Rearrangement Reactions of Lithiated Oxiranes

B. Ramu Ramachandran,*,[†] Shannon Waithe,[‡] and Lawrence M. Pratt[§]

[†]College of Engineering & Science, Louisiana Tech University, Ruston, Louisiana 71272, United States
[‡]Medgar Evers College Preparatory High School, Brooklyn, New York 11225, United States
[§]Department of Physical, Environmental, and Computer Sciences, Medgar Evers College, The City University of New York 1638 Bedford Ave., Brooklyn, New York 11225, United States

S *Supporting Information*
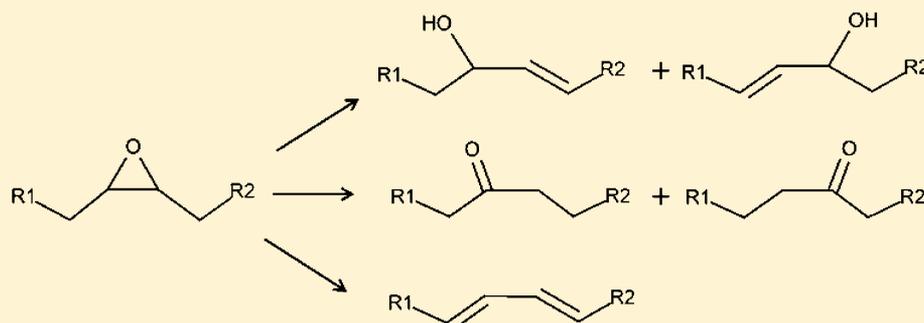
ABSTRACT: The first computational study of the rearrangement reactions of oxiranes initiated by lithium dialkylamides is presented. Aside from the well-known carbenoid insertion pathways, both β-elimination and α-lithiation have been suggested as the exclusive mechanism by which oxiranes react in the presence of organolithium bases. The products of the former are allyl alcohols (and, in some cases, dienes) and are ketones in the case of the latter. The computational studies reported in this work indicate that both mechanisms could be simultaneously operational. In particular, our work shows that the allyl alcohols from β-elimination are unlikely to undergo 1,3-hydrogen transfer to the vinyl alcohols and thus to the ketones, suggesting that ketones are formed through the opening of the oxirane ring after α-substitution. Elimination of LiOH from the lithiated allyl alcohol is found to result in the diene product. Low activation barriers for β-elimination are offered as the explanation for the few special cases where the allyl alcohol is the dominant or exclusive product. These findings are consistent with the product distributions observed in several experiments.

INTRODUCTION

Contradictory reports exist in the literature as to the fate of oxiranes in the presence of organolithium bases. The early studies of Cope and Heeren[1] on deuterated *cis-* and *trans-*4-octene oxides reacting with lithium diethylamide suggested that β-elimination is the exclusive pathway, leading to the allyl alcohol as the exclusive product. On the other hand, more recent studies of Yanagisawa et al.[2] on deuterated 1,2-epoxyalkanes suggest that α-substitution leading to aldehydes is the exclusive mechanism, at least in those compounds. From a survey of the literature, a more common scenario appears to be competition between multiple simultaneously operational reaction pathways. Crandall and co-workers have extensively studied the base-promoted reactions of epoxides[3−7] and have reported not only cases where the allyl alcohol, presumably the product of β-elimination, was the exclusive product but also cases where a mixture of ketones, allyl alcohols, and dienes were observed in addition to bicyclic alcohols formed by carbenoid insertion pathways. Through elegant experiments with deuterium-labeled reactants, *cis-* and *trans-4-tert-*butylcyclohexene oxides in the presence of lithium diethylamide have been shown to yield allyl alcohol exclusively through *syn* β-elimination.[8] More recently, Ramirez and Collum reported the isomerization of *cis-*cyclooctene oxide to a mixture of the allyl alcohol and bicyclic carbenoid insertion products,[9] with a strong solvent dependence on the product distribution. Hodgson et al.[10] have also reported a mixture of products in the reaction of 1,2-epoxy-5-hexene with lithium 2,2,6,6-tetramethylpiperidide, including the bicyclic alcohol from intramolecular carbenoid insertion and the aldehyde, presumably by keto−enol isomerization of a vinyl alcohol.

Thus, it is clear that two pathways are available to oxiranes in the presence of organolithium bases: namely, α-lithiation and β-elimination. The lithiated oxiranes produced by the former are known to undergo carbenoid insertions into C=C double bonds and C−H single bonds to produce bicyclic alcohols and cyclopropane derivatives. We recently reported a detailed computational study of these carbenoid reactions.[11] The lithiated oxiranes also undergo non-carbenoid reactions which lead to vinyl alcohols and thus to ketones or aldehydes. The β-elimination pathway leads to allyl alcohols which appear to be
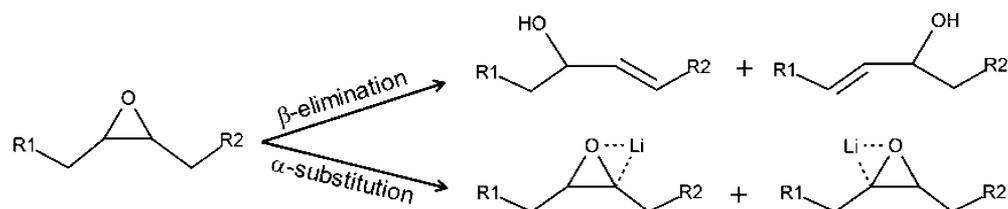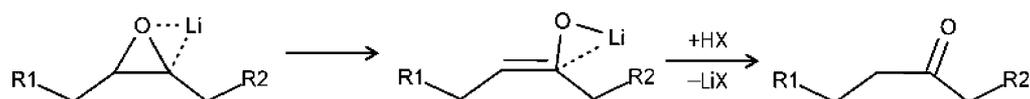
Scheme 1

