refluxed another hour, cooled, and washed thoroughly with 1 l. of 5% HCl. The benzene layer was then washed successively with three 700-ml solutions of 5% NaOH followed by water, and dried over sodium sulfate. The benzene was distilled, and the residue distilled at a range of 75–94° (18 mm). Vpc analysis revealed the presence of alcohol contaminant, and a pentane solution of the product was passed once through a column of acid-washed alumina for purification. After evaporation of the pentane, the resultant ketone (8.6 g, 75.4%) was pure by vpc and nmr standards: nmr (CCl_4) 0.86–1.04 (doublet, 6 H), 1.32–3.23 (multiplet, 6 H). *Anal.* Calcd for $C_7H_{12}O$: C, 75.95; H, 10.78. Found: C, 76.20; H, 10.57.

cis-**3-Isopropylcyclobutanol-*1-d*.** 3-Isopropylcyclobutanone (3.59 g, 0.032 mol) was reduced with 0.7 g (0.167 mol) of lithium aluminum deuteride, to yield 3.35 g (92.4%) of deuterated alcohol after distillation (bp 64–67° (17 mm)). Vpc analysis revealed it to be better than 96% cis isomer. The brosylate (see Table III) was prepared directly from this product and after several recrystallizations gave excellent analytical data.

trans-**3-Isopropylcyclobutanol-*1-d*.** *cis*-Brosylate (4.0 g, 0.012 mol) was refluxed in dry acetone with 6 g (excess) of freshly prepared, dry tetramethylammonium acetate for 20 hr. The precipitated tetramethylammonium brosylate was filtered, and the solution concentrated by distillation. The residual liquid was poured into water and extracted with ether. The ether was dried and evaporated, and the remaining acetate was hydrolyzed by reflux with aqueous KOH for several hours. The resultant alcohol was isolated by ether extraction. After evaporation of solvent, it weighed 0.92 g (67.2%), and was shown to be substantially pure trans isomer by vpc and nmr. This product was used for direct conversion to brosylate, which gave good analytical data (Table III) after several recrystallizations. Both brosylates exhibited sharp melting points which were depressed on admixture, and showed isomeric purity by nmr.

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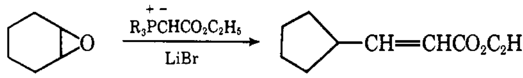
Lithium Salt Catalyzed Epoxide–Carbonyl Rearrangement. I. Alkyl-Substituted Epoxides[1]

Bruce Rickborn*[2] and Richard M. Gerkin[3]

Contribution from the Department of Chemistry, University of California, Santa Barbara, California 93106. Received July 11, 1970

Abstract: Lithium bromide is solubilized in benzene by the addition of an equivalent amount of hexamethylphosphoramide (HMPA) or other phosphine oxide. The resultant complex is an efficient catalyst for the rearrangement of epoxides to aldehydes and/or ketones. The addition of a second equivalent of HMPA quenches this catalytic activity. Evidence is presented which supports a mechanism involving the lithium salt of the bromohydrin as an intermediate in the LiBr-catalyzed rearrangement. Lithium perchlorate is partially solubilized in benzene by epoxides and effects the rapid rearrangement of those systems involving a tertiary center in the oxirane ring. Combined kinetic and product analyses for cyclohexene, 1-methylcyclohexene, and 1,2-dimethylcyclohexene oxides show that the $LiClO_4$-catalyzed reaction occurs by a different mechanism, presumably involving a carbonium ion. This mechanistic dichotomy allows flexibility in choosing the product of rearrangement and enhances the synthetic utility of the reaction. Kinetic data and product analyses are presented for a number of simple cyclic and acyclic epoxides, illustrating the scope and limitations of the reaction.

In an attempt to prepare substituted carbethoxycyclopropanes by the reaction of stabilized ylides with epoxides,[4] we observed instead the formation of acrylic esters,[5] as exemplified by eq 1. This result was most



(1)

easily rationalized in terms of rearrangement of the epoxide to a carbonyl compound (*e.g.*, cyclopentanecarboxaldehyde in eq 1) with subsequent Wittig reaction with the ylide to give the observed product. Initial attempts to demonstrate the intermediacy of the carbonyl compound were unsuccessful,[6] however, and led instead to a number of unexplained experimental observations: (a) the reaction occurred readily with tri-*n*-butylcarbethoxymethylidenephosphorane, this reagent being prepared from the corresponding bromide salt by reaction with butyllithium; (b) no reaction was observed under the same conditions using the analogous triphenyl ylide, which was free of salt contaminants; (c) added lithium chloride had no effect on the reaction; (d) cyclopentene oxide gave cyclopropane product rather than acrylic ester.

Results and Discussion

Tri-*n*-butylcarbethoxymethylidenephosphorane is relatively unstable to water, and consequently the usual aqueous procedure for forming the analogous triphenyl ylide is unsuitable for generation of the aliphatic phosphorane. However, by using the procedure of Payne,[6] we were able to obtain a benzene solution of this ylide which gave a negative halide test; although this mate-

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(1) A part of this work has been described in a preliminary communication: B. Rickborn and R. M. Gerkin, *J. Amer. Chem. Soc.*, **90**, 4193 (1968).

(2) Alfred P. Sloan Fellow, 1967–1969.

(3) NASA Predoctoral Trainee, 1966–1968.

(4) D. B. Denney, J. J. Vill, and M. J. Boskin, *J. Amer. Chem. Soc.*, **84**, 3944 (1962).

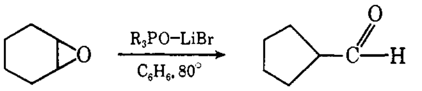
(5) R. M. Gerkin and B. Rickborn, *ibid.*, **89**, 5850 (1967).

(6) G. Payne, *J. Org. Chem.*, **32**, 3351 (1967).

rial gave a rapid, exothermic reaction with benzaldehyde, no reaction with cyclohexane oxide could be detected under our usual reaction conditions. Addition of lithium bromide initiated the formation of the acrylic ester. It thus became evident that we were dealing with a reaction which was catalyzed by the lithium bromide side product of ylide formation.

