Preparation of the starting material (1) begins with the corresponding bromide, RR'CHBr. Reaction of the Grignard reagent, RR'CHMgBr, with phenyl disulfide[7] followed by oxidation of the resulting phenyl thioether with *t*-BuOOH in the presence of a catalytic amount of $Mo(CO)_6$[8] provides the desired sulfone, generally in excellent overall yield.

By taking advantage of the fact that one oxygen atom of BTSP becomes the carbonyl oxygen of the product, it is possible to label an oxygen at a specific position in situ if the appropriate sulfone is used. Following the procedure reported by Davies et al.,[4] $H_2{}^{18}O_2$[9] was converted to $Me_3Si^{18}O^{18}OSiMe_3$, which was used directly for oxidative desulfonylation without further purification.[10] Thus, benzyl phenyl sulfone and cyclohexyl phenyl sulfone were converted to benzaldehyde-^{18}O and cyclohexanone-^{18}O, respectively. The labeled products were purified by Kugelrohr distillation. Their IR and mass spectra are identical with those of samples prepared by ^{18}O exchange of benzaldehyde and cyclohexanone with ^{18}O-enriched water under acidic conditions.

A typical procedure for the conversion of sulfones to unlabeled aldehydes or ketones is as follows. A THF solution (4.4 mL) of benzyl phenyl sulfone (0.501 g) was placed in a dried reaction flask under a nitrogen atmosphere and cooled to −78 °C. After *n*-BuLi (1.00 mL, 2.6 M in hexane) was injected into the reaction vessel, the bright yellow solution was stirred for 15 min. Neat BTSP (0.465 g) was added and the color changed to reddish brown. After the solution was stirred at room temperature overnight, it was poured into ice-cold, saturated aqueous $NaHCO_3$ solution and extracted twice with fresh ether. The combined organic extracts were dried ($MgSO_4$) and condensed under reduced pressure. The residue was chromatographed on a silica gel column, eluting with 20% EtOAc/hexanes, to provide pure benzaldehyde (0.208 g, 91%).[12]

Acknowledgment. This project was supported in part by BRSG Grant SO7 RR7041, awarded by the Biomedical Research Support Grant Program, Division of Research Resource, National Institutes of Health. We are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. We also thank R. Gibbs for his assistance with preliminary studies.

Registry No. 1 (R = H; R¹ = *n*-C_5H_{11}), 16823-63-5; 1 (R = C_2H_5; R¹ = *n*-C_5H_{11}), 87413-31-8; 1 (R = R¹ = CH=CH·$(CH_2)_3$), 87413-32-9; 1 (R = H; R¹ = Ph), 3112-88-7; 1 (R = C_2H_5; R¹ = Ph), 87413-33-0; 1 (R = R¹ = $(CH_2)_5$), 6947-57-5; 1 (R = R¹ = $(CH_2)_4$), 14633-46-6; 2 (R = H; R¹ = *n*-C_5H_{11}), 66-25-1; 2 (R = C_2H_5; R¹ = *n*-C_5H_{11}), 106-68-3; 2 (R = R¹ = CH=CH·$(CH_2)_3$), 930-68-7; 2 (R = H; R¹ = Ph), 100-52-7; 2 (R = C_2H_5; R¹ = Ph), 93-55-0; 2 (R = R¹ = $(CH_2)_5$), 108-94-1; 2 (R = R¹ = $(CH_2)_4$), 120-92-3; BTSP, 5796-98-5; $Me_3Si^{18}O^{18}OSiMe_3$, 87413-34-1; benzaldehyde-^{18}O, 55076-26-1; cyclohexanone-^{18}O, 73007-69-9; 1-bromohexane, 111-25-1; 3-bromooctane, 999-64-4; 3-bromocyclohexene, 1521-51-3; benzyl bromide, 100-39-0; α-ethylbenzyl bromide, 2114-36-5; cyclohexyl bromide, 108-85-0; cyclopentyl bromide, 137-43-9; phenyl disulfide, 882-33-7.

