ice/CCl_4) and 50 mL of 10% aqueous tartaric acid solution was added while stirring; the aqueous layer solidified. After 30 min, the cooling bath was removed and stirring was continued at room temperature for 1 h or until the aqueous layer became clear. After separation of the aqueous layer, the organic layer was washed once with water,[9] dried (Na_2SO_4), and concentrated to afford a colorless oil with an odor revealing contamination by TBHP.[9]

This oil was diluted with 150 mL of ether, and the resulting solution was cooled in an ice bath, and then 60 mL of 1 N sodium hydroxide solution was added. This produced a two-phase mixture which was stirred at 0 °C for $^1/_2$ h.[10] The ether phase was washed with brine, dried (Na_2SO_4), and concentrated to give 4.24 g of a clear oil. Chromatography on silica gel afforded 2.6 g (77%) of 2(*S*),3(*S*)-epoxygeraniol, $[\alpha]^{24}{}_D$ −6.36° (*c* 1.5, $CHCl_3$). Analysis of this material as the MTPA ester[11] gave an enantiomeric excess (ee) of >95% whereas analysis of the derived epoxy acetate by using $Eu(hfbc)_3$ chiral shift reagent gave 94% ee.

The "typical procedure" given for geraniol has a limitation which is important to emphasize. *Very poor yields are realized if the epoxy alcohol produced is fairly water soluble.* For example, although allyl alcohol and crotyl alcohol are epoxidized by this system, it is difficult to extract (even with "salting-out" techniques) more than 10–30% of the intact epoxy alcohol product. We are working on solutions to the isolation problems presented by these and related cases.

The procedure described above for epoxidation of geraniol calls for 1 equiv of both titanium isopropoxide and diethyl tartrate. This is by no means necessary in all cases. With reactive allylic alcohols (**1a**, **2a**, **3a**, and **4a** in Table I), a catalytic amount (e.g., 0.1 equiv) of both $Ti(O\text{-}i\text{-}Pr)_4$ and diethyl tartrate suffices[12] under otherwise identical reaction conditions. However, for the less-reactive substrates in Table I (**5a**, **6a**, and **7a**), the "1-equiv" conditions described above were necessary to achieve reasonable reaction rates. Even under the "1-equiv" conditions, allylic alcohol **7a** required almost 2 days to approach completion. For this first report, the most general method (stoichiometric amount of the chiral catalyst system) was chosen for presentation. The catalytic system (which has some important advantages[13] in addition to the obvious ones) is under further study.

Many other aspects of this unique epoxidation system are also being investigated in our laboratory. Of foremost interest is a good mechanistic rationale for the remarkable selectivities which are seen. Our approach to the mechanism involves both kinetic studies and structural modifications of the chiral ligand. From a synthetic point of view, there are several interesting further developments, among them: (1) this same epoxidation system is effective for the kinetic resolution of racemic allylic alcohols,[14] and (2) predominant inversion of the enantioselectivity pattern shown in Scheme I is observed with certain minor structural modifications of the chiral tartrate ligand.[15] We are also extending our studies to include homo- and bishomoallylic alcohols, and β-hydroxy sulfides.

To the best of our knowledge, this new enantioselective, catalytic process is discriminating to a degree barely[16] rivaled by any other nonenzymatic catalytic process. In its promiscuous acceptance of varied allylic alcohol substrates,[5] it also has some desirable features which would be difficult for even an enzymatic catalyst to achieve.[17]

Acknowledgments. We dedicate this work to Professor Harry S. Mosher. Through patient sharing of his unique insights into asymmetric synthesis, he has had a profound influence on us. The National Institutes of Health (GM24551) is thanked for financial support.

