The Role of Carbenes and Ylides in the Thermal Decomposition of Δ³-1,3,4-Oxadiazolines

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The mechanism proposed by Kassam and Warkentin for the thermal decomposition of 2-(3-butyn-1-yloxy)-2-methoxy-5,5-dimethyl-Δ³-1,3,4-oxadiazoline has been examined using semiempirical PM3 methods supported by low-level *ab initio* calculations. The results may be summarized as follows: The computational chemistry of carbonyl ylides is dependent on their chemical structure as well as their geometry at the time of initial formation. Dialkoxycarbonyl ylides tend to dissociate reversibly to carbenes over a wide range of C–O torsion angles. Collapse to epoxides occurs when the ylide assumes a conformation resembling the epoxide product. Depending on structure, the reactions of carbenes with ketones to form epoxides may be chelotropic reactions or may proceed through a carbonyl ylide intermediate.

Recently, a most remarkable set of observations was recorded in this journal by Kassam and Warkentin,[1] who reported on the thermal decomposition of 2-(3-butyn-1-yloxy)-2-methoxy-5,5-dimethyl-Δ³-1,3,4-oxadiazoline (Scheme 1, **5**). Scheme 1 essentially reproduces their proposed reaction sequence with compounds numbered as per their scheme. This cascade of reactions was accomplished in one pot, giving the complex tricyclic molecule **17**. The mechanistic steps envisioned in this scheme were supported in part by new experimental results and earlier reports from the literature.[2]

The experimental evidence for carbonyl ylides has recently been summarized,[3] and theoretical calculations on their structure and stabilities have been published previously.[4] However, there are still a number of questions raised in Scheme 1 which merit a more detailed examination, including the following: (a) Does the formation of the dialkoxycarbene **7** really require the carbonyl ylide **6** as an intermediate or even a transition state? (b) Is the highly strained **9** actually on the reaction path to carbene **10**? (c) Must **10** form the carbonyl ylide **11** in forming **12**, or might the reaction be more properly described as a cycloaddition to acetone? (d) Is it possible that **12** might pass directly to **14** without the intermediacy of zwitterion **13**? It is not suggested that the mechanism shown in Scheme 1 is wrong in gross outline but rather that the mechanistic details of some of the steps may be refined?

Theoretical Methods. Because of computational limitations, the bulk of the calculations were carried out with the PM3 Hamiltonian of Stewart[5] using MOPAC93.[6] While reaction paths were followed utilizing standard Hartree–Fock methods, energies were corrected by follow up calculations, including a 3 × 3 configuration interaction (CI). Transition structures were approximated by saddle calculations[7] and refined by the "eigenvector following" method of Baker.[8] All transition structures

Scheme 1
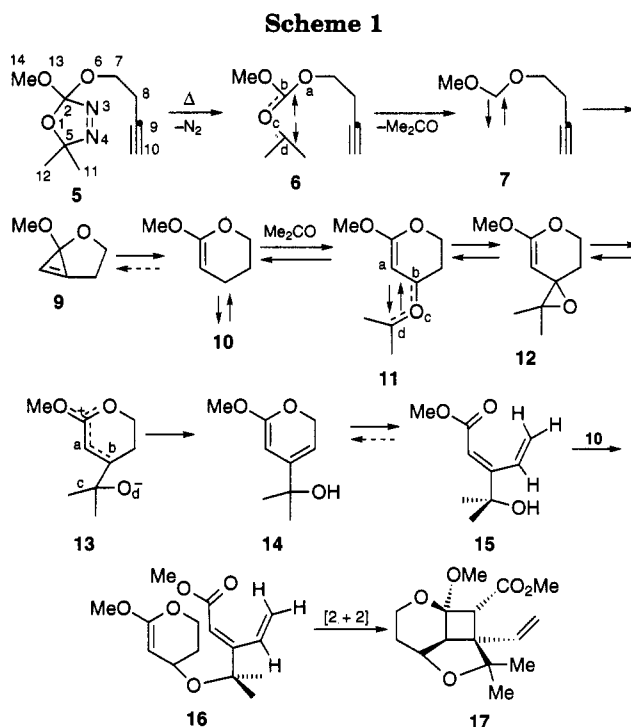
mentioned subsequently meet the criterion that upon a force calculation each gave one negative root to the force matrix as well as one negative frequency. Supporting *ab initio* calculations were carried out at the 3-21G level using Gaussian92 for Windows.[9] For purposes of comparison, the HOMO and LUMO for dimethylcarbene were calculated at the 4-31G level. All of these calculations assume the molecules to be in a vacuum. The actual experiments were carried out in benzene. While the dielelctric constant of benzene is very small, the possible complexing action of the π-system cannot be adequately modeled at this point in time.