Scheme 2

capable of further reaction leading to dienes, at least in some cases. In this paper, we turn our attention to these non-carbenoid pathways. To the best of our knowledge, this is the first computational study of these reactions.

The ring strain in oxiranes makes them useful reagents for a wide variety of synthetic pathways under mild conditions. Their rich chemistry in the presence of organolithium reagents has been discussed in several excellent reviews.[12−16] Although the possibility of competition between α-lithiation and β-elimination in oxirane chemistry has been well-recognized, further evolution of the intermediates produced by these initial steps along the two pathways remain to be studied and motivates the present work.

Neither β-elimination nor α-lithiation is directly studied in this work. Those reactions are likely to be complex processes that depend on the specific lithium base used, as well as its aggregation and solvation states. For example, alkyllithiums commonly exist as dimers, tetramers, or higher aggregates depending on the solvent and steric strain.[17] Structures and solvation states of lithium dialkylamide bases are also complex and any of the multiple species are potential reactive species.[18,19] The influence of the solvent on the reaction pathway has also been reported.[9,20−23]

However, following the fate of the species formed from β-elimination or α-lithiation is sufficient to gain useful insight into the reaction mechanisms. Consider Scheme 1. It is well-established that base-promoted β-elimination of a proton from the epoxide will yield the allyl alcohols as shown. At the same time, α-substitution of a proton on the oxirane ring by Li gives rise to the lithiated oxiranes. These species, represented in the top and bottom rows, respectively, of Scheme 1 subsequently undergo very different reactions. *These reactions* are the subject of our investigations, as summarized below in Schemes 2−4.

Scheme 2 shows the further reaction of the lithiated oxiranes. The ring opening leads to a lithiated vinyl alcohol which, upon final workup, yields the vinyl alcohol and thus the ketone. The rate-determining step in this process appears to be the ring-opening reaction.

The allyl alcohol formed by β-elimination could undergo further reaction if the alcohol functional group is lithiated. As noted above, in several cases where allyl alcohols are observed among the products, dienes are also formed. We conjecture that lithiation of the allyl alcohol followed by the elimination of LiOH may be one mechanism to account for this product, as shown in Scheme 3.
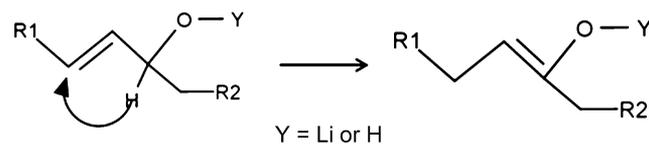
Another source of vinyl alcohols (and thus ketones) that should be considered is through 1,3-hydrogen transfer in the

Scheme 3
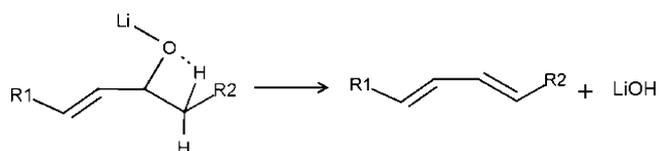
lithiated or nonlithiated allyl alcohol formed from β-elimination, as shown in Scheme 4. Therefore, if the barrier

Scheme 4

for the 1,3-hydrogen transfer is reasonably low, it is plausible that the β-elimination mechanism can account for all the non-carbenoid products observed in the reactions.

Ketones or aldehydes can also be formed by 1,2-hydrogen transfer. However, the work of Morgan et al.[20,22,24] and our own recent study[11] indicate that such reactions are typically part of the carbenoid pathways. In this paper, we restrict ourselves to the noncarbenoid rearrangement reactions.

Our computational investigations will examine *cis*- and *trans*-octene oxides, which were studied by Cope and Heeren.[1] Our primary focus in these calculations is the thermodynamics of formation of the allyl and vinyl alcohols from the starting material and the reaction barrier for the lithiated epoxide ring opening subsequent to α-substitution (Scheme 2). We also examine the reactions of 1,2-epoxy-5-hexene oxide, which was studied by Hogsdon et al.[10] In this case, in addition to the reaction in Scheme 2, we also examine the reaction energetics of the 1,3-hydrogen transfer shown in Scheme 4. However, the majority of our calculations are devoted to the cases studied by Crandall and Chang: apopinene oxide, α-pinene oxide, 2,4,4-trimethyl-2-pentene oxide, and the oxiranes formed from cyclopentene, cyclohexene, and cycloheptene. In the last three cases, the respective cyclic dienes have been observed among the products. The reactant oxiranes studied are shown in Scheme 5.

