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VINYL CATION REARRANGEMENT IN THE SOLVOLYSIS OF 5α-CHOLEST-1-EN-1-YL TRIFLATE[1]

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Abstract: Solvolysis of 1 in buffered aqueous acetone gives a mixture of the rearranged alcohols 2, 3, 4, and 5 as a result of a possibly concerted ionization migration to the double bond.

In spite of their preferred linear geometry, vinyl cations have been established as definite intermediates in the solvolysis reactions of a number of cyclic vinyl substrates, including simple 1-cyclohexenyl triflates.[2] Vicinal alkyl substitution was observed to produce marked rate enhancements in six-membered rings although both rearranged and unrearranged products are invariably obtained.[2a] However, in one case complete rearrangement was observed and a diene was obtained as a result of an exclusive elimination path.[3] A concerted, presumably anchimerically assisted, alkyl migration was suggested.

We wish to describe here the solvolysis of a steroidal 1-cyclohexenyl triflate which affords, near quantitatively, a mixture of rearranged products of substitution.

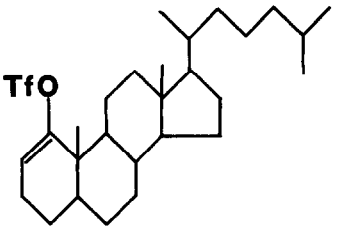
5α-Cholest-1-en-1-yl triflate (1) was obtained from 5α-cholestan-1-one[4] according to literature procedures.[5]

Reaction of 1 in acetone-water (9:1), buffered with sodium acetate, for 89 h at 65 °C gave 2 (2.5%), 3 (14.5%), 4 (41%), and 5 (24%).[6] Each of the four alcohols was found stable to the solvolysis conditions. A 4% of elimination products was found in addition.[7] No cholestan-1-one was observed.

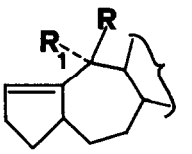
The structure of epimers 2 and 3 was deduced on the basis of spectral data.

The relative orientation of the 10-OH group[8] was assigned from the magnitude of the pyridine-induced solvent shifts of the 13-Me group (Table I).[9]

Inspection of Dreiding model of the assumed intermediate 6 (see later) gave further support to the above assignment for an α-attack by the solvent on the position 10 should be largely favoured over one from the congested β side. $\Delta\delta$ values of the olefinic protons (cf. compounds 17 and 18 of ref. 9b)

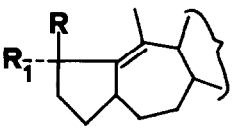


1 (TfO=OSO_2CF_3)



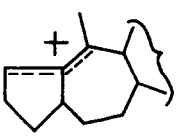
2, R=OH; R_1=Me

3, R=Me; R_1=OH



4, R=H; R_1=OH

5, R=OH; R_1=H



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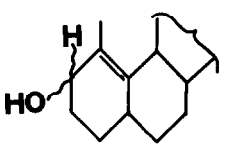
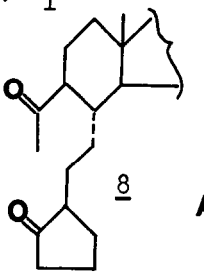


7 (both epimers)



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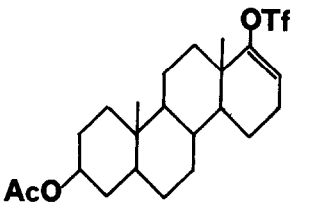

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suggested the existence of ring B as a mixture of the two twist-chair like forms TC_1 and TC_9[10] with a dynamic resultant approaching the favoured twist-chair conformation with the gem-substituents (Me and OH) on the axis carbon.[10a]

A chemical confirmation was conversely required for 4 and 5 in order to rule out alternatives 7 which would exhibit similar spectral properties.

Hydrogenolysis of 4 (or 5) with a mixed hydride ($LiAlH_4$-$AlCl_3$),[11] followed by ozonolysis of the resulting olefins, gave as a main product the diketone 8.[12]

The configuration of the 2-OH group could not be derived unambiguosly from the pattern of the geminal proton as in the case of 17-methylene-16-substituted steroids[13] owing to the flexibility of the A-nor ring.

Slopes observed on $Eu(dpm)_3$ shift analysis (Table I) indicated that the distance r of 13-Me protons from the oxygen atom was in the order $r_4 > r_5$, thus establishing the stereochemistry of 4 and 5 as depicted.[14]

The unexpected independence of the 13-Me signal from the added $Eu(dpm)_3$ in 2 was believed to be the consequence of an accidental close proximity to the critical value (54.7 °) of the angle ϑ, as defined in the McConnell-Robertson equation for pseudo-contact shift.[15] A non negligible influence of the angle factor was also apparent with $Pr(dpm)_3$,[15] for a steeper (or at least equal) shift gradient could be predicted for 2 on merely distance considerations.

