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A Mechanistic Investigation of Ethylene Oxide Hydrolysis to Ethanediol

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The B3LYP/6-311+G(d,p) description is employed to study the heterolytic ring opening mechanisms under microsolvation conditions for ethylene oxide in acidic, neutral, and alkaline environments. In acid and alkaline media, a concerted trans S_N2 reaction is strongly favored as compared to the corresponding cis reaction. The importance of the nucleophile, water in acidic media and hydroxide ion in alkaline media, for lowering the activation enthalpy is emphasized and activation energies of ∼80 and ∼60 kJ mol^{-1} are obtained under acid and alkaline conditions, respectively. Under neutral conditions, the trans S_N2 mechanism becomes inaccessible because it invokes the formation of a transient H^+ and OH^- pair across the 1,2-ethanediol molecule. Rather, epoxide ring opening is achieved by hydrolysis of a single water molecule. The latter mechanism displays significantly greater activation enthaply (205 kJ mol^{-1}) than those in acid and alkaline environments. This is in agreement with experiment. Product distributions of simple olefins in neutral aqueous media, as well as the detrimental impact of acid/base conditions for the selectivity of epoxidation catalysts in aqueous media, are discussed.

1. Introduction

Hydrolysis of epoxides is a longstanding issue, and today it is discussed in the contexts of industrial and biological applications. In biological systems, a large number of compounds are metabolized by pathways involving epoxidation, followed by epoxide hydrolases-catalyzed hydrolysis. Recently an effort based on density functional calculations was performed to obtain a better understanding of the epoxide ring-opening reaction.[1] The reaction was described by an S_N2 mechanism, where the acid-catalyzed ring-opening is associated with formation of an ester, and the diol is formed in the subsequent hydrolysis step involving activated water as the nucleophile.

Industrial production of epoxides utilizes zeolites for the reaction between the alkene and hydrogen peroxide. The most promising zeolite for this purpose is TS-1, where the Ti(IV) active site is tetrahedrally bound in the zeolite structure.[2−7] High selectivity for propene epoxidation has been found, but for larger alkenes, zeolites with wider channels have to be used.[8−14] For example, Ti-Al-β was shown to catalyze the oxidation of oct-1-ene with aqueous hydrogen peroxide. However, the acidic Al(III)-H^+ groups within the zeolite structure catalyzes the hydrolyses of the epoxide and the main product obtained was instead the corresponding diol.[8] In these industrial applications, the reaction takes place in a confined environment, and in this respect, there is a similarity with the biological application mentioned above, which takes place inside cells or in enzymes anchored to the cell membrane[1]

In earlier mechanistic studies of epoxide hydrolysis,[15−20] the two overall reaction mechanisms A-1 (S_N1) and A-2 (S_N2) were discussed, where the A-1 path contains the formation of a stable carbocation. Brønsted et al.[15] studied the kinetics of ethylene oxide and found two kinetically distinct hydrolysis reactions depending on the pH of the solution. One of the most important studies was performed by Long and Pritchard,[20] who found three kinetically distinguished mechanisms for the hydrolysis of simple epoxides in water: acid-catalyzed, pH-independent, and hydroxide-catalyzed hydrolysis. In the pH-independent reaction of propylene oxide, the solvent adds preferentially to the primary carbon, and the mechanism was described as a concerted C−O bond breaking and a nucleophile-assisted O−C bond making. The transition state was considered to be stabilized by strong hydrogen bonding with the solvent.[20] In the second-order reaction of propylene oxide with sodium hydroxide in water solution, hydroxide ion attack at the primary carbon (80%) is favored over attack at the secondary carbon (20%). Thus, it was concluded that the same mechanism holds for hydrolysis in alkaline solutions. However, in acid-catalyzed hydrolysis of propylene oxide, cleavage of the secondary C−O bond is favored over cleavage of the primary C−O bond. These results were taken to support the A-1 mechanism because cleavage of the secondary C−O bond leads to the carbon that can better stabilize a positive charge. However, an A-2 mechanism in which there is a concerted addition of a water molecule to the protonated epoxide has also been suggested. The A-2 mechanism is enforced on the acid-catalyzed hydrolysis of those epoxides that undergo ring-opening to form primary or secondary carbocations because the rate between the carbocation and the solvent is faster than solvent reorganization.[21] Because the lifetime of the carbocation is shorter than the time for solvent reorganization, the epoxide ring-opening may be nearly complete at the transition state. The mechanism of hydrolysis of epoxides was recently reviewed, and it was emphasized that an understanding of the acid- and base-catalyzed mechanisms of epoxide hydrolysis in aqueous solutions is of special interest, in particular how pH, concentrations of added acidic or nucleophilic reagents, and epoxide structure influence the reaction rate.[21] To establish the mechanism is interesting also in the context of epoxide

