Stereochemistry of the Claisen Rearrangement[1]

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Employing arguments based on the experimental findings of Alexander and Kluiber, it had been proposed that the Claisen rearrangement proceeds with retention of configuration. This suggested stereochemical path stands in distinct disagreement with that shown by a number of experimental studies to hold for the closely related S_Ni' rearrangement. In the present study both cis- and trans-α,γ-dimethylallyl phenyl ethers have been prepared and subjected to Claisen rearrangement under mild conditions. The major product in each case was identified as o-(trans-α,γ-dimethylallyl)phenol. The trans ether gives rise to detectable amounts of o-(cis-α,γ-dimethylallyl)phenol, but this isomer is present in the product from the cis ether in an amount too small to be identified with certainty. Both the ethers and the phenols were shown to be effectively stereochemically stable under the conditions of the rearrangement. The Claisen rearrangement thus proceeds with a high degree of stereoselectivity. Its stereochemistry is in good accord with previous findings on the S_Ni' rearrangement. The data can be consistently interpreted by assuming a cyclic transition state with a geometry resembling the chair form of cyclohexane, and applying conventional principles of conformational analysis.

Introduction

Among the large and important group of reactions which involve cyclic transition states, and have been variously termed valence isomerizations, thermal reorganizations, and no-mechanism reactions, the Claisen rearrangement has been examined in the greatest detail from a mechanistic sense.[2] It is interesting then, that when this work was initiated, the only point of stereochemistry which had been carefully elucidated was the "inversion" of the allylic moiety during the rearrangement. The sole experimental study on the over-all stereochemical nature of the rearrangement was that of Alexander and Kluiber,[3] which showed that optically active α,γ-dimethylallyl phenyl ether gave o-(α,γ-dimethylallyl)phenol which retained some portion of the optical activity. Unfortunately neither the configurational relation between the initial and final asymmetric centers, nor the optical purity of the ether and the phenol, was established in this work. In a very interesting paper Hart[4] suggested that the Claisen rearrangement proceeds with *retention* of configuration. This conclusion was based on two pieces of experimental data. Hart and Eleuterio[5] had shown that both O- and C-alkylation of phenol takes place with inversion. Alexander and Kluiber had isolated a C-alkylation product which had the same sign of rotation as the rearranged phenol. Thus the rearrangement was presumed to proceed with retention of configuration.

This idea attracted our attention for three reasons. First, an examination of the activated complex preferred by Hart showed that the *trans* ether should rearrange preferentially to o-(cis-α,γ-dimethylallyl)-phenol. Clearly this would permit a simple experimental verification of the suggested stereochemistry. Second, if it is assumed that the activated complex resembles a cyclohexane ring sufficiently for the principles of conformational analysis to apply, the *trans* ether is predicted to give preferentially o-(trans-α,γ-dimethylallyl)phenol with *inversion* of configuration. This prediction is the exact opposite of the conclusion reached by Hart. Third, there is a certain amount of experimental justification for this opposite prediction. Though a direct stereochemical correspondence between the Claisen and S_Ni' rearrangements is not required, there are good reasons for expecting such a correspondence to exist. Thus it is provocative that the S_Ni' reaction of *trans*-α,γ-dimethylallyl alcohol with thionyl chloride in dilute ether solution has been shown[6a] to give *trans*-α,γ-dimethylallyl chloride with *inversion* of configuration. Similarly the reaction of cis- and trans-5-methyl-2-cyclohexenols gave cis- and trans-5-methyl-2-cyclohexenyl chlorides with *inversion* of configuration.[6b] Further studies on the S_Ni' rearrangement subsequently prompted Goering[7] to question the stereochemistry proposed by Hart.

Relation between Optical and Geometrical Isomerism. In the course of the Claisen rearrangement the α-carbon of the allylic group undergoes a change in bonding which converts the original tetrahedral carbon to a trigonal one. The γ-carbon undergoes a compensating alteration from trigonal to tetrahedral bonding. Similar changes occur at the oxygen and the participating *ortho* carbon of the aromatic ring. The transition state, which must have an intermediate geometry, can be visualized in terms of two planes, one generated by the three atoms of the allylic group, the second by the oxygen, C-1, and an *ortho* carbon of the phenoxy portion of the molecule. Assuming only that bond breaking and bond making occur on the same side in each plane, there must exist a fixed relation between the configurations of the asymmetric centers and the geometries of the double bonds.[8] The relations are shown

(1) A portion of this work was the subject of a brief communication: E. N. Marvell and J. L. Stephenson, *J. Org. Chem.*, **25**, 676 (1960). The authors are pleased to acknowledge the support of this study by the National Science Foundation under Grants G-7432 and G-23072.

(2) This is clearly apparent in the excellent review article on these reactions published recently: S. J. Rhoads, "Molecular Rearrangements," Part I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp. 655–706.

(3) E. R. Alexander and R. W. Kluiber, *J. Am. Chem. Soc.*, **73**, 4304 (1951).

(4) H. Hart, *ibid.*, **76**, 4033 (1954).

(5) H. Hart and H. S. Eleuterio, *ibid.*, **76**, 516, 519 (1954).

(6) (a) F. Caserio, G. E. Dennis, R. H. de Wolfe, and W. G. Young, *ibid.*, **77**, 4182 (1955); (b) H. L. Goering, T. D. Nevitt, and E. F. Silversmith, *ibid.*, **77**, 4042 (1955).

(7) (a) H. L. Goering and R. W. Greiner, *ibid.*, **79**, 3464 (1957); (b) H. L. Goering and R. R. Jacobson, *ibid.*, **80**, 3277 (1958).