When this ylide was generated by treating the phosphorium chloride with butyllithium in benzene, reaction with epoxide was exceedingly slow. The solution was also quite turbid; the low solubility of LiCl under these conditions accounts for lack of reaction, and also the earlier noted absence of any effect by added solid LiCl. Similar treatment of the tri-*n*-butylphosphonium iodide gave material which caused rapid disappearance of cyclohexene oxide in refluxing benzene, showing that LiI more closely resembles LiBr than the chloride.

Interestingly, LiBr alone is totally insoluble in benzene, and refluxing a benzene solution of epoxide with LiBr present gave no reaction. Since the ylide reactions had shown no evidence of salt precipitation, and since tri-*n*-butylphosphine oxide is a product of the reaction (eq 1), a mixture of the latter and LiBr in benzene was prepared. The phosphine oxide exerts a marked solubilizing influence on the salt, such that 1 mol of salt is carried into solution by each mole of R_3PO up to about 0.8 *M* in benzene at 80°. Solutions prepared in this way effected the rearrangement of, *e.g.*, cyclohexene oxide to cyclopentanecarboxaldehyde (eq 2).



(2)

Further, the ylide, which must also solubilize LiBr, is acting only as a normal Wittig reagent with the carbonyl compound, *i.e.*, it is not (in most cases) directly involved in attack on the epoxide. This was demonstrated by preparing equivalent concentration ylide–LiBr and R_3PO–LiBr solutions; the pseudo-first-order rate constants for loss of epoxide were identical within experimental error (±10%), implying strongly that eq 2 is rate determining for eq 1.

Recognition of the mechanism has led to significant improvement in the yields of acrylic esters (eq 1). It is important that the butyllithium solution be in benzene rather than, *e.g.*, hexane solvent, as the latter cosolvent causes LiBr to precipitate. Excess R_3PO–LiBr can also be added to ensure reaction *via* eq 2. As an example of a synthetic application, cyclopentylacrylic ester (*cf.* eq 1) has been obtained in >90% distilled yield by this procedure.

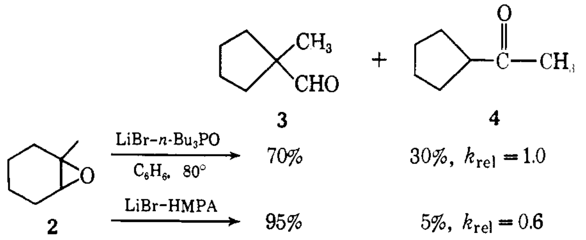
Lithium perchlorate is also completely insoluble in refluxing benzene, but unlike LiBr, a small amount of $LiClO_4$ is carried into solution by added epoxide, sufficient to cause rearrangement with reactive systems.[7] We have proposed[1] a dual mechanism for the lithium salt catalyzed epoxide–carbonyl rearrangement, namely that the LiBr reaction occurs with the intermediacy of the salt of the bromohydrin, while the $LiClO_4$ reaction involves a carbonium ion. This explanation was initially based on kinetic and product examination of 1,2-dimethyl-, 1-methyl-, and cyclohexene oxides; the several alkyl-substituted epoxides subsequently examined support this premise.

Lithium Bromide–HMPA Reaction. Both the ylide tributylcarboethoxymethylidenephosphorane and tri-*n*-butylphosphine oxide solubilize LiBr in benzene, and, as noted earlier, the rate of reaction with cyclohexene oxide and either reagent is the same. Hexamethylphosphoramide (**1**), HMPA, because of its availability and water solubility (facilitating removal at the end of a reaction) was examined to see if it would exert a

$$((CH_3)_2N)_3P\rightarrow O$$

1

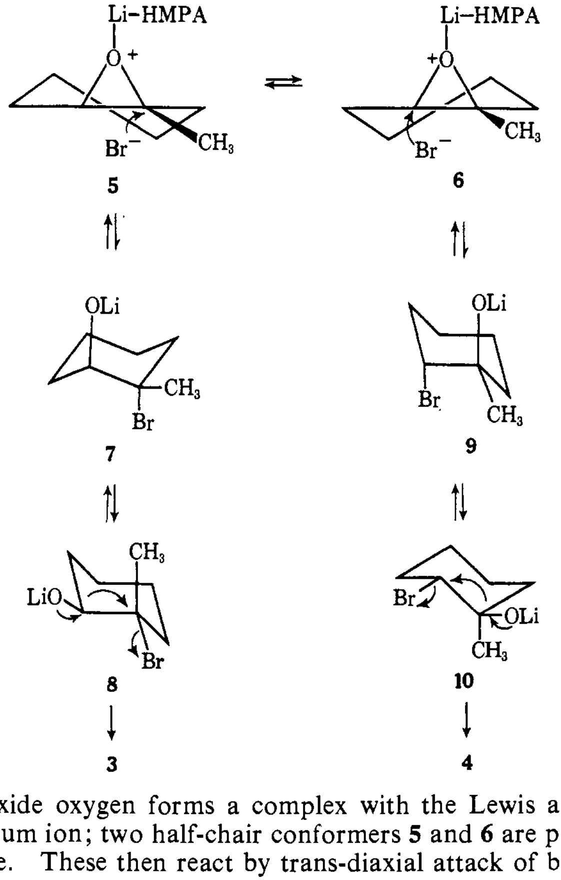
similar influence. An interesting observation was made using 1-methylcyclohexene oxide (**2**) as the substrate for reaction; the rates of reaction using tributylphosphine oxide or HMPA as the solubilizer differed only slightly, but a greater proportion of **3** was formed when HMPA was employed (eq 3). The formation of nearly pure **3** in excellent yield furnishes an example of the synthetic utility of this sequence.