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production because the formation of diols lowers the selectivity and yield of the desired epoxide.[6]

In two previous studies,[22,23] we have addressed the catalytic epoxidation of ethene with hydrogen peroxide. We formulated a mechanism for said reaction and demonstrated how the $[H^{\delta+}O_\alpha-(O_\beta H)^{\delta-}]$ transition state can be stabilized by a hydrogen-bonding network. Because the TS-1 catalyst employs diluted hydroperoxide in a methanol/water mixture, it becomes interesting to investigate to what extent the epoxide is stable toward hydrolysis to form diols by water. This is the aim of the present work, and the results will be discussed in the context of our previous work on the epoxidation reaction.

2. Computational Considerations

The applicability of DFT for heterolytic dissociation reactions was discussed in ref 22. It was concluded that bond dissociation reactions are treated properly by DFT if these can be described as electron pairs displacements propagating via avoided crossings on a potential energy surface where the HOMO−LUMO gap is large in the vicinity of the minimum energy path. The present investigation addresses such a class of heterolytic reactions by employing the B3LYP/6-311+G(d,p) description,[24−26] i.e., the HOMO−LUMO gaps exceed 3.5 eV for all transition states considered. This has been found to be the functional of choice in many studies. Recently, we also compared the activation energy for epoxidation reactions employing CCSD(T), the B3LYP hybrid functional, and the GGA functionals BLYP and BP86.[22] Again, the best agreement was found between the B3LYP and CCSD(T) results. Furthermore, it has been shown how an unrealistically low activation energy was obtained with the BLYP/6-311+G(d,p) description on a binuclear Ti(IV) site.[23]

The B3LYP calculations were performed by employing the GAUSSIAN 03 program package.[27] Molecular structures were optimized, and analytical Hessians were subsequently evaluated for all the optimized geometries. All transition states were characterized by one negative eigenvalue of the Hessian matrix. Besides structural information and vibrational spectra, data from the Hessians was used for the thermochemical calculations. Reaction and activation enthalpies at 298 K are presented.

3. Results and Discussion

The efficiency of an ethene epoxidation catalyst that employs hydrogen peroxide as oxidant is to a great extent determined by its ability to suppress the formation of the 1,2-ethanediol. Below, we explore sensitive parameters which control the formation of the diol. The reaction scheme for ethene oxidation by hydrogen peroxide is displayed in Figure 1. The symmetric reaction to the diol is effectively symmetry forbidden due to orthogonality between the C_2H_4 π orbital and the H_2O_2 σ^* orbital, which are HOMO and LUMO, respectively, in the vicinity of the transition state. Hence, the epoxide will always be an intermediate in the reaction sequence as shown for the asymmetric pathway.

The breaking of the epoxide bond with water is associated with a transition state electron distribution in the ethylene oxide of the type $H_2C^{\delta+}-CH_2O^{\delta-}$. Because this bond breaking is associated with a displacement of electron pairs rather than homolytic dissociation, the minimum energy path results from avoided crossings with sizable HOMO−LUMO gaps. This in turn warrants the applicability of DFT. Conceptually, the transition state comprises a heterolytic ring-opening reaction, which is supported by protonation at the negative end under acidic conditions, and by a hydroxide nucleophile at the positive end in alkaline media. In both cases, the complementary site is coordinated with water, which acts as electrophile and nucleophile, respectively, Figure 2. Indeed, the diol formation effectively transfers H^+ (acidic) or OH^- (alkaline) from one side of the molecule to the other. In case of the neutral system, diol formation may formally involve the transient formation of H^+ and OH^- on either side of the diol, Figure 2b, or hydrolysis of the epoxide bond with a single water molecule, Figure 2c.