The solvolysis of 1 is reminiscent of others in the steroid field involving

Table I. Relevant ^{1}H NMR Data of the Solvolysis Products

Compd / Signal	2	3	4	5
13-Me	0.65(s)[a]	0.67(s)[a]	0.68(s)[a]	0.67(s)[a]
	-0.11[b]	-0.05[b]	+0.01[b]	-0.01[b]
	0.00[c]	1.87[c]	0.98[c]	1.22[c]
	-2.32[d]	-2.52[d]		
10-Me	1.20(s)[a]	1.27(s)[a]	1.75(d,J=1.5Hz)[a]	1.77(d,J=1.5Hz)[a]
	-0.29[b]	-0.30[b]	-0.22[b]	-0.20[b]
			6.65[c]	6.80[c]
C-2 H	5.68(m)[a]	5.70(m)[a]	4.54(m)[a]	4.57(m)[a]
	-0.41[b]	-0.25[b]	-0.41[b]	-0.40[b]
	12.05[c]	11.95[c]		

[a] δ values (ppm) relative to TMS in 0.1 M CCl_4 solutions. [b] Pyridine-induced solvent shifts: $\Delta\delta = \delta_{CCl_4} - \delta_{C_5D_5N}$. [c] Slopes obtained by least squares from plots of $Eu(dpm)_3$ induced shifts *vs.* $Eu(dpm)_3$: substrate molar ratio. [d] Slopes obtained with $Pr(dpm)_3$.

S_N at saturated carbon to give A-nor-B-homo structures,[10b,16] but is uncommon in respect of 1-cyclohexenyl triflates for the mild experimental conditions, and the complete rearrangement and substitution observed.

The abnormal instability of 1 (see note 5), probably as a consequence of compression with the adjacent C-11 H, should account for our result. In fact 3β-acetoxy-D-homo-5α-androst-17-en-17a-yl triflate (9), when reacted as 1 for 96 h at 80 °C, was practically unchanged.

The 5(10→1) *abeo* alcohols arise *via* an exclusive migration of the adjacent cyclohexenyl bond to the vinyl cation centre and formation of the allylic cation 6.

Since no 10-Me migration nor unrearranged products were detected, we suggest, according to Stang,[3] that the reported rearrangement could be a '*concerted* ionization migration to the double bond'.

References and Notes

1) For recent reviews on vinyl triflates and on vinyl cation chemistry, see respectively: P.J. Stang, Acc. Chem. Res., 11, 107 (1978), and M. Hanack, Angew. Chem. Int. Ed. Engl., 17, 333 (1978).
2) a) W.D. Pfeifer, C.A. Bahn, P.v.R. Schleyer, S. Bocher, C.E. Harding, K. Hummel, M. Hanack, and P.J. Stang, J. Am. Chem. Soc., 93, 1513 (1971); b) M. Hanack, E.J. Carnahan, A. Krowczynski, W. Schoberth, L.R. Subramanian, and K. Subramanian, J. Am. Chem. Soc., 101, 100 (1979) and references therein.
3) P.J. Stang and T.E. Dueber, Tetrahedron Lett., 563 (1977).
4) M.P. Cava and B.R. Vogt, J. Org. Chem., 30, 3775 (1965).
5) P.J. Stang and T.E. Dueber, Org. Synth., 54, 79 (1974). 1 was isolated as a brown oil and could not be crystallised. An attempted filtration on silica gel resulted in a partial decomposition to an olefin, probably 5(10→1)abeo-cholesta-1,10(19)-diene, as disclosed by ^{1}H NMR of the eluate [two additional 1:1 signals at δ 4.90 and 5.17 (cf. ref. 16)]. Spectral data of 1: IR ($CHCl_3$) 1390 and 1130 cm^{-1} (OSO_2); ^{1}H NMR (CCl_4) δ 0.65 (3H, s, 13-Me), 1.08 (3H, s, 10-Me), 5.63 (1H, t, J=4.5 Hz, 4C-2 H); MS m/e, rel intensity, 518(M^+, 7), 503(2), 405(3), 386(5), 368(100), 364(22).
6) Yields refer to pure compounds isolated by deactivated (grade III) Woelm neutral alumina [n. hexane-benzene (3:2) as eluant]. 2: mp 74-74.5 °C (MeOH); $[\alpha]_D$ -37° (1%, $CHCl_3$); IR (KBr) 3460 cm^{-1}(OH). 3: mp 112-114 °C (MeOH); $[\alpha]_D$ -50° (1%, $CHCl_3$); IR (KBr) 3340 cm^{-1}(OH). 4: mp 55.5-57.5 °C (MeOH); $[\alpha]_D$ -46° (1%, $CHCl_3$); IR (KBr) 3400 cm^{-1} (OH). 5: mp 104-105.5 °C (MeOH); $[\alpha]_D$ -49° (1%, $CHCl_3$); IR (KBr) 3280 cm^{-1} (OH). Satisfactory analytical data were obtained for all the new compounds described in this paper, 1 excepted.
7) The small olefin fraction was shown by ^{1}H NMR to be a mixture of at least two products and was not further examined.
8) The original steroid numbering is retained according to Rule 2S-9 of IUPAC-IUB 1971 Definitive Rules for Steroid Nomenclature.
9) a) S. Ricca, B. Rindone, and C. Scolastico, Gazz. Chim. Ital., 99, 1284 (1969); b) P.V. Demarco, E. Farkas, D. Doddrell, B.L. Mylari, and E. Wenkert, J. Am. Chem. Soc., 90, 5480 (1968).
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11) J.H. Brewster and H.O. Bayer, J. Org. Chem., 29, 116 (1969).
12) 8 (oil): $[\alpha]_D$ +82° (1%, $CHCl_3$); IR (CCl_4) 1736 (cyclopentanone) and 1709 cm^{-1}(COMe); ^{1}H NMR (CCl_4) δ0.72 (3H, s, 13-Me), 2.05 (3H, s, COMe).
13) F.A. MacKellar and G. Slomp, Steroids, 11, 787 (1968).
14) The angular factor contribution in the McConnell-Robertson equation[15] was neglected.
15) A.F. Cockerill, G.L.O. Davies, R.C. Harden, and D.M. Rackham, Chem. Rev., 73, 553 (1973).
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