Jih Ru Hwu
Department of Chemistry
The Johns Hopkins University
Baltimore, Maryland 21218
Received August 12, 1983

(7) Wiegand, G. H.; Petersen, J. R.; Yu, S.-L. *Int. J. Sulfur Chem., Part A* **1972**, *2*, 295.
(8) Seree de Roch, I.; Menguy, P. Fr. Pat 1 540 284 (Cl. C 07C), 1968, (Appl. Dec 7, 1966), 4 pp. See also: *Chem. Abstr.* **1969**, *71*, 80944*q*.
(9) Sawaki, Y.; Foote, C. S. *J. Am. Chem. Soc.* **1979**, *101*, 6292.
(10) A method for the preparation of $Me_3Si^{18}O^{18}OSiMe_3$ combining the procedures reported by Davies[4] and Foote[9] has been successful only on a small scale in this laboratory. Although a comparison of the rates of decomposition of BTSP and $Me_3CO_2CMe_3$ showed that the silicon compound was more stable than the hydrocarbon at 150 °C (see: Pike, R. A.; Schaffer, L. H. *Chem. Ind. (London)* **1957**, 1294), attempts to purify $Me_3Si^{18}O^{18}OSiMe_3$ by distillation at temperatures up to 80 °C under vacuum gave a siloxane as a rearrangement product.[11]
(11) Yablokov, V. A. *Russ. Chem. Rev. (Engl. Transl.)* **1980**, *49*, 833.
(12) Idenfified by chromatographic as well as IR, NMR, and mass spectral comparison with an authentic specimen.

Total Synthesis of 1α,25(*R*)-Dihydroxy Vitamin D_3 26,23(*S*)-Lactone (Calcitriol Lactone), a Natural Metabolite of Vitamin D_3

Summary: The total synthesis of 1α,25(*R*)-dihydroxy vitamin D_3 26,23(*S*)-lactone (calcitriol lactone) and the 23*R*,25*S* diastereomer via a convergent approach utilizing an ene reaction for C20 and C23 functionalization and the HPLC comparison to the natural metabolite are described.

Sir: The isolation and characterization of a new vitamin D_3 metabolite, termed 1α,25(*R*)-dihydroxy vitamin D_3 26,23(*S*)-lactone (calcitriol lactone, **1a**), has been reported recently.[1,2] Due to the importance of the vitamin D_3 dependent endocrine system in humans and animals[3] and the unknown biological function of this new metabolite, we were interested in obtaining sufficient material for structure verification and biological evaluation. While several partial syntheses of the related metabolite 25-(*R*)-hydroxy vitamin D_3 26,23(*S*)-lactone (calcidiol lactone, **1b**) have been reported[4] and could potentially be used to form **1a**, we have applied our recently published total synthesis in the preparation of this metabolite.[5] With this, we extend the generality of the convergent total synthetic approach to 1α-hydroxy vitamin D_3 metabolites[5] as well as further explore the introduction of steroidal side-chain functionality via the ene reaction.[5,6] At the time we embarked on this project, the C23, 25 configurations of **1a**

(1) Ohnuma, N.; Bannai, K.; Yamaguchi, H.; Hashimoto, Y.; Norman, A. W. *Arch. Biochem. Biophys.* **1980**, *204*, 387. Tanaka, Y.; Wichmann, J. K.; Paaren, H. E.; Schnoes, H. K.; DeLuca, H. F. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 6411.
(2) While this work was in progress, the enzymatic 1α-hydroxylation of 25(*S*)-hydroxy vitamin D_3 26,23(*S*)-lactone and 25(*R*)-hydroxy vitamin D_3 26,23(*S*)-lactone and an HPLC comparison to the natural 1α,25-dihydroxy vitamin D_3-lactone was reported. Ishizuka, S.; Yamaguchi, H.; Yamada, S.; Nakayama, K.; Takayama, H. *FEBS Lett.* **1981**, *134*, 207.
(3) For reviews, see: (a) Norman, A. W. "Vitamin D, Molecular Biology and Clinical Nutrition"; Marcel Dekker: New York, 1980. (b) DeLuca, H. F.; Paaren, H. E.; Schnoes, H. K. *Annu. Rep. Med. Chem.* **1980**, *15*, 288. (c) Norman, A. W. "Vitamin D, The Calcium Homeostatic Steroid Hormone"; Academic Press: New York, 1979. (d) DeLuca, H. F.; Paaren, H. G.; Schnoes, H. K. *Top. Curr. Chem.* **1979**, *83*, 1.
(4) (a) Wichmann, J. F.; Paaren, H. E.; Fivizzani, M. A.; Schnoes, H. K.; DeLuca, H. F. *Tetrahedron Lett.* **1980**, *21*, 4667. (b) Ikekawa, N.; Hirano, Y.; Ishiguro, M.; Oshida, J.; Eguchi, T.; Miyasaka, S. *Chem. Pharm. Bull.* **1980**, *28*, 2852. (c) Yamada, S.; Nakayama, K.; Takayama, H. *Tetrahedron Lett.* **1981**, *22*, 2591. (d) Morris, D. S.; Williams, D. H.; Norris, A. F. *J. Chem. Soc., Chem. Commun.* **1981**, 424. (e) Morris, D. S.; Williams, D. H. Norris, A. F. *J.Org. Chem.* **1981**, *46*, 3422. (f) Eguchi, T.; Takatsuto, S.; Hirano, Y.; Ishiguro, M.; Ikekawa, N. *Heterocycles* **1982**, *17*, 359. Yamada, S.; Nakayama, K.; Takayama, H. *J. Org. Chem.* **1982**, *47*, 4770.
(5) Baggiolini, E. G.; Iacobelli, J. A.; Hennessy, B. M.; Uskokovič, M. R. *J. Am. Chem. Soc.* **1982**, *104*, 2945.
(6) (a) Batcho, A. D.; Berger, D. E.; Davoust, S. G.; Wovkulich, P. M.; Uskokovič, M. R. *Helv. Chim. Acta* **1981**, *64*, 1682. For related systems, see: (b) Dauben, W. G.; Brookhart, T. J. *J. Am. Chem. Soc.* **1981**, *103*, 237. (c) Batcho, A. D.; Berger, D. E.; Uskokovič, M. R.; Snider, B. B. *Ibid.* **1981**, *103*, 1293.

