

1,5-HYDROGEN MIGRATIONS IN MEDIUM-RING 3,4-EPOXYCYCLOALKENES¹

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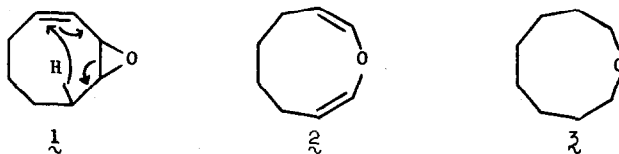
Since their relatively recent recognition as important thermal reactions, 1,5-hydrogen migrations in pentadienyl systems have been amply documented, particularly in medium-ring derivatives.³ An interesting modification of this reaction involves the "homodienyl" analog in which one of the double bonds is replaced by a cyclopropyl ring.³ In this instance the hydrogen-migrated product is a 1,4-diene. We now report that the analogous medium-ring epoxides undergo strikingly similar reactions to those of their carbocyclic counterparts.



Thus, vapor phase pyrolysis of 3,4-epoxycyclooctene (1) in a flow system at 460° and 0.25 mm pressure yields a product mixture which consists of five components, typically in the ratio of 38:1:42:18:1. Isolation of pure samples of these materials by preparative gas chromatography resulted in their identification as cis,cis-3-oxa-1,4-cyclononadiene (2), 9-oxabicyclo[4.2.1]-non-7-ene, starting material, 3-cyclooctenone and 2-cyclooctenone, respectively.⁴

The structure of 2 was established by a combination of physical and chemical data. The mass spectrum of 2 displayed a molecular ion peak at $m/e = 124$ and the infrared spectrum showed bands at 3.28 ($=CH$), 6.04 and 6.10 μ ($C=CO$).⁵ The nmr spectrum consisted of a two-proton doublet ($J = 6$ cps) at τ 3.96 ($C=CHO$), a two-proton overlapping doublet of triplets ($J = 6, 8$ cps) centered at 5.11 ($OC=CH$) and four-proton multiplets at 7.73 ($C=CCH_2$) and 8.38 (CH_2).⁶ Treatment of 2 with aqueous chromic acid resulted in a combined hydrolysis and oxidation to generate suberic acid in high yield. Hydrogenation of 2 took up two moles of hydrogen to give oxacyclononane (3) [infrared: 8.83 and 9.07 μ ; nmr: broad bands at τ 6.48 (CH_2O) and 8.4 (CH_2) in a 1:4 ratio; mass spectrum: molecular ion at $m/e = 128$]. Chromic acid oxidation of 3 also produced suberic acid smoothly. These data serve to define the gross structure of 2, while the simplicity of the nmr spectrum and the magnitude of the coupling between the olefinic

protons (6 cps) strongly support the assigned cis,cis stereochemistry.⁷



The conversion of $\tilde{1}$ to $\tilde{2}$ is considered to involve a 1,5-hydrogen migration in a synchronous process as indicated by the arrows in the structure above. This transformation parallels the thermal conversion of 2-bicyclo[6.1.0]nonene to cis,cis-1,4-cyclononadiene³ almost exactly. As observed for the latter reaction, the $\tilde{1}$ to $\tilde{2}$ conversion is reversible and pyrolysis of a pure sample of $\tilde{2}$ under the standard conditions gave a 14:86 ratio of $\tilde{1}:\tilde{2}$. While equilibrium is not achieved in the flow system, the results obtained by starting from the two isomeric compounds would appear to bracket the equilibrium concentrations and indicate that comparable amounts of each will be present at equilibrium at 460°.

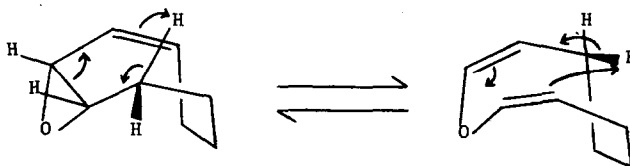
The absence of the other products in the pyrolysis of $\tilde{2}$ leads us to suspect that the observation of these materials in the pyrolysis of $\tilde{1}$ is the result of competing heterolytic processes catalyzed by trace impurities in the starting material or by active sites on the glass surfaces of the pyrolysis chamber. Support for this hypothesis is also found in the deviations of the pyrolysis product ratios from $\tilde{1}$ in different runs and in the pyrolysis of $\tilde{1}$ over Florisil at lower temperatures, which produces only small amounts of $\tilde{2}$ along with substantial quantities of the other products described above. Finally, thermolysis of neat $\tilde{1}$ in a sealed tube at 195° for 2 days gives a 60:40 mixture of $\tilde{1}:\tilde{2}$ which was essentially free of other products.

A further parallel³ of the epoxide rearrangement with those of its carbocyclic analogs is found as the reactive moiety is incorporated into smaller rings. Thus 3,4-epoxycycloheptene pyrolyzes to cis,cis-3-oxa-1,4-cyclooctadiene [infrared: 6.04 and 6.10 μ ; nmr: a two-proton doublet ($J = 7.5$ cps) at τ 3.76, a two-proton overlapping doublet of triplets ($J = 7.5, 8$ cps) centered at 5.72, a four-proton multiplet at 7.62, and a two-proton multiplet at 8.82], starting material, 3-cycloheptenone and 2-cycloheptenone in a 20:15:54:11 ratio. The 1,5-hydrogen migration product is of less importance here than in the larger ring. Pyrolysis of the divinyl ether obtained from the seven carbon epoxide did not regenerate observable starting material; but, rather, a small amount of 3-cycloheptenone was the only product. However, the most reasonable source of this ketone would appear to be by way of the epoxide. This result can be construed to mean that interconversion of the divinyl ether and the epoxide did obtain, although

the equilibrium strongly favors the former. The next smaller ring compound, 3,4-epoxycyclohexene gives no 1,5-hydrogen migration product, only 2- and 3-cyclohexenone are observed. Preliminary examination of several acyclic examples has also failed to uncover products derived from this process.

The 1,5-hydrogen migrations are favorable in the various medium-ring series since the molecular framework aids in achieving the proper geometrical array of atoms in the reactive moiety for the transformation to occur. As the ring size is decreased the resulting loss of flexibility mitigates against an energetically reasonable conformation with the necessary geometry for reaction, consequently the lack of 1,5-hydrogen migration with the cyclohexyl derivative and its lesser importance in the cycloheptyl case.

It should be noted that reaction of both the cyclopropyl and epoxy derivatives apparently proceed by way of a somewhat unfavorable conformation in which the three-membered ring protrudes toward the center of the molecule, whereby destabilizing nonbonded repulsions are experienced. However, the stereoelectronic situation in this conformation allows for better overlap among the orbitals involved in the breaking and forming of bonds as a molecule is converted from reactant to product. In the alternate, more stable conformer with an "equatorial-like" three-membered ring the stereoelectronics are not as good. In addition, a synchronous reaction from this conformation should lead to a cis,trans geometry of the double bonds in the product ether. This product is, of course, not observed and forms the experimental basis for our conclusion regarding the reactive conformation. On the other hand, it is entirely possible that product stability is the controlling feature here and the more strained nature of the cis,trans isomer is the real factor which mitigates against its formation.



This study illustrates that the carbon-carbon σ -bond of an epoxide can replace one of the π -bonds of a dienyl system in facilitating 1,5-hydrogen migrations in the same sense that a cyclopropane σ -bond participates in such reactions. This is so despite the substantial difference in strain energy between a cyclopropane and an epoxide function (26 vs 13 kcal.).⁸

We are currently engaged in elaborating on this work and examining other thermal trans-

formations of epoxides.

References

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