(8) It is, of course, tacitly assumed that the activated complex is cyclic, and that no rotations about the ring bonds are permitted. Should such rotations occur, the relations between configuration and
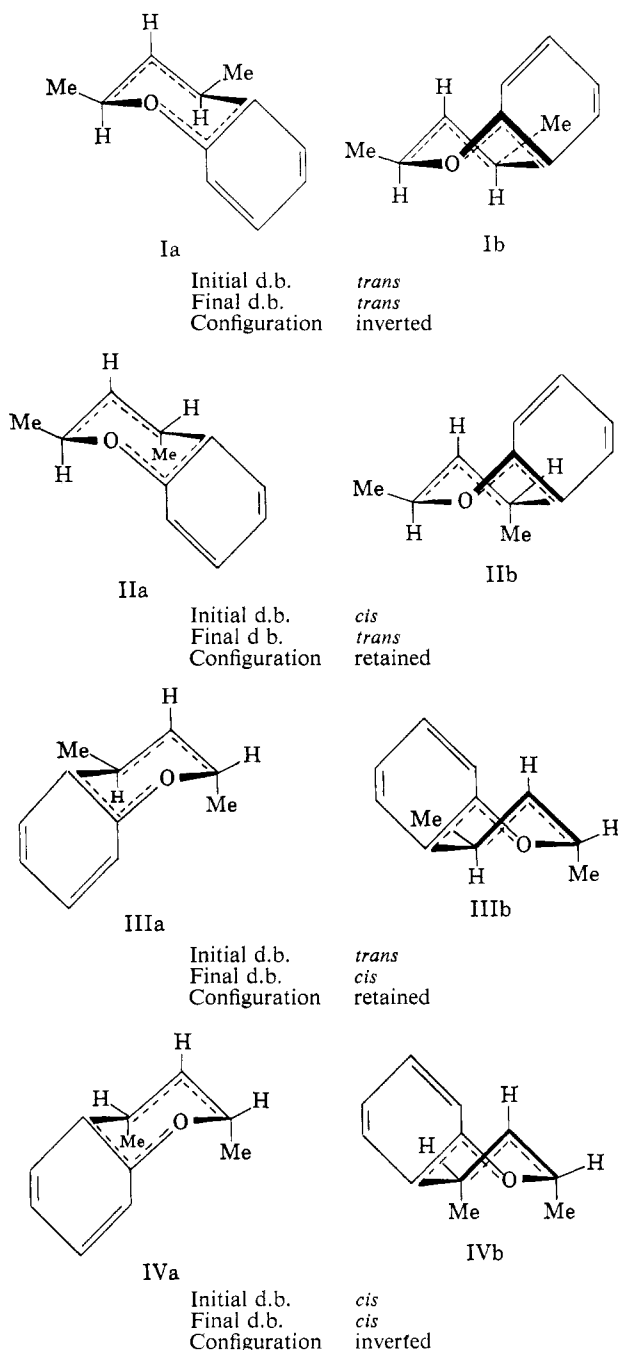
Ia

Ib

Initial d.b.	trans
Final d.b.	trans
Configuration	inverted

IIa

IIb

Initial d.b.	cis
Final d b.	trans
Configuration	retained

IIIa

IIIb

Initial d.b.	trans
Final d.b.	cis
Configuration	retained

IVa

IVb

Initial d.b.	cis
Final d.b.	cis
Configuration	inverted

Figure 1. Relations between configuration and double bond geometry.

for the case of a single initial configuration in Figure 1. Note that both boat and chair forms for the activated complex lead to identical stereochemical predictions.

The arguments presented here indicate that investigation of the stereochemistry of the Claisen rearrangement can be followed either optically or via geometric isomerism. In the unlikely but conceivable event that the relations fail, either tool will serve to investigate the stereochemical course, but neither may be sufficient to provide the complete answer. With these principles in mind, we chose to study the Claisen rearrangement
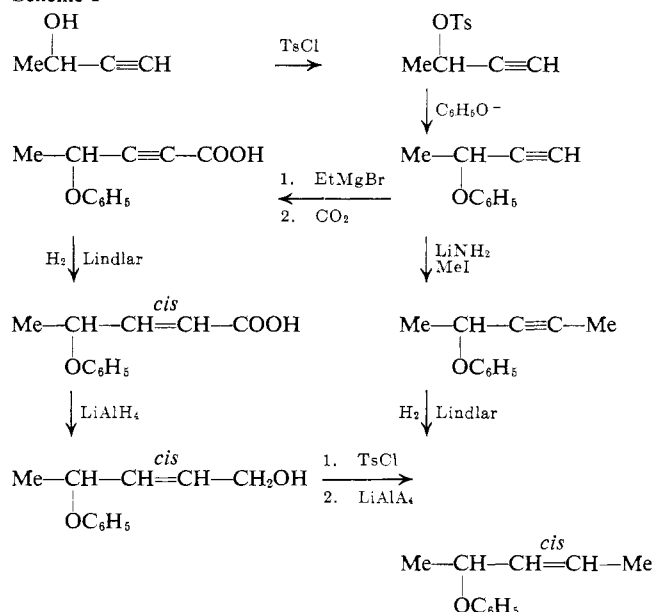
double bond geometry would not be as deduced here. At the same time the stereoselective nature would disappear and this would be revealed by experimental studies using either configuration or geometry as a tool.

of α,γ-dimethylallyl phenyl ether using geometric isomerism as the investigative tool because of its simplicity.
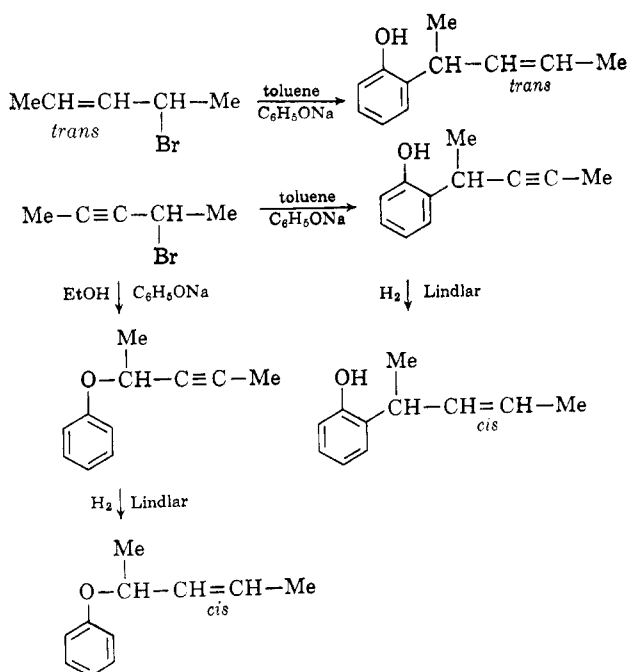
Results

Synthesis of Isomeric Ethers and Phenols. The *trans* ether is a well known compound. It was prepared from *trans*-crotonaldehyde essentially by the route used by previous workers.[3] Synthesis of the *cis* ether had not been achieved previously. Our initial synthesis of this compound was designed to introduce the *cis* double bond at the last possible stage to reduce isomerization problems, and to permit the preparation of an optically active sample should that prove desirable. No difficulty was experienced with the synthesis depicted in Scheme I. A second synthesis shown in

Scheme I

$$MeCH-C\equiv CH \quad \xrightarrow{TsCl} \quad MeCH-C\equiv CH$$
(OH)   (OTs)

$$Me-CH-C\equiv C-COOH \quad \xleftarrow[\text{2. } CO_2]{\text{1. } EtMgBr} \quad Me-CH-C\equiv CH$$
(OC_6H_5)   (OC_6H_5) $\downarrow C_6H_5O^-$

$\downarrow$ H_2 Lindlar $\downarrow$ LiNH_2, MeI

cis
$$Me-CH-CH=CH-COOH \qquad Me-CH-C\equiv C-Me$$
(OC_6H_5)   (OC_6H_5)

