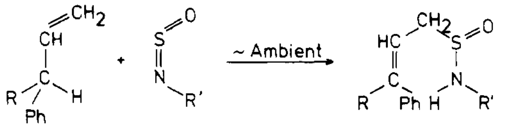
*J. Org. Chem.* **1982**, *47*, 2677-2679

# *Communications*

## Transition-State Geometry in Superene Reactions

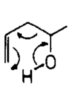
*Summary:* A pseudopericyclic transition state (TS) involving nonlinear H transfer is proposed for the superene reaction (eq 1), characterized by a temperature-independent isotope effect ($k_H/k_D = 2.863$). Ancillary evidence for rapid, reversible formation of a four-membered cyclic charge-transfer complex is also presented to account for the observed regio- and stereoselectivity of the reaction.

*Sir:* The ene reaction[1,2] between olefins with allylic hydrogen and "regular" enophiles is frequently a poor-yielding preparative procedure usually requiring elevated temperatures (>150 °C) and protracted reaction times. A class of enophiles featured by an S=N bond as the reaction site was found in these laboratories[2] to possess superenophilic properties, having the ability to rapidly convert appropriate olefins to the expected addition products in quantitative yields at near or below ambient temperatures. A case in point is the process expressed in eq 1 by analogy to the usual ene-reaction representation[1] as a concerted pericyclic process.[1b] Our objectives in the studies to be reported here were to seek some clues as to the origins of the greatly diminished activation requirements for superenophilic reactivity.



1 2 3 (1)

Some useful perceptions of the TS‡ geometry in a typical ene reaction have been previously gained through studies of the gas-phase retroene reaction. A variety of homoallylic alcohols and acids (O–H bond breaking)[3] such as **4**–**6** and



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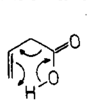

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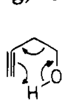

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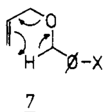

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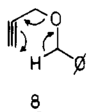

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allylic and propargylic benzyl ethers (C–H bond breaking[4]) such as **7** and **8** have been studied through application of the temperature dependence of the $k_H/k_D$ (TDKIE) criterion of TS‡ geometry.[5] All these cases of unimolecular, gas-phase, thermal rearrangement showed the kinetic isotope effect (KIE) properties associated with a symmetrical (concerted) TS‡ of linear H transfer. Thus, the activation energy difference between corresponding H and D bonds $[\Delta E_a]_D^H$, was found to be nearly identical with the zero-point energy difference of the bond being broken, i.e., $[\Delta E_0]_D^H$, and the $A_H/A_D$ values in each case fell between the limits (≥0.7 and ≤1.2) established for linear H-transfer processes.[5a–c,g] It can therefore be anticipated on the basis of microscopic reversibility that the reverse of each of these processes, all ene reactions, under the very same conditions, must pass through an identically symmetrical TS‡.

Table I. Experimental Method,[a] Data, and Computations of the Temperature Dependence of the Primary Kinetic Deuterium Isotope Effect in the Superene Reaction of $C_6H_5CHDCH{=}CH_2$ (**1**, R = D) with TosN=S=O (**2**, R' = Tos)

| $M_{118}/M_{119}$ | temp, °C | calcd[b,c] $k_H/k_D$ |
|---|---|---|
| 1.8345 ± 0.0002 | 30 | 2.8693 ± 0.0004 |
| 1.8349 ± 0.0001 | 20 | 2.8651 ± 0.0002 |
| 1.8355 ± 0.0002 | 0 | 2.8594 ± 0.0010 |
| 1.8355 ± 0.0001 | −10 | 2.8594 ± 0.0002 |
| 1.8350 ± 0.0011 | 30 | 2.8641 ± 0.0022 |
| 1.8349 ± 0.0003 | 20 | 2.8651 ± 0.0006 |
| 1.8355 ± 0.0006 | 0 | 2.8591 ± 0.0012 |
| 1.8351 ± 0.0007 | 0 | 2.8629 ± 0.0014 |
| 1.8351 ± 0.0002 | −10 | 2.8633 ± 0.0004 |