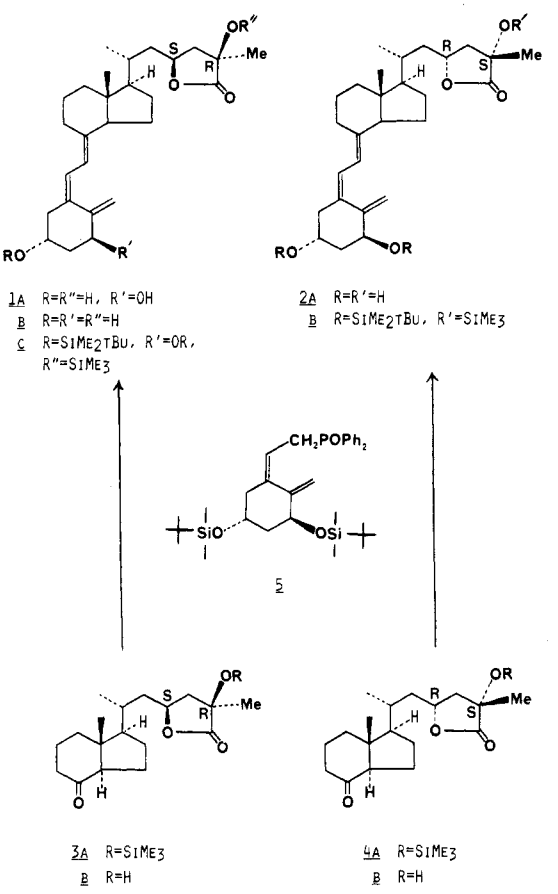
0022-3263/83/1948-4433$01.50/0

and **1b** were not known although the number of possibilities for **1b** had been reduced to two (23*S*,25*R* or 23*R*,25*S*) by NMR correlations.[4a,e] On the assumption that the 1α-hydroxylated metabolite would bear the same C23,25 configuration, we concentrated our attention on the preparation of the 23(*S*),25(*R*)-lactone **1a** and the 23(*R*),25(*S*)-lactone **2a**.[7]

Our synthetic strategy centered on the coupling of ketones **3a** and **4a** with the lithium anion derived from the phosphine oxide **5**[5] (Scheme I). One particular virtue of this convergent approach is the avoidance of the more traditional, usually low yielding, introduction and photolytic–thermal rearrangement of a steroidal 5,7-diene system *after* the construction of the side-chain functionality.

For the preparation of ketones **3a** and **4a**, the ene reaction was enlisted to generate the functionality and stereochemistry at C20 and C23. Exposure of olefin **6**[5,8] to methyl α-bromoacrylate[9] in the presence of ethylaluminum dichloride (CH_2Cl_2, 0 °C → room temperature, 25 h) produced a 13:87 mixture of 20*R*,23*R* and 20*R*,23*S* bromo esters **7** and **8** in 77% yield (Scheme II).[10,11] For the initial synthesis of **3a**, equilibration was selected to produce working amounts of the minor isomer **7**. The C23 equilibration of **8** with lithium bromide (acetone, room temperature) cleanly produced a 1:1 mixture of **7** and **8**, which were separated by silica gel chromatography (hexane/ethyl acetate, 7:1). In this manner, **7** was obtained in 63% overall yield from olefin **6** after four cycles through the equilibration–separation protocol. Reduction of **7** with diisobutylaluminum hydride (THF, 0 °C → room temperature) gave bromo diol **9**[10] (91%), which on treatment with base (KO-*t*-Bu, *t*-BuOH, room temperature) led to the formation of the unsaturated 23*S* epoxide **10**[10] in 84% yield. Hydrogenation of **10** over 5% platinum on carbon in ethyl acetate produced exclusively **11a**[10] with the natural configuration at C17 (72%), which was then converted to the trimethylsilyl ether **11b** with (trimethylsilyl)imidazole