$\downarrow$ LiAlH_4 $\downarrow$ H_2 Lindlar

cis
$$Me-CH-CH=CH-CH_2OH \quad \xrightarrow[\text{2. } LiAlA_4]{\text{1. } TsCl}$$
(OC_6H_5)

cis
$$Me-CH-CH=CH-Me$$
(OC_6H_5)

Scheme II was also convenient for this *cis* ether. The *trans* ether has a strong band at 963 and lacks absorp-

Scheme II

$$MeCH=CH-CH-Me \quad \xrightarrow[C_6H_5ONa]{toluene}$$
trans   (Br)

trans
(product with OH, Me, CH-CH=CH-Me)

$$Me-C\equiv C-CH-Me \quad \xrightarrow[C_6H_5ONa]{toluene}$$
(Br)

(product with OH, Me, CH-C≡C-Me)

EtOH $\downarrow$ C_6H_5ONa H_2 $\downarrow$ Lindlar

Me
$$O-CH-C\equiv C-Me$$

OH Me
(CH-CH=CH-Me, cis)

H_2 $\downarrow$ Lindlar

Me
$$O-CH-CH=CH-Me$$
cis

tion near 720 cm.$^{-1}$. The *cis* ether has a moderate band at 718 and none at 963 cm.$^{-1}$. These clearly identify the geometry of the double bonds in the ethers.[9] In the n.m.r. spectrum the vinyl protons were not sufficiently separated to permit an unequivocal assignment of coupling constants. The *trans* ether was not contaminated by the *cis* isomer as far as could be determined spectrally. The same result pertains for the *cis* isomer in that no band at or near 963 cm.$^{-1}$ can be found. However, the *cis* ether has strong bands at 953 and 1006 cm.$^{-1}$ which could mask a weak absorption in this area. Generally semihydrogenation of a triple bond gives rise to 5–10% of the *trans* isomer.[10] Our case seems to be a particularly favorable one, and we estimate that the amount of *trans* isomer present does not exceed 3%.

Samples of the phenolic products of the rearrangement were synthesized independently as is illustrated in Scheme II. The key step in the scheme is the heterogeneous C-alkylation procedure of Kornblum and Lurie.[11] Both phenols show strong absorption at 750 cm.$^{-1}$ and each was uniform to gas chromatographic analysis. Kornblum and Lurie[11] showed that the entering allyl group appeared exclusively in an *ortho* position. Our results confirm their findings completely. The band at 750 cm.$^{-1}$ is typical of *ortho*-disubstituted aromatic rings,[12] and the overtone pattern in the 1700–2000-cm.$^{-1}$ region confirms this assignment.[13] No trace of *para* product could be found *via* gas chromatographic analysis. The *trans* isomer was free of *cis* isomer as far as spectral analysis could determine. Semihydrogenation of the acetylenic phenol proceeded in a normal manner, and the product contained enough *trans* phenol to give a discrete peak at 968 cm.$^{-1}$. It indicates the presence of 5–6% of the *trans* isomer.

Rearrangement. The rearrangement of both *cis* and *trans* ethers was carried out in 1.0 M solutions in mesitylene at 165–166°. Analysis of the products was by infrared. The *trans* ether gave a mixture of phenols consisting of 90 ± 4% o-(*trans*-α,γ-dimethylallyl)phenol and 10 ± 5% o-(*cis*-α,γ-dimethylallyl)-phenol. The *cis* ether gave 98 ± 4% of the *trans* phenol containing perhaps a trace of the *cis* phenol. Under the conditions employed here no evidence for the presence of o-(α-ethylallyl)phenol, the product of an abnormal Claisen rearrangement,[14] could be found.

Rate Studies. The *cis* and *trans* ethers were rearranged in dilute solution in *n*-octane at 164° using an ampoule technique. Infrared analysis was made directly to determine total phenol content. The residual ether was separated from the phenolic product and both were analyzed separately for *cis* and *trans* double bond content by an infrared method. The over-all

rate constant for the *cis* isomer was 0.95 × 10^{-5} sec.$^{-1}$, while that of the *trans* isomer was 1.52 × 10^{-5} sec.$^{-1}$. The ether which was recovered from each sample during the kinetic runs was checked to ascertain whether geometric isomerism occurred during the course of the rearrangement. Both the *cis* and *trans* ethers were found to be geometrically stable throughout the course of the rearrangement (to at least 85% completion).[15]

Heating the *trans* phenol under the conditions of the rearrangement for what amounts to about 8 half-lives for the *trans* ether led to no change in the double bond geometry. Under the same conditions a sample of *cis* phenol was converted to *trans* phenol to the extent of 14%. Assuming this to be a first-order process its rate constant is *ca.* 0.5 × 10^{-6} sec.$^{-1}$. This is more than ten times slower than the rearrangement of the *cis* ether and will not therefore influence the stereochemical conclusions reached with respect to the Claisen rearrangement. This conclusion is supported by the observation that the ratio of *cis* to *trans* phenol in the product does not vary beyond the experimental error during the reaction. Clearly the product obtained is the kinetic one and any stereochemical observations will be pertinent to the geometry of the activated complexes.

Discussion

The Claisen rearrangement is known to be an intramolecular process.[16] "Inversion" of the allylic group inevitably occurs and within experimental ability to determine is complete.[16,17] The rate of the Claisen rearrangement is relatively insensitive to structural and environmental alterations.[18] These observations have been generally interpreted[2] as indicating a single cyclic transition state for the Claisen rearrangement to the dienone intermediate. The activated complex is considered to lie toward the covalently bonded end of the spectrum of allylic rearrangements which run the gamut from ion pairs to covalently bonded activated complexes. The following discussion of the stereochemical implications of the present work will be made in terms of this framework.

Since our original communication two other groups have reported[19] studies aimed at elucidating the stereochemistry of the Claisen rearrangement. Burgstahler[19a] showed that the rearrangement of *trans*-α,γ-dimethylallyl vinyl and phenyl ethers gave products containing a *trans* double bond. This result is in good agreement with our findings. White and Norcross[19b] as well as

(9) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p. 24.

(10) R. A. Raphael, "Acetylenic Compounds in Organic Synthesis," Academic Press Inc., London, 1955, p. 24.

(11) N. Kornblum and A. P. Lurie, *J. Am. Chem. Soc.*, **81**, 2705 (1959).

(12) See ref. 9, pp. 26, 27.

(13) For the overtone patterns and their use in distinguishing substitution arrangements, see C. W. Young, R. B. DuVall, and N. Wright, *Anal. Chem.*, **23**, 709 (1951).

(14) W. M. Lauer and H. E. Ungnade, *J. Am. Chem. Soc.*, **61**, 3047 (1939); E. N. Marvell, D. R. Anderson, and J. Ong, *J. Org. Chem.*, **27**, 1109 (1962).

