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STEROIDS PART VIII*, BORON TRIFLUORIDE-CATALYSED REARRANGEMENTS OF 5β-METHYL-9,10-EPOXY-STEROIDS

I.G.Guest and B.A.Marples
The Department of Chemistry, The University of Technology
Loughborough.

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The boron trifluoride catalysed rearrangements of steroidal epoxides have been widely reported (1). Recently, considerable interest has been shown in the backbone rearrangement of 4,5-and 5,6-epoxy-steroids (1). In an attempt to elucidate the mechanism of these rearrangements in more detail, we have studied the previously unreported reactions of the 5β-methyl-9,10-epoxides (II) and (III) with boron trifluoride etherate.

The mixed epoxides (II) and (III), prepared by monoperphthalic acid oxidation of the $\Delta^{9(10)}$-methoxy-acetate (I)(2), were separated by preparative t.l.c. on silica gel. Treatment of a benzene solution of the α-epoxide (II) m.p. 86-87°, $[\alpha]_D$+ 10.5°(c**, 1.2) with boron trifluoride etherate in benzene (7 min.) gave the rearranged diene (IV) (56%)$[\alpha]_D$+ 67° (c, 1.1) and small quantities of the related compounds (V) (3%) and (VI) (5%). The products were separated by preparative t.l.c. and identified from spectroscopic data. The i.r. spectrum of (IV) showed the absence of a hydroxyl group and the ^{1}H n.m.r. spectrum *** showed important bands at τ 4.5-4.8 (m,=CH), 5.19 (t, apparent J $\cong$ 7.7 Hz,AcOCH), 6.3-6.8 (m, MeOCH), 6.71 (s, OMe), 7.95 (s,AcO), 8.88 (s, 5β-Me), 9.01 (low field branch of C-21 Me doublet), 9.03 (s, 14β-Me), 9.13 (upfield branch of C-21 Me doublet and low field branch of C-26 and C-27 Me doublets), and 9.22 (upfield branch of C-26 and C-27 Me doublets). Double irradiation at 87 Hz downfield from the signal due to the C-21 Me doublet (τ 9.01) caused its collapse into the adjacent signal at τ 9.03 thus confirming the presence of the 13,17-double bond (1b). The absence of any signals due to olefinic protons in the ^{1}H n.m.r. spectrum of (V) and the

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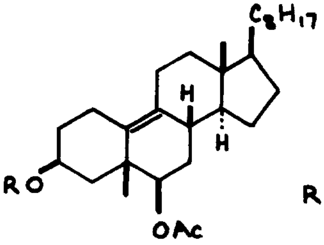
* Part V. I.G.Guest and B.A.Marples, Tetrahedron Letters, 1947 (1969).
Part VI. J.G.Ll.Jones and B.A.Marples, Reference 5.
Part VII. J.G.Ll.Jones and B.A.Marples, Chem.Comm., 1969, in press.

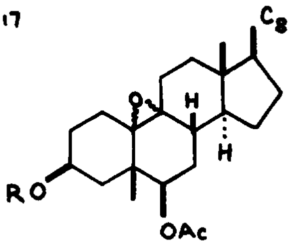
** All rotations are for $CHCl_3$ solutions.

*** All ^{1}H n.m.r. spectra are for $CDCl_3$ solutions.

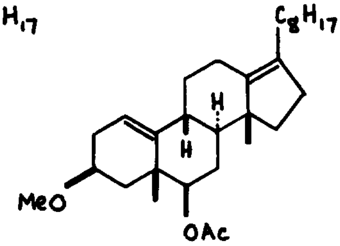
chemical shift of the 5β-Me signal (τ 8.81) suggested the presence of the 9,10-double bond. The i.r. spectrum ($CHCl_3$) of (VI) showed two hydroxyl bands at 3660 and 3450 $cm.^{-1}$ The former is due to the tertiary hydroxyl group since the spectrum of the $\Delta^{9,10}$-3-hydroxy-compound (VII) (3) shows only a band at 3420 $cm.^{-1}$ The ^1H n.m.r. spectrum of (VI) shows the 3-H signal at τ 5.35-5.7 ($W_{\frac{1}{2}} \cong 12$ Hz) confirming the 3β-hydroxyl group. The presence of the 13,17-double bond in (V) and (VI) was confirmed by double irradiation experiments similar to that described for (IV).



