Tetrahedron Letters No. 51, pp 4761-4762, 1976. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF 19/10→9β/ABEO-10α-LANOST-5-ENES

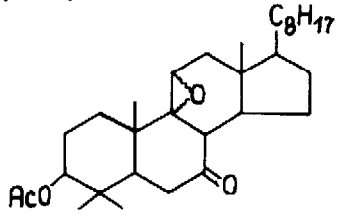
Z. Paryzek
Institute of Chemistry, A. Mickiewicz University
Poznań, Poland

(Received in UK for publication 19 October 1976)

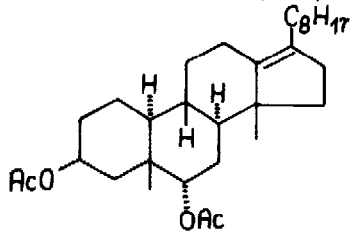
The attempted synthesis of the cucurbitane skeleton from the lanostane skeleton by processes involving the migration of 19-methyl group has either failed[1] or resulted in low yield.[2] We wish to report an efficient entry into the cucurbitane series.

Of the two isomeric epoxides /I/ prepared from 3β-acetoxylanost-9/11/-ene-7-one[3] the rearrangement of the epoxide /Ib/[4] was studied.

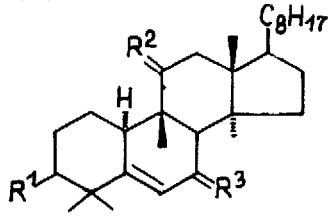
Treatment of /Ib/ with $BF_3 \cdot Et_2O$ in benzene resulted in the formation of 3β-acetoxy-5α-lanostan-7,11-dione.[5] However, the reaction carried out in acetic anhydride with $BF_3 \cdot Et_2O$ gave 3β,11β-diacetoxy-19-nor/10→9β/abeo-lanost-5-ene-7-one /II/ and 3β-acetoxy-lanostan-7,11-dione in 58 and 32% yield respectively. The structure of /II/, mp. 188-190°, follows from its spectral properties: PMR: 6.07 /H-6/, 5.27 /H-11/, 4.86 /H-3/, 2.05 and 2.00 /two CH_3COO singlets/; IR: 1725, 1660, 1260; UV: λ_{max} 245 nm, ε 13500; M^+ 542.[6] The stereochemistry of /II/ follows from the assumption that suprafacial shifts of the C-10 methyl group and of the 5α-hydrogen atom occured. Compound /II/ hydrolysed in ethanolic KOH to monoacetoxy derivative /III/, mp. 214-216°, PMR: 6.12 /H-6/, 5.27 /H-11/, 3.65 /H-3/, 2.06 /CH_3COO/. Prolonged hydrolysis afforded /IV/ as the main product, mp. 230-233°, PMR: 6.11 /H-6/, 4.00 /H-11/, 3.67 /H-3/; IR: 3550, 3400, 1650, 950; M^+ 458. /IV/ was selectively acetylated to /V/, mp. 252-254°, PMR: 6.09 /H-6/, 4.82 /H-3/, 3.98 /H-11/, 1.99 /CH_3COO/; IR: 3635, 3480, 1730, 1655, 1250. /V/ could be further transformed into /II/, thus indicating that no change of stereochemistry was involved under hydrolytic conditions. Jones reagent oxidized /V/ to a cucurbitone /VI/,



Ia 9α,11α Ib 9β,11β



VIII



II	R^1= OAc	R^2=α-H,β-OAc	R^3= O
III	R^1= OH	R^2=α-H,β-OAc	R^3= O
IV	R^1= OH	R^2=α-H,β-OH	R^3= O
V	R^1= OAc	R^2=α-H,β-OH	R^3= O
VI	R^1= OAc	R^2= O	R^3= O
VII	R^1= OAc	R^2= O	R^3= H_2

mp. 225–228°, PMR: 6.13 /H-6/, 4.83 /H-3/, 2.00 /CH_3COO/; IR: 1732, 1700, 1663, 1255; UV: λ_{max} 243 nm, ε 13300; CD: $\Delta\varepsilon$ -0.69 at 339 nm, +6.31 at 295 nm; M^+ 498. The high positive Cotton effect associated with the $n \rightarrow \pi^*$ transition of 11-carbonyl chromophore confirmed the 9β-configuration of compound /VI/ and its precursors. Oxydation of deoxybryogenin acetate /VII/ with CrO_3 in AcOH afforded a substance which was identical with compound /VI/. This transformation provided the evidence that the rearranged compound /II/ and its derivatives were of cucurbitacin type.

The role of acetic anhydride which serves both as the solvent and the reagent is worth of mentioning, since in benzene which is commonly used for epoxide rearrangements the methyl migration does not occur. On the basis of this and other results obtained it is expected that BF_3–Ac_2O system is a useful reagent in which efficient skeletal rearrangements induced by an epoxide cleavage may proceed. For example cholesterol acetate α-epoxide afforded 62% yield of completely backbone rearranged compound /VIII/ which has not been formed in benzene.[7]

The significance of the 7-carbonyl group and of the configuration of 9,11-epoxide for methyl migration is under investigation.

Acknowledgment. - Author thanks Dr. O.E. Edwards of NRC of Canada for his encouragement and comments and also for the sample of deoxybryogenin.

References and notes

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