(15) Our earlier report[1] stated that the *cis* ether was slowly converted to the *trans* ether during the rearrangement. That ether was obtained by methylation of 3-phenoxy-1-butyne with methyl iodide. Traces of iodine could have been responsible for catalysis of this isomerization. The *cis* ether, prepared by semihydrogenation of the 4-phenoxy-2-pentyne obtained by alkylation of phenol, was completely stable.

(16) H. Schmid and K. Schmid, *Helv. Chim. Acta*, **35**, 1879 (1952), and references to earlier papers listed therein.

(17) J. P. Ryan and P. R. O'Connor, *J. Am. Chem. Soc.*, **74**, 5866 (1952); see also ref. 2, pp. 661–663.

(18) H. L. Goering and R. R. Jacobson, *J. Am. Chem. Soc.*, **80**, 3277 (1958); W. N. White, D. Gwynn, R. Schlitt, C. Girard, and W. K. Fife, *ibid.*, **80**, 3271 (1958); W. N. White and E. F. Wolfarth, Abstracts, 140th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1961, p. 52Q.

(19) (a) A. W. Burgstahler, *J. Am. Chem. Soc.*, **82**, 4681 (1960); (b) W. N. White and B. E. Norcross, *ibid.*, **83**, 1968 (1961); (c) W. N. White and B. E. Norcross, *ibid.*, **83**, 3265 (1961).
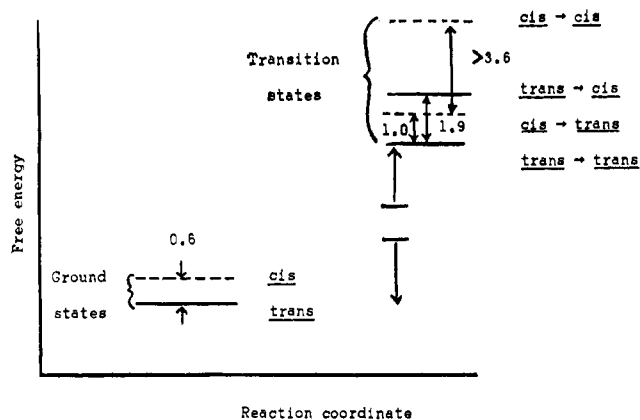
Transition states

cis → cis

>3.6

trans → cis

1.0   1.9

cis → trans

trans → trans

Free energy

0.6

Ground states

cis

trans

Reaction coordinate

Figure 2. Free-energy relations for ground and transition states.

Huestis and Andrews[20] have shown that, of a pair of isomeric cis and trans ethers, the trans generally rearranges more rapidly than the cis. Again our results with the α,γ-dimethylallyl phenyl ethers are in excellent agreement.

Rearrangement of both cis- and trans-α,γ-dimethylallyl phenyl ethers gives mainly o-(trans-α,γ-dimethylallyl)phenol. However, the amount of o-(cis-α,γ-dimethylallyl)phenol in the product is quite different for the two ethers. Rearrangement of the trans ether is ca. 90% stereoselective and the product contains ca. 10% of the cis phenol. On the other hand rearrangement of the cis ether proceeds with notably higher stereoselectivity (98–100%) and the product contains too little cis phenol to permit a reliable identification. This cis ether rearranges more slowly than the trans. These observations rule out the possibility that both cis and trans ethers rearrange via the same transition states. Should that have been the case the same ratio of cis and trans phenols would have to be obtained from each ether, and the cis ether would have reacted faster than the trans. Thus the two ethers must react via separate transition states and four activated complexes are required.[21]

The ratios of cis and trans isomers obtained from each ether in conjunction with the rates of rearrangement permit the relative energies of ground and transition states to be established (Figure 2). The transition state of lowest energy is that which converts the trans ether to the trans phenol. The state used by the trans ether in going to cis phenol lies ca. 1.9 kcal./mole above this, as indicated by the ratio of ca. 9.0 for the rates of formation of these isomeric phenols from the trans ether. The free energy difference between cis → trans and cis → cis states must exceed 3.6 kcal./mole, since for the cis ether the ratio of rates must exceed 19. The energy relation between these two sets can be established from the difference in rates of the cis and trans ethers. This difference is due in part to the difference in transition-state free energies and in part to ground-state free energies. The latter difference can be readily estimated, since the steric situation about the double bond is quite similar to that in 4-methyl-2-pentene.

The energy difference between cis and trans isomers for 4-methyl-2-pentene has been calculated[22] to be 0.6 kcal./mole. Consequently the cis → trans transition state must lie about 1.0 kcal./mole above the trans → trans state.

In applying conformational analysis to the various activated complexes, it will be assumed that for the chair type complexes, Ia–IVa, an equatorial methyl will be more stable than an axial one. Similarly for the boat type complexes, Ib–IVb, an exo-methyl will be assumed to be more stable than an endo-methyl. These are in accord with well established principles of conformational analysis. However the relative energies of one further pair of isomers will have to be established before a complete analysis can be made. The problem is whether a pair of groups larger than hydrogen in an exo-cis position on the boat form (as in form Ib) is more or less stable than the same pair in a trans orientation (as in IIb). We assume here that the former is less stable than the latter.[23]

If at the transition state bond breaking and bond making have progressed about equally and the six-membered ring is therefore nearly symmetrical, these experimental facts cannot be accommodated by the chair form complexes alone, or the boat form complexes alone. For example, the activated complex IIa where the axial methyl is forced up against the face of the aromatic ring would be expected to be less stable than IIIa. However the data show that a type II activated complex must be more stable than a type III. This would be the predicted order if the activated complexes were of the boat form, IIb and IIIb. However Ib would be predicted to be less stable than IIb whereas the experimental results demand the reverse order of stability. Clearly some further assumptions must be made.

There are a number of possible ways to fit the data, but in view of the lack of experimental data which would permit a clear choice among them only two of the more reasonable will be discussed here. It is possible that the activated complex changes from a chair to a boat form, i.e., that the forms Ia, IIb, IIIb, and either IVa or IVb are the actual conformations. This would demand that the free-energy difference between the chair and boat forms be less than 1.0 kcal./mole, an exceedingly low value. Doering and Roth[27] in their elegant study of the Cope rearrangement found a minimum value of 5.7 kcal./mole between the two forms of the activated complex. An alternative which seems more satisfactory to us is that when the transition state is attained the γ-allylic carbon has approached an ortho carbon near enough to permit bond formation to start, but the carbon–carbon bond is stretched to a considerable degree. At the same time the bond be-

(20) L. D. Huestis and L. J. Andrews, J. Am. Chem. Soc., 83, 1963 (1961).

