the equilibrium concentration of CH_2=$CHCH_2SR$ was of about the same magnitude as the estimated uncertainty in measuring the concentrations;[9] furthermore, steric effects should be smaller with SR than with SOR, SO_2R, or OR. In the series n-C_nH_{2n+1} > i-Pr ≈ t-Bu it is again not clear that the observed differences are significant, and it is a series in which steric crowding of the CH_2 group in XCH_2CH=CHY should be less than with OBu-t, SO_2Bu-t, etc. groups. Steric hindrance can decrease resonance interactions with the double bond, as in the first part of the series 2-naphthyl > 1-naphthyl ≈ 9-anthryl, but when there is too much hindrance, this resonance effect is counteracted, presumably by crowding the CH_2 group, as in the last part of the series.

Notes

The Periodination Reaction: Fast One-Step Synthesis of C_6I_6 from C_6H_6

L. S. Levitt* and R. Iglesias

Chemistry Department, College of Science, University of Texas at El Paso, El Paso, Texas 79968

Received April 22, 1981

In an attempt to prepare the unknown compound, periodyl benzene ($PhIO_3$), benzene was added dropwise over a period of around 15 min to a 1.0 M solution of H_5IO_6 in concentrated H_2SO_4 in an open beaker at 0–5 °C, whereupon the colorless solution turns green,[1] then red, and finally light yellow, as a yellow-tan precipitate gradually forms, which, after recrystallization from Me_2SO, is insoluble in all common solvents except Me_2SO and MeCN: mp ~260 °C with decomposition, giving off I_2; elemental analysis, 8.5% C and 91.5% I; $M_r \gtrsim 800$ by freezing point depression of camphor; mass spectrum parent peak at 834 ($C_6I_6^{+\cdot}$) and M − 1 at 707 ($C_6I_5^{+\cdot}$); proton NMR, no resonance absorption; burns with an aromatic sooty flame along with dense purple fumes of I_2, from all of which evidence one would rightly conclude that the compound prepared here is C_6I_6,[2] and, on the basis of the quantity of benzene used, the yield is 48% peridobenzene.

Registry No. H_5IO_6, 10450-60-9; C_6I_6, 608-74-2; $PhIO_3$, 82891-66-5; benzene, 71-43-2.

(1) The green intermediate first formed (presumably $PhIO_3$), and the red one, should be further investigated, as well as the generality of the periodination of aromatics. The authors invite any investigator interested in this unusual reaction, which might be of use in deuterating aromatic compounds, to pursue this research.

(2) The stoichiometric equation used to calculate yield is $2C_6H_6 + 3IO_4^- + 9I^- + 12H_3O^+ \rightarrow 2C_6I_6 + 24H_2O$, the I^- indicating that some of the benzene is oxidized, presumably to CO_2.

Stereoselective Synthesis of (23*S*,25*R*)-23,25,26-Trihydroxyvitamin D_3 and (23*S*,25*R*)-25-Hydroxyvitamin D_3 26,23-Lactol, Presumed Vitamin D_3 Metabolites

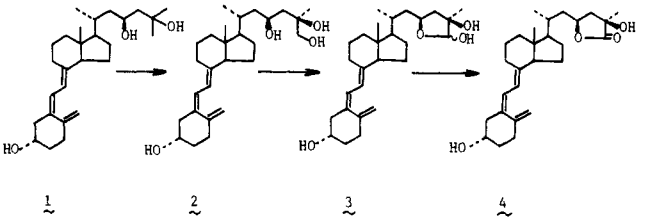
Sachiko Yamada, Keiko Nakayama, and Hiroaki Takayama*

Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199-01, Japan

Received May 7, 1982

Calcidiol lactone, 25-hydroxyvitamin D_3 26,23-lactone (**4**),[1] is a unique metabolite of vitamin D_3 which exhibits a weak activity in intestinal calcium transport and bone calcium mobilization but shows the most potent activity[2] toward vitamin D binding protein in blood plasma of all known vitamin D metabolites. These characteristics have suggested that the metabolite may have an important role in other aspects of vitamin D action. As one of our projects on the stereoselective synthesis of vitamin D metabolites using chiral templates,[3] we have synthesized (23*R*,25*S*)-[4] and (23*S*,25*R*)-calcidiol lactones[5] stereoselectively and for the first time determined the stereochemistry of the natural metabolite[5] to be *S* at C-23 and *R* at C-25. Recently a new metabolite, (23*S*)-23,25-dihydroxyvitamin D_3 (**1**),[6] has been isolated and has been shown to be a biosynthetic precursor of calcidiol lactone (**4**).[7] It can be assumed that biological transformation of 23,25-dihydroxyvitamin D_3 (**1**) to the lactone (**4**) may proceed via 23,25,26-trihydroxyvitamin D_3 (**2**) through 25-hydroxyvitamin D_3 26,23-lactol (**3**; Scheme I) and that these postulated biosynthetic intermediates have the same stereochemical configuration at C-23 and C-25 as those of calcidiol lactone (**4**). So we planned the stereoselective synthesis of these two presumed vitamin D_3 metabolites.

Scheme I. Presumed Metabolic Pathway of (23*S*)-23,25-Dihydroxyvitamin D_3 (**1**) to Calcidiol Lactone (**4**)



1 **2** **3** **4**

In this paper we report the stereoselective synthesis of (23*S*,25*R*)-23,25,26-trihydroxyvitamin D_3 (**2**) and (23*S*,25*R*)-25-hydroxyvitamin D_3 26,23-lactol (**3**). Both compounds have been demonstrated to be converted to

(1) Wichmann, J. K.; DeLuca, H. F.; Schnoes, H. K.; Horst, R. L.; Shepard, R. M.; Jorgensen, N A. *Biochemistry* **1979**, *18*, 4775.

(2) (a) Tanaka, Y.; Wichmann, J. K.; Paaren, H. E.; Schnoes, H. K.; DeLuca, H. F. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 6411. (b) Horst, R. L. *Biochem. Biophys. Res. Commun.* **1979**, *89*, 286.

(3) Takayama, H.; Ohmori, M.; Yamada, S. *Tetrahedron Lett.* **1980**, *21*, 5027.

(4) Yamada, S.; Nakayama, K.; Takayama, H. *Tetrahedron Lett.* **1981**, *22*, 2591.

(5) Yamada, S.; Nakayama, K.; Takayama, H. *Chem. Pharm. Bull.* **1981**, *29*, 2393.

(6) Tanaka, Y.; Wichmann, J. K.; Schnoes, H. K.; DeLuca, H. F. *Biochemistry* **1981**, *20*, 3895.

(7) Tanaka, Y.; DeLuca, H. F.; Schnoes, H. K.; Ikekawa, N.; Eguchi, T. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 4805.

0022-3263/82/1947-4770$01.25/0