(3)

It is proposed that the LiBr-catalyzed reaction of **2** occurs by the sequence shown in Scheme I. The epoxide oxygen forms a complex with the Lewis acid lithium ion; two half-chair conformers **5** and **6** are possible. These then react by trans-diaxial attack of bromide ion to give the lithium salts of halohydrins, **7** and **9**. These conformers are geometrically disposed only

Scheme I



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[7] When any epoxide (even an unreactive one) is added to a boiling mixture of $LiClO_4$ (on the bottom of the flask) and benzene, the salt disappears from the bottom and forms a ring at the surface of the refluxing liquid.

to give the reverse reaction, *i.e.*, epoxide formation. However, ring inversion gives the halohydrin salt conformers **8** and **10**, which now have the proper geometry for backside displacement of bromide by a ring methylene to give the products **3** and **4**, respectively.[8] Two points are especially worth noting; first, this mechanistic scheme precludes 2-methylcyclohexanone as a product, and indeed none is observed. Second, the ratio of products **3** and **4** depends *only* on the concentrations of **8** and **10** and their rates of reaction, *i.e.*, it is not possible with all prior steps being rapidly reversible to directly relate products to, *e.g.*, preference for tertiary *vs.* secondary attack of bromide ion. When cyclohexene bromohydrin (trans), with 1 equiv of HMPA in benzene, was treated with *n*-butyllithium, cyclohexene oxide was immediately formed in very high yield. A similar result was obtained with the derivative of 1,2-dimethylcyclohexene oxide. Thus we would conclude that the halohydrin salts are intermediates on the starting material side of the transition state, *i.e.*, the rate-determining step in the rearrangement is the actual alkyl migration with displacement of halide. The effect of alkyl substituents on the overall rate of reaction is clearly difficult to predict, as results to be presented later will show.

The reaction is, in all cases examined, clearly first order in epoxide. The kinetic order in LiBr–HMPA was determined by altering the concentration of this 1:1 complex and following the reaction with **2**. The results are shown in Table I. These data, when plotted as log [LiBr–HMPA] *vs.* log *k* give a straight line with a slope of one. Although there is some deviation at the highest concentration, over the lower tenfold concentration range it is clear that the reaction is first order in LiBr–HMPA. The kinetic results reported later were obtained with a salt concentration of 0.213 *M*, well within the first-order range.

Table I. Reaction of 1-Methylcyclohexene Oxide with LiBr–HMPA in Benzene, 80°

[LiBr–HMPA]	10^6k, sec^{-1}
0.037	0.23
0.071	0.407
0.106	0.68
0.217	1.11
0.355	2.5
0.71	6.4

The excellent metal cation solvating ability of HMPA has been noted in connection with other studies.[10] It was therefore of interest to examine the effect of changing the ratio of HMPA to LiBr on the course of the rearrangement. Again, 1-methylcyclohexene oxide was chosen as the substrate, and rather remarkable results were obtained. These are shown in the plot of reaction rate constant *vs.* HMPA to LiBr ratio (see Figure 1), with the total LiBr held constant (enough to make the solution 0.1 *M* if all dissolved). As noted previously, in the absence of HMPA solubilizer no LiBr goes into solution, and no reaction occurs. With HMPA/LiBr = 0.5, solid material is still in evidence, and the rate is essentially half that observed when HMPA/LiBr = 1.0. At the latter ratio no solid is visible, and we may therefore conclude that each mole of HMPA carries 1 mol of LiBr into solution. In other words, the equilibrium constant K_1 for eq 4 must be significantly greater than unity.

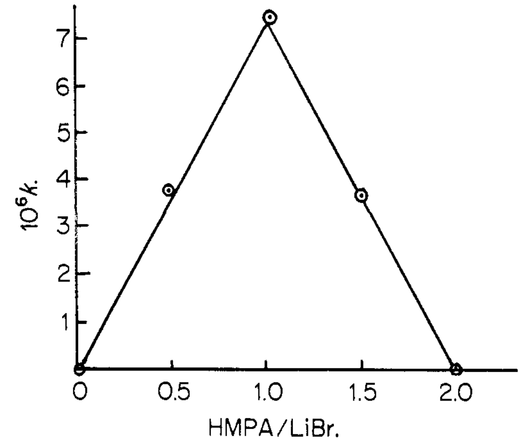

Figure 1. Rate constant for rearrangement of 1-methylcyclohexene oxide *vs.* HMPA/LiBr ratio, with total [LiBr] = 0.1.

$$\text{HMPA} + \text{LiBr(s)} \overset{K_1}{\rightleftarrows} \underset{\mathbf{11}}{\text{LiBr–HMPA}} \text{ (benzene solution)} \qquad (4)$$

As the amount of HMPA is increased further the reaction rate decreases; at HMPA/LiBr = 1.5 the rate is diminished to effectively half its value at the 1:1 ratio. Furthermore, at HMPA/LiBr = 2, no measurable reaction occurs. All reagents remain in solution. A plausible explanation is that a second complex is formed (eq 5), involving 2 mol of HMPA per mole of LiBr, and

$$\mathbf{11} + \text{HMPA} \overset{K_2}{\rightleftarrows} \underset{\mathbf{12}}{\text{LiBr–2HMPA}} \qquad (5)$$

that this complex, **12**, exhibits no catalytic activity for epoxide rearrangement. The equilibrium constant K_2 must also be greater than unity to account for the observed stoichiometric rate effects; further, K_2 cannot be much greater than K_1. If $K_2 \gg K_1$, no sharp maximum would appear in a plot such as Figure 1.

If it is assumed that HMPA solvates the Li cation by interaction with the negative (oxygen) end of the P $\rightarrow$ O dipole, it appears that there are two catalytically active sites on the cation. When only one is occupied by an HMPA molecule, the other (possibly by displacement of the bromide from an ion-pair arrangement) is available for interaction with an epoxide. However, when both sites are taken by HMPA moieties, the relatively weakly basic[11] epoxide is unable to interact strongly with the lithium, and no reaction occurs. In keeping with this interpretation it was observed that adding small amounts of THF[11] or glyme also caused the rate to fall off markedly. No reaction occurs in glyme solvent between cyclohexene oxide and LiBr, even though the salt is quite soluble.

