in a recent paper:[15] With use of known heats of formation at 298 K and $(H_{298}^\circ - H_0^\circ)$[17] and the 6-31G(d) frequencies[16] scaled by a factor of 0.89,[17] "experimental" energy changes are estimated to be −112.0 and −113.6 kcal/mol for propane and cyclobutane, respectively. The theoretical values in Table I overestimate the exothermicity of both reactions.

Higher level calculations on these reactions, as well as the analogous silylene insertions and CH_2 and SiH_2 insertions into strained and unstrained C–Si and Si–Si bonds, are currently under way in this laboratory.

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Registry No. Methylene, 2465-56-7; ethane, 74-84-0; cyclopropane, 75-19-4.

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Gas-Phase Hydrolysis of Protonated Oxirane. Ab Initio and Semiempirical Molecular Orbital Calculations

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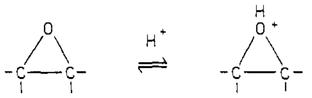
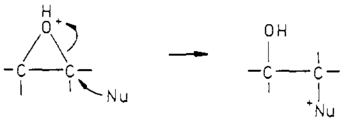
Abstract: MP2/6-31G**//HF/6-31G* ab initio molecular orbital theory predicts the gas-phase unimolecular ring opening of protonated oxirane **2** to lead to protonated acetaldehyde via an activation barrier of 24.6 kcal mol^{-1} with no intervening minima. The gas-phase bimolecular hydrolysis of **2** is predicted to occur via a transition state 9.1 kcal mol^{-1} below the isolated reactants but 4.1 kcal above an intermediate ion–dipole complex. The transition structure is predicted to be "early", but probably less so than for the analogous aqueous phase reactions. Reaction profiles calculated with use of the semiempirical MNDO and smaller basis set ab initio procedures are qualitatively different from those at this level.

Derivatives of the highly reactive three membered heterocycle, oxirane **1**, are intermediates in the metabolic activation of many known or suspected carcinogens. These include the intensively studied polycyclic aromatic hydrocarbons,[1a,2a,3] the aflatoxins,[1b,2b,4] and many vinylic compounds.[5,6] The carcinogenic properties[7] of these epoxides appear to be associated with their ability to alkylate, or aralkylate, nucleic acid base sites.[1-3,8] However, where they have been studied, the kinds and amounts of such adducts formed depend markedly on the structure of the epoxide.[5,9]

1

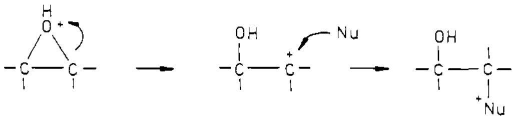


(1)



(2a)

(A2 mechanism)



(2b)

(A1 mechanism)

In neutral aqueous media it is now generally accepted,[10,11] that epoxides undergo initial protonation in a fast reversible step (eq 1) followed by rate determining opening of the conjugate acid. This is usually discussed in terms of two limiting processes.[11] In

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Table I. Calculated Total Energies (au)[a]

molecule[b]	symmetry	optimized geometries		HF/6-31G* geometries	
		HF/3-21G	HF/6-31G*	HF/6-31G**	MP2/6-31G**
2	C_s	-152.32561	-153.17710 (0)	-153.19077	-153.64371
3	C_s	-152.29522 (0)	-153.15306 (1)	-153.16734	-153.59934
4	C_s	-152.36786[c]	-153.22612[c] (0)	-153.24028[c]	-153.68439
5	C_1	*d*	-229.20913 (0)	-229.23533	-229.88629
6	C_1	*d*	-229.20457 (1)	-229.23071	-229.87844
7	C_1	-228.00634	-229.24476 (0)	-229.27085	-229.92140
8	C_1	-227.98068	-229.22779 (0)	-229.25410	-229.90048
9	C_1		-229.22546 (1)	-229.25164	-229.89862

[a] The number of negative eigenvalues of the calculated force constant matrices is given in parentheses. [b] Structures are identified in Figure 1. [c] Data from *Quantum Chemistry Archive*.[35] [d] Not a stationary point at this level.