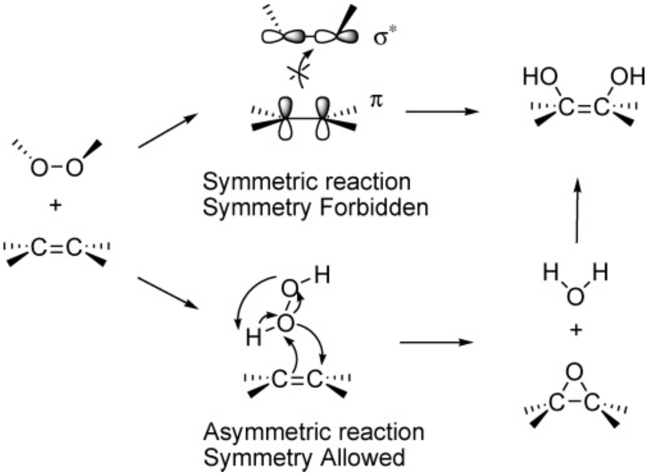

Figure 1. Oxidation of ethene with hydrogen peroxide showing the symmetrically forbidden direct pathway to the diol (top) and the asymmetrically allowed pathway (bottom).

Decisive for the activation energy is the electrostatic interactions at the transition state. Upon introduction of an oxonium ion, the $CH_2O^{\delta-}$ end becomes stabilized by the proton transfer but the $H_2C^{\delta+}-CH_2O^{\delta-}$ attractive coulomb interaction is lost. To compensate for this loss, a water molecule can be introduced as nucleophile. Significant reduction in activation energy is observed (∼60 kJ mol^{-1}); compare the activation enthalpy for **1A** to that of **2A** and **3A** in Figure 3. The great asymmetry in activation energies (∼60 kJ mol^{-1}) between cis (**1A**) and trans (**2A**, **3A**) for the nucleophilic attack supports an S_N2 reaction mechanism. Similar activation energies would have implied the formation of a carbocation and thus an S_N1 mechanism.

Taking a hydroxide ion to act as initiator in the breaking of the epoxide bond, two modes of nucleophilic attack can be envisaged, one cis and one trans with respect to the epoxide oxygen; compare cis $\mathbf{0B_{cis}}$ and **1B** to trans $\mathbf{0B_{trans}}$ and **5B** in Figure 4. The activation energies are 110 kJ mol^{-1} lower for the trans structures because, in the cis attack, both Coulomb and Pauli repulsion between the electron rich $OH^{\delta-}$ and $CH_2O^{\delta-}$ compete with the attraction to the $H_2C^{\delta+}$ subunit. By performing the nucleophilic attack in the trans mode, both the repulsive interactions are minimized while the intramolecular attractive interaction as well as the $H_2C^{\delta+}-OH^{\delta-}$ attraction are preserved. It is interesting to observe the similarity in the reaction barriers for the poorly solvated $OH^{\delta-}$ in **0B** and the significantly better solvated **5B** case, Figure 4. The difference between the two activation energies is only 15 kJ mol^{-1} and emphasizes the role of the nucleophile in the transition state, thus negating any involvement of a carbocation under alkaline conditions. This is also in general agreement with experimental results.[21]

Under neutral conditions, two mechanisms can be envisaged, one where OH^- and H^+ are formed as a result of the hydrolysis reaction, Figure 2b, and a second where the heterolytic decomposition of the epoxide occurs in concert with protolysis of water, which is the limiting bare reaction, Figure 2c. In Figure 5, the results of the bare reaction (**0N**), and the effect of adding a second water molecule (**1N**) are seen to display activation

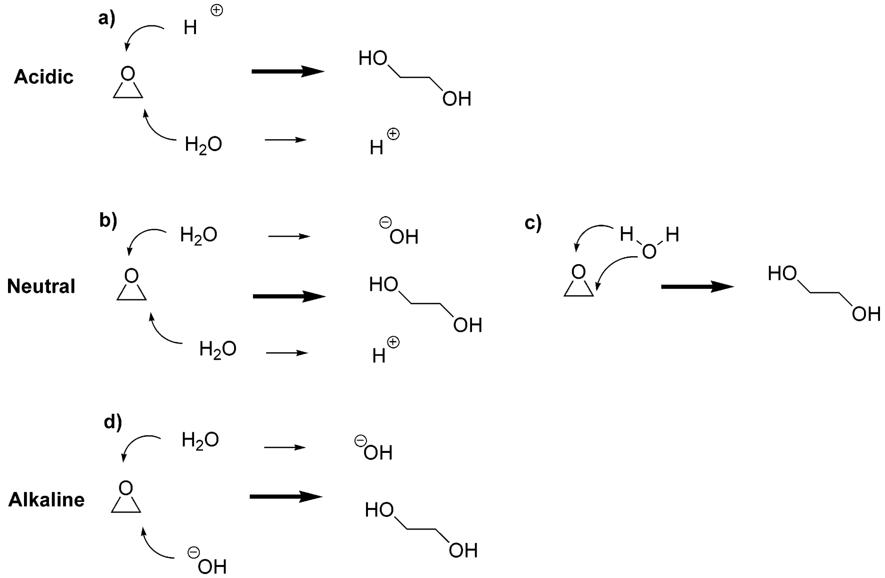

Figure 2. Schematic representation of the hydrolysis of ethylene oxide under acid (a), neutral (b,c), and alkaline (d) conditions. Path (c) represents the bare hydrolysis reaction.