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(9) Due to the small scale, we have chosen to ignore the excess TBHP. If one wishes to remove it, a number of reductive procedures are available.[8]

(10) Do not expose the reaction mixture to this base treatment for longer than $^1/_2$ h as base-catalyzed rearrangements of the epoxy alcohol may occur: G. B. Payne, *J. Org. Chem.*, **27**, 3819 (1962). Diethyl tartrate is fairly soluble in water and hydrolyzes readily under these conditions. We have found that (+)-dimethyl tartrate (Aldrich) is as effective (>95% ee) as the ethyl ester for epoxidation of **4a**. The methyl ester is much more water soluble and may prove advantageous when the hydrolysis step is unacceptable. The isopropyl ester also works well, but leads to increased trouble at the workup stage.

(11) J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, **34**, 2543 (1969). We used MTPA chloride and DMAP in CH_2Cl_2.

(12) Under these catalytic conditions, (0.1 equiv of $Ti(OR)_4$/DET), the yields of **1b**, **2b**, and **4b** were comparable to or somewhat better than those with 1 equiv, and the product isolations were cleaner and easier. The enantiomeric excess was somewhat poorer for **1b** (91% ee) and **2b** (84% ee) but was still >95% ee for **4b**.

(13) The possibilities for product stability problems, transesterification problems, and most other workup and isolation problems are greatly diminished.

(14) M. Ikeda, Y. Yamada, T. Katsuki, V. S. Martin, and K. B. Sharpless, unpublished results.

(15) J. Ryan Zilenovski and K. B. Sharpless, unpublished results.

(16) Asymmetric catalytic hydrogenations can be extremely enantioselective; for an example of 100% ee, see: M. D. Fryzuk and B. Bosnich, *J. Am. Chem. Soc.*, **99**, 6262 (1977). However, these asymmetric hydrogenation processes appear more sensitive to permutation of the olefin substitution patterns than does the asymmetric epoxidation process we have described here.

(17) **Note Added in Proof.** We now have results for two more of the basic substitution patterns of primary allylic alcohols (see note 5). Allyl alcohol itself affords 2(*S*)-glycidol, ca. 15% yield, 73% ee [performed at 0 °C by using (+)-diisopropyl tartrate and $Ti(OiPr)_4$]; the higher temperature probably contributes to the lower ee observed in this case. (*Z*)-2-Methylhept-2-enol gives the 2(*S*),3(*R*)-epoxy alcohol, 80% yield, 89% ee [performed at −20 °C, using (+)-diethyl tartrate and $Ti(OiPr)_4$]. Thus, both conform to the rules stated in paragraph two and only the tetrasubstituted type of primary allylic alcohol remains to be tried.

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2,3-Di-*n*-propyl-1,4-dehydrobenzene

Sir:

Rearrangement and trapping studies[1] have implicated an "open" or biradical form (**2**) of 1,4-dehydrobenzene as an intermediate in the thermal reaction of (*Z*)-hexa-1,5-diyn-3-ene (**1**, R = H; Scheme I). Attempts to obtain kinetic evidence for the existence of a true intermediate in this reaction, however, have been frustrated by the low yield of aromatic products obtained in solution pyrolyses of several compounds of type **1**. In this paper, we report a detailed study of the thermolysis of (*Z*)-4,5-diethynyl-4-octene (**4**).[2] This reaction gives high yields of products formed by rearrangement and intramolecular and intermolecular trapping of the intermediate 1,4-dehydrobenzene **5**. The kinetics of the solution pyrolysis of **4** in the presence and absence of trapping agent establish that the 1,4-dehydrobenzene is a discrete intermediate on the pathway leading to products. By following this reaction in the probe of an NMR spectrometer at high temperature, we have, for the first time, observed CIDNP in a 1,4-dehydrobenzene reaction. This observation, along with kinetic and chemical trapping evidence, indicates the subsequent formation of two additional intermediates on the pathway to products. The observation of CIDNP, coupled with the reactivity exhibited by **5** and the other two intermediates, implicates a biradical description of these molecules.

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(1) (a) Jones, R. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 660. (b) Bergman, R. G. *Acc. Chem. Res.* **1973**, *6*, 25. (c) Johnson, G. C.; Stofko, J. J.; Lockhart, T. P.; Brown, D. W.; Bergman, R. G. *J. Org. Chem.* **1979**, *44*, 4215. See also, however: (d) Breslow, R.; Napierski, J.; Clarke, T. C. *J. Am. Chem. Soc.* **1976**, *98*, 570. (e) Breslow, R.; Khanna, P. L. *Tetrahedron Lett.* **1977**, 3429.