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Table 1. Calculated Energies for 2-Oxatrimethylene and Ethylene Oxide by Various Methods (PM3 in kcal/mol and *ab Initio* Values in Hartrees)

	PM3	STO-3G	HF/6-31G*	MP2/6-31G*
CH_2-O-CH_2	22.66	−150.786229	−150.748592	−153.222790
ethylene oxide	−8.13	−150.928504	−152.865240	−153.303584
difference (kcal/mol)	30.79	89.28	73.20	50.70
∠C−O−C, deg	122.9	129.3		128.9
Bond C−O, Å	1.292	1.298		1.323
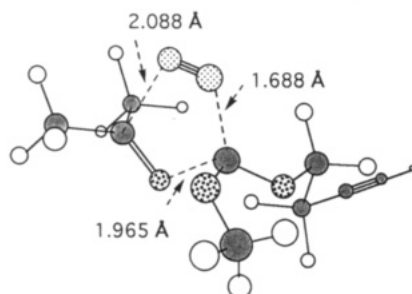
Figure 1. The transition structure for the thermal decomposition of 2-(3-butyn-1-yloxy)-2-methoxy-5,5-dimethyl-Δ³-1,3,4-oxadiazoline.

Two methods of assessing the validity of PM3 calculations for the purposes at hand were employed. The heat of formation of the carbonyl ylide formed by diazomethane in acetone has been measured by photoacoustic calorimetry and reported as 4.5 ± 9.9 kcal/mol.[10] The PM3 value without CI is 3.53 kcal/mol, while with CI the value is 1.43 kcal/mol. Either may be considered as in reasonable agreement with the experimental value. A second check was given by comparing values for the 2-oxatrimethylene ylide and ethylene oxide calculated by a variety of methods as given in Table 1. As is evident, there is a marked decrease in the energy difference between the carbonyl ylide and ethylene oxide as the computational level is increased. On this basis, the PM3 result would seem to offer some advantages over *ab initio* results at lower levels. Whether the difference in C−O−C angle is of great significance is debatable. The C−O bond lengths are in satisfactory agreement.

Results and Discussion

The Conversion of Compound 5 to 7. The thermal decomposition of **5** certainly produces dinitrogen. The question to be answered regards the role of **6** in the decomposition process. A series of calculations were carried out in which the carbon−nitrogen bonds were lengthened while following the energy and the change in molecular structure of the starting material. In the C−N region of about 1.7−1.8 Å, the structure undergoes a dissociation to dinitrogen, acetone, and carbene **7**. This structure was optimized as a transition structure, and shown in Figure 1. A force calculation confirmed this as a valid stationary point with one negative root to the force matrix and one imaginary vibrational frequency. The distances are as shown. The carbonyl carbon of the incipient acetone is still partially pyramidal as the oxygen is 22° out of the plane defined by the three carbons (angle measured from either methyl group). The activation enthalpy is 43.21 kcal/mol. The energies for compounds **5** and **7** are given in Table 2.