As the foregoing discussion indicates, lithiated oxiranes have a very rich chemistry, due at least in part to their intermediate nature between carbenoids and stabilized carbanions.[12,25] They undergo carbanion-like reactions with electrophiles,[26] and the

Scheme 5
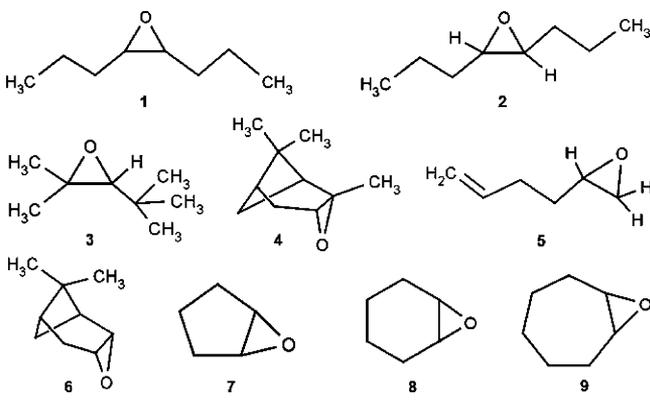
chemical and configurational stability of the oxiranyl anion has been exploited for organic synthesis.[27,28] In addition to the carbenoid cyclopropanation reactions,[10,11,29−33] which are C═C insertion reactions, many examples of C−H insertion reactions have also been reported.[10,34−36]

The remainder of this paper is structured as follows. The next section describes the computational methods and methodology adopted in this study. This is followed by a section in which we present the results and discuss the insights they provide into the reactions of lithiated oxiranes. The final section offers a summary of the main findings and conclusions.

■ COMPUTATIONAL METHODS

All calculations were performed using the Gaussian 09 suite of programs.[37] Calculations were done for molecules in the gas phase, which can be readily extended to nonpolar solvents with appropriate standard state corrections.[38] However, given that the most commonly used solvent in the experimental studies of these reactions has been diethyl ether (abbreviated as Et$_2$O), we also model the effect of the solvent with explicitly coordinated Et$_2$O ligands. Such explicit inclusion of solvent ligands is necessary in organolithium chemistry not only because of the strong coordination of Li to the ether group but also because of the need to account for the electronic and steric effects of the coordinated solvent, which is known to profoundly affect some reactions.[38,39]

Reaction and activation energies were calculated using density functional theory (DFT), specifically the Minnesota functional[40] M062X, with the 6-31++G(d,p) basis set. The inclusion of both polarization and diffuse functions on hydrogen atoms is expected to provide a better description of the hydrogen transfer reactions (Scheme 4). This basis set was retained for all calculations for consistency. Integrals were evaluated with a pruned numerical grid of 99 radial shells and 770 angular points in each shell (grid=99770), which is denser than the "ultrafine grid" option of Gaussian 09. Single-point energy calculations were also performed at the MP2 level of theory with the same basis set, which permitted the evaluation of free energies of each species in the MP2//DFT two-step model chemistry. Intrinsic reaction coordinate (IRC) calculations[41,42] were performed using M06-2X from each transition state to confirm that they connected to the correct reactants and products and to clearly understand the reaction mechanism.

The M06-2X functional and the two-step model chemistry employed here have been benchmarked against the coupled cluster method with explicit single and double excitations and perturbative triple excitation corrections, i.e., CCSD(T), in the context of organolithium compounds and represent excellent compromises between accuracy and computational efficiency, and the two-step model chemistry MP2//DFT based on the M06-2X functional outperforms other combinations of MP2 and DFT in terms of reproducing CCSD(T) results.[39,43]

■ RESULTS AND DISCUSSION

The epoxides whose reactions are studied in this paper are shown in Scheme 5. Molecules **1−4** have been found to exclusively yield the allyl alcohol product,[1,3] and experimental evidence points to β-elimination as the most likely mechanism. Molecules **5−9** yield a mixture of allyl alcohols and ketones,[3,10] while **7−9** also produce dienes.[3]

We begin by examining the oxirane ring-opening reaction (Scheme 2) subsequent to α-lithiation of **1−4**. The M06-2X/6-31++G(d,p) structures of α-lithiated **1**, the corresponding transition state, and vinyl alcohol product are shown in Figure 1. Structures of all molecules studied are given in the
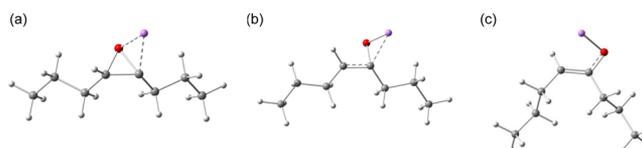
Figure 1. M06-2X/6-31++G(d,p) structures of the ring-opening reaction of the α-lithiated oxirane formed from **1** (Scheme 2): (a) the α-lithiated reactant; (b) the ring-opening transition state; (c) the resulting vinyl alcohol product.