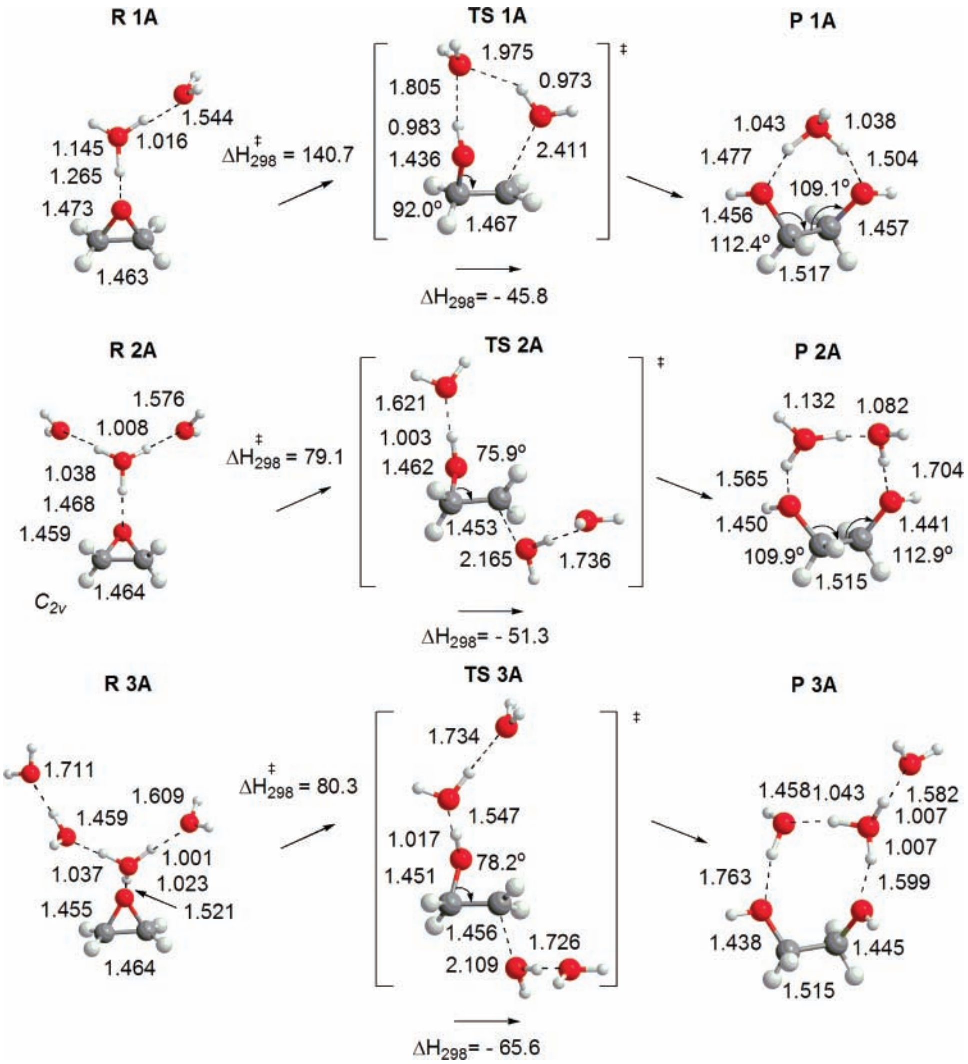

Figure 3. Hydrolysis of ethylene oxide in acidic environment. Reaction and activation enthalpies are given in kJ mol^{-1}and bond lengths in Å. Calculations were made at B3LYP/6-311+G(d,p) level of theory.

energies of 205.0 and 204.1 kJ mol^{-1}, respectively. Formally, both transition states are associated with the protolysis of water, and this is why similar activation energies are expected. No transition state could be determined for the H^{+}−OH^{-} producing diol reaction, Figure 2b, which would be analogous to the trans reactions in the case of acidic and neutral conditions, Figure