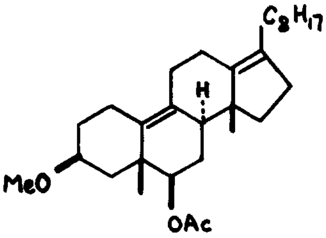
I, R=Me
VII, R=H



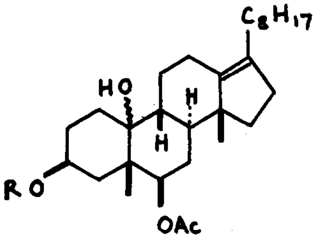
II, R=Me, 9α, 10α
III, R=Me, 9β, 10β
XIII, R=Ac



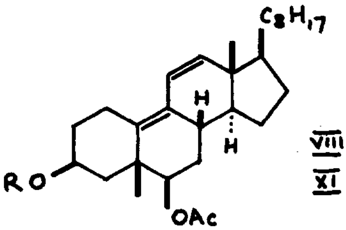
IV



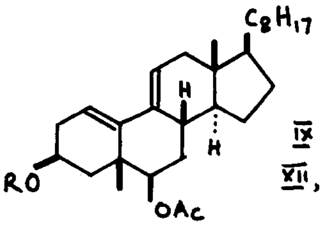
V



VI, R=H, 10α
X, R=Me, 10β



VIII, R=Me
XI, R=Ac



IX, R=Me
XII, R=Ac

Treatment of the β-epoxide (III), $[\alpha]_D$ + 63° (c, 1.1) with boron trifluoride etherate under similar conditions gave the conjugated dienes (VIII) (34%), m.p. 74-76°, $[\alpha]_D$-41° (c, 3.9), and (IX) (17%), $[\alpha]_D$-50° (c, 1.4), and the $\Delta^{13,17}$-compound (X) (15%), $[\alpha]_D$ + 45° (c, 0.7). These were separated by preparative t.l.c. The u.v. spectra of (VIII) ($\lambda_{max.}$ 249 nm., ε , 25,200) and (IX) ($\lambda_{max.}$ 243 nm., ε , 9,200) compare well with those reported (4) for (XI) and (XII) which were prepared from the epoxides (XIII) by treatment with ethanolic hydrochloric acid. The ^{1}H n.m.r. spectrum of (X) showed important peaks at τ 4.65-5.15 (t, apparent J≃7.7 Hz, AcOCH), 6.35-6.9 (m, MeOCH), 6.76 (s, OMe), 7.96 (s, AcO), 9.0 (5β-Me and lower branch of C-21 Me doublet), 9.08 (s, 14β-Me), 9.12 (upper branch of C-21 Me doublet and lower branch of C-26 Me and C-27 Me doublets), and 9.22 (upper branch of C-26 Me and C-27 Me doublets). Double irradiation at 90 Hz downfield from the signal at τ 9.12 caused a reduction in its intensity and that of the signal at τ 9.0, and an increase of the intensity of the signal at τ 9.08. This spin-spin decoupling of the C-21 Me from the 20-H confirmed the presence of the 13,17-double bond (1b). The i.r. spectrum ($CHCl_3$) of (X) showed the presence of a hydroxyl group (3620 and 3440 cm.$^{-1}$). The structure of (X) was finally confirmed by its conversion to (IV) with thionyl chloride in pyridine.

The formation of the 13,17-double bond undoubtedly occurs by heterolysis of the C-9-O-bond and a series of 1,2-shifts in an analogous fashion to the backbone rearrangement of 4,5- and 5,6-epoxides (1). The high yield of $\Delta^{13,17}$-compounds from the α-epoxide (II) would be anticipated since the migration of hydride ion from C-8 and the cleavage of the C-9-O-bond could occur synchronously. Elimination of the oxygen function from C-10 would give the dienes (IV) and (V) while boron trifluoride-catalysed cleavage of the 3-methoxy-group would give the diol (VI). In the β-epoxide (III) the C-8 hydrogen and the epoxy-group have the β-configuration which precludes the concerted process described for the α-epoxide (II). It seems likely that the intermediate will have more carbonium ion character (C-9) and this would explain the relatively high yields of dienes (VIII) and (IX). These results complement our recent observations on the backbone rearrangement of 10β-hydroxy-steroids (5).

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