Supporting Information along with the optimized Cartesian coordinates. The free energies of activation and reaction for all three species are given in Table 1.

Table 1. Free Energies of Activation, $\Delta G^{\ddagger}$, and Reaction, $\Delta_r G°$, at 298.15 K (in kcal/mol) for the Ring-Opening Reaction of α-Lithiated Oxiranes Leading to Vinyl Alcohols (Scheme 2)

	M06-2X		MP2//M06-2X	
α-lithio-oxirane formed from	$\Delta G^{\ddagger}$	$\Delta_r G°$	$\Delta G^{\ddagger}$	$\Delta_r G°$
1	26.7	−50.7	23.7	−51.8
2	30.5	−48.2	27.5	−47.8
3	25.3	−44.8	22.9	−45.4
4	26.9	−46.0	24.2	−47.2
1·2Et$_2$O	30.4	−53.6	27.4	−53.6
2·2Et$_2$O	34.4	−53.7	32.3	−52.2
3·2Et$_2$O	25.6	−47.9	23.1	−47.8
4·2Et$_2$O	30.4	−51.7	28.0	−53.1

In spite of the structural differences among molecules **1−4**, the reaction barriers are fairly similar in magnitude. The average free energy barrier $\langle \Delta G^{\ddagger} \rangle$ and the associated standard deviation of σ for the gas-phase reactions of **1−4** are $\langle \Delta G^{\ddagger} \rangle \pm \sigma = 24.6 \pm 2.0$ kcal/mol, while the Et$_2$O-solvated cases give 27.7 ± 3.8 kcal/mol, at the MP2//M06-2X level of theory. We noted above that molecules **1−4** are experimentally found to give only the allyl alcohol product, and the most plausible mechanism is β-elimination. Thus, the results given in Table 1 suggest that the barrier height for β-elimination in these cases must be considerably lower than the $\Delta G^{\ddagger}$ value for epoxide ring opening.

We now examine the epoxide ring-opening reaction of **5**. Figure 2 shows the reactant, transition state, and vinyl alcohol product structures along the reaction coordinate (IRC) at the M06-2X/6-31++G(d,p) level of theory for the α-lithiated epoxide ring opening to yield the lithiated vinyl alcohol. The reaction of apopinene oxide is examined next. Figure 3 shows structures analogous to those shown in Figure 2: namely, the
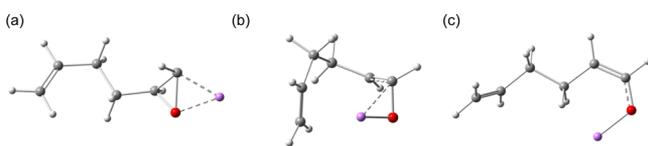
Figure 2. Three structures along the intrinsic reaction path for the ring-opening reaction of the α-lithiated oxirane formed from **5** (Scheme 2): (a) the α-lithiated reactant; (b) the ring-opening transition state; (c) the resulting vinyl alcohol product.
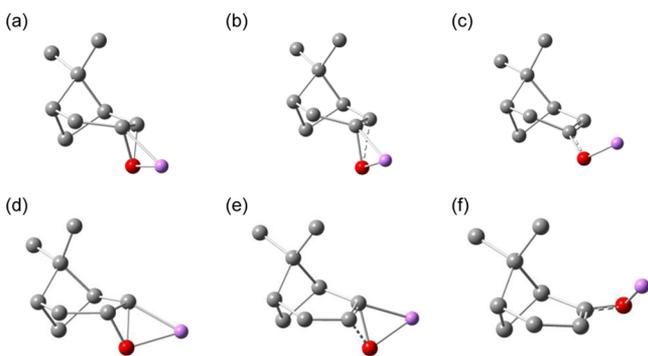
Figure 3. Structures along the intrinsic reaction paths of the two α-lithiated apopinene oxides **6a,b**. Hydrogens are not shown for clarity. Panels a–c are respectivel, the reactant, the ring-opening transition state, and the vinyl alcohol product for **6a**, while panels d–f show analogous structures for **6b**.

reactants, transition state, and products of the α-lithiated oxirane. In this case there are two nonequivalent possibilities, which we identify as **6a,b** in Figure 3.

The energetics of the epoxide ring-opening reaction (Scheme 2) for **5** and **6** as well as the cyclic oxiranes **7–9** are summarized in Table 2. On comparison of Figure 1 with

Table 2. Free Energies of Activation, $\Delta G^{\ddagger}$, and Reaction, $\Delta_r G°$, at 298.15 K (in kcal/mol) for the Ring-Opening Reaction of α-Lithiated Oxiranes Leading to Vinyl Alcohols (Scheme 2) for 5–9