Table II. Calculated Relative Energies for the Unimolecular Reactions of **2**[a–c]

	ΔE			MP2/6-31G**//B			ΔH
	HF/3-21G//A	HF/6-31G*//B	HF/6-31G**//B	ΔE	ΔH	ΔG	exptl
3	19.1	15.1	14.7	27.8	24.6	23.9	24[d,e]
2	0	0	0	0	0	0	0
4	-26.4	-30.8	-31.1	-25.5	-26.3	-27.4	-26[e]

[a] All energies in kcal mol^{-1}. [b] Geometry: A = HF/3-21G; B = HF/6-31G*. [c] Thermodynamic quantities calculated from scaled HF/6-31G* frequencies. Free energies refer to 1 mol of the ideal gas at 1 atm and 298 K. [d] Reference 48. [e] Reference 40.

Table III. Calculated Relative Energies for the Bimolecular Hydrolysis of **2**[a]

	ΔE			MP2/6-31G**//B			ΔH
	HF/3-21G//A	HF/6-31G*//B	HF/6-31G**//B	ΔE	ΔH	ΔG	exptl
H_2O + **2**	0	0	0	0	0	0	0
5		-13.4	-13.2	-14.6	-13.2	-6.1	
6		-10.5	-10.3	-9.6	-9.1	-0.6	
7	-59.5	-35.7	-35.5	-36.6	-33.6	-23.1	~ -28[b]
8	-43.3	-25.1	-24.9	-23.5	-21.0	-11.8	~ -19[c]
9		-23.6	-23.4	-22.3	-20.3	-9.7	

[a] Table II, footnotes *a–c*. [b] From an estimated value of $\Delta H_f(7) \sim 79$ kcal mol^{-1} (see text) and data in ref 40 and 69. [c] From an estimated value of $\Delta H_f(8) \sim 88$ kcal mol^{-1} (see text) and data in ref 40 and 69.

one, the protonated oxirane undergoes nucleophilic attack with concomitant ring opening in a single kinetic step (eq 2a). In the other, ring opening without nucleophilic assistance to form an intermediate 2-hydroxycarbenium ion is envisioned (eq 2b). In Ingold's terminology[12] these are designated A-2 and A-1, respectively.[13] For simple epoxides, the observed stereospecific trans addition[11,14] and lack of skeletal rearrangements[11,15] argue against a limiting Al mechanism. However, the marked tendencies of unsymmetrically substituted oxiranes to open at the more substituted carbon,[11,16] as well as the significant rate acceleration by electron releasing substituents,[17] have been taken as evidence against a fully synchronous bimolecular process and led Parker and Isaacs[11] to suggest a so-called "border-line" A2 mechanism in which the opening of the oxirane ring significantly preceded bond formation to the incoming nucleophile.

The gas-phase unimolecular ring opening and related processes for protonated oxirane **2** have been studied theoretically by Radom[18] and others[19,20] with use of ab initio molecular orbital theory. Larger systems analogous to those occurring in the metabolism of the polycyclic aromatic hydrocarbons[1a,2a,3] have been studied with use of semiempirical molecular orbital theory.[21] The corresponding reactions with nucleophiles, however, have received far less attention.[22]

In ongoing work in our laboratory we are using molecular orbital calculations in an attempt to understand the physicochemical determinants of the widely differing regioselectivities of biologically significant electrophiles toward nucleic acids.[23-27] As a prelude to such studies for substituted oxiranes, we have investigated the gas-phase attack of water on protonated oxirane using both ab initio and semiempirical MNDO molecular orbital calculations. Related MNDO[28] calculations for other nucleophiles are presented elsewhere.[27]

Methods and Results

Ab Initio Calculations. Ab initio molecular orbital calculations were carried out with the GAUSSIAN 77[29] and GAUSSIAN 82[30] pro-

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(13) For a more recent formulation in terms of ion-paired species, see: Lamaty, G.; Meloq, R.; Selve, C.; Sivade, A.; Wylde, J. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1119–1124.