Scheme I



(EtOAc, room temperature, 99%). The remaining three carbons were introduced by the reaction of **11b** with the lithio anion of the ethoxyethyl-protected cyanohydrin of acetaldehyde[12] (THF, −78 °C → room temperature) followed successively by a basic and then acidic workup, which produced a ca. 1:1 mixture of 23*S*,25*R* and 23*S*,25*S* hydroxyl lactones **12a** and **12b** in 60% yield.[10,13] The intermediate **12a** was converted to the required *CD*-ring synthon **3a** by oxidation with 2,2′-bipyridinium chlorochromate (CH_2Cl_2) followed by silylation with (trimethylsilyl)imidazole (90% from **12a**).

In similar fashion, the diisobutylaluminum hydride reduction of **8** produced **13**, which in turn was treated with base (KO-*t*-Bu, *t*-BuOH) to generate epoxide **14** in good overall yield. Hydrogenation (H_2, EtOAc, 5% Pt/C) produced **15a**. The trimethylsilyl ether **15b** gave, on exposure to the ethoxyethyl-protected cyanohydrin anion and workup, 23*R*,25*S* and 23*R*,25*R* hydroxy lactones **16a** and **16b** as a 60:40 mixture. Oxidation and silylation of **16a** yielded **4a**.

(7) For the purpose of discussion, the steroid numbering system is used here.

(8) The fact that this olefin was 95% isomerically pure by GC was of little consequence since, as noted previously,[5,6c] the contaminating *E* isomer reacts substantially slower.

(9) We elected to use the bromoacrylate rather than the chloroacrylate because of its convenient preparation in quantity from methyl acrylate by a modified bromination–dehydrobromination sequence.

(10) Satisfactory combusion analysis as well as IR, NMR, and mass spectral properties were observed. Some proton NMR ($CDCl_3$ except as noted) data are as follows: **1a** (CD_3OD) δ 0.61 (s, 3 H), 1.02 (d, J = 6 Hz, 3 H), 1.45 (s, 3 H), 4.13 (m, 1 H), 4.36 (m, 1 H), 4.52 (m, 1 H), 4.90 (br s, 1 H), 5.31 (br s, 1 H), 6.10 (d, J = 11.5 Hz, 1 H), 6.45 (d, J = 11.5 Hz, 1 H); **2a** δ 0.57 (s, 3 H), 1.01 (d, J = 6 Hz, 3 H), 1.50 (s, 3 H), 4.26 (m, 1 H), 4.48 (m, 2 H), 5.01 (br s, 1 H), 5.33 (br s, 1 H), 6.03 (d, J = 11.5 Hz, 1 H), 6.38 (d, J = 11.5 Hz, 1 H); **7** δ 0.81 (s, 3 H), 1.04 (d, J = 6 Hz, 3 H), 2.04 (s, 3 H), 3.78 (s, 3 H), 4.25 (t, J = 6 Hz, 1 H), 4.98 (dt, J = 4, 11, Hz, 1 H), 5.36 (m, 1 H); **8** δ 0.90 (s, 3 H), 1.08 (d, J = 7 Hz, 3 H), 2.04 (s, 3 H), 3.78 (s, 3 H), 4.22 (dd, J = 5, 10 Hz, 1 H), 4.97 (dt, J = 5, 11 Hz, 1 H), 5.32 (m, 1 H); **9** δ 0.80 (s, 3 H), 1.02 (d, J = 6 Hz, 3 H), 3.80 (m, 3 H), 4.20 (m, 1 H), 5.37 (m, 1 H); **10** δ 0.82 (s, 3 H), 1.10 (d, J = 7 Hz, 3 H), 2.49 (dd, J = 3,5 Hz, 1 H), 2.75 (dd, J = 5, 5.5 Hz, 1 H), 2.93 (m, 1 H), 3.83 (dt, J = 5, 11 Hz, 1 H), 5.39 (m, 1); **11a** δ 0.70 (s, 3 H), 1.07 (d, J = 6 Hz, 3 H), 2.39 (dd, J = 2.5, 5.5 Hz, 1 H), 2.72 (dd, J = 5, 5.5 Hz, 1 H), 2.91 (m, 1 H), 3.58 (dt, J = 5, 10 Hz, 1 H); **12a** δ 0.69 (s, 3 H), 0.98 (d, J = 6 Hz, 3 H), 2.37 (dd, J = 5, 13 Hz, 1 H), 3.59 (m, 1 H), 4.40 (m, 1 H); **12b** δ 0.69 (s, 3 H), 1.02 (d, J = 6 Hz, 3 H), 2.47 (dd, J = 5, 15 Hz, 1 H), 3.61 (m, 1 H), 4.74 (m, 1 H). Ms data: m/e (relative intensity) (%) **1a** 444 (10), 426 (26), 408 (17), 269 (10), 251 (20), 197 (17), 157 (27), 152 (34), 135 (42), 134 (100); **2a** 444 (14), 426 (24), 408 (20), 269 (11), 251 (26), 197 (23), 157 (36), 152 (41), 135 (49), 134 (100). $[\alpha]^{25}_D$ (EtOH) **1a** +24.66° (0.73); **2a** +17.91° (0.24).