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(8) The classical demonstration of the geometrical requirements of the base-catalyzed rearrangement of halohydrins to carbonyl compounds is found in the work of Tiffeneau and Tchoubar.[9]

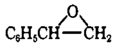
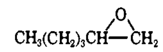
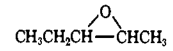
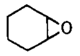
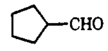
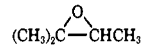
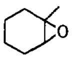
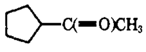
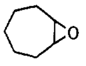
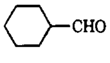
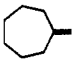
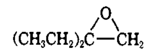
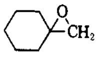
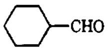
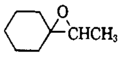
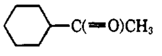
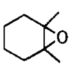
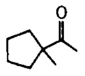
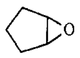
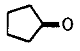
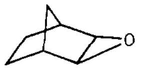
(9) M. Tiffeneau and B. Tchoubar, *C. R. Acad. Sci.*, **216**, 856 (1943).

(10) An excellent review of this very useful reagent and solvent has been presented by H. Normant, *Angew. Chem., Int. Ed. Engl.*, **6**, 1046 (1967).

(11) Equilibrium constants for complex formation with iodine of the oxaheterocycles fall in this order of ring size: 4 > 5 ~ 6 > 3.[12]

(12) M. Brandon, M. Tamres, and S. Searles, Jr., *J. Amer. Chem. Soc.*, **82**, 2129 (1960).

Table II. Rearrangement by LiBr–HMPA (0.213 *M*) in Benzene, 80°

Epoxide	10^4k, sec^{-1}	Products
	7.3	Nonvolatile material
	6.4	$CH_3(CH_2)_4CHO$ (60%) + $CH_3(CH_2)_3C(=O)CH_3$ (40%)
	1.7	$CH_3CH_2C(=O)CH_2CH_3$ + $CH_3C(=O)CH_2CH_2CH_3$ (see text)
	0.35	
	0.17	$(CH_3)_2CHC(=O)CH_3$
	0.11	 (95%) +  (5%)
	0.099	 (74%) +  (26%)
	0.088	$(CH_3CH_2)_2CHCHO$
	0.067	
	0.004	
	0.003	
	≥0.003	
	No reaction	

The rate constants and products of the LiBr–HMPA-catalyzed rearrangement of a variety of epoxides are given in Table II. The rate of the systems covered in this table varies over a range of 10^3.

The effect of alkyl substitution is not easily generalized. Thus, the first few entries in Table II might suggest that the lower the degree of substitution, the higher the rate. However, both 1,1-diethylethylene oxide and methylenecyclohexane oxide rearrange slower than some trisubstituted ethylene oxides (*e.g.*, trimethylethylene oxide) but faster than others (*e.g.*, ethylidenecyclohexane oxide). As pointed out earlier in the discussion of Scheme I, the observed rate depends on several preequilibria of unknown magnitude, and consequently the subtle changes caused by an alkyl substituent are not readily predicted or explained.

All of the systems studied, with the exception of styrene oxide, gave excellent yields of the products as shown in Table II. The yields were determined by vpc using an inert internal standard. The aldehyde products containing α hydrogens were not completely stable under the reaction conditions, presumably because of aldol condensation, and were lost slowly during the course of the reaction.[13] The products mixtures reported in Table II in cases where this could cause a problem represent the ratios formed at very low stages of conversion, where material balances were in general excellent. An exception is 1-hexene oxide, where the loss of hexanal was sufficiently rapid that its yield was determined by difference after complete reaction (see Experimental Section). The absence of volatile product from styrene oxide may be attributable to the formation of phenylacetaldehyde and its facile subsequent condensation, although this was not substantiated by a control reaction where the aldehyde was treated with LiBr–HMPA in refluxing benzene. The 1-hexene oxide results show that very little overall selectivity is observed for product arising from primary attack (2-hexanone) or secondary attack (hexanal) by bromide. Of course, because of the preequilibria problem, the product ratios cannot be taken as a direct measure of preference in nucleophilic attack. In systems containing a tertiary center, much higher regioselectivity is attained; the major or exclusive product is that arising from bromide

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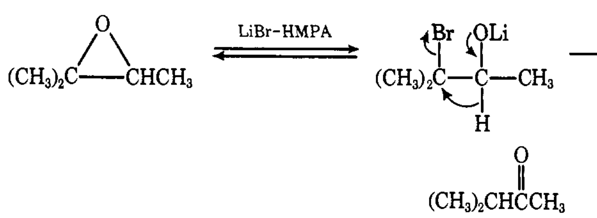
(13) The enhanced basicity of halide ions in dipolar aprotic solvents such as HMPA is well documented.[14]

(14) J. F. Normant and H. Deshayes, *Bull. Soc. Chim. Fr.*, 2455 (1967).

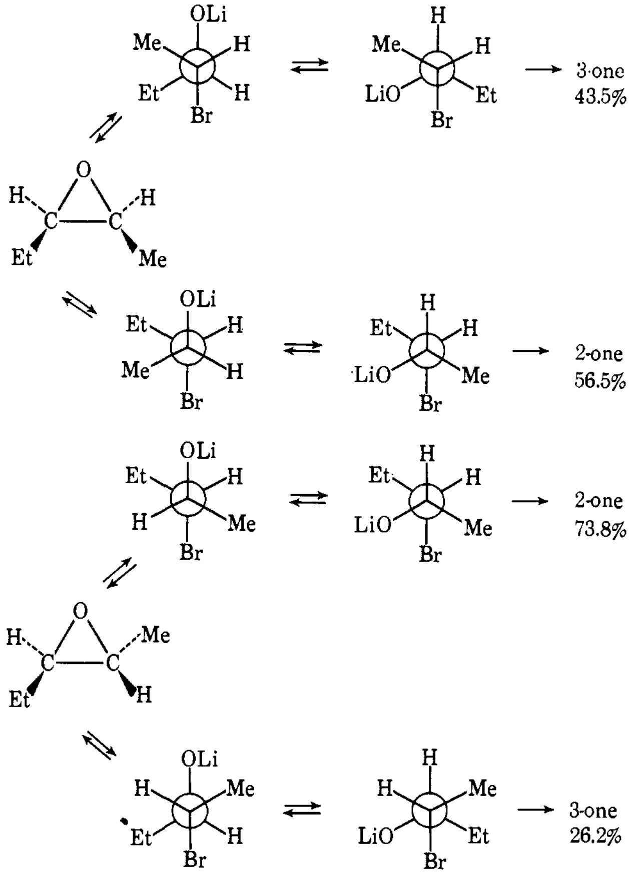
attack at the tertiary center. Examples are provided by 1-methylcyclohexene oxide, 1,1-diethylethylene oxide, methylenecyclohexane oxide, and ethylidenecyclohexane oxide. This result seems to hold generally, and therefore the mechanism of trimethylethylene oxide rearrangement is thought to occur as shown in eq 6; the alternate mode of opening followed by methyl migration appears to be energetically less favorable.



