. The aqueous layer was drawn off and the ether layer washed with brine. Drying over $MgSO_4$, followed by evaporation of solvent, and purification by radial chromatography (Chromatotron, 1-mm plate, 10% EtOAc/low-boiling petroleum ether, 30–60 °C) afforded 34 mg (94%) of the pure silyl ether. Exactly the same procedure was used to prepare the 1*S* silyl ether **12b** (91%) starting from 20 mg (0.05 mmol) of the (1*S*)-vinylallenol **12a**.

Thermolysis of 12a,b and 13a,b to 14 + 16 and 15 + 17, Respectively. Detailed experimental procedures are given in the supplementary material. The results for the thermolysis in refluxing isooctane (98.4 °C) are summarized in Table IV of the text.

[2′-(3″-Cyano-3″-(trimethylsiloxy)-2″-methylcyclohex-1″-en-1″-yl)ethenylidene]cyclohexane (24a). A round-bottom flask was oven-dried and flushed with argon. Vinylallenone **1a** (216 mg, 1.0 mmol) was added to the flask containing ZnI_2 (0.012 mg, 0.04 mmol) and 5 mL of CH_2Cl_2 distilled over P_2O_5, and to this mixture was added 2.0 mL of Me_3SiCN via syringe. The solution was allowed to stir at room temperature for 4 h, after which time TLC examination (10% EtOAc/low-boiling petroleum ether, 30–60 °C) revealed the reaction to be virtually complete. The reaction was quenched with a saturated K_2CO_3 solution, and then the reaction mixture was diluted with ether. The ether extract was washed with H_2O and brine, dried over $MgSO_4$, and then concentrated under reduced pressure to afford a residue. The crude product was immediately purified by radial chromatography (Chromatotron, 10% EtOAc/low-boiling petroleum ether, 30–60 °C) and the resulting oil crystallized spontaneously on storage at 0 °C, yielding 220 mg (0.70 mmol, 70%) of **24a** as a white solid (mp 52–53 °C).

[2′-(3″-(Trimethylsiloxy)-2″-methylcyclohex-1″-en-1″-yl)ethenylidene]cyclohexane (24b). Trimethylsilyl chloride (Me_3SiCl, 0.35 mL, 2.7 mmol) was added to a solution of imidazole (373 mg, 5.4 mmol) in 1 mL of DMF, and to the mixture was added

298 mg (1.4 mmol) of the vinylallenol **4a**. The solution was allowed to stir at room temperature for 8 h, at which time TLC examination (10% EtOAc/low-boiling petroleum ether, 30–60 °C) showed the reaction to be complete. The solution was transferred to a separatory funnel, diluted with ether, and washed with 1 M HCl, aqueous $NaHCO_3$, H_2O, and brine. After being dried ($MgSO_4$) and concentrated, the crude product was purified by radial chromatography (Chromatotron, 10% EtOAc/low-boiling petroleum ether, 30–60 °C) to afford 203 mg (50%) of silyl ether **24b**.

(*Z*)-1-Cyclohex-1′-en-1′-yl-2-[3″-cyano-3″-(trimethylsiloxy)-2″-methylcyclohex-1″-yl]ethene (26a). Vinylallene **24a** was thermolyzed as described below in the general procedure for the kinetic studies. Several ampules containing a total of 38 mg (0.12 mmol) of vinylallene **24a** in isooctane (4 mL) were withdrawn from the constant temperature bath (98.4 °C) after 17 h. The starting material had been essentially completely consumed. The thermolysis product was purified initially by radial chromatography (Chromatotron, 2-mm plate, 2% EtOAc/low-boiling petroleum ether, 30–60 °C) to afford 35 mg (92%) of **26a**. Further purification by HPLC (Whatman M-9 Partisil column) using the same solvent system afforded **26a** as a single peak on the HPLC trace.

