gave IVd (52 mg) as colorless needles. mp 204—205°. $[\alpha]_D^{26.5}$ +90.1° (c=0.16 in MeOH). *Anal.* Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.75; H, 8.53. NMR (1% solution in $CDCl_3$) δ: 0.85 (3H, s, 18-CH_3), 3.49 (1H, d, J=7 Hz, 17α-H), 3.82 (3H, s, 3-OCH_3), 4.18 (1H, m, 16α-H), 6.52 (1H, s, 4-H), 6.81 (1H, s, 1-H).

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Synthesis of 2β-Hydroxycholecalciferol [2β-OH-D_3]

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As part of a general exploration of the structure/activity relationships of the vitamin D system, the 2β-hydroxylated analogue of cholecalciferol (vitamin D_3) has been prepared from 2β-hydroxy-7-dehydrocholesterol obtained in our previous work as starting material *via* (i) photochemical conrotatory opening (2 N_f pericyclic reaction) of the B-ring and (ii) thermal 1,7-antarafacial hydrogen shift (3 N_f pericyclic reaction).

Importance of 1α-hydroxy function of cholecalciferol (vitamin D_3) to induce either intestinal calcium transport or bone calcium mobilization activity has been demonstrated by the studies on 1α,25-dihydroxycholecalciferol [1α,25-$(OH)_2$-D_3][2-4] and 1α-hydroxycholecalciferol [1α-OH-D_3].[5-8] The increased clinical significance[9-16] of these two hydroxylated derivatives of vitamin D has led recently to synthesis and biological testing of various derivatives, hy-

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droxylated in the A ring or in the side chain. Chemical preparations of D_3-analogues with hydroxy groups in positions 1α;[5–7,17,18] 2α;[19] 4α;[20] 1α, 2α[21] 22;[22] 25;[23–25] 20, 25;[26] 24, 25;[27] 25, 26;[28] 1α, 25;[29,30] and 3-deoxy-1α[31] have been described. The present paper reports the synthesis of a new A-ring-hydroxylated derivative, 2β-hydroxycholecalciferol [2β-OH-D_3].

Recently, we have reported the preparation of 1α-OH-D_3 from cholesterol without using 1α-hydroxycholesterol as an intermediate.[32] This process is shown in Chart 1. The 1β,2β-

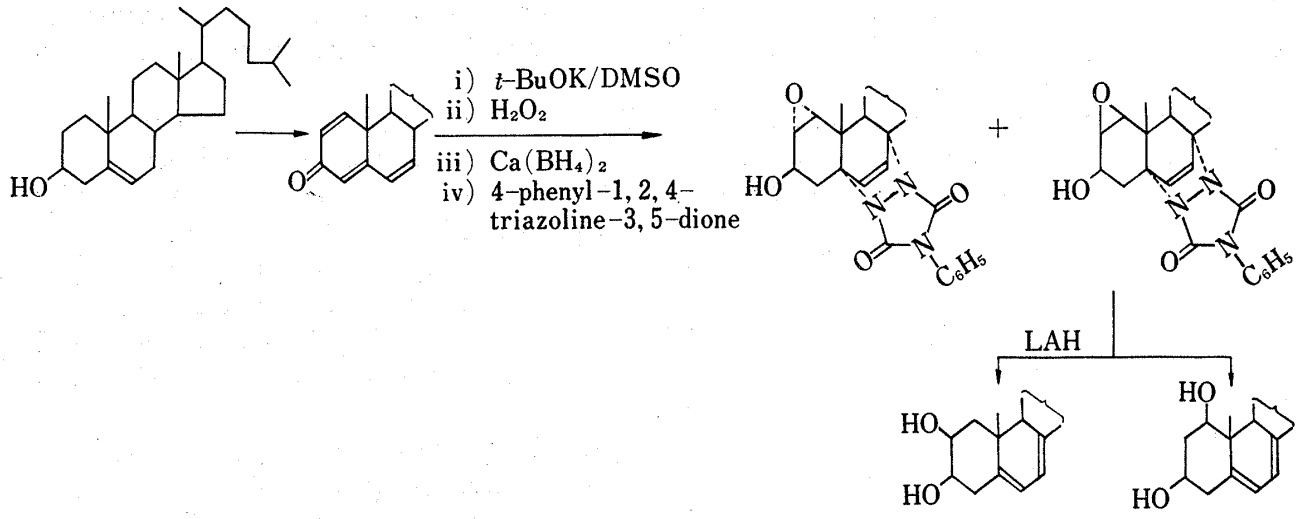
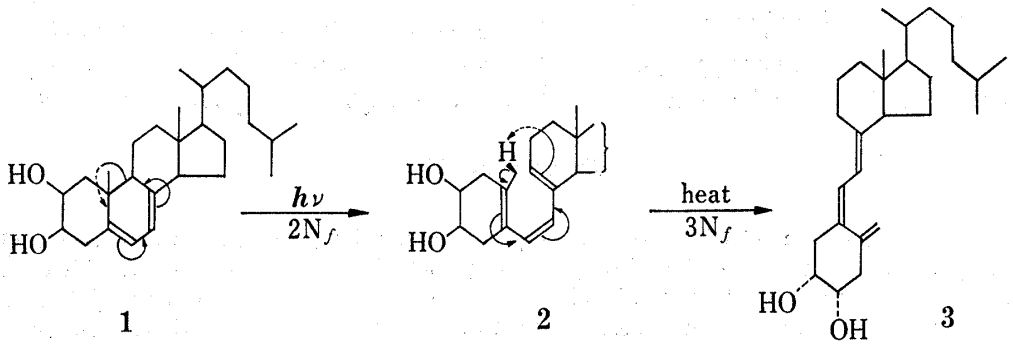