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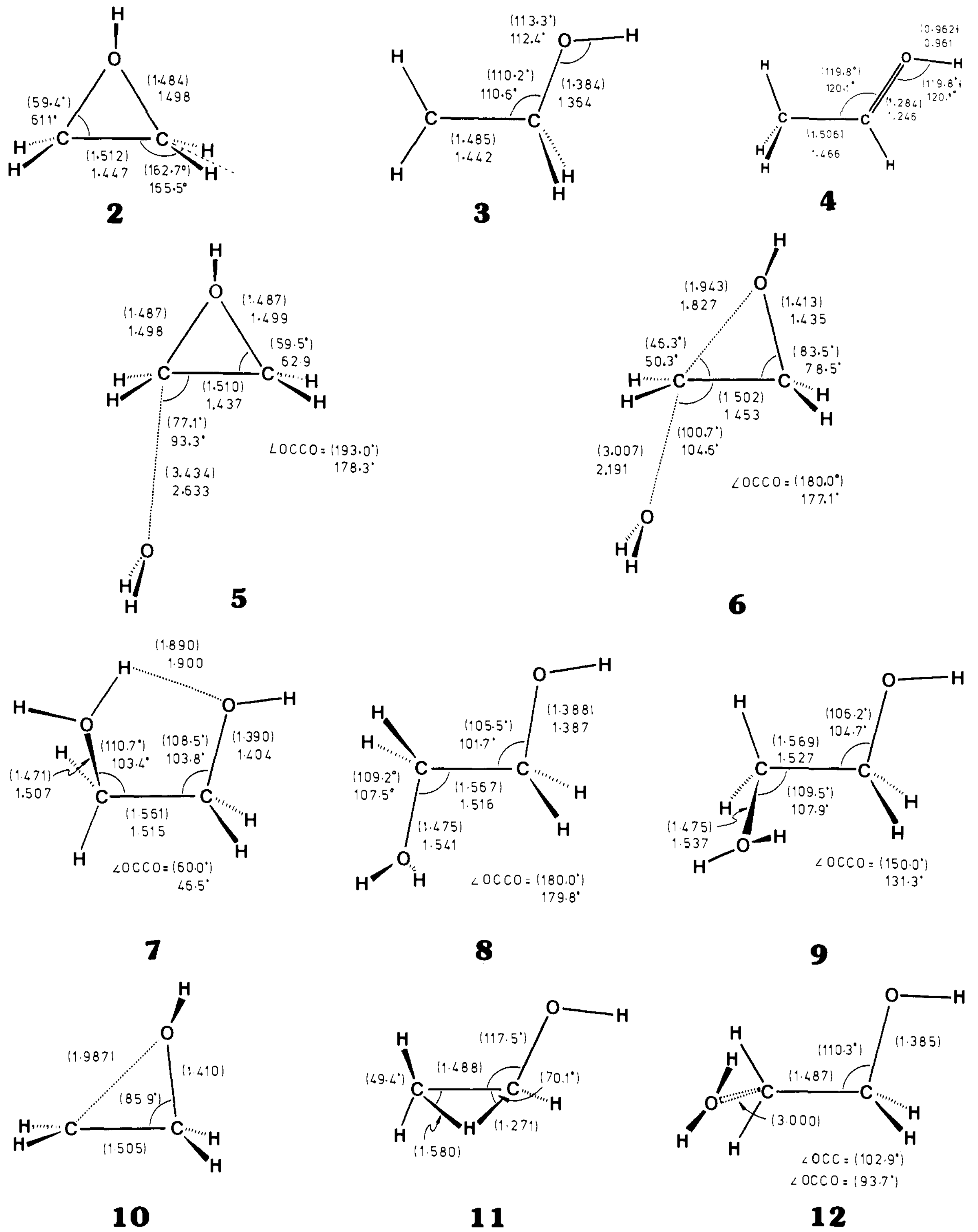

Figure 1. Calculated geometries of structures **2–12**. Unparenthesized data refer to ab initio HF/6-31G* and parenthesized values to semiempirical MNDO calculations. Ab initio data for **4** from ref 35.

gram systems. All geometries were completely optimized within the specified point groups with use of both the 3-21G[31] and 6-31G*[32] basis sets and gradient based algorithms[33] incorporated as standard program options. The optimized HF/6-31G* geometries are displayed in Figure 1. The HF/3-21G geometries are not included here but may be obtained from the authors on request. Single point 6-31G** calculations,[32] including second-order Møller–Plesset[34] (MP2) valence electron correlation corrections, were carried out on the optimized HF/6-31G* geometries.

The calculated total energies are summarized in Table I. These, together with additional data from the Carnegie-Mellon Quantum Chemistry Archive,[35] were used to compute the relative