[a] A typical kinetic run for determining the KIE was conducted as follows. A solution of 2.7 g (23 mmol) of **1** (R = D) in 3 mL of dry $CHCl_3$ was slowly added to a solution thermostated at the stipulated reaction temperature and consisting of an equimolar amount of **2** (R' = Tos) in 17 mL of the same solvent. After 50–70% conversion, the residual solution was drawn off the precipitated reaction product **3**. The latter was triturated with petroleum ether, dried, and then quantitatively decomposed by heating with a ca. 100× excess of water in DME solution for 36 h, similar to the procedure of Sharpless and co-workers.[12] The isotopic composition of the allylbenzene obtained alongside of $TosNH_2$ in accordance with eq 2 was estimated by the high-precesion mass spectrometric method previously developed[5] for the

$$\begin{gathered}\mathrm{PhCHDCH{=}CH_2 + TosN{=}S{=}O} \longrightarrow \\ \mathrm{PhCH(D){=}CHCH_2SOND(H)Tos} \xrightarrow{H_2O} \\ \mathrm{[PhCH(D){=}CHCH_2SO_2H] + TosNH_2} \xrightarrow[-SO_2]{\text{retroene}} \\ \mathrm{PhCH_2CH{=}CH_2 + PhCHDCH{=}CH_2} \qquad (2)\end{gathered}$$

purpose. [b] These values were computed through applying the following relationships:[5g] $M_H/M_{H+1} = 0.0923 \pm 0.0002$, determined on allylbenzene; $M_{D-1}/M_D = 1.545 \pm 0.0001$, determined on the (3-deuterioallyl)benzene; $k_H/k_D = [1 - M_H/M_{H+1}\,(M_{118}/M_{119})]/[(M_{118}/M_{119}) - (M_{D-1}/M_D)]$. [c] Mean $k_H/k_D = 2.863 \pm 0.002$ (standard deviation = $1.95 \times 10^{-4}$. variance = $3.38 \times 10^{-8}$).

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(1) (a) Hoffmann, H. M. R. *Angew. Chem.* **1969**, *81*, 597. (b) Oppolzer, W.; Snieckus, V. *Ibid.* **1978**, *90*, 506. (c) Keung, E. C.; Alper, H. *J. Chem. Educ.* **1972**, *49*, 97.

(2) (a) Schönberger, N.; Kresze, G. *Justus Liebigs Ann. Chem.* **1975**, 1725. (b) Bussas, R.; Kresze, G. *Ibid.* **1980**, 629. (c) Kresze, G.; Bussas, R. *Ibid.* **1980**, 843. (d) Bussas, R.; Kresze, G. *Ibid.*, **1982**, 545.

(3) Kwart, H.; Latimore, M. C. *J. Am. Chem. Soc.* **1971**, *93*, 3770.

(4) Kwart, H.; Sarner, S. F.; Slutsky, J. *J. Am. Chem. Soc.* **1973**, *95*, 5342.

(5) (a) Kwart, H.; Nickle, J. H. *J. Am. Chem. Soc.* **1973**, *95*, 3394; **1976**, *98*, 2881. (b) Janssen, J. W. A. M.; Kwart, H. *J. Org. Chem.* **1977**, *42*, 1530. (c) Kwart, H.; George, T. J.; Louw, R.; Ultee, W. *J. Am. Chem. Soc.* **1978**, *100*, 3927. (d) Kwart, H.; Benko, D. A.; Bromberg, M. E. *Ibid.* **1978**, *100*, 7093. (e) Kwart, L. D.; Kwart, H.; Horgan, A. G. *Ibid.* **1981**, *103*, 1232. (f) Kwart, H.; Horgan, A. G.; George, T. J.; Lin, Y. T. *J. Org. Chem.* **1981**, *46*, 5143. (g) Kwart, H.; Brechbiel, M. *J. Am. Chem. Soc.* **1981**, *103*, 4650.