(2) Details of the synthesis of compound **4** will be presented in a full paper.

0002-7863/80/1502-5976$01.00/0

Scheme I

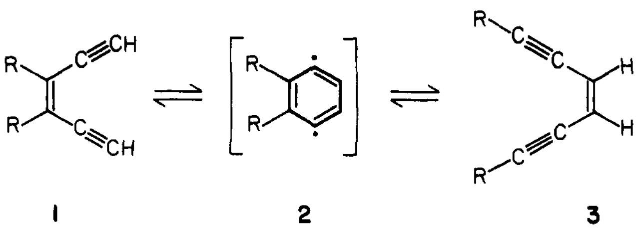


Table I. Product Yields and Rate Constants in the Solution Pyrolysis of 4[a]

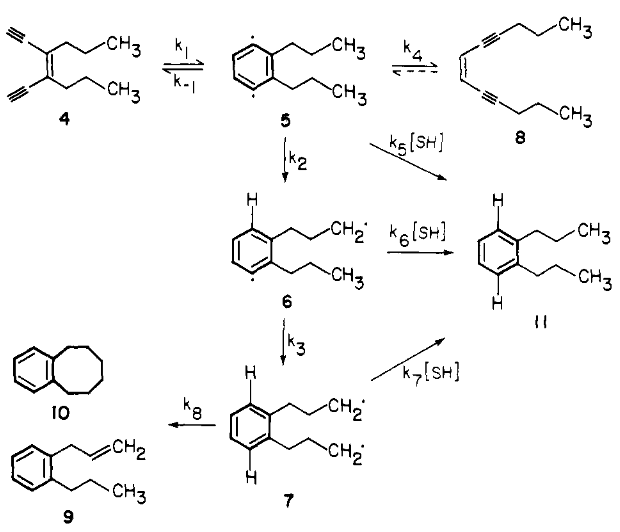
run	T, °C	k_{obsd}, s^{-1}	1,4-cyclohexadiene, M	absolute yield, %[b] 8	9	10	11	total (8-11)
1	196		0.0	20.3	36.9	20.8		78
2	196		0.4	10.1	8.9	5.4	48	71
3	196		10.6	~1.0	<1	<1	76	<79
4	166	1.3×10^{-3}	0.0	13.5	38.5	20.0		72
5	156	6.9×10^{-4}	0.0	11.8	35.8	17.2		65
6	145	2.9×10^{-4}	0.0	9.8	37.3	17.6		65
7	132	9.3×10^{-5}	0.0	7.9	38.5	16.4		63
8	156	7.1×10^{-4}	0.19	8.7	13.5	8.7	27.6	58
9	156	6.4×10^{-4}	0.38	5.2	6.7	3.1	47.4	62

[a] [4] = 0.01 M. [b] Yields determined by digital integration of FID VPC trace and reference to an internal standard.

Reaction of **4** in the gas phase (N_2 flow, 320 °C) quantitatively produces three products: isomeric diyne **8**, *o*-allyl-*n*-propylbenzene (**9**), and benzocyclooctene (**10**).[3] The yield of **8** is dependent on the reaction temperature; at 400 °C, **8**, prepared by independent synthesis, is converted to **9** and **10** in high yield. Products **8**, **9**, and **10** are obtained in high mass balance when compound **4** is heated to 196 °C in a solvent inert toward free-radical hydrogen atom abstraction such as diphenyl ether, chlorobenzene, or benzene.[4,5] At this temperature, the more stable isomer **8** does not react appreciably during the course of the reaction. Pyrolysis of **4** in an inert solvent to which a good hydrogen atom donor (1,4-cyclohexadiene or 9,10-dihydroanthracene) has been added gives reduced product **11** in addition to **8**, **9**, and **10**.[6] Increasing the percent of trapping agent in solution increases the yield of **11** at the expense of the three unimolecular products (see Table I, runs 1-3).