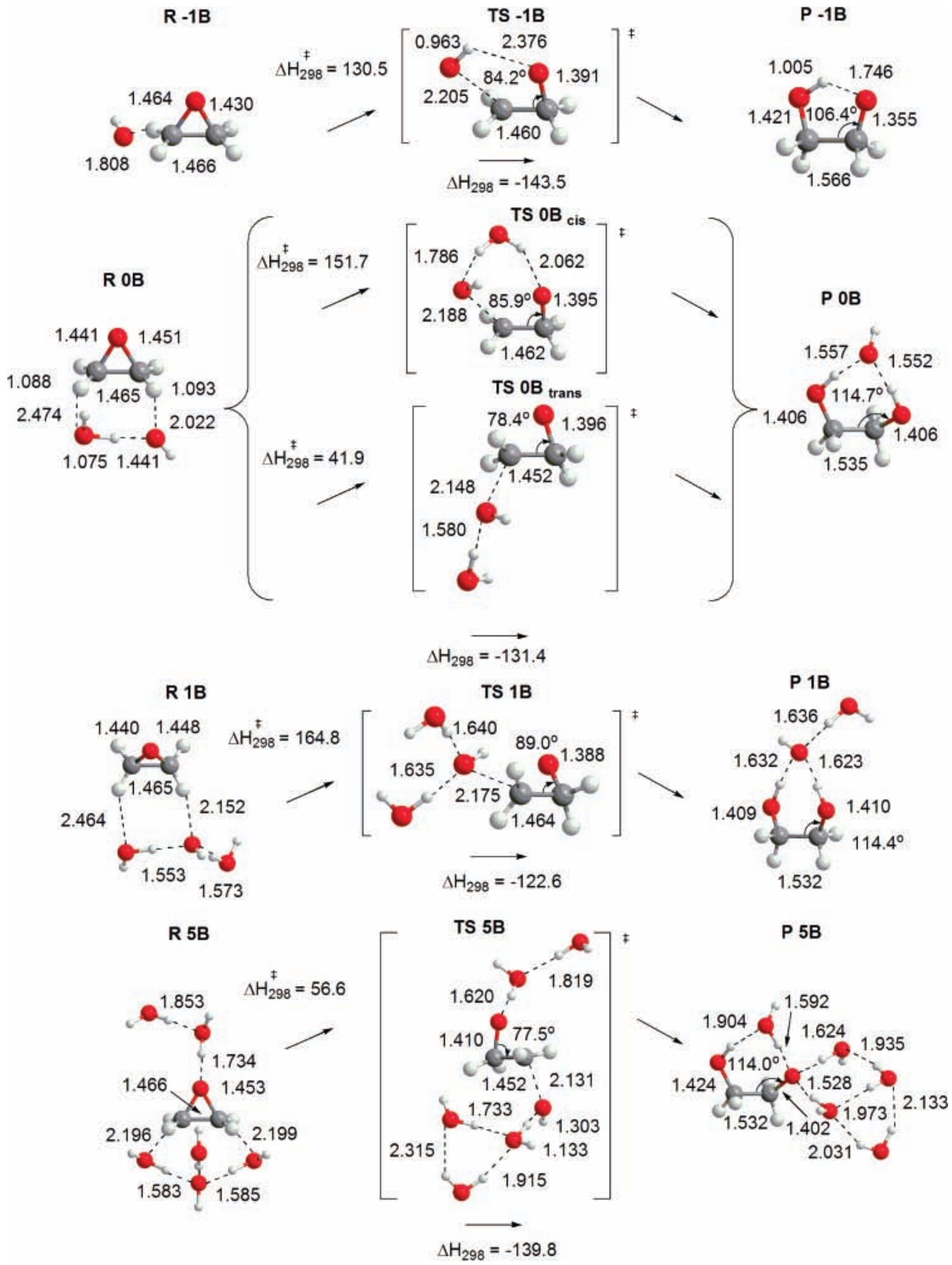

Figure 4. Hydrolysis of ethylene oxide in alkaline environment. Reaction and activation enthalpies are given in kJ mol^{-1}and bond lengths in Å. Calculations were made at B3LYP/6-311+G(d,p) level of theory.

2a,d. This is because of the strong ion pair ($H^+{-}OH^-$) attraction distorts the potential energy surface.