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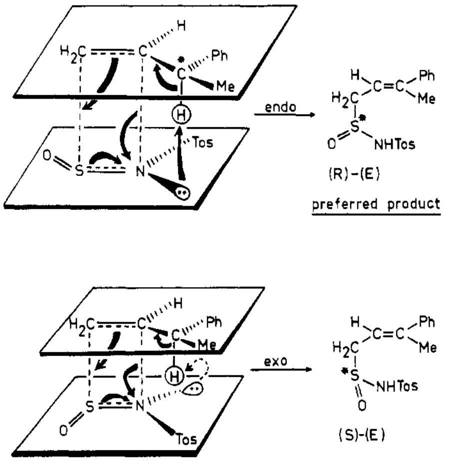


**Figure 1.** The curved arrows are intended to show the motions of the orbitals involved in the bond making and breaking subsequent to the formation of the [2 + 2] CT complex; for example, in development of the tetrahedral nitrogen configuration the n orbital on the nitrogen which is originally coplanar with the Tos substituent rises to angular overlap with the hydrogen being abstracted in the $\mathrm{TS}^{\ddagger}$.

The results of our KIE measurements of the reaction expressed in eq 1, where the substrate olefin 1 used was $PhCHDCH{=}CH_2$ and the superenophile was 2 (R′ = *p*-toluenesulfonyl), are listed in Table I, along with the procedures employed in preparing these reagents and the KIE determinations and computations.

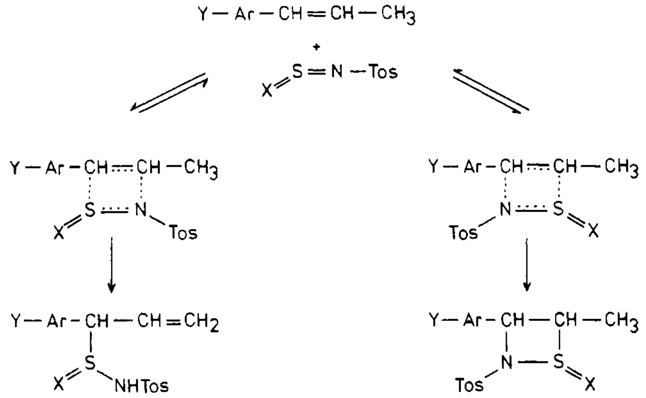
The completely temperature-invariant isotope effect observed in the reaction (eq 1) taking place in chloroform solution over the 40 °C range of study, in which $k_H/k_D = 2.863 \pm 0.002$, is taken as direct evidence[5c,d,g] of a bent $\mathrm{TS}^{\ddagger}$ of H transfer. This conclusion is based on increasingly numerous instances[5] of reactions characterized by such KIE properties. It requires an interpretation which accounts for the geometry of the superene reaction mechanism departing so radically from the addition mode previously elucidated[3] in the gas-phase retroene reaction through recourse to the same temperature dependence of the KIE criterion.

It must first be recognized that the superene reaction is a bimolecular process for which we might ordinarily have expected a lower probability of occurrence than the unimolecular retroene reaction previously studied. These considerations suggest the possibility of preliminary complex formation which orients the reagents (1 and 2) and organizes the subsequent events, including the rate-determining H transfer from carbon to nitrogen in which the process is completed.

In addition to the bimolecular kinetics, other lines of evidence[6] supporting the intervention of a complex in low concentration are (a) the nondetectability of new bonding in the NMR despite color change and thermal manifestations of complexing between the reactants on admixture and prior to the advent of gross product formation, (b) the absence of any likely radical intermediates in measureable concentrations as confirmed by ESR and CIDNP experiments, and (c) the absence of polar intermediates as indicated by the lack of significant solvent effects on the rate.

Other considerations in addition to the nonlinear course of H transfer point to a preliminary complex between the reactants formed with strict regioselectivity. We can presume that the ene and enophile are separately situated in planes which are superposed in an orientation that leads to charge transfer.[7] The product arises from this complex via a bent $\mathrm{TS}^{\ddagger}$ only in the orientation in which the nonbonded electron pair of the nitrogen is in a position to coordinate the allylic H in concert with other bond-making and bond-breaking events in the cycle of atoms comprising the complex (see Figure 1). These circumstances have been described as "pseudopericyclic",[8] implying that the reaction cannot be orbital symmetry forbidden since what is involved is the exchange of mutually orthogonal bonding and nonbonding orbitals on nitrogen. In this sense, it is indeed contrary to the situation prevailing in the "regular" ene reaction for which a pericyclic $\mathrm{TS}^{\ddagger}$ of linear H transfer is stipulated.[1b]

Scheme I[a]



[a] Y = para substituents Cl, $CH_3$, $CH_3O$, H, etc., X = O, NTos.