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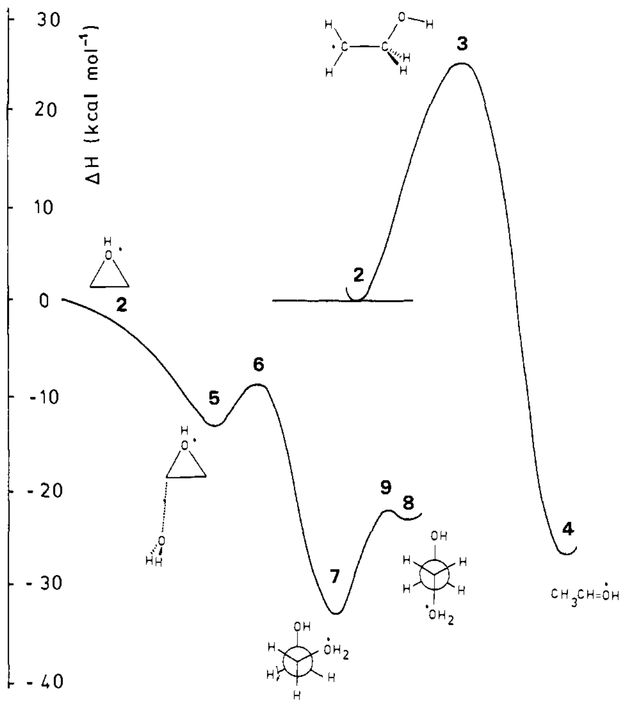

Figure 2. Calculated (MP2/6-31G**//HF/6-31G*) enthalpy profile for reactions of **2**.

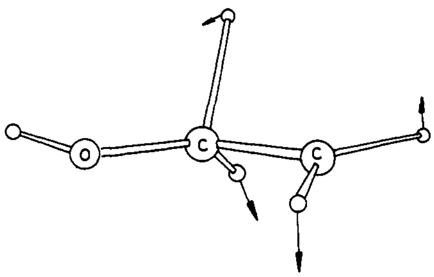

Figure 3. HF/6-31G* transition-state geometry and form of the imaginary vibration interconverting reactants and products for **2** → **4**.

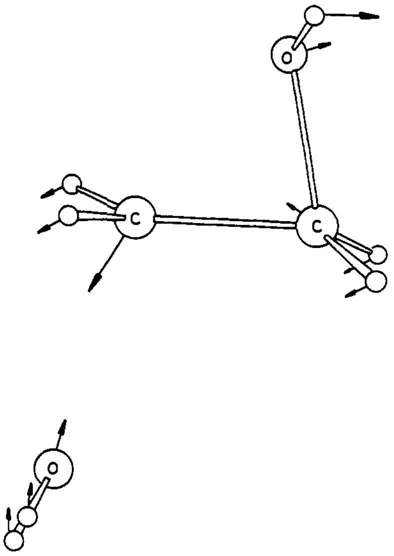

Figure 4. HF/6-31G* transition-state geometry and form of the imaginary vibration interconverting reactants and products for H_2O + **2** → **7**.

energetics summarized in Tables II and III. The energies for the vibrationless species at 0 K were converted to ΔH values by using the classical[36] rigid-rotor harmonic-oscillator approximation (cf. ref 37) and the HF/6-31G* moments of inertia and scaled[38] harmonic frequencies. In an alternative procedure, recommended in the recent book by Pople and co-workers,[37] torsional modes below 500 cm^{-1} were treated as free rotations (each contributing $1/2RT$ to the total enthalpy.) Reaction enthalpies calculated in this way were slightly more negative by $\lesssim 1$ kcal mol^{-1}. The results (MP2/6-31G**//HF/6-31G*) in Tables II and III were combined to generate the overall enthalpy profile shown schematically in Figure 2. Absolute entropies were also calculated[36] from the scaled HF/6-31G* frequencies, in which all modes were treated as harmonic vibrations,[39] and used to estimate reaction free energies.

At the MP2/6-31G**//HF/6-31G* level (including vibrational contributions) the proton affinity of **1** is calculated to be 188.1 kcal mol^{-1}, in quantitative agreement with the experimentally[40] derived 187.9 kcal mol^{-1}. In a careful study of calculated proton affinities Del Bene[41] found that the small errors inherent in (a) the inclusion of limited electron correlation and (b) the less than optimum basis sets partially canceled. Thus, the agreement noted above may be slightly fortuitous. Nevertheless, while it would have been desirable to have included higher levels of correlation, and a somewhat more extensive basis set, the highest level used here, MP2/6-31G**//HF/6-31G*, was judged to represent a useful compromise.

The structure of **2** has been discussed by several groups.[16,22,42] Of special note is the predicted[16,35] elongation of the CO bond and the widening of the angle between the CC bond and CH_2 plane (0.096 Å and 7.1° at the HF/6-31G* level) relative to **1**. Both phenomena are readily understood in terms of the greater π-complex character associated with the protonated ring.[16,43]

At the HF/3-21G level the C_s structure of the 2-hydroxycarbenium ion **3** was calculated to be a local minimum. However, when optimized with the more flexible 6-31G* basis set, it was found to be a transition state (one negative eigenvalue of the force constant matrix[44]) for the concerted rearrangement of **2** to protonated acetaldehyde **4**. The form of the imaginary vibrational mode which interconverts reactants and products is shown in Figure 3.