α-lithio-oxirane formed from	M06-2X		MP2//M06-2X	
	$\Delta G^{\ddagger}$	$\Delta_r G°$	$\Delta G^{\ddagger}$	$\Delta_r G°$
5	24.0	−49.5	20.4	−51.6
6a	26.8	−51.6	23.3	−53.5
6b	26.7	−52.1	23.2	−53.5
7	32.0	−47.4	29.1	−48.3
8	26.9	−53.2	23.6	−54.5
9	24.5	−53.8	20.7	−55.3
5·2Et$_2$O	33.3	−52.3	27.8	−55.2
6a·2Et$_2$O	29.4	−53.4	25.7	−56.0
7·2Et$_2$O	34.1	−49.8	30.7	−50.7
8·2Et$_2$O	27.7	−54.7	23.7	−55.4
9·2Et$_2$O	26.1	−52.8	21.7	−53.3

Figures 2 and 3, it is clear that the transition states are very similar in all cases. Consistent with the observation made earlier in connection to Table 1, the reaction barriers are again similar in magnitude in spite of the structural differences of the molecules **5–9**. In this case, at the MP2//M06-2X level of theory, $\langle \Delta G^{\ddagger} \rangle \pm \sigma = 23.4 \pm 3.1$ and 25.9 ± 3.5 kcal/mol, respectively, for gas-phase and Et$_2$O-solvated reactants. Combining the ring-opening barriers from Tables 1 and 2,

we get $[\langle \Delta G^{\ddagger} \rangle \pm \sigma]_{\text{MP2//M06-2X}} = 23.9 \pm 2.7$ and 26.7 ± 3.5 kcal/mol, respectively, for gas-phase and Et$_2$O-solvated reactants. This suggests that the free energy barriers for α-lithiated epoxide ring opening may generally be about 25 kcal/mol. We conjectured earlier that the reactions in Table 1 exclusively yielded the allyl alcohol product, because the reaction barrier for the β-elimination pathway was significantly lower than that for epoxide ring opening. By the same argument, we conclude that the mixture of products observed in the cases of **5–9**, due to α-lithiation as well as β-elimination, suggests that the free energy barriers for β-elimination in these cases are of comparable magnitude to those for ring opening after α-lithiation, a stark difference from the case of **1–4**.

As noted in the Introduction, the formation of dienes in the base-promoted reactions of epoxides has been characterized as unexpected. Crandall and Chang note that "Resubjecting 2-cycloheptenol and its bicyclic isomer [a carbenoid insertion product] to the reaction conditions established that the former was converted into cycloheptadiene."[3] The most plausible mechanism for this appears to be through the elimination of LiOH from the lithiated allyl alcohols, as shown in Scheme 3. Lithiation of the alcohol group of the allyl alcohol appears to be necessary to stabilize the leaving group because (a) the ether ligands strongly coordinate to the Li atom, creating a tight primary solvation sphere, and (b) the other alternative—elimination of H$_2$O from the unlithiated allyl alcohol in ether medium—is even less likely.

Among the nine molecules in Scheme 5, diene formation is reported only for **7–9**. The IRC for LiOH elimination from cyclopentene-3-ol, the allyl alcohol formed from cyclopentene oxide (**7**), is shown in Figure 4. Following the IRC from the transition state B toward products results in the intermediate structure C, in which the second double bond has not yet formed. Optimizing structure C results in the stationary state D, which is connected to the second transition state E and ultimately to the diene product F. The structures corresponding to the labels A–F in Figure 4 are shown in parts a–f of Figure 4. In contrast to this two-step mechanism, the molecules **8** and **9** appear to undergo a single-step reaction to yield the diene. The IRC for the reaction of cyclohexen-3-ol (**8**) is shown in Figure 5, and the structures corresponding to the labels A–C are shown in parts a–c of Figure 5. The free energy barriers relative to the lithiated allyl alcohols in the gas phase and in diethyl ether are given in Table 3. Once again, the free energy barriers are quite similar in magnitude, with $[\langle \Delta G^{\ddagger} \rangle \pm \sigma]_{\text{MP2//M06-2X}} = 50.2 \pm 2.8$ and 52.7 ± 4.1 kcal/mol for gas-phase and Et$_2$O-solvated reactants.

As noted in the Introduction (Scheme 4), it is possible that a post-β-elimination 1,3-hydrogen transfer in the allyl alcohol as shown in Scheme 4 could lead to the vinyl alcohol. We now examine this possibility using molecules **5** and **6** as candidates. The reactions considered are shown in Scheme 6, and the associated free energies of activation are given in Table 4.