(*Z*)-[2′-(3″-(Trimethylsiloxy)-2″-methylcyclohex-1″-en-1″-yl)ethenylidene]cyclohexane (26b) and (*Z*)-1-Cyclohexylidene-2-[3′-(trimethylsiloxy)-2′-methylenecyclohexylidene]ethane (25b). The silyl ether **24b** was thermolyzed at 98.4 °C as described below in the general procedure for the kinetic studies. An ampule was opened after 8 h, resulting in essentially quantitative conversion of vinylallene **24b** (20 mg) to the previtamin **26b** and vitamin **25b** as determined by ^1H NMR. The mixture of products was not separated at this point but instead treated directly with MeOH (20 mL) and a catalytic amount (28 mg) of citric acid. Stirring at room temperature for 5 h resulted in deprotection of the silyl moiety to afford a mixture of alcohols, which after the usual workup were separated by HPLC (20% EtOAc/Skellysolve B; Partisil M-9 column). The spectra of these compounds were identical with the spectra of the previously characterized alcohols **6a** and **5a**, respectively.

In a separate experiment, 165 mg (0.76 mmol) of vinylallenol **4a** was thermolyzed. The products were separated by using the HPLC conditions described above, resulting in 22 mg (13%) of **5a** and 133 mg (81%) of **6a**. The previtamin (133 mg, 0.61 mmol) **6a** was added to an ice-cooled mixture of imidazole (166 mg, 2.44 mmol) and freshly distilled Me_3SiCl (0.15 mL, 1.22 mmol) in 1 mL of DMF, and then the mixture was stirred overnight. After being diluted with ether, the mixture was washed with 1 M HCl, $NaHCO_3$, H_2O, and brine. Drying over $MgSO_4$ and evaporation of solvent followed by radial chromatography (Chromatotron, 10% EtOAc/low-boiling petroleum ether, 30–60 °C) afforded 158 mg (89%) of the silyl ether **26b**. The same procedure was employed in the preparation of the isomeric silyl ether **25b** (22 mg, 0.10 mmol, of **5a** afforded 25 mg, 85% yield, of silylated product).

2-Methylcyclohexane-1,3-dione (27b) and 2-(Trideuteriomethyl)cyclohexane-1,3-dione (27c). Cyclohexane-1,3-dione (**27a**, 1.7 g, 15 mmol) was added to a 5 M aqueous NaOH solution (3 mL). The solution was placed in an ice bath followed by addition of iodomethane (5.0 g, 35 mmol) via syringe. The ice bath was removed, and the solution was allowed to reflux for 17 h. The crystals were collected and recrystallized from H_2O to afford the pure substituted diketone **27b** (1.1 g, 8.7 mmol, 59%, mp 204–205 °C).

The same procedure was used to prepare the deuterated diketone **27c** (60% yield) using instead the corresponding amount of iodomethane-d_3 (isotopic purity 99.9+%, Aldrich) with cyclohexane-1,3-dione (1.7 g, 0.15 mmol).

3-Isobutoxy-2-methylcyclohex-2-en-1-one (28a) and 3-Isobutoxy-2-(trideuteriomethyl)cyclohex-2-en-1-one (28b). The diketone **27b** (1.9 g, 15 mmol) was dissolved in benzene (25 mL) followed by addition of *p*-toluenesulfonic acid monohydrate (0.15 g, 0.79 mmol) and isobutyl alcohol (8.0 mL). A Dean–Stark apparatus was attached, and the solution was allowed to reflux for 6 h. The crude mixture was transferred to a separatory funnel and washed with aqueous $NaHCO_3$. After dilution with ether, the solution was washed sequentially with aqueous Na_2CO_3, water, and a saturated NaCl solution and then dried over $MgSO_4$. Filtration followed by evaporation of solvent under reduced pressure and Kugelrohr distillation afforded **28a** (2.6 g, 14 mmol, 93%) as a colorless oil (bp 107 °C, 0.55 mm).

Exactly the same procedure was followed to prepare the deuterated enol ether **28b** (2.6 g, 93%) with the exception that the deuterated diketone **27c** (1.9 g, 15 mmol) was used.

General Procedure for the Kinetic Studies. Disposable pipets, washed with 2% aqueous NH_3 solution and then oven-dried, were used for constructing the kinetic reaction vessels. The pipets were sealed at the thin end, and then approximately 1 in. from the opposite end, the pipet was constricted to a smaller diameter so that eventual sealing could be achieved more easily. The reaction solvent was spectral grade isooctane, which was further purified in the following manner. Ferric ammonium sulfate (6 g) was added to approximately 10 mL of distilled H_2O and 1 mL of concentrated sulfuric acid. This solution was transferred to a separatory funnel along with 250 mL of isooctane and the mixture thoroughly agitated. The aqueous layer was removed, and the isooctane was washed three times with distilled water and then dried over $MgSO_4$. The isooctane was then distilled from $LiAlH_4$.

