reaction. This latter observation requires a negative bond dissociation energy for the dimer cation radical[15] and, as such, invalidates the basic assumption of the kinetic argument. On the other hand, one need only make the reasonable assumption that the reorganization energy of the ammonia dimer cation radical is larger than that of quinuclidine, for the reorganization energy hypothesis to unify the ammonia and the quinuclidine dimer cation radical results in a single principle.

In summary, the previously anomalous behavior of amines toward group 15 dimer cation radical formation can now be explained by their uniquely planar monomer cation radical structures and the distortion energy required to form a nonplanar dimer cation radical.

**Acknowledgment.** We are grateful to S. F. Nelsen for a copy of his EPR simulation program and to J. A. Kampmeier for valuable discussions. Support was provided by the National Science Foundation (CHE86-10404), the Research Corporation, and the Camille and Henry Dreyfus Foundation for research and by the National Science Foundation for an instrumentation Grant (CHE78-03089).

(15) Dimer cation radicals with negative bond dissociation energies may still have activation barriers to dissociation. Guilhaus, M.; Brenton, A. G.; Beynon, J. H.; Rabrenović, M.; Schleyer, P. v. R. *J. Chem. Soc., Chem. Commun.* **1985**, 210.

## A Study of the [1,7]-Sigmatropic Shift of a 1-Hydroxylated 3-Desoxy Previtamin D to Vitamin D: Observation of a Modest Primary Deuterium Kinetic Isotope Effect[1]

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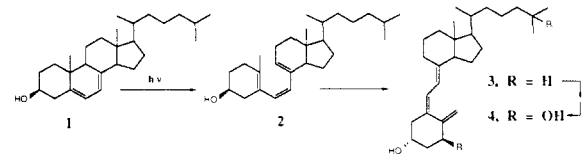
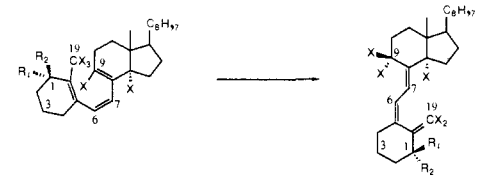
*Received September 3, 1987*

The primary metabolic pathway (Scheme I) leading to the active form of vitamin D, namely 1$\alpha$,25-dihydroxyvitamin $D_3$ (**4**),[2] formally incorporates two classical pericyclic processes. These include the photochemical electrocyclic ring opening of 7-dehydrocholesterol (**1**) to previtamin $D_3$ (**2**) and then the thermal transformation (a [1,7]-sigmatropic hydrogen shift) of previtamin $D_3$ to vitamin $D_3$ (**3**). The latter transformation in solution has been well studied.[3] In 1965, Akthar and Gibbons firmly established the pathway of the thermal transformation through studies using C-19 tritium-labeled materials.[4] In 1979, Mazur and co-workers synthesized 19,19-dideuteriovitamin $D_3$ and reported that the transformation of previtamin $D_3$ to vitamin $D_3$ occurs with an exceptionally large primary deuterium kinetic isotope effect ($k_H/k_D$) of ~45 at 80 °C.[5] Our interest in studies of

**Scheme I**




**Scheme II**



5a, $R_1$=OH; $R_2$=X=H
b, $R_1$=OH: $R_2$=H: X=D

6a, $R_1$=OH: $R_2$=X=H
b, $R_1$=OH; $R_2$=H; X=D

7a, $R_1$=H; $R_2$=OH; X=H
b, $R_1$=H; $R_2$=OH; X=D

8a, $R_1$=H; $R_2$=OH; X=D
b, $R_1$=H; $R_2$=OH; X=D

**Table I.** Summary of Kinetic Data for **5** and **7**

| substrate | $T$,[a] °C | $k^b \times 10^4$, $s^{-1}$ | $k_H/k_D$[c] |
|---|---|---|---|
| **5a** (1*S*-$d_0$) | 80.35 | 7.67 (±0.34) | 6.06 ± 0.02 |
| **5b** (1*S*-$d_5$) | 80.35 | 1.25 (±0.04) | |
| **7a** (1*R*-$d_0$) | 80.35 | 6.20 (±0.15) | 6.13 ± 0.21 |
| **7b** (1*R*-$d_5$) | 80.35 | 1.02 (±0.06) | |

[a] ±0.05 °C. [b] The errors are maximum errors (absolute deviations from the mean). [c] For the previtamin D to vitamin D transformation at 80.35 °C.