In summary, we have shown that the mechanism for ring opening is fundamentally the same under acidic and alkaline conditions, i.e., a trans reaction associated with an electrophile and a nucleophile, both contributing to the lowering of the activation energy. Under acidic conditions, the oxonium ion is the electrophile while water acts as nucleophile, whereas water acts as electrophile and the hydroxide ion as nucleophile under alkaline conditions. However, under neutral conditions, the ring-opening mechanism is associated with the protolysis of a single water molecule in that the H^+ end acts as electrophile and OH^- as nucleophile. This cis-type pathway is contrary to what is expected in bulk water, where the trans pathway is generally found,[28] Figure 2b. In the absence of bulk water, however, the reaction channel depicted in Figure 2b becomes highly unfavorable in that the proton and hydroxide ions become effectively nonsolvated in the zeolite environment. In contrast, the direct addition of molecular water to the epoxide, Figure 2c, is affected to a much lesser extent by the absence of bulk water. Thus an enhanced ratio of epoxide hydrolysis products, which display retention of configuration at the carbon, is expected in zeolites.

A direct comparison with experiment is hampered by the asymmetry between the electrophilic and nucleophilic sites of the epoxide backbone ($H_2C^{\delta+}{-}CH_2O^{\delta-}$) with respect to solvation in bulk water. While the $-CH_2O^{\delta-}$ site becomes part of the hydrogen-bonded network, the $-H_2C^{\delta+}$ site is hydrophobic. This would imply that, under increasingly more acidic conditions, the ring opening will appear more S_N1-like. This is because protonation would occur more readily and a carbocation would form prior to solvent reorganization. However, this is contradictory to experimental findings for primary and secondary epoxides, for which the lifetime of the carbocation is much shorter than the reorganization time for water.[21]

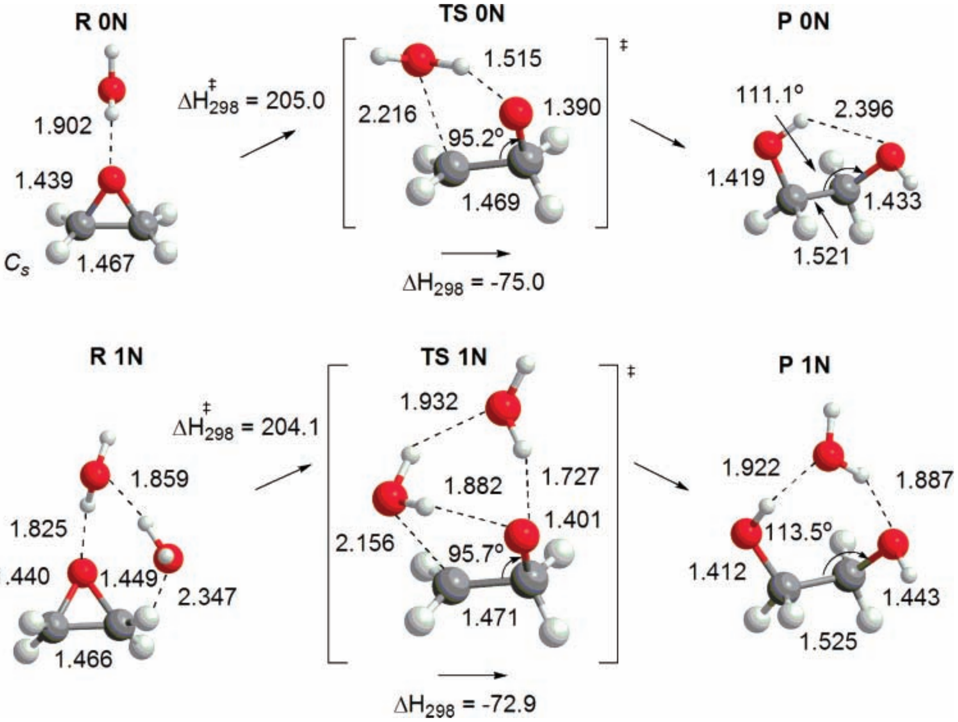

Figure 5. Hydrolysis of ethylene oxide in neutral environment. Reaction and activation enthalpies are given in kJ mol^{-1}and bond lengths in Å. Calculations were made at B3LYP/6-311+G(d,p) level of theory.