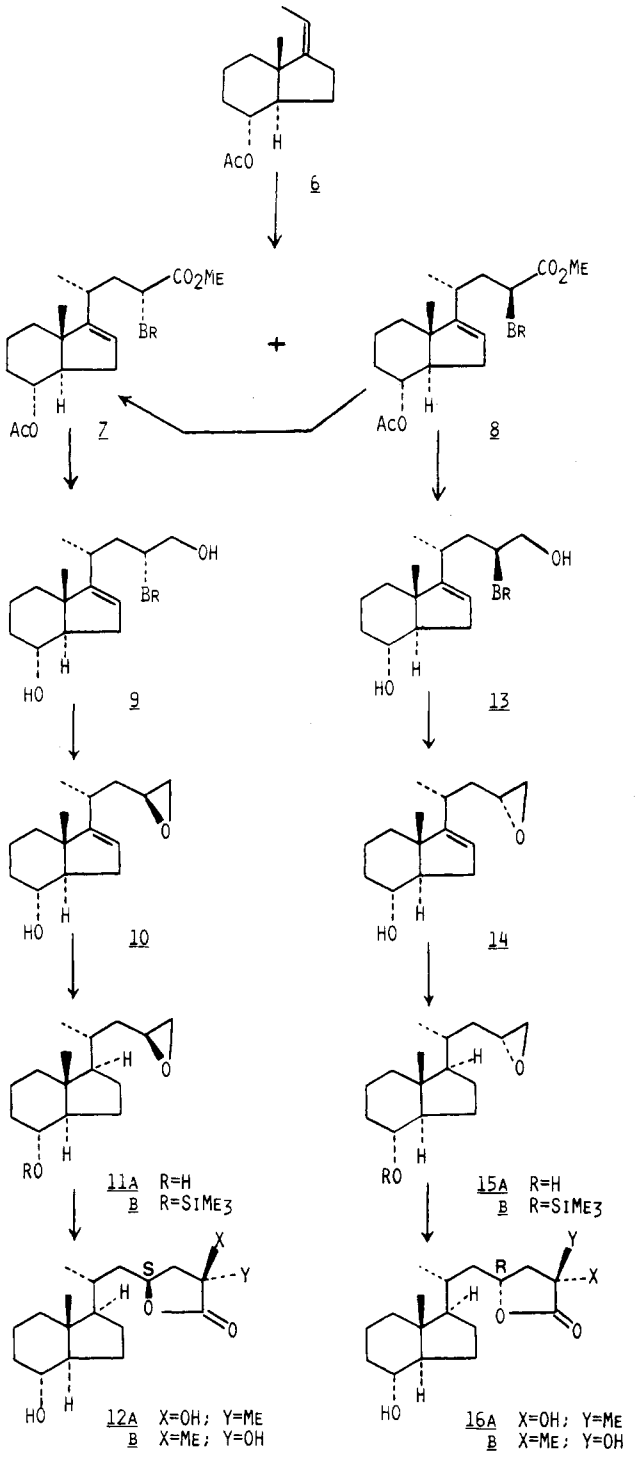
(11) The configuration at C26[6] of **7** and **8** was deduced by correlation with the cholesterol analogues in which the proton at C23 appears as triplet (J = 6 Hz) at δ 4.23 for the *R* isomer and as a doublet of doublets (J = 5, 10 Hz) at δ 4.26 for the *S* isomer. A similar trend was also observed in the chloro esters. This was affirmed by conversion of **8** to **16b**, the structure of which was determined by an X-ray crystallographic analysis.