19,19,19-trideuteriated derivatives of previtamin $D_3$ and their various 1-hydroxylated counterparts stems from the possibility of utilizing previtamins as biochemical or chemical research tools. It was anticipated that a heavy isotope at C-19 would attenuate the rate of the [1,7]-sigmatropic shift so as to facilitate handling of the thermally unstable previtamins. Thus, in the case of 1$\alpha$,25-dihydroxyvitamin $D_3$ (**4**), its previtamin form might be anticipated to exist in nature, and its more stable 19,19,19-trideuterio counterpart would facilitate evaluation of its biological profile. Moreover, the latter might have practical application as a "slow release" source of the highly potent, and potentially toxic, natural hormone **4**. In this communication we describe our initial studies in this area through kinetic investigations of the isomerization of 3-deoxy-1-hydroxyprevitamin $D_3$ epimers **5** and **7** (Scheme II),[6] a [1,7]-sigmatropic shift model for the previtamin form of the natural hormone.

The synthesis of the previtamins used in this study is outlined in Scheme III. Grundmann's ketone **9a** (or **9b**; available by three cycles of base-catalyzed exchange of the acidic protons of **9a** with $NaOCH_3$, $CH_3OD$) was reacted with the monoanion of bis(trimethylsilyl)acetylene and subsequently benzoylated to give **10a** (or **10b**). Flash vacuum pyrolysis (FVP) of the benzoate **10a** (or **10b**) yielded the CD-ring fragment **11a** (or **11b**), which was coupled to A-ring fragment **12a** (or **12b**).[7] Subsequent Lindlar hydrogenation of the resulting **13a** (or **13b**) gave the previtamin ketone **14a** (or **14b**), which was reduced to the previtamins **5a** and **7a** (or **5b** and **7b**). The epimeric previtamins were separated and then stored at −80 °C.

Overall deuterium incorporation was measured at each stage by mass spectroscopy and was found to be >98% complete. Site specific deuterium incorporation was checked by $^1H$ NMR and proved to be complete within the limits of detection. The kinetic studies were performed in a manner previously described.[8] Stock

(1) This is paper 33 in the following series: "Studies of Vitamin D (Calciferol) and Its Analogues". For paper 32, see: Gibbs, R. A.; Okamura, W. H. *Tetrahedron Lett.*, in press.

(2) Norman, A. W. *Vitamin D, the Calcium Homeostatic Steroid Hormone*; Academic Press: New York, 1979.

(3) (a) Hanewald, K. H.; Rappoldt, M. P.; Roborgh, J. R. *Recl. Trav. Chim. Pays-Bas* **1961**, *80*, 1003. (b) Velluz, L.; Armiad, G.; Petit, A. *Bull. Soc. Chim. Fr.* **1949**, 501. (c) Verloop, A.; Koevoet, A. L.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1957**, *76*, 689. (d) Verloop, A. Ph.D. Thesis, State University Leiden, **1956**, p 44. (e) Legrand, M.; Mathieu, J. *Compt. Rend. Seances Acad. Sci.* **1957**, *245*, 2502. (f) Schlatmann, J. L. M. A.; Pot, J.; Havinga, E. *Recl. Trav. Chim. Pays-Bas* **1964**, *83*, 1173.

(4) (a) Akhtar, M.; Gibbons, C. J. *Tetrahedron Lett.* **1965**, 509. (b) Akhtar, M.; Gibbons, C. J. *J. Chem. Soc.* **1965**, 5964.

(5) Sheves, M.; Berman, E.; Mazur, Y.; Zaretskii, Z. V. I. *J. Am. Chem. Soc.* **1979**, *101*, 1882.

(6) See: Condran, P., Jr.; Hammond, M. L.; Mouriño, A.; Okamura, W. H. *J. Am. Chem. Soc.* **1980**, *102*, 6259 and references cited therein for earlier chemical and biochemical studies of 3-deoxy-1$\alpha$-hydroxyvitamin $D_3$ (**6a**).

(7) Barrack, S. A.; Okamura, W. H. *J. Org. Chem.* **1986**, *51*, 3201.

(8) Hoeger, C. A.; Johnston, A. D.; Okamura, W. H. *J. Am. Chem. Soc.* **1987**, *109*, 4690.

