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THE ACID-CATALYSED REARRANGEMENT OF A DITERPENOID EPOXIDE[1]

R.D.H. Murray, R.W. Mills and J.M. Young

Department of Chemistry, University of Glasgow, Glasgow W.2.

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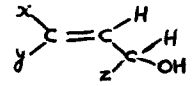
Our observation[2] that CrO_3-acetic acid oxidation of erythroxylol A epoxide (1) induced carbon-carbon bond cleavage, prompted us to study the effect of formic acid as solvent. At least 13 compounds were formed but, surprisingly, the same product mixture was obtained in the absence of CrO_3. Since treatment of dihydroerythroxylol A (2) with 95% formic acid afforded only the derived formate, the products from 1 necessarily resulted from fission of the epoxide ring, with concomitant esterification of the primary hydroxyl group. Indeed, all the rearrangement products contain the grouping $-CH_2OCHO$ as shown by their IR ($\nu_{max}^{CCl_4}$ 1731 and 1175 cm^{-1}) and NMR spectra ($\tau \sim 5.6$ and 6.1, 2H, J = 11Hz).

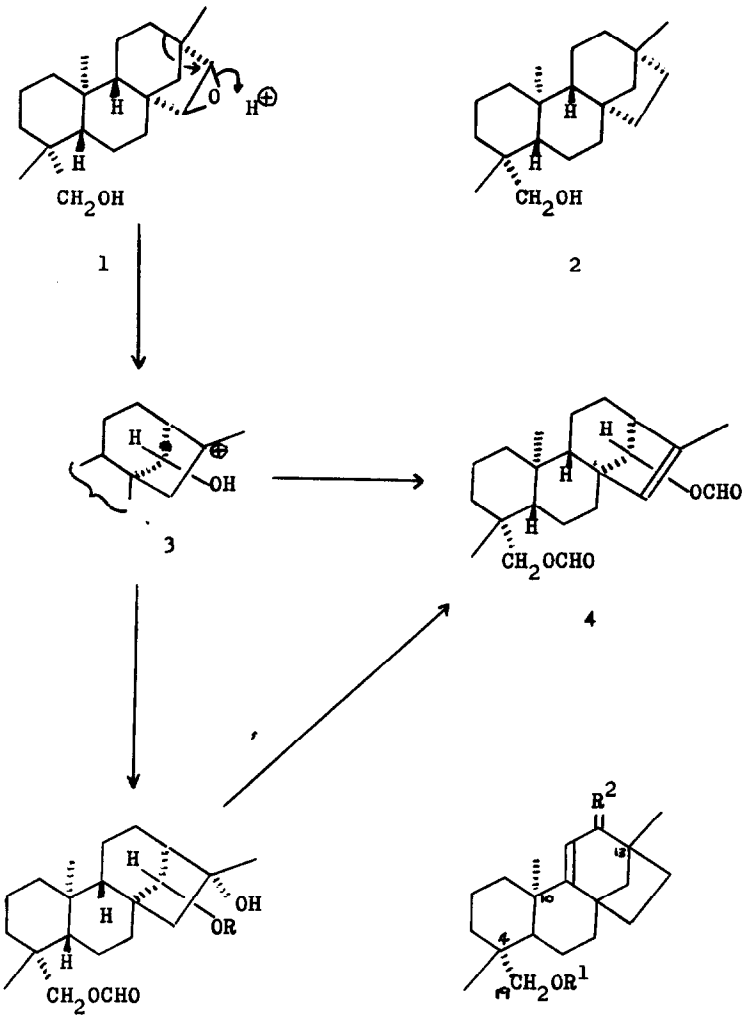
Two distinct concentration dependent rearrangement processes appear to be operative. Exposure of 1 to 95% formic acid (85 mg/ml) for 5 min. gave mainly an enediol diformate, m.p. 135-136°, the NMR of which reveals two tertiary methyls (τ 9.05 and 8.87) and a vinyl methyl (τ 8.28, d, J = 1Hz) adjacent to one vinyl proton (τ 4.98, m). The compound possesses both a primary and a secondary formate group, the methine proton associated with the latter being considerably deshielded (τ 4.50, bs). Bearing in mind the hibaene epoxide rearrangement,[3] the spectroscopic data is consistent with structure 4, which can arise from the carbonium ion (3) by deprotonation and esterification. Two related compounds, a triol diformate (5), m.p. 126-128° and a triol monoformate (6), m.p. 161-164°, were also formed in significant amounts under these conditions. The former possesses three tertiary methyls and a tertiary hydroxyl and was smoothly dehydrated to 4 with $POCl_3$/pyridine. 5, which slowly hydrolyses to 6 on standing, can arise from 3 by solvent capture, probably from the less hindered α-face.[3]

