

A NOVEL NEIGHBORING GROUP PARTICIPATION IN THE SOLVOLYSIS OF
 α -3,4-EPOXYCARANE WITH A CARBOXYLIC ACID

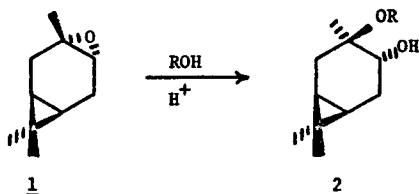
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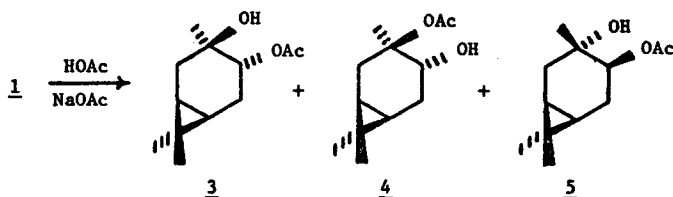
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The recent interest in the conformational and configurational relationships in the carane series¹ prompts us to report an abnormality observed in the solvolysis of (+)- α -3,4-epoxycarane, 1, with a sodium acetate buffered solution of glacial acetic acid.²

The acid catalysed solvolytic opening of α -3,4-epoxycarane, 1, in alcohols (R = CH₃, -C₂H₅)³ or water (R = H)⁴ is known to give good yields of 3-substituted 4-neocaranol⁵, 2, with only very small percentages of the opposite 3-hydroxy-4-neoisocaranyl derivatives being produced.⁶ These results are in full accord with observations recorded by us and others for the opening of alkyl substituted cyclohexane epoxides.⁷ However, when α -3,4-epoxycarane was solvolyzed

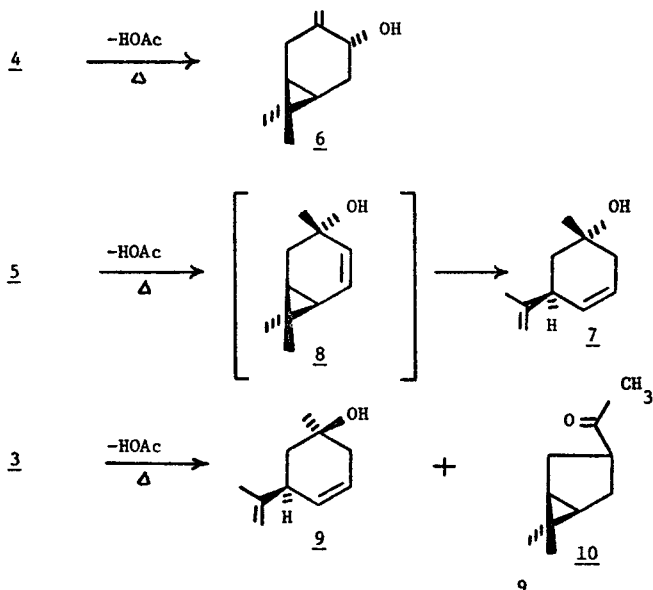


in an anhydrous sodium acetate buffered solution of glacial acetic acid at room temperature three different hydroxyacetates were produced in the ratio 3 : 1 : 1 (compounds 3 : 4 : 5)



The major hydroxyacetate 3 (m.p. 69.5 - 70.5°) was easily isolated by crystallization from the mixture and identified by direct comparison of its spectra (I.R., N.M.R., M.S.) and mixed melting point

with an authentic sample of (+)-3-hydroxy-4-neocaranylacetate prepared by the procedure of Kropp.⁵ The minor components, 4 and 5 were isolated as a mixture contaminated by 3 and identified by isolation of their respective vapor phase pyrolysis (485°) products via preparative GLPC. 3-Acetoxy-4-neocaranol, 4, gave 3(10)-carene-4-ol⁵, 6, in the pyrolysis mixture while 3-hydroxy-4-neoisocaranylacetate, 5, gave cis-4,8-m-menthadiene-1-ol⁸, 7, via a sigmatropic rearrangement of the intermediately formed 3-hydroxy-4(5)-carene, 8.