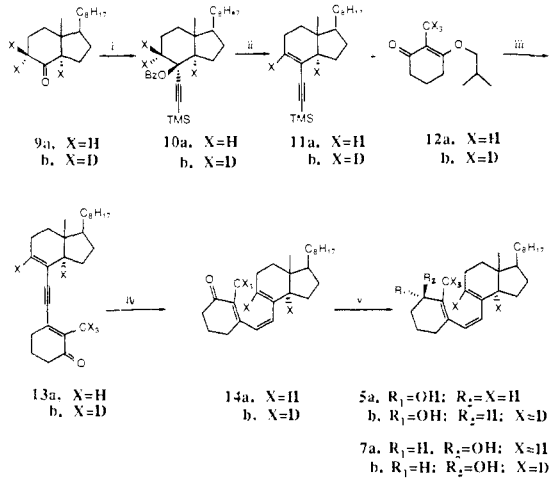
0002-7863/88/1510-0973$01.50/0 

Table II. Activation Parameters[a] for the Previtamin D → Vitamin D Transformation

| substrate | $E_A$[b] | log A[c] | $\Delta G^{\ddagger}$[b] | $\Delta H^{\ddagger}$[b] | $\Delta S^{\ddagger}$[d] |
|---|---|---|---|---|---|
| **5a** (1*S*) | 18.8 (±0.07) | 8.5 (±0.03) | 25.9 (±0.1) | 18.1 (±0.1) | -22.2 (±0.1) |
| **7a** (1*R*) | 19.1 (±0.5) | 8.6 (±0.2) | 26.1 (±0.7) | 18.4 (±0.5) | -21.7 (±0.6) |
| previtamin $D_3$[e] | 19.1 (±0.5) | 8.5 (±0.2) | 26.3 (±0.7) | 18.4 (±0.5) | -22.2 (±0.6) |

[a] At 80.0 °C. The rate constants were determined over the temperature range, 60.55-87.70 °C (±0.05 °C). [b] kcal/mol. [c] A in $s^{-1}$. [d] cal/mol K. [e] Data at 80.0 °C from ref 3a.

Scheme III[a]




[a] 1. TMS-CC-TMS/MeLi, LiBr, THF; 2. Benzoyl chloride (neat), -78 °C to RT, room temperature (**10a**, 91%; **10b**, 86%); (ii) FVP, quartz tube with quartz chips, 480 °C, $N_2$ flow, 5 mmHg vacuum (**11a**, 51%; **11b**, 40%); (iii) MeLi/LiBr/THF; **12**; $HOAc/H_2O$ (**13a**, 71%; **13b**, 79%); (iv) Lindlar catalyst, quinoline, benzene (**14a**, 89%; **14b**, 88%); (v) $NaBH_4$, $CeCl_3$, methanol (**5a**, 49%; **7a**, 33%; **5b**, 36%; **7b**, 28%).

solutions of the previtamins in isooctane ($10^{-3}$ molar) were prepared, and aliquots were introduced into capillary reaction vessels, which were then sealed and stored at -80 °C. No detectable isomerization or decomposition of previtamin was noticed for samples handled in this manner. For the kinetic measurements, each sample during heating was removed at appropriate time intervals and was immediately cooled to -80 °C and later analyzed by analytical HPLC (10% ethyl acetate in hexanes, Waters Radial-Pak; calibrated silica cartridge column, UV detection at 254 nm). Peak areas were integrated by using the cut and weigh method. The weights obtained were transformed into concentrations by using the measured extinction coefficient at 254 nm for each of the species: **5a** or **5b**, $\epsilon$ = 8900; **6a** or **6b**, $\epsilon$ = 16 300; **7a** or **7b**, $\epsilon$ = 8200; **8a** or **8b**, $\epsilon$ = 16 800. A plot of ln [fraction of starting material remaining] versus time [s] (followed to a low 20-30% conversion) afforded a straight line with slope $-k$ representing the first-order rate constant. In one study, the product composition determined by $^1H$ NMR integration (C-18 angular methyl group) proved identical (within ± 3%) with that determined by the HPLC integration method.