The stability of proposed intermediate **6** was examined next. The graphics capability of PCMODEL[11] was em-

Table 2. The PM3(CI) Energies (kcal/mol) for Scheme 1 Structures

structure	PM3(CI)	structure	PM3(CI)
5	−47.37	**11**	−93.12
6	−29.08	**12**	−94.82
7	−7.58	**14**	−108.64
9	17.02	**15**	
10	8.41		

ployed to describe the molecule which was then minimized with the MMX force field.[12] The torsion angle *abcd* (Scheme 1) was found to be 165°, and the pertinent C−O−C angle was 127°. When minimized, the PM3 energy for **6** was found to be −29.08 kcal/mol. However, the fragment corresponding to **6** in starting material **5** has a torsion angle of −139° which changes only slightly during the reaction. Minimization of this structure resulted in the decomposition of the carbonyl ylide to **7** and acetone (HF −54.39 kcal/mol). A study in which the angle *abcd* was systematically rotated indicated a region of ±40° about the 165° angle in which all structures minimized to a stable carbonyl ylide **6**. Upon exceeding ±40° of twist, all structures decomposed to acetone and carbene **7** with an energy decrease of 27.5 kcal/mol. Since the comparable angle in **5** (−139°) is well within the decomposition range and does not change appreciably during the decomposition, it follows that **6** is not a true intermediate on the reaction pathway. These PM3 results were subsequently confirmed on **6** by *ab initio* calculations at the 3-21G level.

The importance of carbonyl ylides in two major steps of Scheme 1 made a further investigation of the role of carbene and ylide structure on these and related reactions desirable. Toward this end, dimethoxycarbene, dimethylcarbene, and phenylcarbene have each been allowed to react with acetone via a series of saddle calculations. The former was chosen as an obvious model to **6** above. Phenylcarbene is a computationally simpler analog of fluorenylidene which has been shown to add to acetone to form the corresponding dimethylethylene oxide through the observed intermediacy of a carbonyl ylide.[13] Dimethylcarbene was selected as an intermediate case where resonance interactions with a substituent should be slight or nil. For each example, the carbene was placed approximately 2.8−3.0 Å above the midpoint of the C−O bond perpendicular to the acetone molecular plane. The energies of the starting duo, the transition structure and the epoxide product are given in Table 3. Ball and stick representations of the transition structures are given in Figure 2 as are the activation enthalpies. Pertinent bond lengths, bond angles and charges are given in Table 4.

Surprisingly, the three carbenes gave unique transition structures. A computer search of the literature suggested

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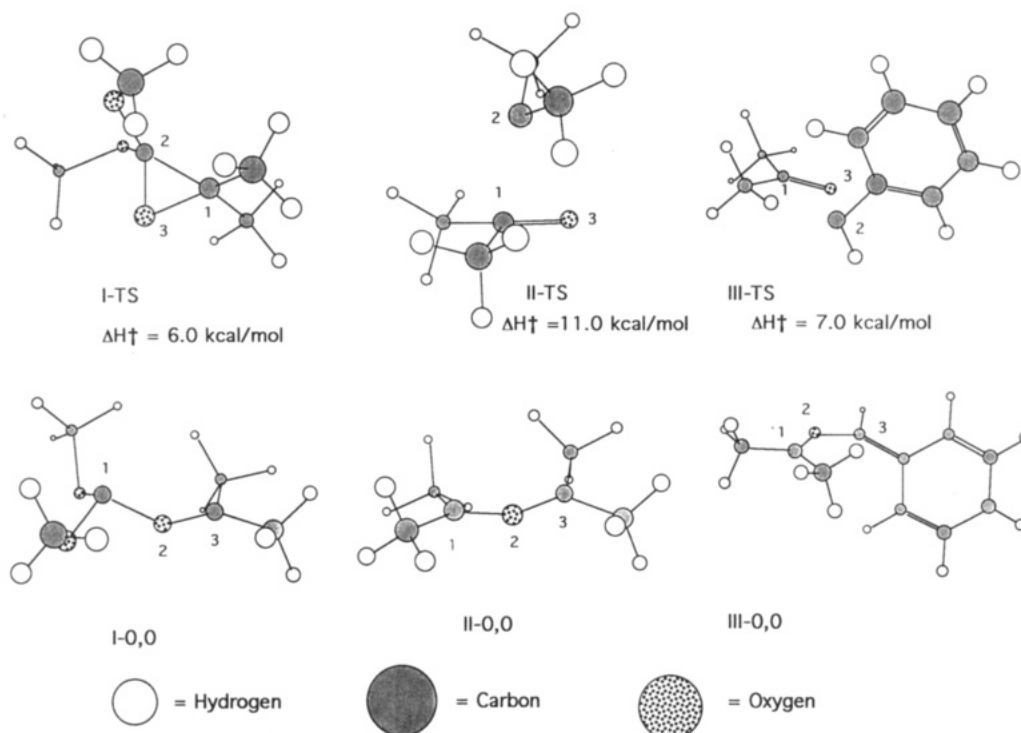
Figure 2. Transition structures (ball and stick representations) for the addition of dimethoxycarbene (**I-TS**), dimethylcarbene (**II-TS**), and phenylcarbene (**III-TS**) to acetone as well as the corresponding carbonyl ylides in their 0°,0° conformations. The designation 0°,0° implies that the substituents attached to the C—O—C backbone are in the plane defined by these atoms. This is not quite true for the dimethoxy species as the carbon with the methoxyls is obviously pyramidal.