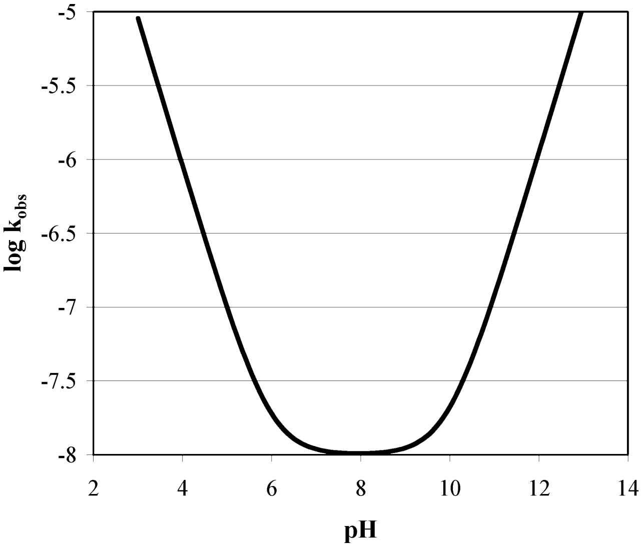

Figure 6. pH dependence of the rate constant for ethylene oxide hydrolysis as adopted from ref 20.

The pH dependence of ethylene oxide hydrolysis was estimated by Long and Pritchard[20] and is reproduced in Figure 6. Indeed, enhanced rates of hydrolysis are observed under both acidic and alkaline conditions, while under neutral conditions, low and apparently pH-independent rates are observed. These observations are in perfect accord with the results presented above, i.e., low activation energy for the trans S_N2 reaction mechanism in both acidic and alkaline solutions and high activation energy for molecular water hydrolysis under neutral conditions.

The neutral mechanism for ethylene oxide hydrolysis can be generalized to explain the product distribution of other simple epoxides, taking into consideration both steric and electronic properties, Figure 7. Asymmetric steric hindrance will favor oxygen coordination to the less crowded carbon (C_β); compare parts a and b of Figure 7. In the case of electron withdrawing groups, water will attack at the more positive carbon, Figure 7c, while the opposite is true for an electron-releasing substituent, in agreement with experimental results.[21]

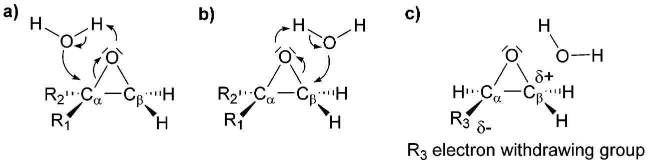

Figure 7. Schematic representation of steric (a and b) and electronic effects (c) on the product distribution of simple epoxides.

Ford and Smith addressed hydrolysis of protonated ethylene oxide in the gas phase.[29] The authors argued that this model is relevant to bulk water, assuming rapid proton exchange under neutral conditions, and report low activation energies for the subsequent hydrolysis. It may be questioned to what extent ethylene oxide is protonated at pH ~ 7. In contrast, we have discussed a high barrier reaction path for direct hydrolysis, which may compete with the unlikely though possible proton exchange driven mechanism in bulk water. Protonated ethylene oxide is expected to be further suppressed in low-dielectrics media, which is the main context of the present study. It is experimentally observed that, in the case of zeolites with large cavities and acidic sites,[8,9] ethylene oxide is found to hydrolyze to a much greater extent than in, e.g., TS-1 under neutral conditions.[30] Yet, hydrolysis products are observed.[30] These are proposed to originate from the direct hydrolysis reaction pathway reported in the present work because this reaction channel does not require bulk water.

The high selectivity obtained in using TS-1 as a catalyst for epoxidation of alkenes with hydrogen peroxide is partly due to the low activity of water for the ring-opening reaction. However, the reactivity of the epoxidation reaction is low and other zeolite systems have been tested. Higher reactivity is indeed found for proton-containing zeolites, but the selectivity is lower due to acid-catalyzed ring-opening reactions.[9] Also in biological applications, the ring opening is acid catalyzed with a subsequent hydrolysis step involving water as the nucleophile.[1]

4. Conclusions

A. The hydrolysis of ethylene oxide was shown to follow two different reaction mechanisms: (1) Under neutral conditions, the ring-opening reaction involves only one water molecule that is protolyzed in the transition state. The activation barrier for this reaction is high, which is in agreement with the low reaction rate observed experimentally. (2) Under acidic and alkaline conditions, an S_N2 reaction is observed, with water and hydroxide ions acting as nucleophiles and oxonium ions and water acting as electrophiles, respectively. The activation enthalpies for these reactions are significantly lower than those for the reaction under neutral conditions. This agrees with experimental results.

B. The mechanism prevailing under neutral conditions was generalized to understand also the product distribution observed experimentally for more complex epoxides, i.e., in terms of steric and electronic effects.

