The Cyclohexane-1,4-diyl Mechanism for Cope Rearrangements. Phenyl Substitution in the Oxy-Cope System

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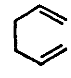
Summary Phenyl substituted oxy-Cope systems give rate ratios for the two competing components which rule out the intermediacy of cyclohexane-1,4-diyl diradicals in these rearrangements, although such intermediates have recently been implicated in the rearrangements of some phenyl hexa-1,5-dienes.

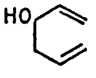
In 1971 Doering and his co-workers suggested the intermediacy of 1,4-cyclohexylene, (**1**), as a possible pathway for the Cope rearrangement.[1] Recently, Dewar and Wade[2] reported experimental verification of this pathway in the 2-phenyl and 2,5-diphenyl derivatives of hexa-1,5-diene, (**2**).

(1)



(2)

(3)



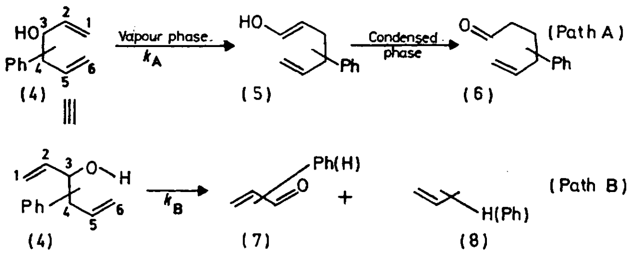
(4)

The relative rates of rearrangement of these two derivatives were 41 and 2000 times that of unsubstituted (**2**). This factor was consistent with the intermediacy of a diradical, such as (**1**), and not with a pericyclic mechanism, as in (**3**). A 3-phenyl substituent, however, gave an 18-fold rate enhancement, which was thought to indicate the pericyclic mechanism in that particular derivative.

Table. Ratio of Cope: cleavage products at 350°.

Substituent	k_A/k_B
None, (**4**)	1·5
1-phenyl, (**4a**)	0·5
2-phenyl, (**4b**)	1·2
3-phenyl, (**4c**)	2·2
4-phenyl, (**4d**)	1·4
5-phenyl, (**4e**)	1·6

We now report preliminary results of a study of phenyl substitution effects on the oxy-Cope rearrangement.[3] The oxy-Cope system[4] consists of two competitive, first order, unimolecular reactions, one of which is a Cope process (path A), and the other a β-hydroxyolefine cleavage (path B). Surprisingly, the Cope component does not appear to be an equilibrium and the ratio of products observed, in a flow system, is independent of the residence time in the heated zone.[4] The enol (**5**) formed in the gas phase, ketonizes only upon condensation to produce the observed carbonyl product, (**6**).



a; 1-Ph d; 4-Ph
b; 2-Ph e; 5-Ph
c; 3-Ph

Although only crude rate data for the two reaction pathways in (**4**) have been reported,[5] the relative rate of the two pathways is simply the weight ratio of products (**6**): (**7** + **8**). The reported[5] product ratio in the thermolysis of (**4**) is 1·5 at 350°. For derivatives (**4a**—**e**), it may be assumed that the effect of the phenyl substituent upon each path can be added to the effect of the hydroxyl or the vinyl substituent, respectively. Since phenyl substitution effects upon the Cope and cleavage reaction components are known, a comparison of product ratios, and thus k_A/k_B, is possible.

The five phenyl derivatives (**4a**—**e**) were prepared by the reaction of appropriate Grignard reagents upon the appropriate carbonyl component.† In all cases the reaction

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† The alcohols, (**4a**—**e**) and products, (**6a**—**e**) all gave satisfactory C and H analyses and consistent n.m.r. and i.r. spectra. Product structures were established by further chemical means where necessary.

proceeded readily at 350°, under a pressure of 10 mm and in a nitrogen atmosphere. The values of k_A/k_B, experimentally determined by g.l.c. with an expected accuracy of $\pm 6\%$, are listed in the Table.

The minimal variations‡ in the observed ratios are consistent only with a concerted pathway for both the cleavage and [3,3] rearrangements, whereas a diradical Cope pathway would be expected to respond differently to the phenyl substituents. For example, in the case of (**4b**), the phenyl substituent should not affect the cleavage reaction since it is quite distant from the reaction site. A forty-fold rate enhancement is to be expected for the [3,3] component if it proceeds by the diradical path, but none if it proceeds by the pericyclic route.[2] The value of k_A/k_B is 60, if the diradical path is involved, or 1·5 if the reaction is pericyclic. In the cases of (**4c**) and (**4d**) the rate enhancement for the cleavage component is expected[6] to be about 20, while that for a pericyclic Cope process[2] is 18. The product ratio expected is therefore 1·5, in good agreement with observed results,§ whereas a diradical Cope process, unaffected by phenyl substitution at these sites,[2] would result in a ratio of 0·08. The largest observed deviation in k_A/k_B, that of (**4a**), is not unexpected since steric considerations alone demand a decrease in the rate of the Cope process, and hence of k_A/k_B, regardless of the mechanism involved.

If more than one mechanism exists for the Cope rearrangement, then the reaction may be swayed in one direction or the other by substituents. If this is the case, the radical stabilizing effect of a phenyl substituent can be negated by an hydroxyl function which stabilizes the forming double bond¶ in the requisite pericyclic transition state.

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‡ The small variations in experimental Cope : cleavage ratios do not necessarily imply small substituent effects on individual reaction rates. That both reaction components are speeded up considerably in (**4c**) and (**4d**), in relation to (**4**), is indicated by the much lower temperatures required to drive the reaction to completion under otherwise identical conditions.

§ The agreement between observed and calculated pericyclic ratios for (**4c**) and (**4d**) becomes even closer when conformational differences in the requisite transition states, leading to paths A and B, are considered together with the unknown *threo–erythro* ratio in (**4d**). These factors will be discussed in a full paper.

¶ The stabilizing influence of a hydroxy function upon a double bond, as in (**5**), is not known, but it must be this factor which is responsible for the essential irreversibility of the oxy-Cope rearrangement. The stabilization energy due to a methoxy function upon a carbon–carbon double bond has been evaluated at 5·1 (ref. 7) to 6·8 (ref. 8) kcal mol.$^{-1}$

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