(21) Possibly more transition states may actually be involved. It is a moot question whether an intermediate may be involved in the Claisen and Cope rearrangements. Since our experiments provide no evidence for or against an intermediate, this important question has been put aside here and only the minimum number of states invoked.

(22) J. E. Kilpatrick, E. J. Prosen, K. S. Pitzer, and F. D. Rossini, J. Res. Natl. Bur. Std., 36, 559 (1946).

(23) Not only is this an apparently reasonable estimate based on the energy difference between exo- and endo-methyls and eclipsed and skew butane forms, it is also supported by some experimental data. Although the relative free energies of exo-cis- and trans-2,3-dimethylnorbornanes have not been determined, the trans isomer has the lower refractive index and density[24] and presumably then the lower enthalpy.[25] Also exo-cis-3-methylnorbornane-2-carboxylic acid rearranges to trans-exo-3-methylnorbornane-endo-2-carboxylic acid.[26]

(24) K. Alder and W. Roth, Chem. Ber., 87, 161 (1954).

(25) E. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 216.

(26) K. Alder, W. Günzl, and K. Wolff, Chem. Ber. 93, 809 (1960).

(27) W. von E. Doering and W. Roth, Tetrahedron, 18, 67 (1962).

tween the oxygen and the α-allylic carbon is not stretched to a comparable degree. Thus the activated complex is distorted considerably from a nearly symmetrical cyclohexane ring to one having a considerably longer distance between the γ-allylic carbon and an *ortho* carbon than between the α-allylic carbon and the oxygen atom. This explanation also permits a convenient rationalization of the observation that the size of an *ortho*-alkyl group does not markedly alter the rate of the *para*-Claisen rearrangement.[28]

Relation to Other Allylic Rearrangements. The Claisen rearrangement is an example of a double allylic rearrangement. For allylic rearrangements in general the stereochemical results may be expected to fall into two patterns. When the group leaving the α-carbon and that being substituted at the γ-carbon are attached to one another, the pattern should follow that established here, or for the Cope rearrangement.[27] If the leaving and substituting groups are discrete entities, the stereochemical alterations at the double bond will again follow the pattern found in the case here, but the changes at the asymmetric centers will depend upon whether the groups enter and leave on the same side of the plane of the allyl group, or on the opposite sides. Thus from the viewpoint of geometric isomerism the results in the Claisen, Cope, SNi', and SN2' reactions should all fit one coherent pattern. This is indeed the case.

Examples of the SNi' type which have been found to fit this stereochemical pattern are the reaction of α,γ-dimethylallyl alcohol with thionyl chloride,[6a] the rearrangement of *trans*-3-hepten-2-yl acetate to *trans*-2-hepten-4-yl acetate during pyrolysis,[29] and the facile rearrangement of allyl azides.[30] In this latter case no stereochemical conclusions were reported, but the data suggest that α-methylallyl azide gives *trans*-γ-methylallyl azide.

The SN2' rearrangement also fits the pattern. This stereochemistry was first suggested on theoretical grounds,[31] and later confirmed by Stork and White.[32] They found that, in a cyclic system where the initial and final double bonds were *cis*, the configuration inverted. They also reported that α-methylallyl 2,6-dichlorobenzoate reacts with piperidine to give a mixture of *cis*- and *trans*-N-(γ-methylallyl)piperidines, apparently with the *trans* isomer predominating though no quantitative data were reported. The reaction of α-methylallyl chloride with trimethylamine has been shown[33] to give an SN2' product composed of 90% *trans* and 10% *cis* isomers, while with dimethylamine it is reported[34] to give only the *trans* isomer.

Somewhere in the spectrum of allylic reaction types lies the reaction of 3,4-dibromo-1-butene with lithium aluminum hydride. Apparently a reduction with rearrangement is followed by a normal reduction.[35]

The sole product of the reaction is *trans*-2-butene which fits the stereochemical pattern. Even reactions which must involve allylic carbonium ions follow the same general path. Braude and Coles[36] originally reported that acid-catalyzed rearrangement of 1-*cis*-4-hexadienol-3 gives *cis*-3,5-hexadienol-2. This result, which is contrary to the general rule, was attributed by the authors to hydrogen bonding between the methyl group and the terminal double bond. More recently Bell, Jones, and Whiting[37] have shown that *trans*-4-hexen-1-ynol-3 gives a mixture containing 75% of *trans*-3-hexen-5-ynol-2 and 25% of this *cis* isomer. A report[38] that similar results are obtained with the dienol corrects the lone exception reported by Braude and Coles.

Experimental

3-Phenoxy-1-butyne. One-molar amounts of 1-butynol-3[39] were treated with *p*-toluenesulfonyl chloride according to the procedure of Reppe.[40] After recrystallization from hexane the tosylate melted at 51.5–52.5°. To a solution containing 37.6 g. (0.40 mole) of phenol and 26.4 g. (0.40 mole) of potassium hydroxide in 150 ml. of 95% ethanol was added over a 40-min. period 74.0 g. (0.33 mole) of the recrystallized tosylate. The solution was stirred for 1 hr. at 25° and for 3 hr. at 60–65°. The reaction mixture was diluted with water and extracted with ether. The combined ether extracts were washed with 5% sodium hydroxide followed by distilled water and dried over anhydrous magnesium sulfate. After removal of the ether by evaporation the product was distilled, b.p. 40–41° (0.6 mm.), n^{20}D 1.5191, giving 28 g. (58%) of a clear mobile liquid.

Anal. Calcd. for $C_{10}H_{10}O$: C, 82.15; H, 6.90. Found: C, 82.23; H, 7.07.

4-Phenoxy-2-pentynoic Acid. To an ethereal solution containing 0.1 mole of ethyl magnesium bromide was added dropwise a solution of 14.6 g. (0.1 mole) of 3-phenoxy-1-butyne in 30 ml. of ether. The resultant solution was heated at reflux for 8 hr. A beaker containing 600 g. of Dry Ice was placed in a steel autoclave and the ether solution was poured onto the Dry Ice. The autoclave was sealed and allowed to stand 24 hr. at room temperature. The sticky product was covered with ether and hydrolyzed carefully with ice-cold 15% sulfuric acid. The ether layer was extracted several times with saturated sodium bicarbonate solution. The bicarbonate solutions were combined, extracted with ether, and after being cooled were acidified with cold 15% sulfuric acid. The product was taken up in ether and the solution was dried over anhydrous magnesium sulfate. Evaporation of the ether gave 11.8 g. (62%) of a tan solid. After recrystallization from hexane the acid melted at 82.6–83.6°.

Anal. Calcd. for $C_{11}H_{10}O_3$: C, 69.47; H, 5.30; neut. equiv., 190. Found: C, 69.70; H, 5.51; neut. equiv., 189.

