Synthesis of C(19)-Acetoxy Precalciferol$_3$ and Its Conversion into the Vitamin D$_3$ Analogue

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Summary A modified Bamford–Stevens reaction on the tosylhydrazone derivative of 7-ketocholest-5-ene-3β,19-diol diacetate afforded the ring B-diene which upon photolysis and thermal isomerization yielded the vitamin analogue.

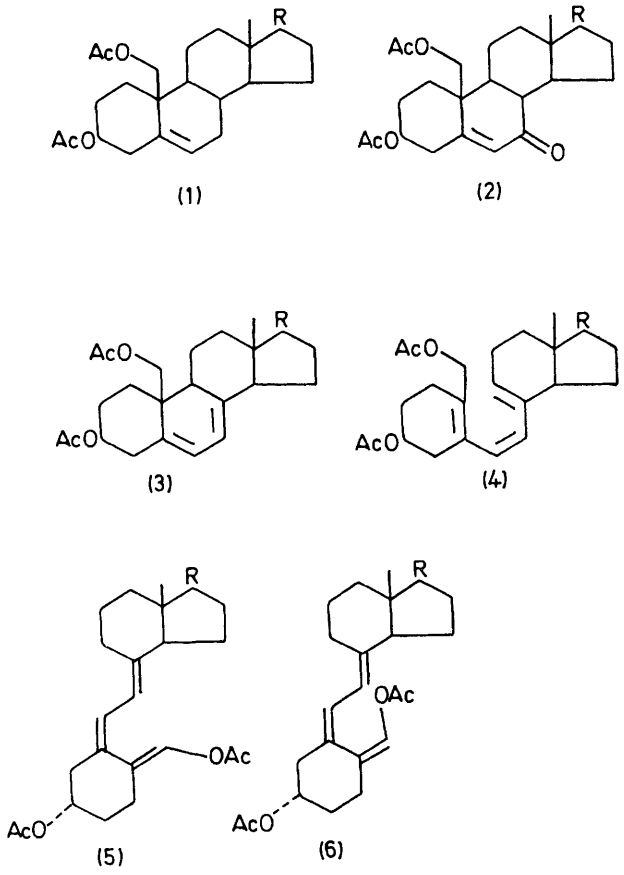
PHOTOCHEMICAL and thermal conversions in the vitamin D series have proved to be an interesting area of organic chemistry.[1] Since the C(19) methyl group undergoes a critical change in the thermal formation of the vitamin from the previtamin, namely, a 1,7-antarafacial hydrogen shift,[2] we became curious about the comparative behaviour of C(19) functionalized analogues. Accordingly the synthesis of such a compound was undertaken and accomplished as shown in the Scheme.

Allylic oxidation of (**1**) (CrO_3–py–CH_2Cl_2) yielded (**2**) (68%) m.p. 94·5—95·5°. The conjugated ketone (**2**) was converted into the tosylhydrazone and without isolation treated with LiH in benzene at reflux for 6 h,[3,4]† to give (**3**) (80%), m.p 113·5–114·0°.

Irradiation of (**3**) (15 min, 125 W Hanovia 8A36, C_6H_6–EtOH, 9:1) and subsequent column chromatography gave the previtamin (**4**) (68%) as an oil which was then heated at reflux in CCl_4 for 2·5 h under N_2 to give the vitamin analogue which was isolated as an oil (65%) λ_{max} (EtOH) 266 nm.

Only one of the two possible vinyl 19-acetoxy-isomers is formed in the thermolysis reaction as indicated by n.m.r. spectroscopy. Dreiding models reveal that the structure corresponding to (**5**) is much less hindered than the other possible isomer (**6**).

Since the 1,7-hydrogen shift is an equilibrium process[2] we tentatively assign structure (**5**) to the vitamin analogue in this series.



SCHEME

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† All new compounds had the appropriate spectral properties and the required composition by elemental analysis.

[1] H. H. Inhoffen and K. Irmscher, *Fortschr. Chem. Org. Naturstoffe*, 1959, **17**, 70; H. H. Inhoffen, *Angew. Chem.*, 1960, **72**, 875; G. M. Sanders, J. Pot, and E. Havinga, *Fortschr. Chem. Org. Naturstoffe*, 1969, **27**, 131.
[2] J. L. M. A. Schlatmann, and E. Havinga, *Rec. Trav. chim.* 1961, **80**, 1101.
[3] L. Caglioti, P. Grasselli, and G. Maina, *Chimica e Industria*, 1963, **45**, (5), 559.
[4] Attempted introduction of the additional double bond into (**1**) by the customary procedure of allylic bromination–dehydrobromination (F. Hunziker and F. X. Muller, *Helv. Chim. Acta*, 1958, **41**, 70) gave significant amounts of the 4,6-diene.