The location of the completely asymmetric transition state **6** for the bimolecular attack of water on protonated oxirane **2** proved to be significantly more difficult. A two-dimensional energy surface was constructed at the HF/3-21G level with use of the opening CCO angle and the distance to the approaching nucleophile, r(CO), as independent reaction coordinates. Each geometry was then fully optimized with respect to all remaining geometrical variables. Initially CCO was varied from 65 to 95° in steps of 10° and r(CO) from 2.2 to 2.8 Å in steps of 0.2 Å. Further calculations provided additional points in the vicinity of the anticipated transition state; those in obviously less critical regions were obtained by quadratic interpolation of the original grid. However, the resulting two dimensional energy contour diagram revealed a monotonically descending pathway between reactants and products. In other words the water assisted ring opening of protonated oxirane was predicted to take place without activation and with no intervening minima at the HF/3-21G level.

We next investigated the potential surface for the same process at the higher HF/6-31G* level. To circumvent the substantial

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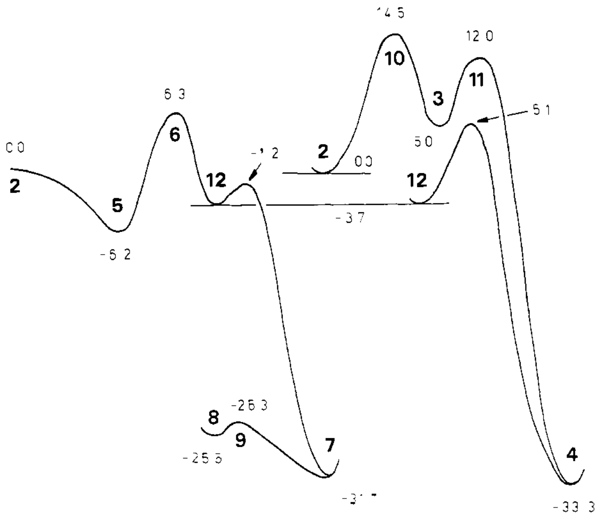

Figure 5. Calculated (MNDO) enthalpy profile for reactions of **2**. Structures are identified in Figure 1.

computational expense required to generate the full surface with this basis set single point HF/6-31G* calculations were carried out with use of the HF/3-21G geometries. Here we identified a saddle point at $\angle$CCO ~ 77° and r(CO) ~ 2.25 Å. Complete optimization with the 6-31G* basis set then led to a transition structure with the necessary[44] single negative force constant (Figure 4). The energy of the latter was calculated to be below that of the isolated reactants. It therefore followed that another minimum energy structure must separate the reactants and transition state. This was identified as the electrostatically bound complex **5**.

The gauche **7** and anti **8** conformations of the ring opened products were predicted to be local minima at both the HF/3-21G and HF/6-31G* levels. The transition state for their interconversion **9** was also located at latter level by using a short reaction path followed by gradient minimization.

MNDO Calculations. Parallel MNDO[28] calculations were carried out[45] with complete geometry optimization with use of standard gradient methods.[46] Transition-state geometries were located by one-dimensional reaction paths or two-dimensional grid searches followed by gradient refinement and vibrational analysis. The resulting MNDO reaction profile and relative enthalpies are summarized in Figure 5. The optimized geometries are shown in parentheses in Figure 1.

MNDO, which systematically underestimates the proton affinities of ethers,[47] leads to a proton affinity for oxirane (177.2 kcal^{-1}) which is too low[40] by 10.9 kcal mol^{-1}. Like the present HF/3-21G, and previous smaller basis set ab initio calculations,[18] MNDO predicts the 2-hydroxycarbenium ion **3** to be a local minimum separating individual transition states for the ring opening **10** and H-shift **11**, cf. Figure 5. The construction of detailed energy contour maps for these reactions revealed no concerted pathway between **2** and **4** at the MNDO level.