A stock solution of the substrate (~100 mg sample in 10 mL of isooctane) was prepared. Aliquots (1 mL) were introduced into the pipet derived reaction ampules via syringe. These reaction vessels or ampules were flushed with argon, placed in dry ice, and sealed under vacuum. In several experiments, the kinetic reaction medium consisted of refluxing isooctane (98.8 ± 0.9 °C) from which aliquots were periodically removed by syringe and then analyzed. In one case, it was shown that the rate constant determined in this way was in good agreement (<±3%) with values obtained by the ampule method in constant temperature baths (see below).

The ampules were immersed in a constant temperature bath maintained at 98.40 ± 0.05 °C. Subsequent experiments for the determination of Arrhenius parameters employed the following temperatures: 88.51 ● 0.05, 77.52 ± 0.05, and 68.56 ± 0.05 °C. A small initial drop in temperature (~0.5 °C) of the bath was observed upon introduction of the samples, but approximately 2 min later, the bath equilibrated back to the original temperature. The first sample was withdrawn and designated t_0. Subsequent samples were withdrawn from the bath at various time intervals. Each vessel was opened, and the solution was filtered through a small glass frit while rinsing with ether. The solvent was removed by initial rotary evaporation under water aspirator pressure followed by high-vacuum drying on an oil pump.

The ^1H NMR spectrum (Jeol FX-200 spectrometer; $CDCl_3$ as solvent) was obtained for each sample. Proton resonances for starting material and product could be clearly seen in the olefinic region of the spectrum. Photocopies of the expanded ^1H NMR spectra of this region were integrated by the cut and weigh method. Each peak was cut out and weighed three times in order to obtain an average value. From these values, the fraction of starting material remaining could be calculated.

A plot of ln (fraction starting material) vs. time (in seconds) afforded a straight line with slope k representing the first-order rate constant for the reaction. A more detailed account of the kinetic measurements is presented in the supplementary material.

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Registry No. **1a**, 74483-09-3; **1b**, 102724-85-6; **3a**, 74483-13-9; **3b**, 102724-87-8; **4a**, 74483-10-6; **4b**, 102724-88-9; **5a**, 74483-11-7; **5b**, 102724-89-0; **6a**, 74483-12-8; **6b**, 102724-90-3; **7a**, 74398-26-8; **7b**, 102724-91-4; **10a**, 75154-93-7; **10b**, 102724-93-6; **11a**, 75154-94-8; **11b**, 102724-92-5; **12a**, 67670-78-4; **12b**, 102724-95-8; **13a**, 67632-48-8; **13b**, 102724-94-7; **14a**, 53954-32-8; **15a**, 67619-72-1;

24a, 102724-96-9; **24b**, 102724-97-0; **25b**, 102724-99-2; **26a**, 102724-98-1; **26b**, 102725-00-8; **27a**, 504-02-9; **27b**, 1193-55-1; **27c**, 71277-46-8; **28a**, 37457-15-1; **28b**, 102724-86-7; **29**, 10575-77-6; **30**, 74398-28-0; **31a**, 74398-27-9; iva, 75154-97-1; ivb, 75154-98-2; va, 75154-96-0; vb, 75154-95-9; via, 67672-93-9; vib, 67670-81-9; viia, 67619-73-2; viib, 67619-74-3.

Supplementary Material Available: Spectral and detailed kinetic analyses data (28 pages). Ordering information is given on any current masthead page.

