

THE CYCLIZATION OF EPOXYOLEFINS. (1) V. A MODEL FOR
SYNTHESIS OF RING A OF THE DITERPENE ACIDS

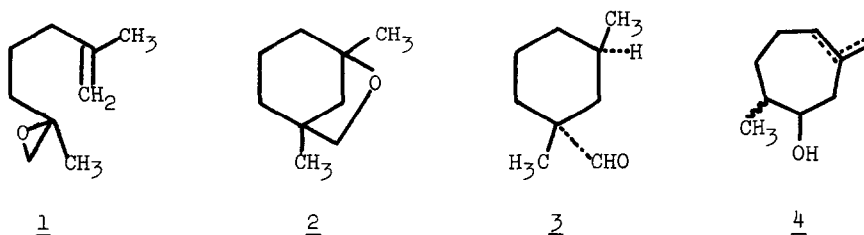
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In the previous communication (3) we showed the feasibility of generating a cyclohexyl system, bearing an oxygenated carbon atom in the typical Ring A exocyclic position of diterpene acids, from an epoxyolefin precursor. We wish to report here the synthesis of a model system for diterpenoids bearing the characteristic C-4 methyl-carboxyl or methyl-hydroxymethyl substituents.

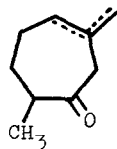
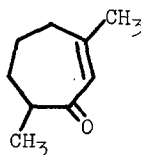
The epoxide 1 was prepared by treating 6-methyl-6-hepten-2-one with dimethyloxosulfonium methylide (4). Cyclization of 1 was carried out employing



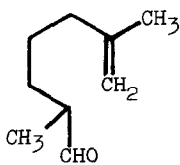
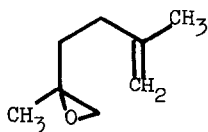
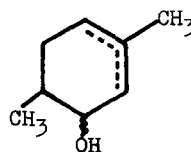
a number of acid catalysts and the product composition varied with the catalyst. Using boron fluoride etherate in benzene for 15 min. at 5-15° an 80% yield of volatile materials was obtained (5) comprised of 42% of the bicyclic ether 2 (6), 35% of the saturated aldehyde 3, 20% of a mixture of unsaturated alcohols 4, and 3% of an unidentified fraction. The aldehyde 3 was identified by its conversion with oxygen to 1,3-dimethylcyclohexanecarboxylic acid (7) and its stereochemistry follows from the pathway of its formation; a → b.



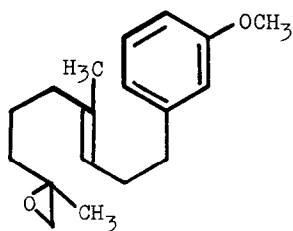
The alcohol fraction 4 contains at least four isomeric substances having varying positions of the double bond. The seven-membered ring structure was demonstrated by chromic acid oxidation of 4 to the β,γ -unsaturated ketones 5 (the double bond positions shown by NMR measurements) and isomerization of the latter with p-toluene sulfonic acid in chloroform to the α,β -unsaturated ketone 6. The NMR spectrum of 6 shows resonance lines for a methyl group on a saturated carbon atom (1.05 p.p.m.) and a single vinyl hydrogen alpha to a carbonyl group (5.79 p.p.m.). Other spectral measurements ($\lambda_{\max}(\text{EtOH})$ 236 m μ , ϵ 11,500; $\bar{\nu}_{\max}(\text{CCl}_4)$ 1660, 1640 (shoulder)) are also in accord with the structural assignment of 6.

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The formation of 4 apparently occurs after opening of the oxirane ring of 1 without participation to yield the aldehyde 7. We have also found that the same type of sequence, epoxyolefin \rightarrow unsaturated aldehyde \rightarrow unsaturated cyclic alcohol is the only reaction pathway followed in the cyclization of epoxide 8. The product in this case is a mixture of the alcohols 9. This latter cyclization is essentially the same type as recently reported by Johnson and co-workers (8).

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In a subsequent communication we shall report the results of the acid catalyzed cyclization of epoxide 10 which yields a number of tricyclic products.



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References

1. This work was generously supported by a grant from the Public Health Service, GM-11728.
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5. Satisfactory elemental analyses were obtained for all new compounds reported. NMR chemical shifts are reported relative to TMS as internal standard. Relative yields were obtained from gas chromatographic peak area measurements using cyclohexanol as an internal standard.
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