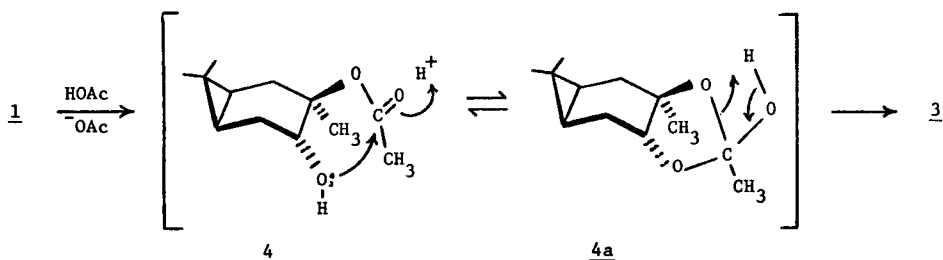


Similarly, pyrolysis of 3 afforded trans-4,8-m-menthadiene-1-ol⁹, 9, along with the ring contracted ketone, 6,6-dimethyl-3-acetyl-bicyclo[3.1.0]-hexane,^{10, 11}, 10, in a ratio of 76 : 24.

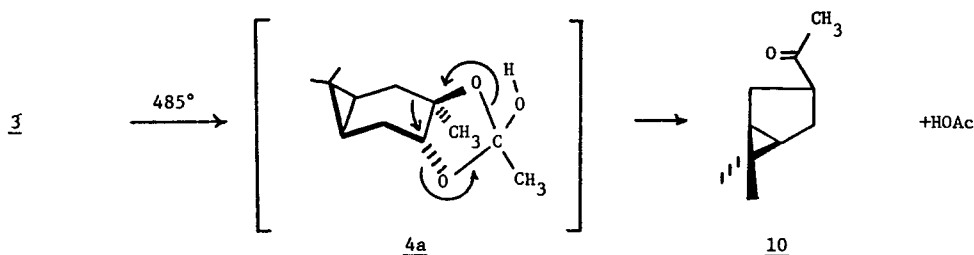
The formation of 4 and 5 in the epoxide solvolysis arises via classical attack¹² of the nucleophilic acetate ion on the protonated oxirane with inversion of configuration at the carbon atom attacked. 3-Hydroxy-4-neocaranylacetate, 3, however, cannot arise either by direct nucleophilic attack or by a free secondary carbonium ion (as has been suggested for formation of minor products in the solvolysis of cis-4,5-epoxycarane¹³) since this would require the unlikely situation of inversion of configuration at both C-3 and C-4. Therefore, under the solvolytic conditions employed, 3 must arise by neighboring group interchange of the initially formed 4 through 4a. While such neighboring group interchange occasionally occurs in cyclohexyl systems in the form of cis hydroxy ester interchange, this is the first report of such exchange of a trans system derived during solvolysis of a cyclohexyl epoxide system¹⁴. In confirmation

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of this postulate, when 4 was treated under similar solvolytic conditions, rapid transformation to 3 occurred. Significantly, neither cis or trans diacetates were formed during solvolysis under our anhydrous reaction conditions thus indicating an internal collapse of the intermediate



ortho acid 4a rather than a further solvolytic course¹⁵. The related observation that 3 is converted pyrolytically into the ring contracted ketone 10 affords additional indirect support for the formation of the intermediate 4a since the most reasonable rationale for such pyrolytic

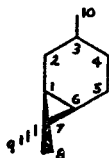


ring contraction would envision a concerted elimination - rearrangement of 4a \rightarrow 10¹⁶.