At higher concentrations of 1 in formic acid (750 mg/ml) a more deep-seated rearrangement predominated. The main product (35%) was a diol monoformate,

$C_{21}H_{32}O_3$, m.p. 105-106° which was not formed when 4, 5 or 6 were resubjected to formic acid and must therefore arise from 1 by an alternative pathway. This compound contains a primary formate grouping (τ 5.53 and 5.85, 2H, $\underline{J}$ = 11Hz) necessarily located at C-19, three tertiary methyls and the grouping  with one vinyl hydrogen (τ 4.58, d, $\underline{J}$ = 4Hz) coupled to the methine proton (τ 6.38, d, $\underline{J}$ = 4Hz) of a secondary alcohol (ν_{max} 3600 cm^{-1}). Since the former signal appears as a sharp doublet while the latter doublet is only slightly broadened, probably by 'W' coupling,[4] the groups x, y and z are probably all  . This tetracyclic alcohol was readily oxidised to a conjugated cyclohexenone, $C_{21}H_{30}O_3$, (ν_{max} 1676 cm^{-1}; λ_{max}^{EtOH} 245 nm, ε 12,900), the one vinyl proton resonating as a sharp singlet at τ 4.22. The available evidence can be accommodated by tentatively assigning structure 7 to the alcohol, though a satisfactory mechanism for its formation from 1 is not yet apparent to us. Support for structure 8 for the enone is provided by the NMR of the derived hydrolysis product (9). This discloses three tertiary methyls at τ 8.83, 8.90 and 9.05 (in $CDCl_3$) which move to τ 8.76, 9.12 and 9.15 (in C_6H_6) and are therefore[5] attached to C-13, C-10 and C-4 respectively. Hydrolysis of 7 gave an enediol (10) catalytic hydrogenation of which stereoselectively afforded only one saturated alcohol, m.p. 130-131°, isomeric with 2. Although their IR spectra differed slightly, the NMR and mass spectra of the two isomers were virtually identical. Again, the two alcohols could not be distinguished by GLC but while their m.p's were identical, admixture resulted in depression. From these observations, it is likely that the structure of the hydrogenolysis product is very similar to 2, possibly differing only in stereochemistry.

Although the rearrangement of epoxides to allylic alcohols is well established,[6] it is not possible for 1 to rearrange in this simple manner owing to the absence of hydrogens on the carbons adjacent to the epoxide moiety. Thus the formation of 7 from 1 must be the result of a much more complex rearrangement. Significantly perhaps other novel epoxide rearrangements have recently been reported.[7]

Work is in progress to confirm the structure of 7 and to elucidate the structures of the remaining reaction products, a number of which have been found



1 2

3 4

5: R=CHO

6: R=H

7: R^1=CHO, R^2=H, OH

8: R^1=CHO, R^2=O

9: R^1=H, R^2=O

10: R^1=H, R^2=H, OH

to emanate from 7 on further formic acid treatment. Preliminary results suggest that one such compound is an unsaturated pentacyclic ether, $C_{20}H_{30}O$, which remarkably must involve both the hydroxymethyl group attached to ring A and the epoxide on ring D.

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