In each case, the activation barrier is lower when Y = Li as opposed to that when Y = H. However, these are significant energy barriers to overcome, even under the multiday reflux conditions for these reactions. Given the relatively small variation in reaction barriers in Tables 1–3, it seems reasonable to conclude that, in general, 1,3-hydrogen transfer in lithiated allyl alcohols is less favorable than the elimination of LiOH to give the diene, while 1,3-hydrogen transfer is likely to be an extremely minor source of vinyl alcohols and thus ketones in the case of nonlithiated allyl alcohols.
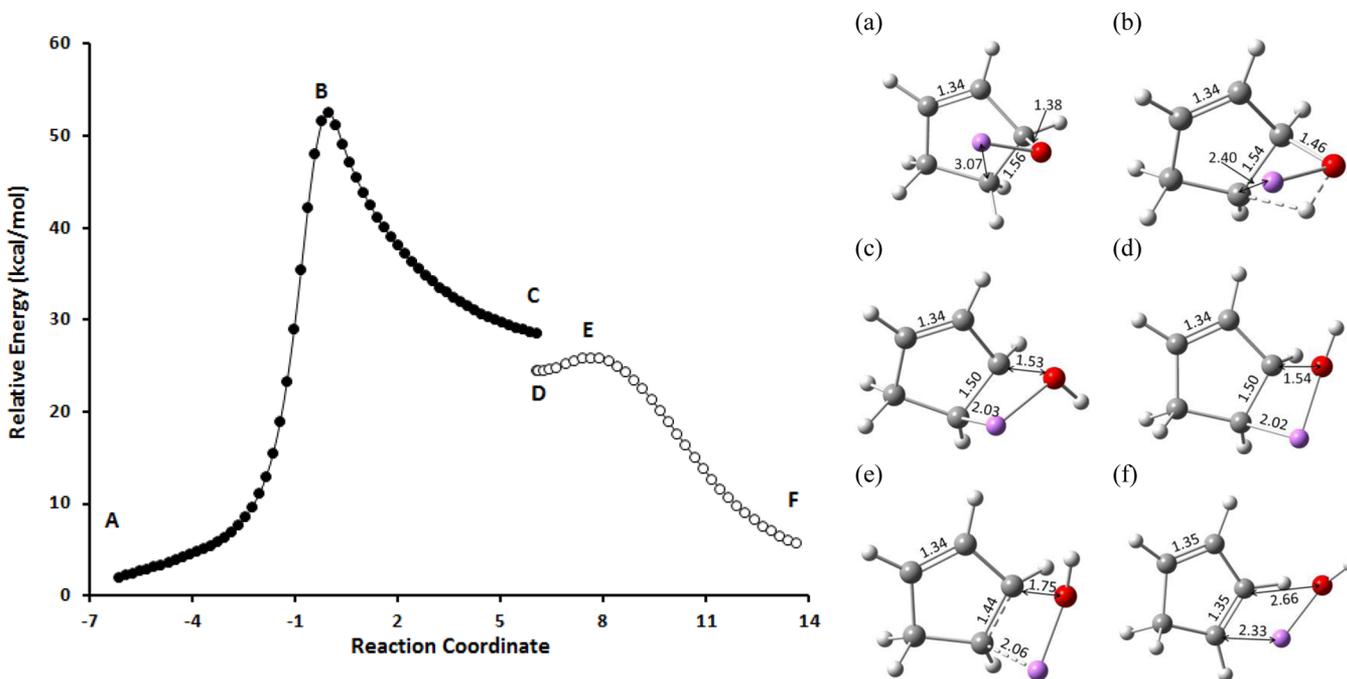
Figure 4. Intrinsic reaction coordinate in $(amu)^{1/2}$ bohr for LiOH elimination from lithiated cyclopenten-3-ol in the gas phase. The structures corresponding to the labels A−F along the IRC are shown in panels a−f.
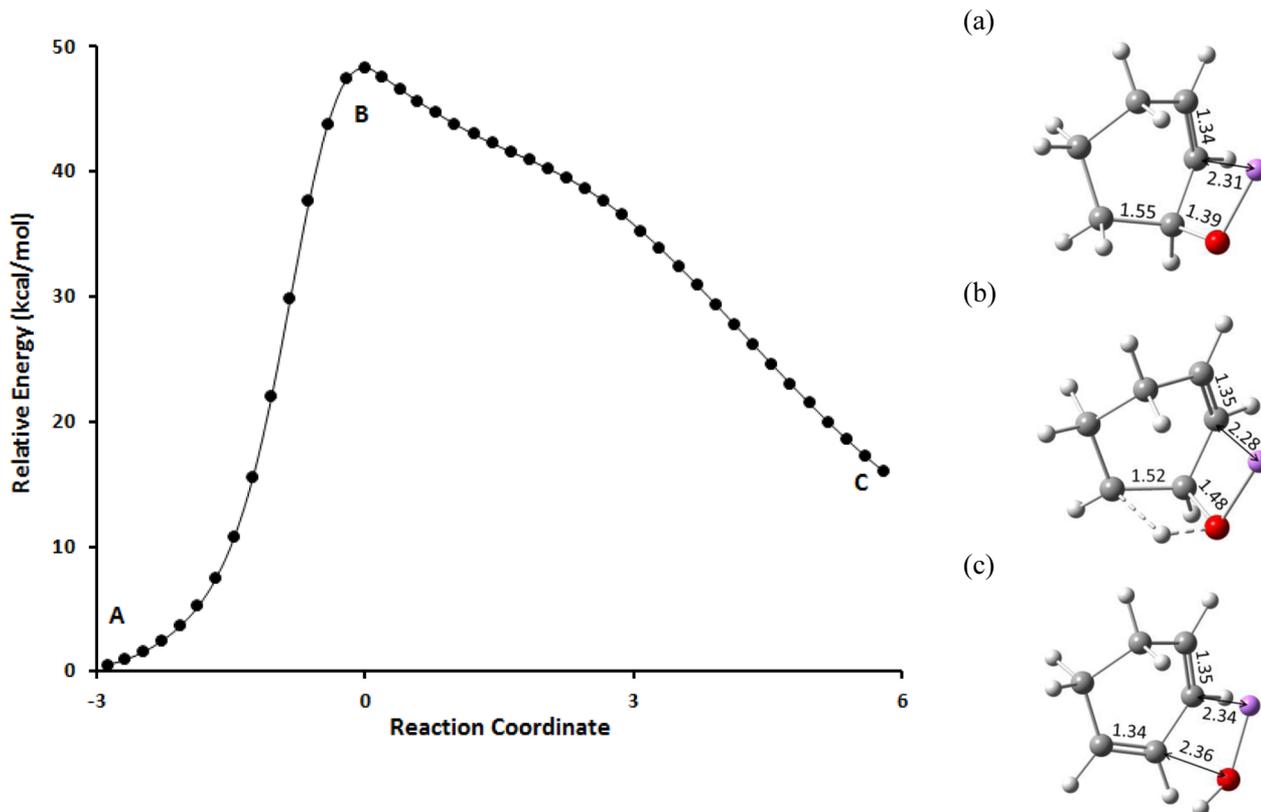
Figure 5. Intrinsic reaction coordinate in $(amu)^{1/2}$ bohr for LiOH elimination from lithiated cyclohexen-3-ol in the gas phase. The structures corresponding to the labels A−C along the IRC are shown in panels a−c.