Table 3. Enthalpies (kcal/mol) for Starting Systems, Epoxide Products, and Transition Structures shown in Figure 2

	$(CH_3O)_2C$	$(CH_3)_2C$	PhCH
carbene and acetone	−110.05	4.40	59.99
dimethyl epoxide	−104.85	−40.50	0.32
transition structure	−104.05	15.42	67.04[a]
			31.60
carbonyl ylides (0°,0°)	−93.74	−27.13	21.43

[a] These correspond to the first and second transition structures.

Table 4. Bond Lengths (Å), Bond Angles (deg) and Charges for Transition Structures and Carbonyl Ylides in Figure 2

	I-TS	II-TS	III-TS	I-0°,0°	II-0°,0°	III-0°,0°
1−2	1.506	1.983		1.400	1.308	1.306
1−3	1.460	2.215				
2−3	1.422	1.258	2.13	1.271	1.308	1.401
∠132			105.8			
∠123				129.9	128.1	129.1
q_1				−0.009[a]	−0.015	0.040
q_2				−0.300	0.200	−0.300
q_3				−0.249	0.166	−0.247

[a] The charges on the two methoxy oxygens were −0.275.

that the epoxide formed by dimethoxycarbene and acetone is not a known compound. Unlike the other two cases, this reaction is endothermic by a small amount; the transition structure resembles the epoxide product with the C—O bonds stretched by 0.020 Å. The activation enthalpy for the dissociation of the epoxide is less than 1 kcal/mol, a result consistent with the literature search. As with compound **6** above, the dimethoxycarbonyl ylide (Figure 2, **I-0°,0°**) displayed spontaneous dissociation over a wide range of torsion angles about the C—O bonds. Only conformers close to the 90°,90° conformation collapsed to the epoxide.

The addition of dimethylcarbene to acetone is an overall exothermic process by 36 kcal/mol. In a one-step chelotropic addition of the carbene, one would expect the transition structure to resemble the starting material (Hammond's postulate) which corresponds to the observation in Figure 2 (**II-TS**). The carbene has moved slightly closer to the carbon end of the carbonyl dipole, suggesting that it may be exhibiting nucleophilic character. Rondan, Houk, and Moss[14] have characterized the reactivity of 12 carbenes using an empirically defined parameter (m_{CXY}) as well as the HOMO and LUMO values determined for each at the 4-31G level. Dimethylcarbene was not included on their list. The HOMO and LUMO 4-31G values for dimethylcarbene are −8.68 and 3.20 eV, respectively. This result is consistent with the described transition structure. The possible intermediacy of the carbonyl ylide cannot be excluded on the basis of energy alone, since the formation of the ylide from this transition structure is exothermic as is the formation of the epoxide. However, a dynamic reaction coordinate calculation[15] indicated that **II-TS** is converted smoothly into the epoxide without the intervention of the carbonyl ylide as an intermediate. Examination of the molecular orbitals for the transition structures of both the dimethoxy- and dimethylcarbene additions showed a strong bonding MO covering the three atomic centers of the transition structures. A rendition of the MO for the latter case is given in Figure 3. The transition structure for the dimethoxycarbene case is just farther along the reaction coordinate.