(12) Stork, G.; Maldonado, L *J. Am. Chem. Soc.* **1971**, *93*, 5286. This reaction was carried out by addition of the epoxide to a cooled (−78 °C) solution of the anion. The cooling bath was removed and the reaction stirred at room temperature until starting material was consumed. A few milliliters of water was then added and the mixture refluxed 30 min. An excess of 1.3 M tartaric acid solution was added and the mixture refluxed an additional 45 min. The crude product obtained by extractive workup was treated with toluenesulfonic acid in methanol to remove protecting groups. The isomers were separated by silica gel chromatography, eluting with hexane/ethyl acetate (1:1).

(13) The configuration at C25[6] are assigned on the basis of ^{1}H NMR signal for the C23[6] proton as commented on previously by Williams et al.[4e] The trend was also observed for **16a** and **16b**. In the cholesterol series, this trend appears to be unperturbed by derivatization of the C25 hydroxyl moiety where we have obtained an X-ray crystallographic analysis for three of the four possible C23,C25 isomers.[14]

(14) Wovkulich, P. M.; Williams, A.; Barcelos, F., unpublished results.

Scheme II



The Wittig–Horner coupling reaction of **3a** with the lithium anion of **5**[5] proceeded smoothly at −78 °C in THF to give **1c** in 90% yield. Removal of the silyl protecting groups was accomplished by exposure to methanol and an ion exchange resin (AG 50W-X4, 200–400 mesh, H^+ form, Bio-Rad Laboratories) to give quantitatively the desired metabolite **1a**. In like fashion, the 1α,25(*S*)-dihydroxy vitamin D_3 26,23(*R*)-lactone (**2a**) was prepared from ketone **4a**.

The HPLC comparisons of the natural metabolite[15] to the 23*S*,25*R* and 23*R*,25*S* synthetic hydroxy lactones as

(15) Isolated according to the procedure described in ref 1.

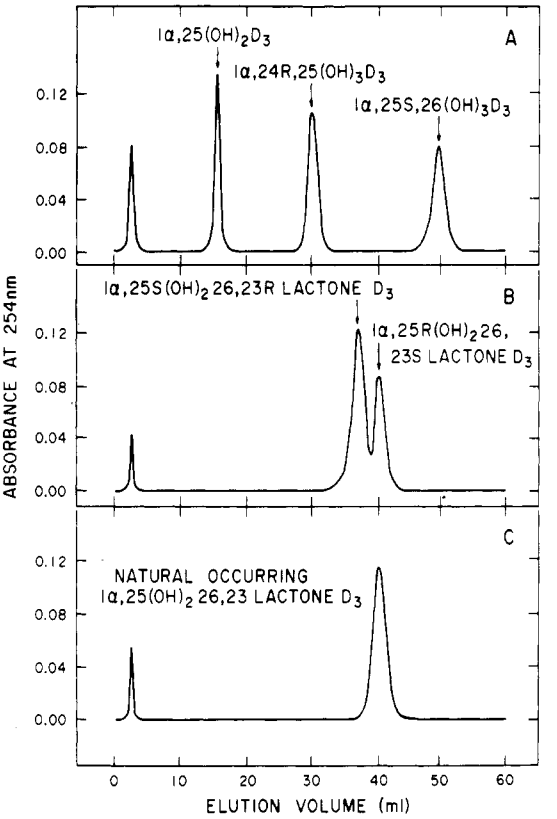


Figure 1. Elution profile of 1α,25$(OH)_2D_3$, 1α,24*R*,25$(OH)_3D_3$ and 1α,25*S*,26$(OH)_3D_3$ (A), 1α,25*S*$(OH)_2$ 26,23(*R*)-lactone D_3 and 1α,25R$(OH)_2$ 26,23(*S*)-lactone D_3 (B) and natural 1α,25$(OH)_2$ 26,23-lactone D_3 (C) on a μPorasil column (0.29 × 30 cm) eluting with *n*-hexane/isopropyl alcohol (555/65) a flow rate of 2 mL/min. The naturally occurring 1,25$(OH)_2$ 26,23-lactone D_3 was isolated from rabbit serum by using a procedure described in detail elsewhere.[1]

well as to other known metabolites, given in Figure 1, show that the retention volume of the natural metabolite is identical with the 23*S*,25*R* diastereomer **1a**, thereby supporting the earlier configuration assignments.[2,16]

In summary, the generality of the convergent total synthesis approach to vitamin D_3 metabolites has been further exemplified by the synthesis of 1α,25(*R*)-dihydroxy vitamin D_3 26,23(*S*)-lactone (calcitriol lactone, **1a**) and its 23*R*,25*S* isomer (**2a**). The identity of the natural metabolite as the 23(*S*),25(*R*)-lactone **1a** was indicated by an HPLC comparison. An alternate utilization of the bromo esters **7** and **8** for vitamin D_3 metabolite synthesis is presently under investigation and will be reported in due course.