The kinetic isotope effect data and activation parameters for **5** and **7** are summarized in Tables I and II, respectively. The activation parameters for **5a** and **7a**, both of which bear $C_1$-OH groups, are very similar to those previously reported for isomerization of the parent previtamin $D_3$, which bears a $C_3$-OH group. However, the isomerization of **5** and **7** to their corresponding vitamin D forms occurs with a primary kinetic isotope effect, $k_H/k_D$, of ~6, nearly an order of magnitude smaller than that reported for previtamin $D_3$. The $k_H/k_D$ value of ~6 (80 °C) reported in this study is thus not particularly unusual in magnitude and only modestly larger than the values 2.6-4.0 (at 98.6 °C) recently reported by this laboratory for a [1,7]-sigmatropic shift in a different heptatriene system.[8] The parent previtamin $D_3$ isomerization (**2** → **3**) for which the large $k_H/k_D$ of ~45 was reported clearly needs to be reevaluated.[9]

**Acknowledgment.** This study was supported by NIH Grant DK-16595. Dr. Menso Rappoldt of Duphar, B.V. (Weesp, The Netherlands), generously provided starting materials. K.J.M. acknowledges receipt of a President's and N. T. Coleman undergraduate research awards. We are especially grateful to H. Y. Elnagar, Dr. G.-Y. Shen, and Dr. A. Palenzuela of this laboratory for valuable input.

(9) During the review of this manuscript, Professors Y. Mazur and M. Sheves have kindly informed us that the $k_H$ value ($1.2 \times 10^{-3}$ $s^{-1}$ at 80 °C) utilized in their computation of $k_H/k_D$ (ref 5) is in error. We believe the $k_H$ value reported in ref 3a would have been more appropriate.

## Dissociative versus Molecular Chemisorption of Nitric Oxide on Small Bare Cationic Cobalt Clusters in the Gas Phase

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The surface chemistry of nitric oxide (NO) has been the focus of intense study due, in part, to its importance in environmental concerns.[1] These investigations have emphasized the characterization of the molecular structure of NO on surfaces,[2] dynamics of dissociation,[3] factors (substrate geometry, presence of other adsorbates, temperature, etc.) affecting dissociation or activation,[4] and reaction with other adsorbates.[5] Of relevance to these studies is the investigation of small metal cluster ions in the gas phase.[6] Techniques have been developed that allow both the size of the cluster and the presence of adatoms or molecules to be controlled and their effects on reactivity monitored. As an example we recently reported that $Co_2NO^+$ undergoes oxide transfer to CO, process 1, whereas $Co_2(CO)NO^+$, $Co_3NO^+$, and $Co_4NO^+$ are unreactive with CO.[7]

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(1) See, for example: (a) Kummer, J. T. *J. Phys. Chem.* **1986**, *90*, 4747. Egelhoff, W. F., Jr. *The Chemical Physics of Solid Surfaces and Heterogeneous Catalysis*; Kind, D. A., Woodruff, D. P., Eds.; Elsevier: Amsterdam, 1982; Vol. IV, p 397.

(2) (a) Sung, S.-S.; Hoffmann, R.; Thiel, P. A. *J. Phys. Chem.* **1986**, *90*, 1380 and references cited therein. (b) Root, T. W.; Fischer, G. B.; Schmidt, L. D. *J. Chem. Phys.* **1986**, *85*, 4687. (c) Conrad, N.; Scala, R.; Stenzel, W.; Unwin, R. *Surf. Sci.* **1984**, *145*, 1.

(3) (a) Villarrubia, J. S.; Ho, W. *J. Chem. Phys.* **1987**, *87*, 750. (b) Villarrubia, J. S.; Richter, L. J.; Gurney, B. A.; Ho, W. *J. Vac. Sci. Technol. A* **1986**, *4*, 1487. (c) Thiel, P. A.; Weinberg, W. H.; Yates, J. T., Jr. *Chem. Phys. Lett.* **1979**, *67*, 403.

(4) (a) Broden, G.; Rhodin, T. N.; Brucker, C. *Surf. Sci.* **1976**, *59*, 593 and references cited therein. (b) Mason, R.; Roberts, M. W. *Inorg. Chem. Acta.* **1981**, *50*, 53.

(5) (a) Lesley, M. W.; Schmidt, L. D. *Surf. Sci.* **1985**, *155*, 215. (b) Dubois, L. H.; Hansma, P. K.; Somorjai, G. A. *J. Catal.* **1980**, *65*, 318. (c) Roberts, M. W.; Au, C. T. *Proc. R. Soc. London A* **1984**, 396.

(6) (a) Alford, J. M.; Weiss, F. D.; Laaksonen, R. T.; Smalley, R. E. *J. Phys. Chem.* **1986**, *90*, 4480. (b) Jacobson, D. B.; Freiser, B. S. *J. Am. Chem. Soc.* **1984**, *106*, 5351. (c) Freas, R. B.; Campana, J. E. *J. Am. Chem. Soc.* **1986**, *108*, 4660.

0002-7863/88/1510-0974$01.50/0 