C. The effect of pH on the ring opening of ethylene oxide was explored, and the crucial role of the nucleophile in both acidic and alkaline media was emphasized. While this puts constraints on any successful strategy to produce epoxides in aqueous media, the stability of the epoxide under neutral conditions is inspiring and can be utilized in the development of epoxidation catalyst.

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References and Notes

(1) Lau, E. Y.; Newby, Z. E.; Bruice, T. C. *J. Am. Chem. Soc.* **2001**, *123*, 3350.

(2) Bordiga, S.; Boscherini, F.; Coluccia, S.; Genoni, F.; Lamberti, C.; Leofanti, G.; Marchese, L.; Petrini, G.; Vlaic, G.; Zecchina, A. *Catal. Lett.* **1994**, *26*, 195.

(3) Bordiga, S.; Coluccia, S.; Lamberti, C.; Marchese, L.; Zecchina, A.; Boscherini, F.; Buffa, F.; Genoni, F.; Leofanti, G.; Petrini, G.; Vlaic, G. *J. Phys. Chem.* **1994**, *98*, 4125.

(4) Clerici, M. G.; Bellussi, G.; Romano, U. *J. Catal.* **1991**, *129*, 159.

(5) Clerici, M. G.; Ingallina, P. *J. Catal.* **1993**, *140*, 71.

(6) Nijhuis, T. A. Towards a New Propene Epoxidation Process, Transient Adsorption and Kinetics Measurement Applied in Catalysis. Ph.D. Thesis, Delft University of Technology, Delft, The Netherlands, 1997.

(7) van Vliet, M. Selective Epoxidation with Hydrogen Peroxide. Ph.D. Thesis, Delft University of Technology, Delft, The Netherlands, 2001.

(8) Sato, T.; Dakka, J.; Sheldon, R. *J. Chem. Soc., Chem. Commun.* **1994**, 1887.

(9) Takeuchi, H.; Kitajima, K.; Yamamoto, Y.; Mizuno, K. *J. Chem. Soc., Perkin Trans. 2* **1993**, 199.

(10) Blasco, T.; Camblor, M. A.; Corma, A.; Esteve, P.; Guil, J. M.; Martinez, A.; Perdigon-Melon, J. A.; Valencia, S. *J. Phys. Chem. B* **1998**, *102*, 75.

(11) Blasco, T.; Camblor, M. A.; Corma, A.; Perez-Pariente, J. *J. Am. Chem. Soc.* **1993**, *115*, 11806.

(12) Blasco, T.; Corma, A.; Navarro, M. T.; Perez Pariente, J. *J. Catal.* **1995**, *156*, 65.

(13) Hutter, R.; Mallat, T.; Baiker, A. *J. Catal.* **1995**, *153*, 177.

(14) Maschmeyer, T.; Rey, F.; Sankar, G.; Thomas, J. M. *Nature (London)* **1995**, *378*, 159.

(15) Brönsted, J. N.; Kilpatrick, M.; Kilpatrick, M. *J. Am. Chem. Soc.* **1929**, *51*, 428.

(16) Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737.

(17) Pritchard, J. G.; Long, F. A. *J. Am. Chem. Soc.* **1956**, *78*, 2667.

(18) Taft, R. W. *J. Am. Chem. Soc.* **1952**, *74*, 5372.

(19) Wohl, R. A. *Chimia* **1974**, *28*, 1.

(20) Long, F. A.; Pritchard, J. G. *J. Am. Chem. Soc.* **1956**, *78*, 2663.

(21) Whalen, D. L. *Adv. Phys. Org. Chem.* **2005**, *40*, 247.

(22) Lundin, A.; Panas, I.; Ahlberg, E. *J. Chem. Phys. A* **2007**, in press.

(23) Lundin, A.; Panas, I.; Ahlberg, E. PCCP, **2007**, submitted.

(24) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(25) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650.

(26) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(27) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision B.05; Gaussian, Inc.: Pittsburgh, PA, 2003.

(28) Ross, A. M.; Pohl, T. M.; Piazza, K.; Thomas, M.; Fox, B.; Whalen, D. L. *J. Am. Chem. Soc.* **1982**, *104*, 1658.

(29) Ford, G. P.; Smith, C. T. *J. Am. Chem. Soc.* **1987**, *109*, 1325.

(30) Laufer, W.; Meiers, R.; Hölderich, W. *J. Mol. Catal. A: Chem.* **1999**, *141*, 215.