The regioselectivity, which characterizes the reaction with even the simplest olefins, is readily understandable in terms of the formation of a four-membered cyclic complex in which the electrophilic sulfur is affiliated with the more electron-donating center of the π bond. In many cases this is probably due to the polarization of the double bond. Certainly the regioselectivity of the superene reaction is much more pronounced than that in what is presently recognized as the "regular"[1] ene reaction. A prominent example is that of 2-pentene where the Markovnikov product is exclusively formed with 2 (R′ = Tos) regardless of which isomer, *E* or *Z*, is used.[2b,c]

The high degree of chirality transfer when (*S*)-3-phenyl-1-butene is converted by reaction with 2 (R′ = Tos) into a excess of the *R–E* product rather than the *S–E* enantiomer, as shown in Figure 1, is a reflection of the strong stereoselective control exercised by preliminary complex formation.[6] The endo orientation in which is realized both the maximum superpositioning of unsaturated centers and in which the allylic H is within interacting distance of the lone pair on the nitrogen leads to the predominant, kinetically preferred product. The "pseudopericyclic" $\mathrm{TS}^{\ddagger}$ accommodates both the stereoelectronic requirements for reaction and the nonlinear geometry of H transfer. The linear H transfer specified for the pericyclic $\mathrm{TS}^{\ddagger}$ of the "regular" ene and retroene mechanisms[1,3] does not provide adequately for either the manifest regioselectivity[2] or the stereoselectivity[6] of the superene reaction.

Another strong indication that the preliminary complex has a [2 + 2] structure, as represented in Figure 1, is the fact that actual competition between [2 + 2] cycloaddition and ene reaction has been observed in some cases, and in

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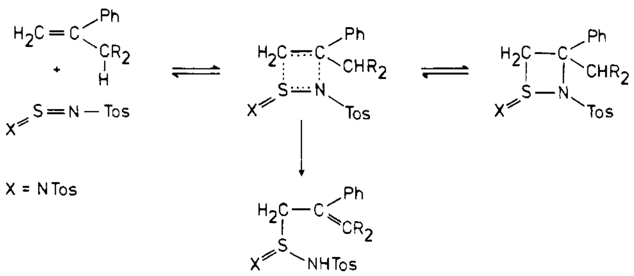
(6) Results to be reported in full detail in future publications.

(7) For a review of the Alder rules to which this proposal beares some analogy, see: Kloetzel, M. C. *Org. React.* **1948**, *4*, 1.

(8) (a) Ross, J. A.; Seiders, R. P.; Lemal, D. M. *J. Am. Chem. Soc.* **1976**, *98*, 4325. (b) Bushweller, C. H.; Ross, J. A.; Lemal, D. M. *Ibid.* **1977**, *99*, 629. For further examples see ref 5c,d.

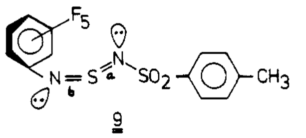
Scheme II



certain others the [2 + 2] cycloaddition is noted to be the only reaction occurring. Two categories of results, each implicating the intervention of a four-membered cyclic complex in its reaction pathway, have thus far been identified. For example, in a series of propenylbenzenes (illustrated in Scheme I) competition exists for the formation of two different orientations of the reactant planes, only one of which can achieve the ene-reaction product while the other results in the [2 + 2] cycloaddition. The most electron-releasing substituents on the aromatic (Ar) group tend to foster the complex which precedes (only) the cyclic product, since an allylic H in this complex is not available for abstraction by the nonbonding pair of the nitrogen. Even where the phenyl ring is unbiased by substitution, the ease of formation of the pre-ene-reaction complex is greatly diminished compared to 1-alkyl-substituted propenes; thus, the ene product from propenyl benzene is found to form at rates which are orders of magnitude lower.[2b,c]