The addition of phenylcarbene to acetone stands in marked contrast to the cases above. The carbene moves

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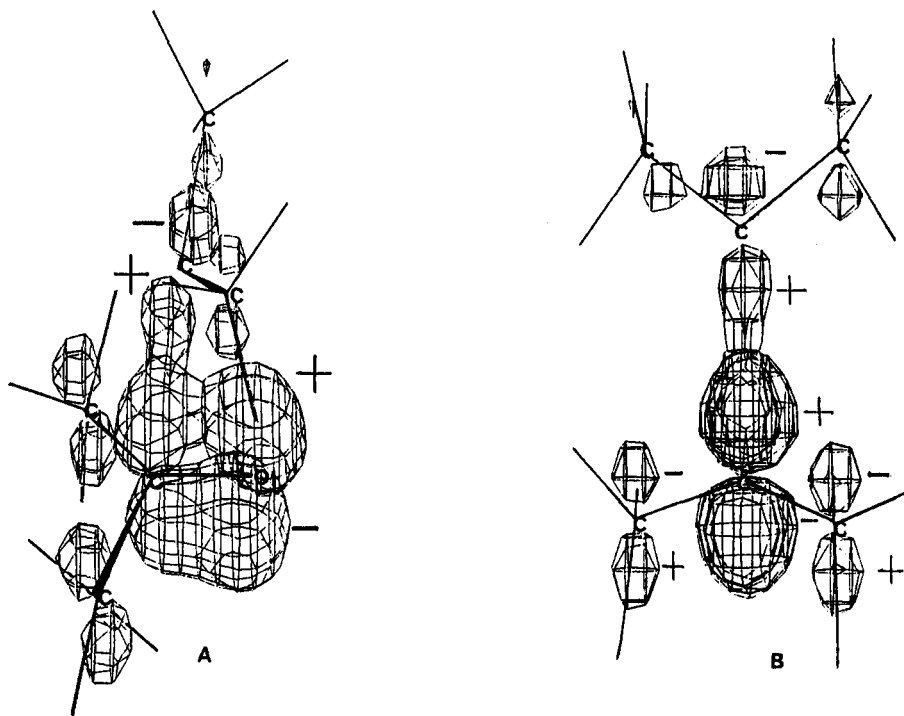
Figure 3. Orbdraw[11] rendering of the binding molecular orbital for the addition of dimethylcarbene to acetone. The threshold has been set high and the resolution low to facilitate the viewing: (A) view from slightly above the plane of the acetone with designations of orbital signs. (B) View from the carbon down the C=O axis.
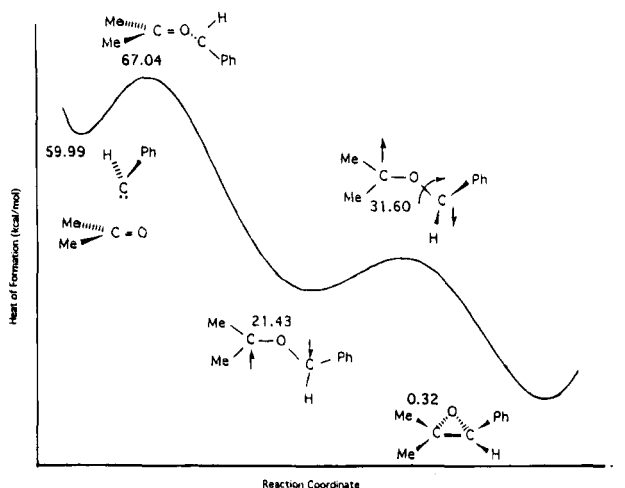

Figure 4. Activation enthalpy plot for the addition of phenylcarbene to acetone.

from above the plane of the acetone carbonyl group to a position in the plane. A bonding MO involving one of the oxygen lone pairs is formed. This transition structure was clearly a precursor to carbonyl ylide formation. Indeed, a second transition structure leading from the carbonyl ylide (III-0°,0°) to the product epoxide was found. A reaction coordinate plot for the phenylcarbene addition is given in Figure 4.