The mechanism outlined in Scheme II accounts for the observed products. We postulate that 1,4-dehydrobenzene **5** is the initial intermediate. Intramolecular hydrogen transfer from the ends of the alkyl chains sequentially converts **5** into **6** and then **7**. Performing the thermal reaction in the presence of 2,2,5,5-tetradeuterio-1,4-cyclohexadiene[7] provides information about the amount of reduced product **11** arising from each of these intermediates since **5** gives rise to **11** containing only aromatic deuterium, **7** leads to **11** containing only aliphatic deuterium, and **6** gives **11** containing one aliphatic and one aromatic deuterium.[8] Assay for these three differently labeled products was performed by selectively[9] washing out aromatic deuterium by using acid-catalyzed exchange and then analyzing the resulting *o*-dipropylbenzene for d_0, d_1, and d_2 isomers by mass spectroscopy. These experiments demonstrated that when a solution of **4**, 0.8 M in cyclohexadiene-d_4, is subjected to thermal reaction, 66% of product **11** is formed directly from the 1,4-dehydrobenzene, 33% is formed from the singly rearranged biradical **6**, and only 1% arises from **7**. As might be expected, therefore, biradical **7** undergoes intramolecular ring closure and hydrogen transfer considerably faster than intermolecular reaction with deuterated cyclohexadiene.

Scheme II



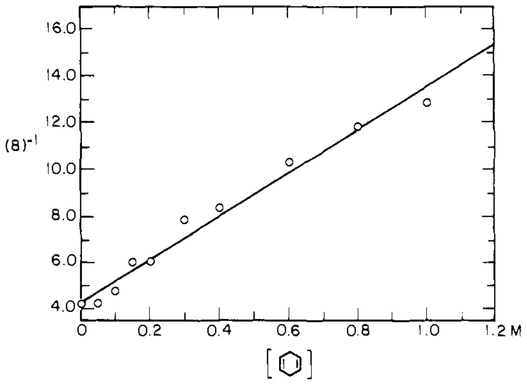


Figure 1. Plot of $(8_{normalized})^{-1}$ vs. concentration of 1,4-cyclohexadiene.

The kinetics of disappearance of **4** in chlorobenzene solution ([**4**] = 0.01 M) are well behaved. First-order plots are linear for

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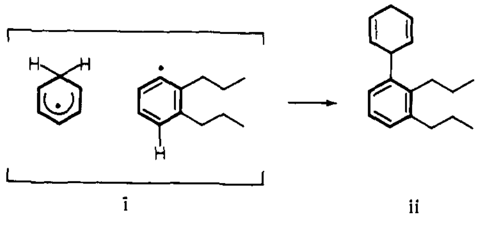
(3) Satisfactory analytical data were obtained on all new compounds.

(4) Samples were prepared for pyrolysis by placing a 0.01 M solution of **4** into hexamethyldisilazane-treated Pyrex tubes and freeze-pump thawing four times to 0.02 torr. The tubes were then sealed under vacuum.

(5) In addition, several isomeric products were observed which appear to be derived from the addition of radical intermediates to the aromatic solvent [<5% total yield, identified by VPC/mass spectroscopy (MS)].

(6) Several new isomeric products of molecular formula $C_{18}H_{24}$ and $C_{18}H_{22}$ were observed by VPC/MS (total yield ca. one-fourth that of compound **11**). These compounds presumably arise from combination of the radical pairs (e.g., i, ii) produced upon transfer of hydrogen from the trapping agent to the intermediate biradicals.



(7) 1,4-Cyclohexadiene-d_4 was prepared by base-catalyzed exchange of the allylic protons for deuterium by treatment with dimsyl-d_5 anion in Me_2SO-d_6. Deuterium incorporation = 98%.