Acknowledgment. We thank the staff of the Physcial Chemistry Department of Hoffmann-La Roche Inc. for the determination of physical and analytical data, particularly Dr. J. F. Blount, who carried out the X-ray structure de-

(16) One curious difference emerged between the results presented here and those reported in ref 2. Under our HPLC conditions (Figure 1) the 23(*R*),25(*S*)-lactone was eluted before the 23(S),25(R)-lactone whereas Takayama et al.[2] reports the opposite order of elution using a Zorbax Sil column (isopropanol/hexane, 20:80). The separations shown in traces B and C were run alternately a number of times to verify the reliability of this result. Additionally, the elution volumes for each of the two synthetic diastereomers were virtually identical with their respective elution volumes when chromatographed as a mixture. That their order of elution did not reverse when combined was demonstrated by chromatographing mixtures containing known proportions of the isomers. The differences between the present work and Takayama's[2] do not, however, alter the 23*S*,25*R* assignment for the natural isomer.

termination. We also thank Mr. A. Williams for technical assistance.

Peter M. Wovkulich,* Enrico G. Baggiolini
Bernard M. Hennessy, Milan R. Uskoković
Chemical Research Department
Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Eberhard Mayer, Anthony W. Norman
Department of Biochemistry
University of California, Riverside
Riverside, California 92521

Received August 2, 1983

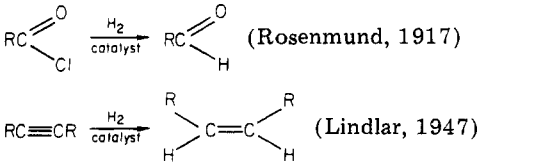
Metallic Palladium, the Actual Catalyst in Lindlar and Rosenmund Reductions?

Summary: We provide evidence that the poisons used in the preparation of Lindlar and Rosenmund catalysts do not block active sites but act to rearrange the surface structure of the catalyst.

Sir: The hydrogenation of alkynes to *cis*-alkenes (Lindlar reduction) and the catalytic hydrogenolysis of acid chlorides to aldehydes (Rosenmund reduction) are well-known textbook examples of reactions with "selectively poisoned" catalysts (Scheme I).[1] The partial hydrogenation of alkynes to give *cis*-alkenes, an important reaction in natural product synthesis, is usually achieved by heterogeneous hydrogenation with "poisoned" Lindlar catalysts. There has been considerable effort in the past to replace this "mythical" catalyst by homogeneous methods. Thus, Li in THF,[2] Na with BF_3 in diglyme,[3] diisobutylaluminum hydride and methyllithium,[4] chloroborane in ether,[5] $PdCl_2$ and H_2 in DMF,[6] $LiAlH_4$ and $TiCl_4$,[7] $Rh(NBD)(PPhMe_2)_3$,[8] and CuI[9] can be used to hydrogenate alkynes to give *cis*-alkenes. None of these methods, however, has replaced the Lindlar catalyst, which is used in the total synthesis of leukotrienes,[10] prostaglandins,[11] carbohydrates,[12] and various other natural products.[13]

The Lindlar catalyst and its modifications generally consist of deactivated palladium supported on $BaCO_3$ or $CaCO_3$, although Pd/C has also been used.[14] Historically, Lindlar catalysts are poisoned by lead acetate, with

Scheme I



quinoline as additional cataylst poison.[15] Successful reactions with untreated catalysts have also been reported.[16] In a very recent paper Dev describes the effects of using various transition-metal chlorides to modify Lindlar catalysts. Dev finds that the $MnCl_2$-modified catalyst is the most selective for alkyne hydrogenation to alkenes;[17] however, no data concerning the stereoselectivity (cis/trans ratio) of the $MnCl_2$-poisoned catalyst were reported.

The Rosenmund reduction[18] catalyst is palladium supported on barium sulfate poisoned by sodium acetate,[19] *N,N*-dimethylaniline,[20] thiourea,[21] thiophene,[21] dibenzothiophene,[21] ethyldiisopropyl amine,[22] or, most commonly, quinoline (with and without sulfur).[23] While the Rosenmund reduction has long been replaced by more practical homogeneous procedures with metal hydrides, the secret of the selective catalyst deactivation has never been uncovered. The very similar preparation procedures suggest that the Rosenmund catalysts are related to Lindlar catalysts; although the literature, surprisingly, does not draw any comparison.

The broad range of poisons used to cause identical or similar modifications of the catalytic activity of supported palladium to give either Lindlar or Rosenmund catalysts is suggestive that the poisons are not involved in the catalytic process but rather change the surface of the catalyst. The generally accepted rationale for the effect of catalyst poisoning suggests that the "poison" blocks the most active catalyst sites and thus prevents undesired further reactions. However, as described below, we find that the poisons do not block certain active sites but rather act to rearrange the palladium structure in a very drastic way.