(28) E. N. Marvell, B. Richardson, R. Anderson, J. L. Stephenson, and T. Crandall, *J. Org. Chem.*, in press.
(29) F. L. Greenwood, *J. Org. Chem.*, **24**, 1735 (1959).
(30) A. Gagneux, S. Winstein, and W. G. Young, *J. Am. Chem. Soc.*, **82**, 5956 (1960).
(31) W. G. Young, I. D. Webb, and H. L. Goering, *ibid.*, **73**, 1076 (1951).
(32) G. Stork and W. N. White, *ibid.*, **78**, 4609 (1956).
(33) W. G. Young, R. A. Clement, and C.-H. Shih, *ibid.*, **77**, 3063 (1955).
(34) W. G. Young and I. J. Wilk, *ibid.*, **79**, 4793 (1957).
(35) L. F. Hatch, P. D. Gardner, and R. E. Gilbert, *ibid.*, **81**, 5943 (1959).

(36) E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 2078, 2085 (1951).
(37) I. Bell, E. R. H. Jones, and M. C. Whiting, *ibid.*, 2597 (1957).
(38) Noted by P. B. D. de la Mare, "Molecular Rearrangements," Part I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p. 78.
(39) K. N. Campbell, B. K. Campbell, and L. T. Eby, *J. Am. Chem. Soc.*, **60**, 2882 (1938).
(40) W. Reppe, et al, *Ann.*, **596**, 38 (1955).

4-Phenoxy-cis-2-pentenoic Acid. The above acid, 0.95 g. (5 mmoles), was reduced in ethyl acetate over 20% of the compound weight of Lindlar catalyst. A drop of synthetic quinoline was added to the reaction mixture. The acid took up 104% of 1 mole of hydrogen and the uptake ceased. The reduced acid was recrystallized from hexane, m.p. 112–113°, 0.86 g. (90%).

Anal. Calcd. for $C_{11}H_{12}O_3$: C, 68.74; H, 6.30; neut. equiv., 192. Found: C, 68.91; H, 6.51; neut. equiv., 192.

4-Phenoxy-cis-2-pentenol-1. A solution of 2.0 g. (0.01 mole) of 4-phenoxy-*cis*-2-pentenoic acid in 40 ml. of anhydrous ether was added to an ether solution containing 0.50 g. (0.013 mole) of lithium aluminum hydride at a rate which maintained a gentle boil. The mixture was stirred for 45 min. longer and 4 ml. of water was added slowly. The reaction mixture was made acid with 10% sulfuric acid, and the product was taken up in ether. The combined ethereal solutions were washed with dilute sodium hydroxide, then with water, and dried. After the ether had been removed by evaporation, the solid product was recrystallized from petroleum ether (b.p. 60–90°), m.p. 41.8–42.6°, 1.57 g. (88%).

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.12: H, 7.92. Found: C, 73.86; H, 7.81.

4-Phenoxy-cis-2-penten-1-yl p-Toluenesulfonate. 4-Phenoxy-*cis*-2-pentenol-1, 2.19 g. (0.012 mole), and 2.35 g. (0.012 mole) of *p*-toluenesulfonyl chloride were dissolved in 20 ml. of anhydrous ether. To this well stirred solution was added at −5° 2.18 g. (0.033 mole) of finely pulverized potassium hydroxide in small portions. The mixture was stirred for 4 hr. at 0° and enough water was then added to dissolve the solids. The product was taken up in ether and the ether solution was dried over anhydrous magnesium sulfate. Evaporation of the ether gave 3.70 g. (90%) of a light tan solid. Recrystallization from petroleum ether gave white needles, m.p. 41.3–42°.

Anal. Calcd. for $C_{18}H_{20}O_4S$: C, 65.04; H, 6.06. Found: C, 64.81; H, 6.15.

trans-3-Pentenol-2. This alcohol was prepared according to the procedure of Alexander and Kluiber.[3] It was a clear liquid, b.p. 64–66° (64 mm.), $n^{20}D$ 1.4280, and was obtained in 57% yield. Alexander and Kluiber report $n^{20}D$ 1.4280.

trans-4-Chloro-2-pentene. Conversion of 3-pentenol-2 to the chloride was carried out in 85% yield by the procedure of Levene and Haller.[41] The chloride was a clear liquid, b.p. 31–34° (54 mm.), $n^{20}D$ 1.5330 (lit.[41] $n^{20}D$ 1.5337).

trans-4-Bromo-2-pentene. The bromide was obtained from *trans*-3-pentenol-2 in 51% yield according to the procedure of Young and Ferrolane.[42] The product was purified by distillation through a concentric tube column, b.p. 65–66° (130 mm.), $n^{23}D$ 1.4721 (lit.[43] b.p. 70–77° at 145 mm.).

3-Pentynol-2. Three 60-ml. portions (*ca.* 3 moles) of methylacetylene were condensed in a cold trap

cooled in Dry Ice and allowed to bubble slowly into an ether solution containing 3.0 moles of ethylmagnesium bromide. Any methylacetylene not absorbed was trapped in a cold trap and recycled. The cold reaction mixture was stirred overnight and then heated under reflux for 4 hr. To this mixture, cooled in an ice-salt bath, was added slowly 3.0 moles of freshly distilled acetaldehyde. The reaction mixture was stirred for 3 hr. in the cold, for 3 hr. at reflux, and allowed to stand overnight.

To this was added 1.5 l. of saturated ammonium chloride. The product was extracted with ether, the ether extracts were dried, and the solvent was removed by distillation. Distillation of the residual liquid, b.p. 61–61.5° (29 mm.), $n^{24}D$ 1.4445, was carried out with a concentric tube column and 164 g. (65%) of a clear liquid was obtained. This alcohol was reported[44] to have $n^{25}D$ 1.4467.

4-Bromo-2-pentyne. The above alcohol was converted to the bromide according to the directions of Smith and Swensen.[44] A 57% yield of clear liquid, b.p. 49–49.5° (28 mm.), $n^{27}D$ 1.4888, was obtained (lit.[44] $n^{25}D$ 1.4903).

2-Phenoxy-3-pentyne. A. Methylation of 3-Phenoxy-1-butyne. A suspension of lithamide from 1.4 g. (0.2 g.-atom) of lithium was prepared in 500 ml. of liquid ammonia. To this was added dropwise a solution of 29.2 g. (0.2 mole) of 3-phenoxy-1-butyne in 40 ml. of anhydrous ether. The mixture was stirred for 4 hr. and then 35 g. (0.25 mole) of methyl iodide in 30 ml. of ether was added over a 20-min. period. The reaction mixture was stirred for 8 hr. Ten grams of ammonium chloride was added and the ammonia was allowed to evaporate. The organic material was taken up in ether, and the solution was washed with 3 N sulfuric acid, 3 N sodium hydroxide, and water. The solution was dried, the ether was allowed to evaporate, and the residue was distilled through a Vigreux column, b.p. 59.5–60° (0.6 mm.), $n^{20}D$ 1.5254, 23.7 g. (74%). The product gave no precipitate with silver nitrate.