Chart 1



1 2 3

Chart 2

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epoxide of the 1,4-addition product gave 2β- and 1β-hydroxy-7-dehydrocholesterol in the ratio 8: 1 by reduction with $LiAlH_4$.

While other routes to the more efficient synthesis of 1β-hydroxy-7-dehydrocholesterol are under examination, we have used 2β-hydroxy-7-dehydrocholesterol (**1**) as the starting material in the present synthesis. Thus, the photochemical conrotatory opening of the B-ring of this diene (**1**) and the subsequent thermal 1,7-antarafacial hydrogen migration of the previtamin D_3 (**2**) led to 2β-OH-D_3 (Chart 2). The arrow symbolism used in the Chart is that developed recently by one (C.K.) of the present authors in order to describe concurrently, electron shifts, stereospecificities, and selection rule for pericyclic reactions within the electronic theory.[33,34]

Irradiation of an ethereal solution of the diene (**1**) with a high-pressure mercury lamp (a Vycor filter) gave a mixture of products from which the corresponding precholecalciferol (**2**), tachysterol derivative and the starting material were separated by column chromatography over Sephadex LH-20. The precalciferol was then converted to 2β-OH-D_3 (**3**) by standing it in ether for two weeks at room temperature. The final purification of 2β-OH-D_3 was achieved by column chromatography over Sephadex LH-20.

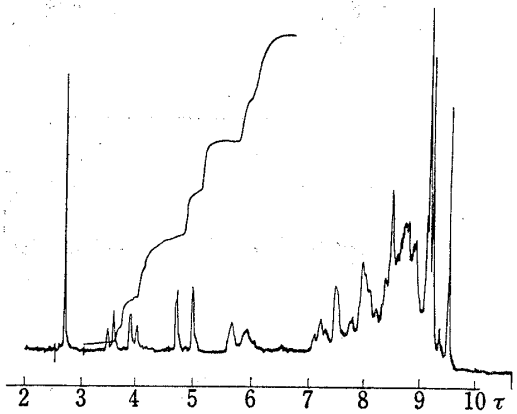

Fig. 1. NMR Spectrum of 2β-Hydroxycholecalciferol in Deuterochloroform

2β-Hydroxycholecalciferol (**3**) exhibited the expected ultraviolet (UV) and mass spectra. The nuclear magnetic resonance (NMR) spectrum of 3 (Fig. 1) showed the resonances of the olefinic protons in the vitamin D chromophore as well as C_2- and C_3-protons with chemical shifts almost identical with those observed in 2β-hydroxy-17-nor-17,17-ethylenedioxyvitamin D_3.[35]

Experimental[36]

Photochemical Conversion of 2β-Hydroxy-7-dehydrocholesterol (1) to 2β-Hydroxyprecholecalciferol (2)——Fifty milligrams of 2β-hydroxy-7-dehydrocholesterol (**1**) was dissolved in 600 ml of distilled ether. After bubbling of argon for 5 min, the whole was irradiated by 200 W high-pressure Hg lamp (Hanovia 654A-36) through a Vycor filter under argon atmosphere for 20 min. After evaporation of the solvent *in vacuo* below 20°, the residue was chromatographed on Sephadex LH-20 (20 g) with hexane–$CHCl_3$ (1: 1 v/v). 2β-Hydroxyprecholecalciferol (**2**) (8.5 mg), 2β-hydroxytachysterol (3.7 mg) and the starting material (30 mg) were eluted in this order. The previtamin D (**2**) showed characteristic UV spectrum: λ_{max}^{Ether}; 260 nm.