We end this section with a recap of the results discussed so far and the main inferences drawn from them. Two non-carbenoid pathways are available to oxiranes in the presence of organolithium bases such as lithium dialkylamides: namely, β-elimination and α-lithiation. The β-elimination is clearly the most likely pathway to allyl alcohols. On the basis of the observation that the exclusive product is the allyl alcohol in the case of **1−4** in the presence of lithium dialkylamides and the calculated barriers for ring opening in the α-lithiated oxiranes (Table 1), we conclude that the free energy of activation for β-

Table 3. Free Energies of Activation, $\Delta G^{\ddagger}$, at 298.15 K (in kcal/mol) for the Diene Formation Reaction of Lithiated Allyl Alcohols 7−9 (Scheme 3)

lithiated allyl alcohol formed from	M06-2X	MP2//M06-2X
7	49.1	50.4
8	44.3	52.9
9	46.3	47.4
7·2Et$_2$O	51.1	48.8
8·2Et$_2$O	55.6	52.5
9·2Et$_2$O	59.2	56.9

Table 4. Free Energies of Activation, $\Delta G^{\ddagger}$, and Reaction, $\Delta_r G°$, at 298.15 K (in kcal/mol) for the 1,3-Hydrogen Transfer Reaction of Allyl Alcohols Formed from 5 and 6 Leading to Vinyl Alcohols (Scheme 6)

	M06-2X		MP2//M06-2X	
allyl alcohol formed from	$\Delta G^{\ddagger}$	$\Delta_r G°$	$\Delta G^{\ddagger}$	$\Delta_r G°$
5 (Y = H)	71.1	−1.6	72.2	−0.29
5 (Y = Li)	66.0	−10.7	66.0	−5.2
6 (Y = H)	126.7	−5.1	131.4	−4.1
6 (Y = Li)	102.4	−14.5	106.1	−11.5

elimination in these cases must be significantly lower than that for epoxide ring opening after α-lithiation.

It is well-known that β-elimination is favored when the H−C−C−X atoms can easily exist in an antiperiplanar conformation, where X is the leaving group, in this case the oxiranyl oxygen. If an *anti* periplanar arrangement is not possible or not energetically favorable, a *syn* periplanar arrangement can also undergo β-elimination and is sometimes the preferred pathway.[9] Those geometries provide maximum overlap of the sp^3 orbitals as they are converted to p orbitals of the forming π bond. Thus, in some strained-ring systems, β-elimination may be disfavored. The experimental and computational study of Morgan and Gronert has examined some of these issues in the context of cyclic oxiranes.[22] From Scheme 5, it is clear that molecules 1−4 can easily achieve the geometry most favorable for β-elimination by rotations of the bond between the α- and β-carbons, making this pathway overwhelmingly favorable.

Oxiranes 5−9 yield a mixture of allyl alcohols, ketones, and dienes in addition to bicyclic alcohols resulting from carbenoid insertion pathways. The most likely sources of ketones are vinyl alcohols generated by epoxide ring opening subsequent to α-lithiation (Scheme 2). This suggests that in the cases of 5−9, in sharp contrast to 1−4, the β-elimination reaction has high enough activation barriers to make the α-lithiation pathway competitive. In the case of 5, it has been reported that 2-cyclopentenol and cyclopentanone are formed in a 7:2 ratio,[10] while for 9, "cycloheptadiene, cycloheptanone, 2-cycloheptenol, and *endo,cis*-2-bicyclo[4.1.0]heptanol in roughly equivalent amounts".[3] An alternate source of vinyl alcohols and thus ketones is 1,3-hydrogen transfer in the allyl alcohol subsequent to β-elimination (Scheme 4). Comparing the activation barriers in Table 2 for post-α-lithiation ring opening with those in Table 4 for 1,3-hydrogen transfer, we are led to conclude that the latter pathway is, at best, a minor source of vinyl alcohols. Moreover, if the alcohol group in allyl alcohols 7−9 gets lithiated, it seems reasonable to conclude on the basis of Table 4 that 1,3-hydrogen transfer is less favorable than the formation