B. Alkylation of Phenoxide. To a solution of 0.123 mole of sodium phenoxide in absolute ethanol was added dropwise 20.6 g. (0.123 mole) of 4-bromo-2-pentyne. The reaction mixture was stirred for 10 hr. at 65°. The ethanol was largely removed *in vacuo*, and enough water was added to dissolve the solid material. The aqueous layer was extracted with ether and the combined extracts were washed with dilute sodium hydroxide and then water. The ether solution was dried over anhydrous sodium sulfate and the ether was removed by evaporation. Distillation, b.p. 48–49° (0.1 mm.), gave 11.8 g. (60%) of a clear liquid, $n^{24}D$ 1.5220, $\bar{v}$ 2260 and 1235 cm.$^{-1}$.

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.48; H, 7.55. Found: C, 82.56; H, 7.56.

cis-2-Phenoxy-3-pentene (cis-α,γ-Dimethylallyl Phenyl Ether). A. Semihydrogenation of 2-Phenoxy-3-pentyne. A mixture of 5.12 g. (0.032 mole) of 2-phenoxy-3-pentyne dissolved in 10 ml. of anhydrous ethyl acetate and 0.5 g. of Lindlar catalyst was treated with hydrogen. After 3 hr. 104% of the theoretical amount of hydrogen had been absorbed and the uptake

(41) P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **81**, 703 (1929).
(42) W. G. Young and J. Ferrolane, *J. Am. Chem. Soc.*, **59**, 2051 (1937).
(43) S. P. Mulliken, R. L. Wakeman, and H. T. Gerry, *ibid.*, **57**, 1605 (1935).

(44) L. I. Smith and J. S. Swensen, *ibid.*, **79**, 2963 (1957).

had virtually ceased. The product was isolated by distillation: b.p. 31–32° (0.03 mm.); n^{24}D 1.5068; $\bar{\nu}$ 1603, 1496, 1350, 1240, 753, 718, and 690 cm.$^{-1}$; 4.35 g. (85%). The n.m.r. spectrum shows a doublet (3H) at τ 8.61 (CH_3—CH=C), a doublet (3H) at 8.29 (CH_3—CH—O), a multiplet centered at 4.85 (CH_3—CH—O), and two complex series of bands between 4.12–4.71 and 2.44–3.19.

B. Preparation from 4-Phenoxy-cis-2-penten-1-yl p-Toluenesulfonate. A mixture of 2.32 g. (7 mmoles) of 4-phenoxy-*cis*-2-penten-1-yl *p*-toluenesulfonate, 0.43 g. (0.011 mole) of lithium aluminum hydride, and 80 ml. of anhydrous ether was heated under reflux for 1 hr. After 5 ml. of water had been added dropwise, the mixture was stirred for 15 min. and acidified with 30 ml. of 8% sulfuric acid. The ether layer was separated and the aqueous layer was extracted with ether. The combined ether layers were washed with dilute sodium hydroxide followed by distilled water. The ether solution was dried and the product was isolated by distillation, b.p. 43–45° (0.6 mm.), n^{20}D 1.5097, 0.91 g. (80%).
Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.55; H, 8.58.

trans-2-Phenoxy-3-pentene (trans-α,γ-Dimethylallyl Phenyl Ether). The ether was prepared from phenol and *trans*-4-chloro-2-pentene using the directions of Alexander and Kluiber.[3] The clear liquid (b.p. 36–37° at 0.07 mm., n^{20}D 1.5103; $\bar{\nu}$ 1375, 1235, 960, 750, and 693 cm.$^{-1}$) was obtained in 33% yield (lit.[3] n^{20}D 1.5110).

o-(trans-α,γ-Dimethylallyl)phenol. A mixture of 15 g. (0.136 mole) of anhydrous sodium phenoxide, 20.5 g. (0.136 mole) of *trans*-4-bromo-2-pentene, and 225 ml. of anhydrous toluene was stirred for 3 days at 65° under an oxygen-free nitrogen atmosphere. Water was added to dissolve the solid materials and the toluene layer was extracted with dilute sodium hydroxide. The cold alkaline extract was acidified with cold dilute hydrochloric acid, and the product was extracted into ether. The phenol was isolated by distillation: b.p. 49–50° (0.02 mm.); n^{23}D 1.5331; $\bar{\nu}$ 3460, 1600, 1506, 1250, 967, and 750 cm.$^{-1}$; 10.7 g. (50%). The phenol has been reported[19a] to boil at 71–74° (0.05 mm.), n^{25}D 1.5318.

o-(1-Methyl-2-butynyl)phenol. A mixture of 11.6 g. (0.1 mole) of dry sodium phenoxide, 14.8 g. (0.1 mole) of 4-bromo-2-pentyne, and 150 ml. of anhydrous toluene was stirred for 72 hr. at 65° under a nitrogen atmosphere. The product was isolated as described in the preparation of *o*-(*trans*-α,γ-dimethylallyl)phenol and distilled: b.p. 78–80° (0.3 mm.); n^{23}D 1.5430; $\bar{\nu}$ 3475, 1595, 1270, 1215, and 790 cm.$^{-1}$; 7.45 g. (46%).
Anal. Calcd. for $C_{11}H_{12}O$: C, 82.47; H, 7.55. Found: C, 82.39; H, 7.71.

o-(cis-α,γ-Dimethylallyl)phenol. A freshly distilled sample of *o*-(1-methyl-2-butynyl)phenol was mixed with 10% of its weight of Lindlar catalyst in anhydrous ethyl acetate containing a drop or two of synthetic quinoline. The hydrogenation was interrupted after 1 mole of hydrogen had been absorbed. The liquid phenol was isolated by distillation: b.p. 63–65° (0.25 mm.); n^{23}D 1.5347; $\bar{\nu}$ 3460, 1600, 1506, 1250, 750, and 705 cm.$^{-1}$. The n.m.r. spectrum shows a

doublet (J = 7 c.p.s., 3H) at τ 8.73 (CH—CH_3), a second doublet (J = 5.5 c.p.s., 3H) at τ 8.32, an apparent quintet ($J = ca.$ 7 c.p.s., 1H) at τ 6.0, a multiplet (3H) between 300 and 350 c.p.s. (CH=CH and OH), and a second complex series of bands (4H) between 375 and 430 c.p.s. (aromatic H).
Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.61; H, 8.90.