Thermal Conversion of 2β-Hydroxyprecholecalciferol (2) to 2β-Hydroxycholecalciferol (2β-OH-D_3; 3)——The previtamin (8 mg) obtained above was dissolved in 100 ml of distilled ether and stored in dark place (20—25°) under argon atmosphere. During the storage, the absorption maximum shifted gradually from 260 nm to 264 nm and the intensity increased up to 1.7 times than that of the original solution. After 10 days (by that time, the UV spectrum of the solution showed its maximum at 264 nm with a constant intensity), the solvent was removed *in vacuo*. The residue was purified by column chromatography on Sephadex LH-20 (10 g) with hexane–$CHCl_3$ (1: 1 v/v). The UV spectrum of each fraction was measured and pure 2β-hydroxy-

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34) The number of full arrows (a solid (→) or a dotted (⇢) arrow) in a given pericycle which is abbreviated to N_f determines whether the reaction is allowed or forbidden. Thus, an odd N_f corresponds to a thermally allowed reaction and an even N_f to a photochemically allowed one.

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cholecalciferol (3) (*ca.* 5 mg) was obtained. The yield of 2β-OH–D_3 (3) was calculated as 5.2 mg [λ_{max}^{Ether}: 264 nm (ε 18300 taken as standard for calculation)[37] and λ_{min}^{Ether}: 228 nm]. The NMR spectrum ($CDCl_3$) of 3 showed the characteristic resonances of the olefinic protons with vitamin D chromophore and the chemical shifts of these and C_2-protons almost identical with those observed in 2β-hydroxy-17-nor-17,17-ethylenedioxy-vitamin D[35]; τ 3.55 (1H, d, J=11 Hz) and 3.95 (1H, d, J=11 Hz) (6- and 7-H), 4.73 (1H, d, J=2 Hz) and 5.00 (1H, d, J=2 Hz) (19-H_2), 5.67 (1H, m) and 5.93 (1H, m) (2- and 3-H). The mass spectrum of 3 showed a molecular ion at *m/e* 400 and fragment ion peaks at *m/e* 382, 367, 364, 269, and 251.

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Studies of Alicyclic α-Amino Acids and Their Derivatives. V.[1] Decyanization of Alicyclic α-Acetylaminonitriles with Sodium Borohydride

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Upon treatment with sodium borohydride in pyridine, 1-acetylamino-*cis*-4-*t*-butylcyclohexane-1-carbonitrile, 2-acetylaminonorbornane-*endo*-2-carbonitrile and 2-acetylaminobornane-*endo*-2-carbonitrile underwent decyanization to give a mixture of isomeric acetylamino compounds in high yields, respectively. The product distribution can be explained in terms of the preferential attack of a hydride ion on the less-hindered side of the molecules.

In a previous report from our laboratory,[1] the stereochemical courses of the Strecker and Bucherer reactions in the synthesis of alicyclic α-amino acids have been proposed, *i.e.*, the former reaction gives the α-amino acids corresponding to thermodynamically stable alicyclic α-aminonitriles, whereas the latter reaction leads to the predominant formation of the isomeric α-amino acids which are derived from alicyclic α-aminonitriles formed under the kinetic control.

Yamada, *et al.*[3] have exploited the decyanization of various α-aminonitriles possessing a hydrogen at the α-position with sodium borohydride and applied this procedure to the synthesis of some natural products.

The subject of the present investigation is to examine the stereochemistry of the decyanization on the carbon substituted by an α-aminonitrile function. For the purpose, we attempted decyanization of some alicyclic α-acetylaminonitriles, which have definite stereochemistry and are readily available *via* the Strecker reaction of the corresponding alicyclic ketones followed by acetylation.

The reduction of 1-acetylamino-*cis*-4-*t*-butylcyclohexane-1-carbonitrile[4] (I) with excess sodium borohydride in pyridine at 95° completed after 12 hr (disappearance of I was checked by thin-layer chromatography). Employment of other solvents (ethanol or diglyme) did not give satisfactory results. Careful post-treatment of the reaction mixture gave a solid

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