The Conversion of Compound 10 to 12. Given the variation in transition structures for the three cases above, the expectations for the addition of compound **7** to acetone were unclear. The reversible addition of carbenes to carbonyl groups is certainly well established.[1,13] However, the vinylcarbene **10** might be expected to enjoy conjugative stabilization and behave like phenylcarbene. Such an expectation would be naive, however, as an examination of the molecular orbitals for

vinylcarbene showed the carbene electrons occupying the HOMO and lying in the molecular plane orthoganol to vinyl π-system.

When **10** was placed 3.8 Å above the carbonyl bond of acetone and minimized, an energy of −49.48 kcal/mol was found; *ca.* 4.5 kcal/mol below the algebraic sum for the isolated parts and indicative of a considerable interaction even at this distance. The transition structure for the reaction is shown in Figure 5A and closely resembles that for the addition of dimethylcarbene. The activation enthalpy is 11.18 kcal/mol, while the overall reaction is exothermic by 42.13 kcal. Thus, the proposed intermediacy of carbonyl ylide **11** (Scheme 1) is seen to be untenable.

The Conversion of 7 to 10. Kassam and Warkentin[1] envision the conversion of carbene **7** to carbene **10** as possibly occurring via the formation of the cyclopropene **9**. They point out that dialkoxycarbenes are generally considered as nucleophiles and that no examples are known of their addition to carbon–carbon triple bonds; the presumption being that ring formation justifies this novel step. The conversion of **7** to **9** is endothermic by 25.6 kcal/mol, while the conversion of **7** to **10** is endothermic by only 16 kcal/mol. The more direct pathway requires that attack by the initial carbene be at the terminal carbon of the triple bond forming the product in one step.

Both pathways have now been investigated. The two energy plots are given in Figure 6, while the transition structures are given in Figure 5. The activation enthalpy for the one-step process is 17.6 kcal/mol. As expected, the transition structure resembles a slightly distorted version of product **10** (the RMS bond length difference between the TS and product is 1.104 Å). The two-stage process first requires an activation enthalpy of 27 kcal/mol in forming **9** and an additional 9.2 kcal/mol in proceeding to **10**. The TS for forming **9** is a slightly
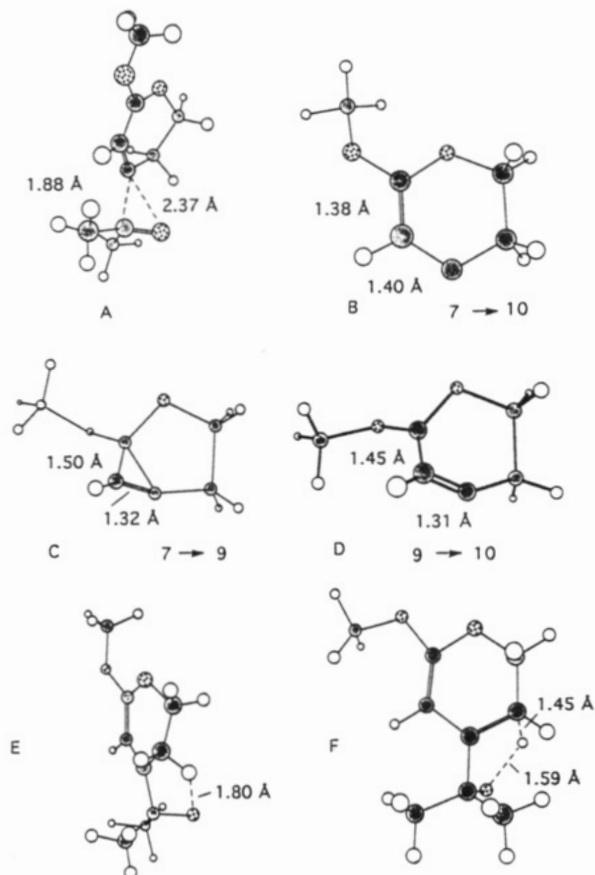
Figure 5. Ball and stick representations for the various transition structures in this study: (A) the addition of **10** to acetone; (B) the direct addition of **7** to form **10**; (C) the conversion of **7** to **9**; (D) the conversion of **9** to **10**; (E) the rearrangement of **12** to **14**; and (F) the diradical rearrangement of **12** to **14**.