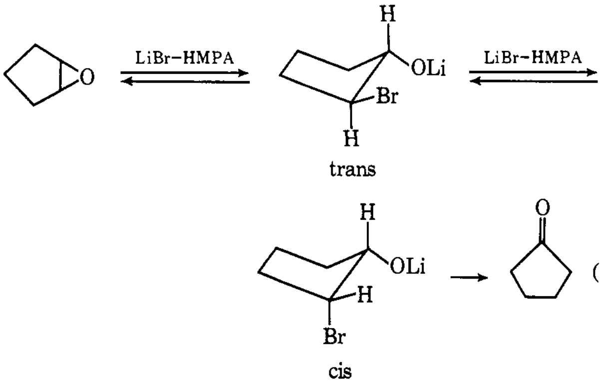
(6)

Two different mixtures of *cis*- and *trans*-2-pentene oxide were used in this work, and the results extrapolated to give the data shown in Scheme II. No difference in rate of reaction for the two isomeric epoxides could be detected. The *cis*-epoxide gave nearly equal amounts of 2- and 3-pentanone; the *trans*-epoxide favored 2-pentanone by a factor of about three. Both the rate and product results suggest very small preference for one reaction pathway over another with these epoxides, a conclusion that is reinforced by the absence of any obvious large differences in the Newman projection formulae in Scheme II.[15]

Scheme II



The three cyclohexene oxides (unsubstituted, 1-methyl, and 1,2-dimethyl) all give rearrangement products as predicted on the basis of the bromohydrin salt mechanism outlined in Scheme I. Specifically, cyclohexanone products have been excluded in the LiBr–HMPA reactions; these are expected and found for the methyl-substituted cyclohexene oxides in which a carbonium ion mechanism occurs (see discussion of the $LiClO_4$ reaction). It was therefore interesting to find that cycloheptene oxide and cyclopentene oxide do give the corresponding cycloalkanone products. Models indicate that the *trans*-bromohydrin salts in both ring systems cannot attain the necessary antiperiplanar H–C–C–Br configuration needed for rearrangement to ketone, and therefore an alternate mechanism is needed. A carbonium ion process appears to be a possibility, and receives support from the observation that cycloheptene oxide gives a similar product mixture (17% cycloheptanone) when treated with $LiClO_4$ (*cf.* Table III). However, other facts argue against this conclusion; the absence of "carbonium ion products" for tertiary epoxides (*e.g.*, 1,2-dimethylcyclohexene oxide), the very slow reaction of these systems, and the failure of norbornene oxide to react at all. We suggest as an alternative mechanism that the *trans*-bromohydrin salt (present in low concentration) undergoes displacement by a second bromide ion to yield the cis derivative, as shown for cyclopentene oxide in eq 7. The latter is geometrically suited for hydride migration to give the ketone. In the cycloheptene oxide reaction, this process competes with the "normal" rearrangement yielding cyclohexanecarboxaldehyde (74%); the latter process is inhibited relative to a simple secondary–secondary epoxide system (the overall rate is diminished), in all probability by transannular hydrogen–hydrogen interactions which develop as the *trans*-bromohydrin salt assumes the necessary geometry for ring contraction.[17]



(7)

The general mechanism proposed for the LiBr–HMPA rearrangement, involving bromohydrin salt, requires a net double inversion at the center adjacent to the carbonyl group in the product. An initial attempt to examine the stereochemical course of the reaction involved working with the isomeric methylene-4-methylcyclohexane oxides[18] (eq 8). The less stable trans isomer[19,21] reacts at exactly the same rate as the unsubsti-

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(15) House[16] has presented data which suggest that 2-bromo-3-pentanol and 3-bromo-2-pentanol, on treatment with ethylmagnesium bromide, rearrange to the corresponding pentanones faster than they close to epoxide. The lithium and magnesium salt reactions differ fundamentally in this regard.

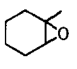
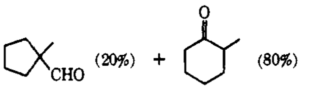
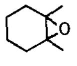
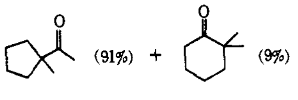
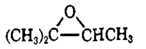
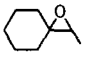
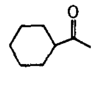
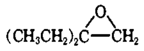
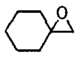
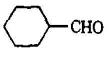
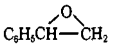
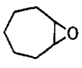
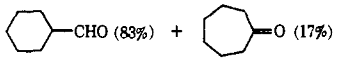
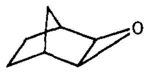
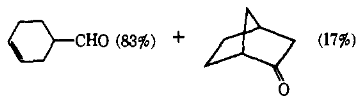
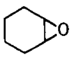
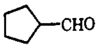
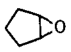
(16) H. O. House, *J. Amer. Chem. Soc.*, 77, 5083 (1955); see also T. A. Geissman and R. I. Akawie, *ibid.*, 73, 1993 (1951).

(17) The relative inertness of cyclopentene oxide explains the earlier observation[5] that this material is preferentially attacked by carbethoxy ylide to give the carbethoxycyclopropane product.