Rearrangement. One-molar solutions of the ethers in mesitylene (b.p. 163–165°) were heated under reflux in a nitrogen atmosphere for 24 hr. The mesitylene was removed under reduced pressure and the residual oil was taken up in hexane. The hexane solution was extracted with 10% sodium hydroxide. The combined alkaline extracts were washed with hexane and acidified with cold 6 N hydrochloric acid and the organic material was taken up in hexane. The hexane solution was dried over anhydrous magnesium sulfate and the phenolic product was isolated by distillation. The product from the *trans* ether boiled at 64–65° (0.2 mm.), n^{20}D 1.5333, while that from the *cis* ether boiled at 68–70° (0.3 mm.), n^{20}D 1.5315. The geometric isomer content was determined by infrared analysis.

Thermal Isomerization of Phenols. A 10-ml. sample of 0.3 M *o*-(*trans*-α,γ-dimethylallyl)phenol in *n*-octane was heated in a sealed tube at 165° for 72 hr. The recovered phenol showed no trace of absorption in the infrared near 710 cm.$^{-1}$.

A 0.3 M solution of *o*-(*cis*-α,γ-dimethylallyl)phenol in *n*-octane was heated in a sealed tube at 165° for 72 hr. The recovered phenol showed a small peak at 965 cm.$^{-1}$ which indicated the presence of 14% of the *trans* ether. Assuming this to be a first-order reaction this corresponds to a rate constant, $k_1 = 0.5 \times 10^{-6}$ sec.$^{-1}$.

Rate Studies. Solutions of the *cis* or *trans* ether in *n*-octane, varying in concentration from 0.1 to 0.6 M, were sealed under vacuum in carefully cleaned Pyrex bombs. The bombs were placed in a constant temperature bath maintained at 164 ± 0.5°. Samples were removed at given time intervals, cooled quickly to room temperature, and concentrated *in vacuo* in weighed flasks. The weighed concentrate was analyzed

Table I

Sample	Time, hr.	% trans phenol
cis ether, 0.3 M solution, 165°		
11	8	98
12	14	97
13	18	98
trans ether, 0.6 M solution, 165°		
5	8	91
7	14	93
8	18	90

by an infrared method for total phenol concentration. The concentrate was then diluted with petroleum ether and this solution was extracted with three portions of 20% sodium hydroxide followed by two portions of Claisen's alkali. The unreacted ether was recovered from the petroleum ether layer and analyzed by infrared for *cis* and *trans* isomers. All samples showed no change in the double bond geometry.

The alkali extracts were combined, cooled in an ice bath, and acidified with cold, dilute hydrochloric acid. The phenolic product was taken up in ether, the solution was dried, and the ether was removed *in vacuo*. The residue was weighed and analyzed for *cis* and *trans* isomer by the infrared method. The concentration of *trans* phenol was effectively invariant as the reactions proceeded, as is shown in typical runs (see Table I).

Analysis. All analyses were carried out on a Perkin-Elmer Model 21 infrared spectrometer using a single fixed cell with sodium chloride windows and having a 0.05-mm. path length. Total phenol concentration was determined using the band at 3460 cm.$^{-1}$ in carbon disulfide solutions have concentrations lying in the range of 10–15%. The bands at 965–970 and 705–715 cm.$^{-1}$ were used to determine the *trans* and *cis* double bond contents, respectively. Samples of the pure isomeric ethers and phenols in known concentrations were used to establish standard curves for the relation between absorbance and concentration, and these were used to ascertain concentrations of the unknown solutions.

N.m.r. Spectra. The n.m.r. spectra were determined using a Varian A-60 spectrometer,[45] in carbon tetrachloride solutions using tetramethylsilane as an internal standard.

Effects of Nonpolar Solvents on an Ionic Reaction. II. Catalyst Basicity, Activation Parameters, Salt Effects, and Deuterium Isotope Effects in the Ionic Decomposition of *t*-Butylperoxy Formate

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Formate C–H bond breakage in the initial step for base-catalyzed decomposition of t-butylperoxy formate to carbon dioxide and t-butyl alcohol in nonhydroxylic solvents is established by kinetic deuterium isotope effect ratios (k_H/k_D = 4.1 for the pyridine-catalyzed reaction in heptane or chlorobenzene at 90°). For a wide variety of bases, the Brønsted relation (with log k_2 = 0.64pKₐ − 5.35) is followed in chlorobenzene with no steric effect observed for ortho-substituted bases. Triethylamine is 660 to 1380 times more effective as a catalyst than pyridine but the pattern of solvent effects remains the same (heptane << benzene < chlorobenzene < nitrobenzene). Changes in media by addition of salts to polar solvents (LiClO₄ to acetonitrile) or polar compounds to nonpolar solvents (pyridine to heptane) cause small increases in rates. The rates in heptane–benzene mixtures and the lower activation energies and more negative activation entropies found in benzene are consistent with the expected effect of polarization of solvent. Solvent effects in some other dipolar reactions in nonhydroxylic solvents are similar to those found in ionic decomposition of t-butylperoxy formate, but no general relationship is found.

t-Butylperoxy formate (I) (TBF), a peroxide highly stable toward thermal free radical decomposition, readily decomposes to carbon dioxide and *t*-butyl alcohol when catalyzed by bases.[1] The kinetic acceleration of this catalyzed decomposition when the solvent is made more ionic or more polarizable indicates formation of a polar transition state. Rate and prod-

uct comparisons[1] suggest that attack by base occurs directly on the formate hydrogen with concerted formation of carbon dioxide in the rate-determining step.
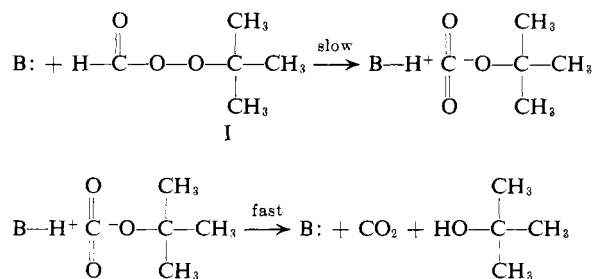
In this mechanism the formation of a dipolar transition state, with separation of the charged centers by the CO_2 unit, is made possible even in nonpolar, weakly polarizable solvents by concurrent partial formation of the stable carbon dioxide molecule.

To establish definitely that this reaction involves hydrogen transfer in the slow step, the deuterium isotope effect for ionic reaction of *t*-butylperoxy formate-*d* has been investigated. In addition, the possibility that the dipole moment of the transition state might be varied by changes in the basic strength of the catalyst or by a change in solvent has been investigated. Further aspects of solvation for this ionic elimination reaction in nonpolar, nonhydroxylic solvents are also reported here. These include studies of salt effects, rates in mixed solvents, and measurements of activation parameters.

(1) R. E. Pincock, *J. Am. Chem. Soc.*, **86**, 1820 (1964).