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A FACILE AROMATIZATION OF VITAMIN D

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DANNENBERG and HEBENBROCK obtained a fluorescent hydrocarbon, $C_{27}H_{34}$, by refluxing vitamin D_3 with chloranil in anisole (bp 155.5°C) for 1 hr (35% yield), to which a structure possessing the styryl indene chromophore was assigned (*1*). During the course of our study on a fluorometric determination of vitamin D, we found this reaction to be unsuited for analytical purposes mainly because of its drastic reaction condition. We wish to report a very easy method of aromatization of vitamin D under extremely mild reaction conditions, and to emphasize the biosynthetic significance of this reaction.

Treatment of vitamin D_2 (I) in acetone with an equimolar amount of N-bromosuccinimide at room temperature for a period of 10 min led to a complete disappearance of the initial vitamin. Extraction of the diluted aqueous acetone solution with *n*-hexane gave a reaction mixture consisting principally of the two fluorescent components A and B, in approximately 3:1 proportion (*2*) as estimated by NMR (*3*). No other reaction products were detected on gas chromatographic tracings (*4*). Successive column chromatographic separation on silica gel, using *n*-hexane, afforded the ingredient A in a pure state (*5*). On the basis of the following data and of a comparative examination with the known vitamin isomers such as isovitamin D_2 (II) and isotachysterol$_2$ (III), the structure (IV) has been determined unequivocally for the compound A, and (V) was assigned tentatively to the compound B.

Compound A (IV) (3-Dehydroxy-1,2,3,4-tetradehydroisotachysterol$_2$) (4)

$C_{28}H_{40}$; colorless oil; UV (nm), 297 (shoulders at 328 and 313; weak absorptions at 243, 234.5, and 227.5) (alkylated 1-phenyl-butadiene chromophore (*6*)); IR (cm^{-1}), 1633 (C=C), 1598 (aromatic C=C), 968 and 957 (strong, *trans*-CH=CH–), 743 (strong, *o*-disubstituted benzene), and no indication of the OH group; NMR (δ ppm), 0.76–1.22 (15H, 5 saturated CH_3) (*7*), 1.22–2.75 (17H; 2.30 [*s*, 19-CH_3] and CH_2, CH), 5.15–5.33 (*m*, 2H; 22, 23-CH=CH–), 6.53 and 6.74 (*AB q*,

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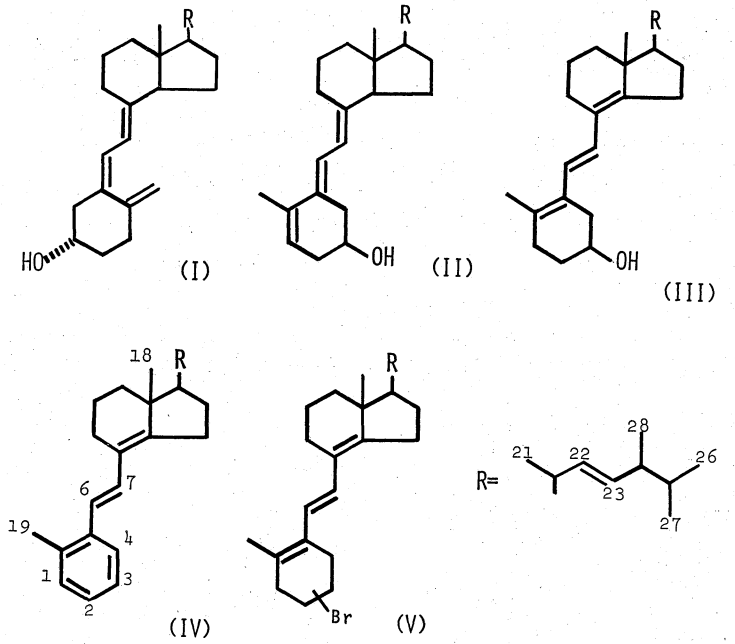

J=15.8 Hz, 2H; 6,7-*trans*-CH=CH–), and 6.97–7.50 (*m*, 4H, aromatic H); MS *m/e*, 376.3129 (M^+, 91%), 361 (M–CH_3, 6%), 333 (M–C_3H_7, 4%), 251 (M–C_9H_{17}, 100%), and no indication of the OH group.