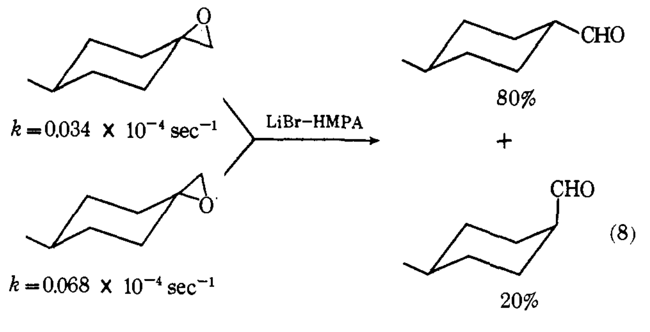
(18) The experiments were actually carried out with two different known mixtures of the two epoxides (see Experimental Section).

(19) The stereochemical designation refers to the position of the oxygen relative to the 4-methyl group. Recent studies have indicated

Table III. Rearrangement by $LiClO_4$ in Benzene, 80°

Epoxide	10^4k, sec^{-1}	Products
	>14 (too fast to measure)	 (20%) + (80%)
	>14	 (91%) + (9%)
 $(CH_3)_2C(O)CHCH_3$	5.7	$(CH_3)_2CHC(=O)CH_3$
	2.2	
 $(CH_3CH_2)_2C(O)CH_2$	0.9	$(CH_3CH_2)_2CHCHO$
	0.6	
 $C_6H_5CH(O)CH_2$	0.26	$C_6H_5CH_2CHO$
	0.099	 (83%) + (17%)
	0.039	 (83%) + (17%)
	0.032	Trace  + nonvolatile material
	<0.03	No reaction

tuted analog, methylenecyclohexane oxide (see Table II), while the cis isomer reacts only half as fast. No obvious explanation for this difference can be offered, but about half of the effect may be attributed to ground-state energies.[19] Unfortunately both isomers give the



same (equilibrium) mixture of *cis*- and *trans*-4-methylcyclohexanecarboxaldehyde (eq 8), precluding any stereochemical interpretation. The aldehydes once formed are rapidly equilibrated, presumably by the same process (enolate) responsible for the loss of aldehydes bearing α hydrogens and the double bond migration in acrylic esters reported earlier.[5]

Rearrangement by $LiClO_4$. The small amount of $LiClO_4$ solubilized by an epoxide in refluxing benzene is sufficient to cause rearrangement of reactive oxiranes. In fact, if HMPA or other phosphine oxide is added to enhance salt solubility, diminished and irreproducible rates are obtained. The HMPA–$LiClO_4$ complex, even though present in much greater concentration, is less effective catalytically than the epoxide-solubilized salt. Using only $LiClO_4$, reproducible first-order (in epoxide) kinetics are observed. Since only a small amount of $LiClO_4$ is carried into solution (the bulk remaining undissolved), the true ground state for the reaction is the free epoxide and insoluble salt. This fact allows kinetic arguments to be based on epoxide structural features, unencumbered by an unknown but presumably variable epoxide–$LiClO_4$ complex concentration.

Kinetic data and product distributions are shown in Table III. The rate sequence is very roughly the reverse of that found with LiBr–HMPA. All tertiary epoxides react rapidly with $LiClO_4$, and both this fact and the observed products are best explained by a carbonium ion mechanism. The cyclohexanone products from 1-methyl- and 1,2-dimethylcyclohexene oxide are formed by a process which allows the development of a planar carbonium ion at the cleaved tertiary center. The major product from 1-methylcyclohexene oxide then reflects the greater migratory aptitude of hydrogen over ring methylene (eq 9). It is interesting that 1,2-dimethylcyclohexene oxide gives the same products, in effectively the same ratio, as reported by Bunton and Carr[22] for the $HClO_4$-catalyzed pinacolone rearrange-

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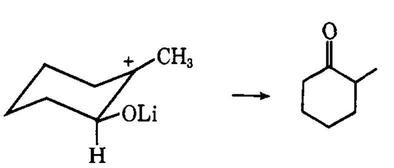
that the conformer of methylenecyclohexane oxide with the CH_2 "equatorial" is favored by 0.27 kcal/mol.[20]

[20] R. C. Carlson and N. S. Behn, *Chem. Commun.*, 339 (1968).

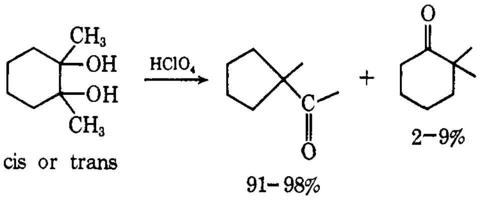
[21] J. J. Ubel, *Tetrahedron Lett.*, 4751 (1967).

[22] C. A. Bunton and M. D. Carr, *J. Chem. Soc.*, 5854 (1963).



(9)

ment shown in eq 10. In both reactions the products



(10)

are best rationalized by a planar carbonium ion, with the product distribution determined by both migratory aptitudes and subtle conformational preferences.

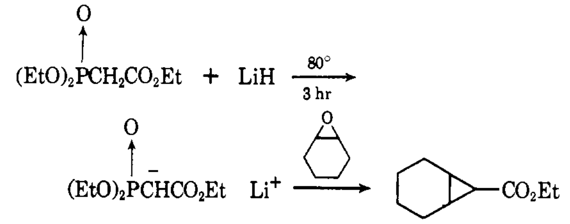
It appears that a fully opened carbonium ion is not a good transition state model for the nontertiary epoxides listed in Table III. In particular, styrene oxide and *exo*-norbornene oxide might have been expected to react faster than is observed; the latter gives mainly skeletally rearranged aldehyde, but at a rate that is typical for secondary–secondary epoxides, *e.g.*, cyclohexene oxide. The $LiClO_4$ procedure failed to give appreciable volatile product with cyclohexene oxide and cyclopentene oxide was completely unreactive, while cycloheptene oxide rearranged smoothly to the products shown. Both the cyclohexanecarboxaldehyde and the phenylacetaldehyde formed from styrene oxide appeared to be reasonably stable to these reaction conditions.