We find that untreated, commercial palladium foil catalyzes the hydrogenation of alkynes to *cis*-alkenes with high selectivity. The following test reactions were carried out in the presence of 6 cm^2 of palladium foil (see Table I). 5-Decyne is converted to *cis*-5-decene with no trans byproduct detectable. Diphenylacetylene as well gives pure *cis*-stilbene. Even dimethyl acetylenedicarboxylate, hydrogenated at 100 °C for 160 h, resulted in dimethyl maleate (cis/trans ratio 30:1).

Our results are especially remarkable for two reasons: (1) Conventional Lindlar hydrogenations use supported catalysts with surface areas much larger than 100 m^2/g, whereas our palladium foil has a surface area of only 6 cm^2. The conversion achieved (turnover frequency = 4 (molecules/(surface atom × second))) is even more surprising, when we consider that such turnover frequencies larger than 1 have only been observed under ultrahigh vacuum conditions with extremely clean surfaces.[24]

(1) See common organic textbooks such as: Heathcock, C.; Streitwieser, A. "Introduction to Organic Chemistry", 2nd ed.; MacMillan: New York, 1981.
(2) Levin, G.; Jagur-Grodzinski, J.; Szwarc, M. *J. Org. Chem.* **1970**, *35*, 1702.
(3) Charlson, A. J.; Richtmeyer, N. K. *J. Am. Chem. Soc.* **1959**, *81*, 1512.
(4) Zweifel, G.; Steele, R. B. *J. Am. Chem. Soc.* **1967**, *89*, 5085.
(5) Brown, H. C.; Ravindran, N. *J. Org. Chem.* **1973**, *38*, 1617. Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1972**, *94*, 4370.
(6) Sisak, A.; Ungvary, F. *Chem. Ber.* **1976**, *106*, 531.
(7) Hooz, J.; Martimer, R. *Tetrahedron Lett.* **1976**, 805.
(8) Schrock, R. R.; Osborn, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 2143.
(9) Crandall, J. K.; Collonges, F. *J. Org. Chem.* **1976**, *41*, 4089.
(10) Rosenberger, M.; Newkom, C.; Aig, E. R. *J. Am. Chem. Soc.* **1983**, *105*, 3656. Cohen, N.; Banner, B. L.; Lopresti, R. J.; Wong, F.; Rosenberger, M.; Lui, Y.-Y.; Thom, E.; Liebman, A. A. *Ibid.* **1983**, *105*, 3661.
(11) Stork, G.; Raucher, S. *J. Am. Chem. Soc.* **1970**, 1583. Stork, G.; Kowalski, C.; Garcia, G. *Ibid.* **1975**, *97*, 3258. Corey, E. J.; Fleet, G. W. J.; Kato, M. *Tetrahedron Lett.* **1973**, 3963.
(12) Jones, J. K. N.; Szanek, W. A. In "The Total Synthesis of Natural Products", ApSimon, J, Ed.; Wiley-Interscience: New York, 1973; Vol. 1, pp 8-19.
(13) Mori, K. In "Total Synthesis of Natural Products"; ApSimon, J, Ed.; Wiley-Interscience: New York, 1981; Vol. 4, pp 9-31.
(14) Dobson, N. A.; Eglinton, G.; Krishnamurti, M.; Raphael, R. A.; Willis, R. G. *Tetrahedron* **1961**, *16*, 16.
(15) Lindlar, H. *Helv. Chim. Acta* **1952**, *35*, 446.
(16) See: Marvell, E. N.; Li, T. *Synthesis* **1973**, 457.
(17) Rajaram, J.; Narula, A. P. S.; Chawla, H. P. S.; Dev, S. *Tetrahedron* **1983**, *39*, 2315.
(18) Mosettig, E.; Mozingo, R. *Org. React. (N.Y.)* **1948**, *4*, 362.
(19) *Chem. Eng. News* **1970**, *48*, 41.
(20) Sakurai, Y.; Tanabe, Y. *J. Pharm. Soc. Jpn.* **1944**, *64*, 25.
(21) Affrosman, S.; Thomson, S. J. *J. Chem. Soc.* **1962**, 2024.
(22) Peters, J. A.; Bekkum, H. v. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 1323.
(23) Rosenmund, K. W.; Zetzsche, F. *Chem. Ber.* **1921**, *54*, 425. Marvell, E. N.; Tashiro, J. *J. Org. Chem.* **1965**, *30*, 3991.

0022-3263/83/1948-4436$01.50/0