(8) Deuterium substitution in 1,4-cyclohexadiene substantially reduces its efficiency as a radical trap. In the pyrolysis of **4**, k_H/k_D = 4.3. The overall yield of tractable products suffers as a result; **8**, **9**, **10**, and **11** were obtained in a total yield of about 40%.

(9) Pyrolysis solutions were concentrated and then heated with 4% HCl in H_2O at 260 °C for 42 h; cf.: Werstiuk, N. H.; Kadai, T. *Can. J. Chem.* **1973**, *51*, 1485. The exchange was repeated, at which time all aromatic deuterium had been exchanged for protons. This method is very effective for exchanging aromatic protons *without* exchanging the protons in pendant alkyl groups. We confirmed this by exchanging the deuterium in toluene-d_8 for protons under identical conditions to those employed in the dipropylbenzene experiment. The exchange stopped at toluene-d_3 (by mass spectral analysis), and NMR showed no proton incorporation into the methyl group.

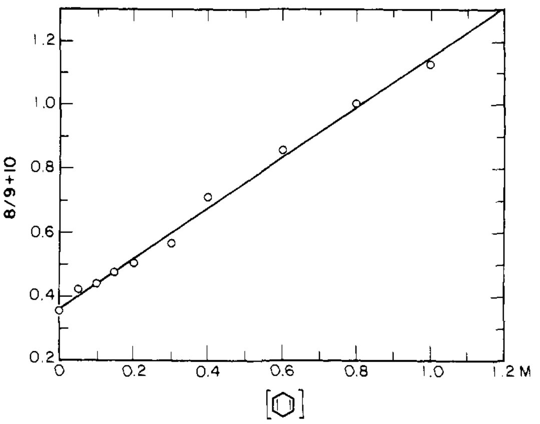


Figure 2. Dependence of the ratio **8**/(**9** + **10**) on 1,4-cyclohexadiene concentration.

two to three half-lives over a range of 34 °C (Table I). These data give $E_a = 27.4 \pm 0.5$ kcal/mol and log $A = 10.8 \pm 0.3$ s^{-1}.

If 2,3-di-*n*-propyl-1,4-dehydrobenzene is a true intermediate in the reaction of **4**, and the reaction rates leading to **6**, **8**, and **11** are fast with respect to k_{-1}, then the rate of disappearance of **4** should be independent of added 1,4-cyclohexadiene trapping agent. The yield of unimolecular products, however, should be strongly dependent on the presence of trapping agent in the reaction solution. The rate data obtained at 0.19 M and 0.38 M added 1,4-cyclohexadiene at 156 °C are identical, within experimental error, with the data obtained in the absence of trapping agent (Table I, runs 5, 8, and 9). Thus, while the rate of reaction of **4** is unchanged, the increase in cyclohexadiene concentration increases the yield of **11** from 0 to 47%, in accord with the prediction.

A specific relationship of the yield of diyne **8** to the 1,4-cyclohexadiene concentration is predicted by Scheme II. Application of the steady-state approximation to the concentration of **5** (Scheme II) leads to the prediction that the reciprocal of the yield of **8** should be proportional to the concentration of 1,4-cyclohexadiene in solution (eq 1). As shown in Figure 1, this relationship is observed experimentally.

$$\frac{1}{\mathbf{8}} = 1 + \frac{k_2}{k_4} + \frac{k_5}{k_4}[\mathrm{SH}] \qquad (1)$$

The absolute yields of products **8**, **9**, and **10** show pronounced, but different, dependences on the concentration of trapping agent. The yields of both **9** and **10** fall off rapidly as the 1,4-cyclohexadiene concentration increases; the dependence of **8** is much smaller. From the cyclohexadiene-d_4 trapping experiments, we know that a negligible amount of **11** arises from **7**; thus, d[**9** + **10**]/d$t \simeq k_3$[**6**] (Scheme II), and we obtain the relationship in eq 2 which relates the ratio of **8** to **9** + **10** as a function of added trapping agent.

$$\frac{\mathbf{8}}{\mathbf{9} + \mathbf{10}} = \frac{k_4}{k_2} + \frac{k_4 k_6}{k_2 k_3}[\mathrm{SH}] \qquad (2)$$