Notes

Synthesis of Derivatives of the Novel Tricyclo[4.4.2.0^{1,5}]dodecane Skeleton

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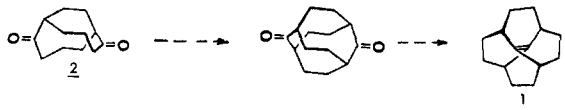
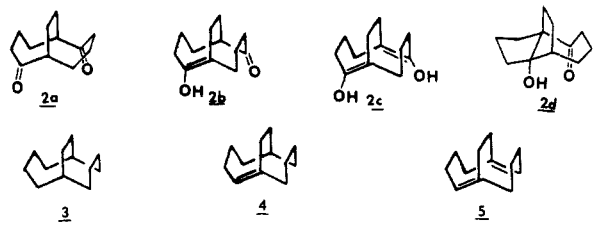
During experimental studies toward the synthesis of orthogonene (**1**)[1] we became interested in diketone **2** as a potential synthetic intermediate. **2** can exist in three



tautomeric forms **2a**, **2b**, and **2c**, which are related to the theoretically interesting hydrocarbons **3**–**5**. In 1981, we predicted that certain bridgehead olefins, termed hyperstable, can be stabilized relative to their parent alkanes by strain effects.[2] This prediction was based on the lower



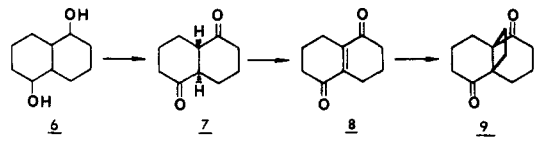
strain energy for the bridgehead olefin relative to the parent hydrocarbon as calculated by molecular mechanics methods (MM1). One of the systems studied was bicyclo[4.4.2]decane (**3**), which was predicted to be more strained by 13 kcal/mol than the corresponding bridgehead olefin. This prediction was confirmed by the synthesis of bicyclo[4.4.2]dodec-1-ene (**4**), which formed selectively upon hydrogenation of the *exo*-10-chlorobicyclo[4.4.2]-dodeca-1,4,7-triene.[3] The considerable reduction in the rate of hydrogenation of the bridgehead double bond to the parent hydrocarbon **3** as well as the lack of isomerization with potassium *tert*-butylate is the first experimental evidence for the predicted hyperstability of bridgehead double bonds.

In a molecular mechanics study (we used a modification of Allinger's MM2 program[4]) on compounds **2**–**5** (see Table I) the keto enol **2b** is predicted to be more stable and less strained than the desired diketone **2a**. **2b**, if existent, would represent the first nonconjugated aliphatic enol more stable than the corresponding ketone.

Table I

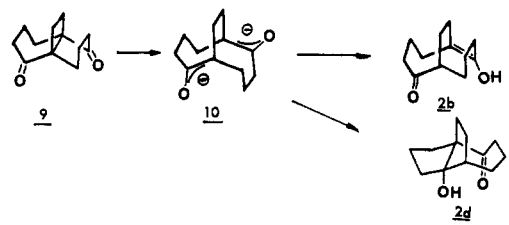
compd	dH_f, kcal/mol	strain energy, kcal/mol	olefinic strain[2]
2a	-81.95	30.80	
2b	-84.83	22.54	-8.26
2c	-69.43	24.32	-6.48
2d	-97.74	30.86	
3	-20.07	40.02	
4	-5.27	29.21	-10.79
5	16.73	25.61	-14.41
11a	-101.28	41.28	
11b	-94.81	37.25	
11c	-84.80	33.64	
11d	-108.84	30.52	

In our synthesis of **2** we followed the procedure of Peet and Cargill[5] with one exception: Jones oxidation of commercially available diol **6** to dione **7** by the biphase method described by Johnson[6] was found to give higher yields of the desired trans dione **7** (65%) than the method described by Kleinfelter.[7] Chlorination and elimination afforded



the enedione **8** in up to 70% yield. The purification of **8** by column chromatography was found to be crucial in order to achieve good yields in the photoaddition of ethylene.

In analogy to Alder's attempted synthesis of a hyperstable [4.4.4] diene system,[8] Grobtype fragmentation of **9** was attempted by dissolving metal reduction. This reaction, which presumably goes through the intermediate dianion (or radical-anion) **10**, can also lead to **2d** by an intramolecular aldol type reaction. Molecular mechanics



calculations (see Table I) predict **2d** to be more stable (lower heat of formation), although more strained than the expected keto enol **2b**. These energy differences are reasonable when we consider that a vinyl alcohol double bond

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