The MNDO bimolecular reaction pathway differs from the 6-31G* one by the appearance of **12**, a stable hydrate of **3**. Despite considerable effort, we found no evidence for such a structure at any of the ab initio levels. We also examined the corresponding pathway involving approach of the attacking water molecule from "above". Here the transition state was calculated to be somewhat less stable than **6** ($\Delta H^{\ddagger}$ = 7.4 kcal mol^{-1}) and the complex separating reactants and products somewhat more stable (7.4 kcal mol^{-1} below the reactants) than **5**. Since we were primarily concerned with the gas-phase counterpart of the aqueous-phase reaction, which is known to involve inversion at the reaction site,[11,14] this pathway was not pursued in detail.

Discussion

Unimolecular Ring Opening. The absence of a stable primary carbenium ion in the gas-phase ring opening of **2** was anticipated by Williams and co-workers in their studies of the appearance potentials of related ions.[48] They estimated the heat of formation of a structure analogous to **3** to be ~189 kcal mol^{-1}, i.e., ~24 kcal mol^{-1} above that of **2**,[40] in quantitative agreement with the MP2/6-31G**//HF/6-31G* result. The overall barrier for the unimolecular rearrangement, and the absence of a distinct A1 pathway in the gas-phase, is thus associated with the special instability of primary carbenium ions[49] especially those bearing electronegative substituents β to the sp^2 center.[50] Although the details of the intervening potential surfaces at the MNDO and smaller basis set ab initio levels differ, all methods predict the overall rearrangement (**2** → **4**) to be exothermic by about the same amount. At the highest ab initio level the agreement with the experimental value[40] (-26 kcal mol^{-1}) was quantitative. MNDO predicts the rearrangement to be somewhat too exothermic.

It is noteworthy that the rates and orientation of Lewis acid catalyzed ring opening of substituted oxiranes in non-nucleophilic solvents strongly suggest a transition state with carbenium ion character.[11,51]

The Bimolecular Hydrolysis of 2. The absence of a definite transition state on the HF/3-21G surface for the bimolecular hydrolysis of protonated oxirane **2** is probably an artifact of the unrealistically large exothermicity predicted for the overall reaction with this basis set. At the HF/6-31G* and higher levels, where the predicted heat of reaction is similar to our best experimental estimate (see below), the reaction profile is of the form now familiar for the gas-phase substitution reactions of anions[52,53] and, for which evidence[54] is also accumulating, for cations. Thus, the transition state itself (**6**) is preceded by an electrostatically bound ion–dipole complex. According to the highest level ab initio calculations the complex **5** lies 13.2 kcal mol^{-1} below the reactants with a 4.3 kcal mol^{-1} barrier hindering its conversion to products via **6**. Thus, most of the driving force for the gas-phase reaction can be attributed to the electrostatic attraction between the reactant moieties. From the calculated transition-state geometry it appears that bond formation to the incoming water molecule plays a significantly smaller role than would have been anticipated for a fully concerted process. While the extent of bond formation, or cleavage, in the transition state is difficult to quantify in terms of the bond lengths themselves, this is conveniently[27] accomplished, at least in an approximate manner, using the related bond orders. Equation 3 expresses the extent to which a given bond is formed (or cleaved) in the transition state as a percentage of that for the

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(45) The majority of the MNDO calculations were carried out on programs adapted for Harris Corp. minicomputers from CDC versions originating in the laboratories of M. J. S. Dewar, University of Texas, Austin. Others used an IBM version of the MOPAC package: Olivella, S. *QCPE Bull.* **1984**, *4*, 109.

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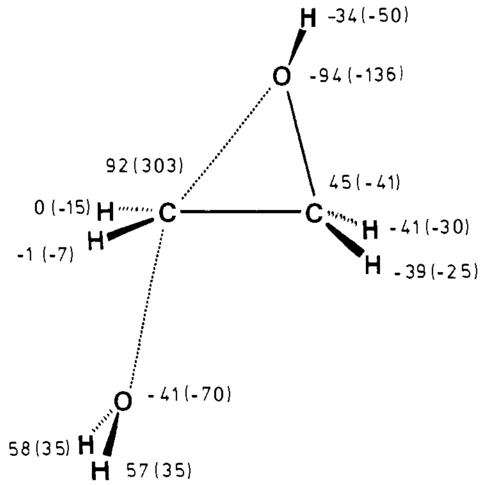

Figure 6. Calculated HF/6-31G* (MNDO) charge development in the transition state for H_2O + **2** → **7**. Data refer to the difference $q^{\ddagger} - q^{R}$, where $q^{\ddagger}$ is the calculated Mulliken[56] atomic charge at the specified atom in the transition state and q^{R} is the corresponding quantity in the reactant in units of 10^{-3}e.