Comparison with Other Catalysts for Epoxide Rearrangement. The lithium salt catalyzed rearrangement of epoxides involves very mild conditions and a degree of selectivity depending on the nature of the epoxide and the choice of lithium salt, as outlined in Tables II and III. Epoxide–carbonyl rearrangements have been known for many years, and numerous catalysts have been utilized to effect this conversion. All have significant limitations. Reagents which have been used, and their limitations, include: 48% HBr (only tertiary epoxides rearrange and then in low yield[23,24]); HCl, H_2SO_4, or H_3PO_4 in hydrocarbon solvent (tertiary epoxides, aldehydes unstable);[25] anhydrous HF in acetonitrile (except for the difficulties of working with HF, this method appears to be generally applicable, giving results similar to those obtained in the present work);[26] H_2SO_4 in $CHCl_3$ has been used very successfully to cause the rearrangement of substituted cyclobutene oxides to the corresponding cyclopropanecarboxaldehydes[27] (not generally applicable). Boron trifluoride has been widely used to effect rearrangement of epoxides, but numerous problems are encountered, including polymerization,[28] low yields,[29] and fluorohydrin formation.[30] Recently CF_3CO_3H–BF_3 has been shown to convert tri- and tetrasubstituted olefins directly to ketones.[31] Zinc halides in aromatic hydrocarbon solvents will cause the rearrangement of tertiary epoxides,[32] while cyclohexene oxide is reported to give only the stable halozinc salt of the halohydrin when treated with $ZnCl_2$ in ether.[33] Magnesium halides behave analogously.[34]

An unusual reaction involving epoxide, alkyl iodide, and sodium iodide in warm (80°) DMSO has recently been reported.[35] Cyclohexene oxide yields cyclohexanone (90%), and 1-octene oxide gives octanal (80%).

The lithium iodide generated in the formation of an alkyllithium reagent can complicate the subsequent reaction with epoxides.[36] LiI has also been reported to cause the rearrangement of a cyclobutene oxide to the analogous cyclopropanecarboxaldehyde.[37] We have briefly investigated the use of this salt under our reaction conditions, where it appears to be somewhat more reactive than LiBr. Its extremely hygroscopic nature, however, makes it much more difficult to handle.

Finally, it was of interest to examine the reaction of epoxides with the lithium analog of the Wadsworth–Emmons reagent,[38] to determine whether the rearrangement reaction would intervene. The reaction was carried out in refluxing benzene, giving the results indicated in eq 11. The ethyl 7-norcaranecarboxylate was isolated in 58% yield (comparing favorably with literature results on other epoxides[38]); none of the acrylic ester, as shown in eq 1, was formed (vpc).



(11)

Experimental Section

Olefins. 1-Hexene, 2-pentene (mixture, cis and trans), 2-methyl-2-butene, cycloheptene, cyclopentene, and ethylidenecyclohexane were obtained from commercial sources. Methylenecyclohexane was prepared by a literature procedure.[39]

Epoxides. Cyclohexene oxide, styrene oxide, and norbornene oxide were obtained from commercial sources and distilled prior to use. The 1-methylcyclohexene oxide and 1,2-dimethylcyclohexene oxide have been described previously.[40] Cyclopentene oxide[41] (bp 99–100°), cycloheptene oxide[42] (bp 155–158°), methylenecyclo-

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(23) J. G. Traynham and O. S. Pascual, *Tetrahedron*, 7, 165 (1959).

(24) A. J. Sisti, *J. Org. Chem.*, 33, 3953 (1968).

(25) E. J. Gasson, A. R. Graham, A. F. Millidge, I. K. M. Robson, W. Webster, A. M. Wild, and D. P. Young, *J. Chem. Soc.*, 2170 (1954).

(26) K. Wiechert and P. Mohr, *Z. Chem.*, 7, 229 (1967).

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(31) H. Hart and L. R. Lerner, *J. Org. Chem.*, 32, 2669 (1967).

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(35) D. Bethell, G. W. Kenner, and P. J. Powers, *Chem. Commun.*, 227 (1968).

(36) J. K. Heeren, T. C. Flood, and R. H. Cunningham, *J. Organometal. Chem.*, 9, P18 (1967).

(37) D. L. Garin, *J. Org. Chem.*, **34**, 2355 (1969).

(38) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1733 (1961).

(39) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).

(40) D. K. Murphy, R. L. Alumbaugh, and B. Rickborn, *J. Amer. Chem. Soc.*, **91**, 2649 (1969).

(41) W. P. Emmons and A. S. Pagano, *ibid.*, 77, 89 (1955).

(42) L. N. Owen and G. S. Saharia, *J. Chem. Soc.*, 2482 (1953).

hexane oxide[43] (bp 145–146°), 1-hexene oxide[41,44] (bp 113.5–115°), 2-pentene oxide[44,45] (various fractions bp 80–86.8°), 2-methyl-2-butene oxide[44,46] (bp 70–73°), and ethylidenecyclohexane oxide[44,47] (bp 158–160°) were prepared in fair to excellent yields using the olefins and peracetic acid.[48]

1,1-Diethylethylene Oxide.[49] This material, bp 105–107°, was prepared in 65% yield from 3-pentanone and dimethylsulfoxonium methylide.[50]

4-Methylmethylenecyclohexane Oxide (Cis and Trans). The procedure of Corey and Chaykovsky[50] was again followed to give distilled product, bp 157–159°. Vpc analysis (10% Carbowax 20M) showed two peaks, in order of retention time 93% cis[19] and 7% trans. The stereochemical assignment is based on analogy with the results reported by Corey for 4-*tert*-butylcyclohexanone (exclusive cis product).[50] Our preparation was repeated, giving the same product mixture.

A separate sample of the epoxide mixture was prepared by peracetic acid oxidation of 4-methylmethylenecyclohexane, giving 70% *cis*- and 30% *trans*-epoxide.[51]

Tri-*n*-butylcarbethoxymethylidenephosphorane (Salt-Free). The procedure was suggested by the successful two-phase preparation of sulfur ylides described by Payne.[6] To efficiently stirred benzene (150 ml) was added 25 g (0.067 mol) of tri-*n*-butylcarbethoxymethylenephosphonium bromide in 50 ml of water, followed immediately by 20 ml of 6.7 *M* NaOH solution. After stirring rapidly for 10 min, the benzene layer was separated, dried over sodium sulfate, and rotary evaporated (vacuum pump) to yield 16.1 g (84%) of a semisolid mass. A small amount of this crude material was dissolved in ether and treated with benzaldehyde. A vigorous reaction occurred, yielding ethyl cinnamate (by vpc). Another sample of the ylide was treated with distilled water and acidified with nitric acid; addition of silver nitrate solution gave no precipitate.