Circumstances have also been encountered where difficulties of steric, conformational and/or bond-strength origin can arise in the rate-controlling H-abstraction step, while formation of the preliminary complex is uninhibited by substitution. Here, it is often detected that the kinetic product is the [2 + 2] cycloadduct which is rapidly and reversibly formed; in fact, this side product can frequently be isolated. A class of examples where the development of the equilibrium ene-reaction product takes place at the expense of the more rapidly formed [2 + 2] cycloadduct is depicted in Scheme II. Analogous observations of steric and conformational substituent effects have been made in the hydroperoxidation of allylic olefins with singlet oxygen[9a], an ene-like reaction for which an actual intermediate or a complex between the reactants prior to the rate-determining allylic-H-abstraction step has been deduced[9b] through KIE studies.

Further evidence supporting this proposal is to be found in the reactions of unsymmetrical (potentially) bifunctional superenophiles. For example, the reagent **9**, *N*-(penta-



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fluorophenyl)-*N*′-tosylsulfur diimide, compared with ditosylsulfur diimide, exhibits very greatly diminished reactivity (ca. factor of >1000 in rate reduction) in the ene reaction at bond b. The X-ray-determined structure of **9** shows[6] that the fluorinated benzene ring is *not* coplanar with the bond b orbitals and tends to sterically mask the *n* orbitals of the nitrogen at bond a from participating in any such "pseudopericyclic" process depicted in Figure 1.

The full details of these and other arguments supporting a mechanism of the superene reaction requiring four-center preliminary complex formation,[10] from which a "pseudopericyclic" TS of nonlinear H transfer emerges, will be discussed in future publications. But this reaction scheme is not unprecedented. Thus, even homolytic processes of allylic H abstraction have been most recently shown[11] to involve the formation of an orienting complex between an abstracting *tert*-butoxy radical and the double bond, preliminary to a nonlinear H transfer occurring in a "pseudopericyclic" TS$^{\ddagger}$.

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**Registry No.** 1 (R = D), 63523-01-3; (*S*)-1 (R = Me), 58717-85-4; *2* (R′ = Tos), 4104-47-6; *3* (R = Me; R′ = Tos), 81654-84-4.

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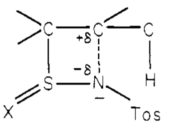
(9) (a) Foote, C. S. *Acc. Chem. Res.* **1968**, *1*, 104. (b) Frimer, A. A.; Bartlett, P. D.; Boshung, A. F.; Jewett, J. G. *J. Am. Chem. Soc.* **1977**, *99*, 7977. (c) See also for full discussions: Frimer, A. A. *Chem. Rev.* **1979**, *79*, 359. Gorman, A. A. *Chem. Soc. Rev.* **1981**, 205.

(10) The possibility that this complex may be better represented by a dipolar structure such as **10** or the corresponding diradical structure



**10**

has not as yet been resolved. Whatever the outcome, however, the evidence indicating the involvement of the lone pair on nitrogen in a "pseudopericyclic" TS of this superene reaction is unaffected by the nature of the carbon–nitrogen bonding in this complex.

(11) Kwart, H.; Brechbiel, M.; Miles, W.; Kwart, L. D., submitted for publication in *J. Org. Chem.*

(12) Hori, T.; Singer, S. P.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 1956.

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## An Approach to the Quadrone Skeleton via a Tandem Aldol-Pinacol[1]

*Summary:* The preparation of a key tricyclic intermediate for the synthesis of quadrone has been accomplished efficiently from a bicyclo[2.2.2]octenone precursor by a regioselective rearrangement to a substituted bicyclo[3.2.1]octenedione and then generation of the tricyclic nucleus by a novel intramolecular aldol–pinacol rearrangement.

*Sir:* The tetracyclic lactone quadrone (1) represents a novel class of sesquiterpenes which possess significant

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[1] This investigation was supported by Grant No. CA 26985, awarded by the National Cancer Institute, DHHS.