The experimental data are plotted in Figure 2. The straight line obtained confirms that a second intermediate exists and is being trapped by added cyclohexadiene. From the *y* intercept, $k_4/k_2 = 0.36 \pm 0.01$. The ratio k_6/k_3, given by the slope/*y* intercept, = 2.0 M^{-1}. In the absence of trapping agent, the ratio of unimolecular products, **8**/(**9** + **10**), gives k_4/k_2 directly. The value obtained experimentally, 0.35, falls almost exactly on the line in Figure 2. This indicates that cyclohexadiene does not produce a significant solvent effect on the reaction rates at the concentrations studied.

It is informative to estimate the absolute rate constants and activation energies for the processes shown in Scheme II. A reasonable model for k_6 is the rate constant for reaction of phenyl radical with diphenylmethane (7.7×10^6 M^{-1} s^{-1} at 60 °C)[10] which gives $k_6 = 10^7$ M^{-1} s^{-1} at 60 °C. The unimolecular rate constants k_2, k_3, and k_4 are thus expected to lie between 10^6 and 10^7 s^{-1}; k_8 must be at least one or two orders of magnitude slower (vide supra). The ratio of products **8**/(**9** + **10**) shows a marked dependence on the reaction temperature (Table I). This is convincing evidence that at least one of the intramolecular processes leading from **5** is activated. A good linear plot of ln [**8**/(**9** + **10**)] vs. $1/T$ is obtained over a range of 64 °C; from the slope of the line, $\Delta E_a[E_a(k_4) - E_a(k_2)]$ is found to be 5.2 ± 0.4 kcal/mol. The E_a for [1,5] hydrogen transfer in **5** should be similar to that for exothermic [1,5] hydrogen transfer in the 2,2-dimethylpentoxyl radical ($E_a \simeq 5.0$ kcal/mol).[10] The conversion of **5** to **8** should therefore have an E_a of about 10 kcal/mol.

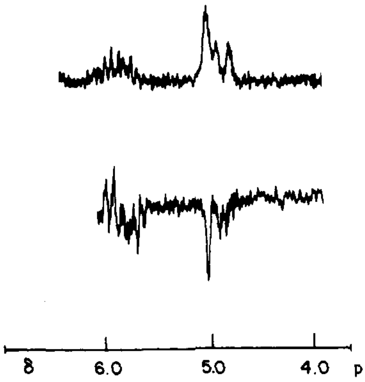


Figure 3. The upper spectrum (90 MHz, ^{1}H NMR) shows the vinyl region of a purified sample of *o*-allyl-*n*-propylbenzene recorded at 30 °C. The lower spectrum shows the emissive ^{1}H NMR signals observed during pyrolysis of **4** at 160 °C in a 90-MHz NMR probe. The signals appearing in absorption on the left side of the lower spectrum are spinning sidebands of the solvent (*o*-dibromobenzene).

When **4** is pyrolyzed in diphenyl ether or *o*-dibromobenzene at 160 °C in the probe of an NMR spectrometer, several emissive signals are observed (Figure 3). We assign these CIDNP signals to the vinyl protons and, tentatively, to the alkyl protons (terminal methyl and methylene) in **10**. The assignment of the polarized protons and the peculiar observation that all enhancements are emissive suggest strongly that the polarization arises from biradical **7**.[11]

The observations reported here constitute strong support for the mechanism outlined in Scheme II and provide information about the relative rates of the fast reactions of intermediates **5**, **6**, and **7**. Experiments now in progress are aimed at determining the reactive spin state of **5**.

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(10) Ingold, K. U. In "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. I, Chapter 2.

(11) For reviews of CIDNP observed in the products of biradical reactions, see: (a) Kaptein, R. *Adv. Free-Radical Chem.* **1975**, *5*, 319. (b) Closs, G. L. In "Chemically Induced Magnetic Polarization"; Lepley, A. R.; Closs, G. L., Eds.; Wiley: New York, 1973; p 130.

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