of dienes through the elimination of LiOH (Scheme 3 and Table 3). Another pathway to alchols and ketones in lithiated oxiranes is 1,2-hydrogen transfer subsequent to α-lithiation or elimination, which has been studied experimentally and computationally by Morgan et al.[24] and also computationally by us.[11] We have not discussed this pathway in the present paper because available evidence suggests that the reactants in this case are strongly carbenoid in nature.

Further support for competition between α-lithiation and β-elimination is provided by the carbenoid insertion products such as the *endo,cis*-bicyclo[4.1.0]heptan-2-ol reported for 9[3] and *trans*-bicyclo[3.1.0]hexan-2-ol in the case of 5.[10] These can be explained only by invoking α-lithiated epoxides as the parent carbenoids. The intramolecular C=C double-bond insertion of the carbenoids generated from 5 was studied in ref 11 using a variety of DFT functionals as well as two-step model chemistries, all of which yielded activation barriers that are less than half of the barriers for Scheme 2 reported in Table 2. The bicyclic alcohol product from 9, namely *endo,cis*-bicyclo-[4.1.0]heptan-2-ol, can be explained by invoking intramolecular C−H single-bond insertion by the α-lithiated carbenoid generated from 9. Such reactions are well-known in the chemistry of lithiated oxirane carbenoids.[12,34−36]

■ SUMMARY AND CONCLUSION

The first computational study of the noncarbenoid rearrangement reactions of oxiranes initiated by lithium dialkylamides is presented. The equilibrium geometries and transition states for the species involved in these reactions as well as the associated free energy changes and reaction barriers are calculated using the M06-2X hybrid density functional and supplemented by second-order Moller−Plesset perturbation theory energies computed at the DFT-optimized geometries. These computational strategies have been validated against high-level wave function methods specifically in the context of organolithium compounds in previous work. A split-valence double-ζ quality basis set with polarization and diffuse functions on all atoms was used. The presence of both polarization and diffuse

Scheme 6
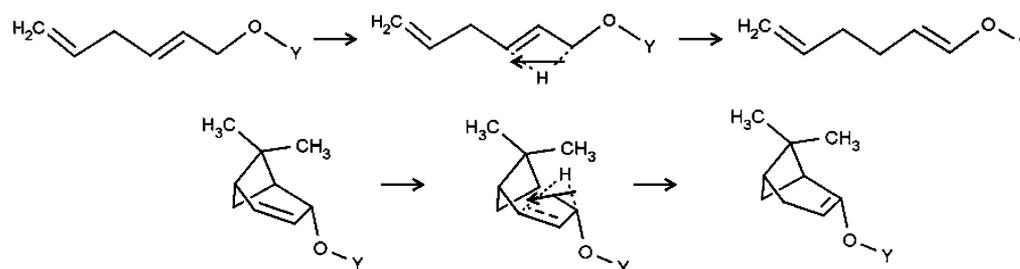
functions on hydrogen atoms is expected to provide a better description of the hydrogen transfer reactions (Schemes 4 and 6). This basis set was retained for all calculations for consistency.

Early experimental studies of Cope et al. on organolithium bases reacting with deuterated *cis-* and *trans-*4-octene oxides (**1** and **2**, respectively) suggested that β-elimination leading to allyl alcohols was the exclusive mechanism,[1] but later studies on other species have concluded that the dominant non-carbenoid mechanism was α-lithiation followed by opening of the epoxide ring, ultimately leading to ketones.[2] In some reactions, the diene has also been observed and has been described as an "unexpected" product.[3]

The computational studies reported in this work provide indirect evidence that both mechanisms are operational. In particular, our work shows that the allyl alcohols from β-elimination are unlikely to undergo 1,3-hydrogen transfer to the vinyl alcohols and thus to the ketones, suggesting that the ketones are formed through keto−enol isomerization of the vinyl alcohols formed by the opening of the oxirane ring after α-substitution. Elimination of LiOH from the lithiated allyl alcohol (product of β-elimination) is found to result in the diene product. These findings are consistent with the product distributions observed in some of the reactions of lithiated oxiranes by Crandall and Chang in 1967[3] and lend additional support to the current understanding that oxiranes in the presence of lithiated bases must undergo both β-elimination and α-lithiation, except in a few special cases where β-elimination appears to be strongly or exclusively favored. In all of these special cases **1−4**, it is noteworthy that the reactant structure readily yields the periplanar H−C−C−O geometry which makes β-elimination favorable, while structural and steric factors in the cases **5−9** allow the other pathways to become competitive.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Tables and figures giving converged M06-2X/6-31++G(d,p) energies and structures of all molecules studied. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail for B.R.R.: ramu@latech.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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