distorted version of **9** (RMS difference 0.364 Å). The TS for the formation of **10** is a more highly distorted version of **10** itself (RMS difference 2.240 Å). On the basis of these calculations, the postulation of **9** as an entity of importance on the pathway would seem not to be required.

The Conversion of Compound 12 to 14. The conversion of epoxide **12** to stable compound **14** has been proposed to proceed through the intermediacy of zwitterion **13**. A computational examination of **13**, however, revealed some complex behavior. Minimizations of **13** were highly dependent upon the torsion angle *abcd* (Scheme 1, **13**). The only recognizable minimum structures for **13** itself were found in the region ±(0−40°). The lowest energy found was −43.22 kcal/mol. Beyond ±40° over the range to ±170° the structures minimized to the epoxide **12**.

This result was confirmed by an ab initio calculation at the 3-21G level. Between +170° to −170° the structures disintegrated to ethylene and an irrationally strained epoxide.
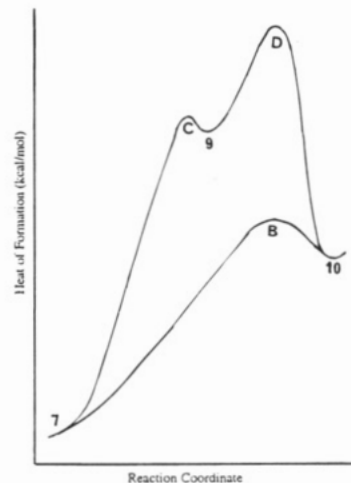

Figure 6. Activation energy plots for two scenarios of **7** forming **10**.

A saddle calculation converting **12** to **14** clarified the matter. A transition structure was found corresponding to an activation enthalpy of 54.4 kcal/mol. This is depicted in Figure 5E. The developing charge on the oxygen is −0.69, which may be compared to a value of −0.80 for the oxygen in *tert*-butoxide ion. The migrating hydrogen bears a charge of 0.24, well above the normal range for a neutral C−H bond. Furthermore, this C−H bond is 0.06 Å longer than its geminal partner. Thus, a structure resembling **13** does appear in the reaction sequence but as a transition structure rather than as an intermediate.

A referee has suggested the interesting possiblity that the opening of the epoxide **12** might yield a diradical analog of **13**. Treatment of **13** as a singlet diradical gave an energy some 12 kcal/mol lower than the zwitterion form. When the transition structure (Figure 5) was subjected to a single point calculation as a singlet diradical the energy was raised by 1.5 kcal/mol. Optimization and a force calculation, however, showed that this diradical was not a transition structure. Subsequently, a new saddle calculation was carried out with the specific intention of identifying any diradical intermediates or transition structures on the path from **12** to **14**. As a result a new transition structure (Figure 5F, HF = −13.12 kcal/mol) was indentified. While (Figure 5) met the criteria for a transition structure, the high activation enthalpy of 79.54 kcal/mol ruled in favor of the path proceeding via structure E.

Conclusions. As stated in the opening paragraph, the mechanism for the decomposition of the Δ^3-1,3,4-oxadiazoline in the work of Kassam and Warkentin is correct in general outline. However, the postulation of carbonyl ylides **6** and **11** as reaction intermediates is unwarranted. Structure **9** is also not found on the reaction pathway. Structure **13** is a transition structure, not an intermediate.