overall reaction. Here, $n^{\ddagger}$, n^{R}, and n^{P} are the orders of the corresponding bond in the transition state, reactant, and product respectively. Introducing the Pauling relationship[55] (eq 4) leads

$$n(\%) = 100(n^{\ddagger} - n^{R})/(n^{P} - n^{R}) \qquad (3)$$

$$n = \exp[(r_0 - r)/0.26] \qquad (4)$$

$$n(\%) = 100[\exp(-r^{\ddagger}/0.26) - \exp(-r^{R}/0.26)]/[\exp(-r^{P}/0.26) - \exp(-r^{R}/0.26)] \qquad (5)$$

to a convenient form (eq 5) in which r_0, the length of a "normal" bond of the same kind (arbitrarily assigned a bond order of unity), does not explicitly appear. Setting the length of the forming bond in the reactant (r^{R}) to ∞ and those in the transition state ($r^{\ddagger}$) and products (r^{P}) to their HF/6-31G* values (2.191 and 1.541 Å, respectively) suggests that in the transition state this bond reaches 8% of its final strength. Similarly cleavage of the breaking bond (r^{R} = 1.498; $r^{\ddagger}$ = 1.827; r^{P} = 2.309) is predicted to be 75% complete in the transition state.

As described in the introduction, an early transition state in the corresponding reactions of **1** and its derivatives in aqueous acid had long been assumed.[11] This so-called borderline A2 mechanism[11] allowed the rate and regiochemical data for substituted oxiranes to be reconciled with the observed[11,14] Walden inversion. Thus, while free carbocations were excluded, a significant buildup of positive charge at the reaction site was envisioned.[11] The HF/6-31G* calculations do indeed predict a rather early transition state. However, positive charge development at the reaction site is predicted to be a rather modest 0.092e (cf. Figure 6).

Unlike the ab initio calculations the MNDO transition structure **6** lies 6.2 kcal mol^{-1} above the reactants, 12.4 kcal mol^{-1} above the complex. It seems likely (cf. ref 53a and 58) that MNDO, which overestimates nonbonded repulsions in crowded systems,[59] predicts both to be too unstable.

The calculated transition structures themselves are qualitatively similar. In both, the water molecule approaches in the plane of the three-membered ring with an angle between the entering and leaving atoms of somewhat less than the ideal 180°. The principal difference lies in the length of the bond to the incoming water molecule which is calculated to be considerably longer at the MNDO level. Thus the latter predicts the transition state to be even "earlier" than does the ab initio HF/6-31G* procedure.[60] Applying the analysis of eq 5 (forming bond, $r^{\ddagger}$ = 3.007 and r^{P} = 1.475; breaking bond, $r^{\ddagger}$ = 1.943, r^{R} = 1.484, and r^{P} = 2.355) cleavage of the endocyclic bond in the MNDO transition state is 86% complete while the bond to the incoming water molecule reaches less than 1% of its final strength. Unlike the HF/6-31G* calculations described above, MNDO does predict a significant accumulation of positive charge[57] at the reaction site (cf. Figure 6). The well known basis set dependence[56] of the Mulliken population analysis precludes quantitative comparison of the ab initio and semiempirical results. However, at least some of the qualitative difference appears to be associated with the earlier character of the MNDO transition-state geometry. When the HF/6-31G* calculations were repeated with the MNDO transition-state geometry, for example, the predicted positive charge development at the reaction site increased from 0.092 to 0.154e. It is interesting to speculate that the inherent shortcomings of the MNDO method (overestimation of nonbonded repulsion) may quite accidently result in transition-state geometries that are in fact more akin to the true solution phase than to the gas-phase structures.

An unexpected feature of the MNDO potential surface was the presence of a second minimum (**12**) on the pathway linking **6** (and the corresponding transition state for attack from "above") to the product conformational manifold. Structure **12** is a hydration complex of **3**, from which it is also formed without activation. Thus, at least in MNDO, **12** is a common intermediate in both the unimolecular and bimolecular pathways. However, this rather appealing intermediate is probably again an artifact of the tendency of MNDO to overestimate nonbonded repulsions.[59]

Protonated 1,2-Ethanediol. At the highest level of theory the gauche conformation of protonated ethanediol **7** is predicted to be more stable than the anti **8** by 12.6 kcal mol^{-1}. While 1,2-ethandiol itself also adopts a gauche conformation in the gas phase the energetic difference is only about 1 kcal mol^{-1}.[65] The extra stability in the former case presumably derives from favorable charge dipole interactions, as well as the intramolecular hydrogen bond present in this conformation. As suggested by Meot-Ner,[66] the latter is formed at the expense of some angle strain (cf. structures **7** and **8**) resulting in a far weaker hydrogen bond than the ~30 kcal mol^{-1} typical in clusters of the type **13**.[67]