Ylide Reaction with Cyclohexene Oxide. The crude ylide described above (6.5 g) was taken up in benzene and 2.2 g (0.022 mol) of cyclohexene oxide was added. The mixture was refluxed for 24 hr, during which time no product was formed, and no epoxide was lost. At this point 2.0 g of LiBr (0.022 mol) was added to the refluxing mixture; a sample withdrawn immediately showed some product, ethyl 3-cyclopentylpropenoate, had formed.

A number of related experiments were performed. High yields of the acrylic ester were obtained by treatment of the above phosphonium iodide or bromide with LiH in refluxing benzene followed by cyclohexene oxide addition. The iodide gave the fastest reaction; a similar experiment using the phosphonium chloride gave a low (9%) yield of product after 22 hr. The analogous salt-free triphenyl ylide[53] failed to react with cyclohexene oxide in refluxing benzene, but when generated from the phosphonium bromide by treating with LiH in benzene, a 62% yield of ester was obtained after 21 hr of refluxing.

Ethyl Bicyclo[4.1.0]heptane-7-carboxylate. Carbethoxymethylenediethylphosphonate, bp 121–123° (3.6 mm), was prepared in 96% yield by the reaction of triethyl phosphate and ethyl bromoacetate (15 hr, steam bath). A mixture of this material, 9.65 g (0.05 mol), LiH, 0.4 g (0.05 mol), and 70 ml of benzene was refluxed (magnetic stirring) in a closed system connected to a gas buret. After 3 hr, 1.14 l. of hydrogen (100%) had been evolved. Cyclohexene oxide, 4.9 g (0.05 mol), was added and reflux continued. The initial reaction was smooth, but after 7 hr a precipitate (lithium diethylphosphate?) formed, and the rate of loss of epoxide decreased. After 23 hr the mixture was quite viscous and some epoxide remained (vpc). The mixture was cooled, washed with water, dried (Na$_2$SO$_4$), and distilled to give 4.9 g (58%) of ethyl norcarrane-7-carboxylate,[54] bp 92° (4 mm).

Kinetics Procedure. A 0.71 *M* stock solution of HMPA in benzene was prepared and stored under nitrogen.[55] Reactions were run in a 25-ml flask equipped with a magnetic stirrer, reflux condenser, and rubber septum. The appropriate amount of commercial anhydrous LiBr was weighed into this flask under nitrogen, and HMPA stock and benzene added to bring the volume to 10 ml. The mixture was then brought to reflux, whereupon the salt dissolved; at this point the internal standard (inert material for vpc reference) and the epoxide were added. At intervals 0.1-ml aliquots were withdrawn and shaken in a test tube with a small (0.2 ml) volume of water. The organic phase was removed by pipet, dried (Na$_2$SO$_4$), and analyzed by vpc.[56] Rate constants were obtained graphically from plots of log epoxide peak area (normalized by reference to internal standard) vs. time. Very good first-order behavior was observed in all cases examined, with estimated rate constant error limits of ±5%.

Product Identification. In most instances the products were known, commercially available aldehydes and ketones, and identification was made by vpc retention times and spectra of collected materials. In a few cases the vpc columns used failed to separate the products. An example is 1-hexene oxide; hexanal and 2-hexanone were not separated. The rearrangement product mixture was reduced and analysis carried out on the easily separable 1- and 2-hexanols. Similarly 2- and 3-pentanone (from 2-pentene oxide) were not separated, but the corresponding alcohols were. The solvent benzene interfered with the 3-methyl-2-butanone (from 2-methyl-2-butene oxide), and again analysis was effected by prior reduction. All reductions were carried out using LAH, and on mixtures containing no unreacted epoxide.

The *cis*- and *trans*-4-methylcyclohexanecarboxaldehydes were not separated by any of the vpc columns employed. LAH reduction was again employed, but after 48 hr when about two-thirds of the epoxide remained unreacted.[57] Using a Carbowax 20M column, the two primary alcohols (in order of increasing retention time) were *trans*- (80%) and *cis*-4-methylcyclohexylmethanol (20%). Both samples of 4-methylmethylenecyclohexane oxide described previously gave the same result, ±1%.

The stereochemistry of these alcohols was determined by conversion to the methanesulfonate derivative, followed by LAH reduction. The 1,4-dimethylcyclohexane mixture, which corresponded very closely percentage-wise to the starting alcohol mixture, was identified by vpc comparison with known materials.

Additional structural evidence for several of the aldehyde products reported here is obtained from the acrylic esters reported earlier.[5,58] Cyclopentanecarboxaldehyde,[59] methylcyclopentyl ketone,[60] and methylcyclohexyl ketone[61] were synthesized by alternate procedures.

Acknowledgment. Partial support of this work by the National Science Foundation (GP 9383) is gratefully acknowledged.

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(44) The authors wish to thank Mr. Sam Tokuyama (H. D.) for carrying out this preparation.

(45) H. van Risseghem, *Bull. Soc. Chim. Fr.*, 1161 (1959).

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(55) The HMPA was distilled material, bp 112.5–113° (11 mm). The benzene was distilled and stored over sodium wire.

(56) Vpc columns of Carbowax 6M, Carbowax 20M, and TCEOP were used at various temperatures. Internal standards employed were bromobenzene, chlorobenzene, toluene, or mesitylene. Details are given in the Ph.D. Dissertation of R. M. Gerkin (U.C.S.B., Dec 1968), and specifics will be gladly furnished on request.

(57) A separate experiment showed that, as expected,[40] LAH reduction of the epoxides gave only tertiary alcohols.

(58) The absence of acrylic esters derived from the ketones found in the present work is due to the very much faster ylide reaction with aldehydes than with ketones.

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