R E F E R E N C E S

1. P. Teisseire, A. Galfre', M. Plattier, P. Rouillier and B. Corbier, *Recherches* 16, 119 (1967); K. Gollnick and G. Schade, *Ann.* 721, 133 (1969); S. P. Acharya and H. C. Brown, *J. Am. Chem. Soc.*, 89, 1925 (1967).
2. The solvolysis of α -3,4-epoxycarane in acetic acid has previously been found by Z. Chabudzinski and H. Kuczynski, *Roczniki Chem.*, 33, 871 (1959), to give p-cymene, (-)-4-caranone, an unknown ketone (probably carvenone) and, as the major product, a monoacetate of a carandiol (no structure designated).
3. Z. G. Isaeva and B. A. Arbuzov, *Zh. Obshch. Khim.* 19, 893 (1949); *Chem. Abstr.* 44, 3467 (1950); Z. G. Isaeva and I. S. Andreeva, *Dokl. Akad. Nauk SSSR*, 152, 106 (1963); *Chem. Abstr.*, 59, 15314 (1963).

4. B. A. Arbuzov and B. M. Mikhailov, *J. Prakt. Chem.*, 127, 1 (1930); H. Schmidt, P. Richter and M. Muhlstadt, *Chem. Ber.*, 96, 2636 (1963).
5. P. J. Kropp, *J. Am. Chem. Soc.*, 88, 4926 (1966).
6. The numbering system employed for the carane ring corresponds to the IUPAC rules as follows:



7. (a) B. Rickborn and J. Quartucci, *J. Org. Chem.*, 29, 3185 (1964); (b) H. Kuczynski and A. Zabza, *Roczniki Chem.*, 37, 773 (1963); *ibid.*, 35, 1621 (1961); (c) R. M. Bowman, A. Chambers and W. R. Jackson, *J. Chem. Soc.*, (C), 612 (1966); (d) A. A. Akhrem, A. M. Moiseemlpv and V. N. Dobrynin, *Russ. Chem. Rev. (Eng. Trans.)*, 37, 448 (1968); (e) J. C. Leffingwell and E. E. Royals, *Tetrahedron Letters*, 3829 (1965); (f) E. E. Royals and J. C. Leffingwell, *J. Org. Chem.*, 31, 1937 (1966).
8. G. Ohloff, *Tetrahedron Letters*, 3795 (1965).
9. All new compounds gave appropriate I.R., N.M.R. and mass spectra.
10. M. Walkowicz and H. Kuczynski, *Roczniki Chem.*, 40, 1231 (1966).
11. This appears to be the first report of the formation of ring contracted ketones via the pyrolysis of *trans*-1,2-cyclohexane hydroxyacetates. This type reaction has subsequently been observed by us in a reinvestigation of the *p*-menthane series, also (see ref. 16).
12. R. E. Parker and N. S. Isaacs, *Chem. Revs.*, 59, 737 (1959).
13. G. Ohloff and W. Giersch, *Helv. Chim. Acta*, 51, 1328 (1968); These authors use a historical numbering system for the carane ring (see ref. 6).
14. To the best of our knowledge, there have been no reported examples of a neighboring group ester exchange in any *trans* cyclohexyl systems in which both groups were directly participating (that is, neither functional group was a "leaving group"). Additional evidence for a transition state such as 4a has also been derived during the basic hydrolysis of 3-acetoxy 4-neoisocaranylacetate (the diacetate corresponding to 3) in that the hydrolysis of the intermediate formed product 4 is extremely rapid relative to the diacetate. This observation is strong evidence for neighboring group participation during base hydrolysis.
15. B. Capon, *Quart. Rev.*, 18, 45 (1964) and ref. therein; E. S. Gould, "Mechanisms and Structure in Organic Chemistry," H. Holt and Co., Inc., New York, 1959, pp. 565-566.
16. J. C. Leffingwell and R. E. Shackelford, *Tetrahedron Letters*, 2003 (1970).

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