Compound B (*V*) (*3-Dehydroxy-3 or 2-bromoisotachysterol*$_2$) (*4,8*)

$C_{28}H_{43}Br$; colorless oil; UV (nm), 302, 289.5, and 279 (isotachysterol$_2$ chromophore); IR (cm^{-1}), 1632 (C=C), 968 and 951 (strong, *trans*-CH=CH–), and no indication of the OH group; NMR (δ ppm), 0.73–1.20 (15H, 5 saturated CH_3) (*7*), 1.20–2.88 (23H; 1.79 [broad *s*, 19-CH_3] and CH_2, CH), *ca.* 4.28 (broad *m*, 1H, >CHBr), 5.15–5.33 (*m*, 2H; 22, 23-CH=CH–), and 6.22 and 6.35 (*AB q*, J=16.0 Hz, 2H; 6,7-*trans*-CH=CH–); MS *m/e*, 460.2527 (M+2, 25%), 458.2539 (M^+, 25%), 445 (M+2–CH_3, 4%), 443 (M–CH_3, 4%), 417 (M+2–C_3H_7, 2%), 415 (M–C_3H_7, 2%), 378 (M–HBr, 100%), 335 (M+2–C_9H_{17}, 28%), 333 (M–C_9H_{17}, 28%), 253 (M–C_9H_{17}–HBr, 51%).

Gas chromatographic analysis (*4*) clearly indicates that the reaction proceeds smoothly, *via* (II) and (III), to give the final products (IV) and (V). Because of its relatively weak fluorescence and heterogeneity of the reaction product, usefulness of this reaction for analytical purposes might be restricted. However, this simple and efficient aromatization procedure should be very useful for biogenetic-like synthesis of natural aromatic carotenoids from their counterparts possessing the terminal methylenecyclohexanol (*e.g.* in I) or the cyclohexenol structure (*e.g.* in III).

REFERENCES AND FOOTNOTES

1) DANNENBERG, H. and HEBENBROCK, K.-F., *Ann.*, **662**, 21 (1963).

2) When an equi-molar amount of N-bromosuccinimide is used at room temperature, reaction rate and formation ratio of the products seem to be affected by solvent employed, *e.g.*, the CCl_4 solution usually requires 1–2 hr for terminating the reaction which yields A and B in 3: 2 proportion.

3) The proportion of A to B in the crude reaction mixture can be estimated from the diagnostic signals and their integral intensities, *viz.*, signals at δ 6.97—7.50 ppm (4H of A) and at δ 5.15 –5.33 ppm (2H of A+2H of B).

4) UV were taken in *n*-hexane, NMR in CCl_4 solutions, and IR in films. New compounds described gave satisfactory high resolution mass spectral analysis. Glc: 1.5% OV–1, column 0.4×150 cm, injector 260°, column 250°, detector 300°, N_2 60 ml/min.

5) The compound B, even highly purified, is usually contaminated with small amount of the compound A as estimated by NMR analysis.

6) GRUMMITT, O. and CHRISTOPH, F. J., *J. Am. Chem. Soc.*, **73**, 3479 (1951).

7) Among the signals, the chemical shift of the 18–CH_3 group is characteristically different from those of (I) and (II), and can be deduced from the NMR data on isotachysterol$_2$ acetate using the shift reagent Eu(DPM)$_3$ (δ 0.93 *s* in A and δ 0.91 *s* in B).

8) All spectral data are almost consistent with those of the specimen prepared from isotachysterol$_2$ and PBr_3 in pyridine.