From the known[40] heat of formation of **14**, which exists in the analogous intramolecularly hydrogen bound gauche conformer,[67]

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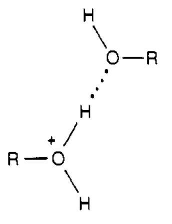
we estimate[68] an upper limit of around 79 kcal mol^{-1} for the heat of formation of **7**. The actual value is probably somewhat lower since the intramolecular hydrogen bond in **7** should be stronger than that in the more congested **14**. Our estimated heat of formation for **9** proceeds from the isodesmic process[70] represented by eq 6. Here, ΔH, which corresponds to the destabilization of

$$CH_3CH_2OH_2^+ + HOCH_2CH_2OH \rightarrow CH_3CH_2OH + HOCH_2CH_2OH_2^+ \quad (6)$$

the onium group by a vicinal OH, is just the difference between the proton affinities of EtOH and $HOCH_2CH_2OH$. This should[71] be of the same order as the corresponding difference[72] (2.4 kcal mol^{-1}) between the proton affinities of cyclohexylamine and the amino alcohol **15** in which the NH_3^+ group is analogously destabilized. An estimate of $\Delta H_f(\mathbf{9}) \sim 88$ kcal mol^{-1} then follows from the known[40,69] heats of formation of the remaining species. Given the uncertainties involved, both the estimated overall heats of reaction and conformation energy differences are consistent with our best ab initio calculations. They do, however, imply that the overall heat of reaction predicted at the HF/3-21G level is far too negative. As suggested above, the resulting distortion of the potential energy surface almost certainly accounts for the absence of a distinct transition state at this level.



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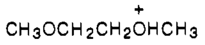
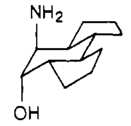


$$CH_3OCH_2CH_2\overset{+}{O}HCH_3$$

14



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On the basis of these estimates MNDO predicts the overall reaction to be slightly too exothermic and the conformational energy difference (5.1 kcal mol^{-1}) too small. The latter reflects the known[73] failure of the method to properly describe hydrogen bonds.

Summary and Conclusions

At the highest level of ab initio theory studied, MP2/6-31G**//HF/6-31G*, the inductively destabilized 2-hydroxycarbenium ion **3** is predicted to be a transition state for the rearrangement of protonated oxirane **2** to the conjugate acid of acetaldehyde **4** ($\Delta H^{\ddagger} = 24.6$; $\Delta G^{\ddagger} = 23.9$ kcal mol^{-1}). At this level of theory there is apparently no gas-phase counterpart of the classical A1 hydrolysis.

In contrast, the water assisted bimolecular ring opening, the gas-phase counterpart of the classical A2 reaction, is predicted to be extremely facile proceeding via an early, or reactant-like, transition state lying 9.1 kcal mol^{-1} *below* the reactants on the enthalpy surface. The transition state is separated from the reactants by an electrostatically bound complex **5**, itself 13.2 kcal mol^{-1} below the isolated reactants. The transition structure leads directly down to the product gauche $\rightleftharpoons$ anti interconversion manifold, the intramolecularly hydrogen bound *gauche* conformer **7** being the more stable by 12.6 kcal mol^{-1}.

Apart from the predicted intermediacy of **12**, a stable carbenium ion hydrate separating the transition state and product manifold, the MNDO bimolecular reaction profile is qualitatively similar to the ab initio MP2/6-31G**//HF/6-31G* one. The predicted existence of **12**, the substantially looser geometries and lower stabilities of the transition state **6** and ion–dipole complex **5**, and the smaller energetic difference between the product gauche and anti conformers, are probably all related to the tendency of MNDO to overestimate nonbonded repulsions.

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Registry No. **2**, 27659-85-4; **3**, 38607-31-7; **4**, 18682-96-7; **7**, 103363-92-4.

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[68] Estimated assuming group additives from the following approximate relationship: $\Delta H_f(HOCH_2CH_2OH_2^+) \sim \Delta H_f(cH_3OCH_2CH_2OH^+CH_3) + PA(EtOMe) - PA(EtOH) + 2[\Delta H_f(EtOH) - \Delta H_f(EtOMe)]$. Heats of formation and proton affinities (PA) are from ref 40 and 69.

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