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ACID-CATALYZED CYCLIZATION OF 2-(3-BUTENYL)-1-VINYLCYCLOPENTANOL[1]

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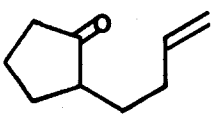
As part of a study on the stereochemistry[1] and synthetic utility of cationic olefin cyclizations we have included an examination of cyclizations involving cyclopentyl systems. We now report the initial results from our cyclization studies with the vinylcyclopentanol 2. The unexpected behavior of this system toward acid-catalyzed cyclization offers insight into the mechanisms of biogenetic-like olefin cyclizations as well as into constraints on synthetic applications of such reactions.

The known[2] 2-(3-butenyl)cyclopentanone (1) was prepared by alkylation of the potassium salt of ethyl 2-oxocyclopentanecarboxylate with 4-bromobutene followed by decarboethoxylation with lithium iodide in refluxing collidine. Treatment of this ketone with vinyllithium gave, after removal of hydrocarbon impurities by column chromatography, the allylic alcohol 2 in 94% yield: ir(film) 3450 (-OH), and 913 and 995 cm^{-1}(-CH=CH_2); nmr(CCl_4)δ 4.7-6.2 ppm(-CH=CH_2). Since this alcohol could only be evaporatively distilled[3] at <0.001 mm in small amounts, the crude product was used in cyclization studies.

Treatment of alcohol 2 with anhydrous formic acid[4] at room temperature for a period of 7.5 min led to cyclic formates in 91% yield: ir(film) 1725 and 1180 cm^{-1} (-OCHO). Analysis by vpc[5a] showed only two long retention-time peaks in a ratio of ~30:70. The ratio of these products could be varied only slightly (range - 15:85 to 36:64) by changes in reaction conditions (changes in temperature, reaction time, concentration, addition of sodium formate). Hydrolysis of the formate group with potassium carbonate in methanol-water at room temperature gave two alcoholic products which have been assigned structures 3 and 4. Separation of these two products could be effected only by preparative vpc.[5b]

Isolation of the minor product by vpc gave alcohol 3 which gave an infrared spectrum with strong bands at 910 and 990 cm^{-1} ($-CH=CH_2$). The nmr spectrum showed the characteristic absorption for a terminal vinyl double bond at δ 4.7-6.2 ppm. The structure and stereochemistry of this alcohol was proven conclusively by oxidation to the ketone 5 with Jones reagent.[6] This ketone was shown to be identical (ir, nmr, vpc, and mp of semicarbazone: 174-179°, dec.) with an authentic sample.[7]



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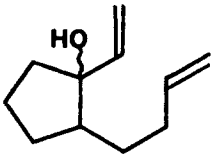

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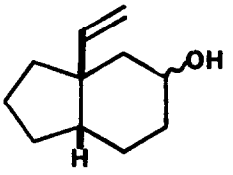

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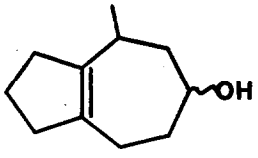

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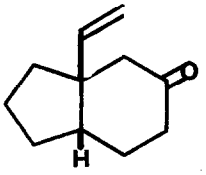

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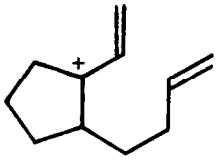

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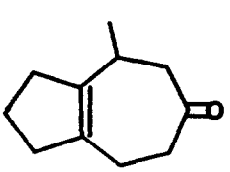
The formation of hydrindane products with a cis ring fusion as observed in this cyclization is predicted on the basis of maximum orbital overlap of the double bond with the ring carbon in cation 6. Examination of models shows the approach of the double bond to form cis products to be much more favorable than the approach leading to trans products.

The major alcohol from the cyclization was also isolated by preparative vpc and has been assigned structure 4. High resolution mass spectra confirmed the elemental composition (Calculated for $C_{11}H_{18}O$: 166.135758; Found: 166.135424). The ir and nmr spectra showed the absence of a terminal vinyl double bond. The nmr spectrum did show a sharp doublet centered at δ 1.07 ppm (CCl_4, J=7.0 Hz, 60 and 100 MHz, $-CH-CH_3$). Oxidation with Jones reagent gave the corresponding ketone which has been assigned structure 7: ir(film) 1700 cm^{-1}(C=O). The nmr spectrum showed absorption for a secondary methyl group at δ 1.06 ppm (CCl_4, J=6.5 Hz, 100 MHz). Strong virtual coupling was observed for this absorption in the 60 MHz spectrum.

The evidence for a secondary methyl group in the nmr spectra of products 4 and 7 and the position of the carbonyl absorption in the infrared spectrum of ketone 7 eliminate alternative

structures such as ketone 8 that could be reasonably derived from cyclization of alcohol 2. Further evidence for structure 4 was obtained by conducting the cyclization in the presence of deuterium. A sample of alcohol 2 was treated with deuterioformic acid, and the product was converted to ketones 5 and 7 which were then separated by vpc. The mass spectrum of ketone 5 showed no significant incorporation of deuterium. However the spectrum of ketone 7 showed almost exclusive incorporation of at least one deuterium into this product.



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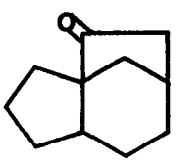

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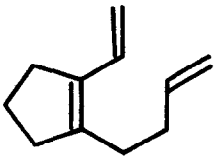

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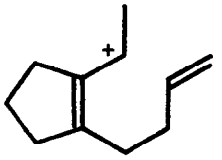

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The above results are readily explained through a mechanism involving the intermediacy of triene 9. The hydrindane product 3 would be formed by direct cyclization of cation 6. However, deprotonation of cation 6 or direct dehydration of allylic alcohol 2 would give the triene 9. This reaction might be expected to be relatively rapid on the basis of the known rapidity of elimination reactions in cyclopentanes relative to cyclohexanes.[8,9] Reprotonation of triene 9 would then lead to cation 10, the logical precursor of alcohol 4, rather than the initial cation 6.

The unexpected diversion of the cyclization of alcohol 2 to hydroazulene products suggests that direct means for generating cation 10 could serve as an efficient hydroazulene synthesis.[10,11]

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8. Cf. E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Interscience, New York, N.Y., 1965, pp. 205 and 206.

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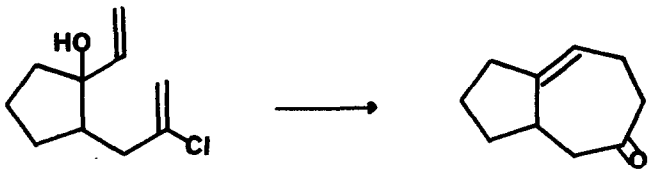

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11. The research reported herein was conducted as partial fullfillment of the requirements for the Doctor of Philosophy Degree by W. D. N.