The Peroxy Acid Dioxirane Equilibrium: Base-Promoted Exchange of Peroxy Acid Oxygens

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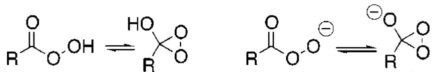
Peroxy acids, **1**, are among the most versatile oxidation reagents in organic chemistry. Olefin epoxidation[1] and Baeyer−Villiger oxidation of ketones[2] are signature reactions of peroxy acids but other oxidative transformations utilizing peroxy acids also have frequent synthetic application.[3] Even oxygen insertion into carbon−hydrogen bonds, a reaction difficult to achieve by nonradical methods, has been reported to result from the reaction of alkanes with trifluoroperoxyacetic acid.[4] The mechanisms of the reactions of peroxy acids have been of longstanding interest[5] and recently there have been several computational studies reported on the mechanism of peroxy acid reactions. The chemistry of peroxy acid conjugate bases, **2**, has also been the focus of several mechanistic studies although these species appear to have received little, if any, theoretical consideration.[6]



Mimoun[7] has suggested the possible intervention of a peroxy acid dioxirane isomer, **3**, in the chemistry of peroxy acids although there is no experimental evidence for and little theoretical consideration of this species. Given the importance of peroxy acids in synthesis and the fact that dioxiranes are now established as one of the most potent of oxidants, we have undertaken a computational and experimental study to assess the relevance of hydroxydioxirane **3** and its conjugate base **4** in the chemistry of peroxy acids and their conjugate bases. Our computations suggest that an alkoxy dioxirane is readily accessible from the peroxy acid conjugate base, and consistent with this, we observe a base-promoted interchange of peroxy acid peroxide oxygens.

The hydroxydioxirane forms of 7 peroxy acids are found to be true isomers at the B3LYP/6-31G(d)[8] level of theory[9] (Table 1). The corresponding conjugate bases of the dioxirane and the percarboxylates are also found to be isomers. The energy differences between the two isomers are relatively large in the neutral species, but much smaller in the anions, suggesting that under basic conditions the dioxirane isomer is in equilibrium with the peroxy acid. Indeed, the dioxirane isomer of trifluoroperacetate (R = CF_3) is lower in energy than the open form by 3.6 kcal/mol.

Table 1. Relative B3LYP Electronic Energies of Isomers **1** (RC(O)OOH) and **3** and Their Anion Isomers **2** ($RC(O)OO^-$) and **4**

R	neutral E1−E3 (6-31G(d))[a]	anion E2−E4 (6-31G(d))[b]	anion E2−E4 (6-31+G(d,p))[b]	anion G2−G4 (6-31+G(d,p))[b,c]
H	17.5	7.6	11.8	4.1
CH_3	18.6	8.7	12.5	5.8
CF_3	14.4	−3.6	1.2[d]	−2.0[e]
Ph	21.4	3.7	7.4	5.5
m-ClPh	20.9	3.1	6.3	5.4
p-NO_2Ph	20.1	3.5	7.0	1.6
C_6F_5	19.0	3.6	7.7	1.9

[a] Peroxy acids (RC(O)OOH, **1**, and the dioxirane isomers **3**. [b] ($RC(O)OO^-$) **4** and their anions, **2**. [c] Solution phase free energies of the anions in dichloromethane using the COSMO solvation model. [d] With the triple-ζ, 6-311+G(d,p) basis set, this value is 2.4 kcal/mol. [e] When this calculation is done in water using the COSMO algorithm, this value is −4.0 kcal/mol.

When calculations of the relative electronic energies of the anions are done with the larger 6-31+G(d,p) basis set, which includes diffuse functions to better describe the electron density around the anionic oxygen, there is a dramatic increase in the Δ*E* values between the anionic isomers. None of the dioxirane isomers are lower in energy than their corresponding peroxy acids with this larger basis set. When the structures were re-optimized by the same method, but now including the conductor-like solvation model (COSMO),[10] with a dielectric constant of 8.3 (that of dichloromethane), the substituent−anion interactions are attenuated, as the hydroxydioxirane is better solvated than the peroxy acid for all R, e.g. for R = CF_3, $\Delta G_{\text{solv}} = -52.5$ kcal/mol for the hydroxydioxirane versus −49.6 kcal/mol for the peroxy acid.

Transition state optimizations for the isomerizations of the anions using the quadratic synchronous transit-2 (QST2) algorithm[11] reveal structures in which the terminal (anionic) oxygen is raised out of plane to close the distance between it and the carbonyl carbon. The barriers to ring-closure are small for each of the peroxy acid anions studied, with values of 9.9, 11.3, and 4.6 kcal/mol for performate, peracetate, and trifluoroperacetate, respectively. The imaginary vibrational modes corresponding to these ring-closings were −160.71, −144.65, and $-162.98\ \text{cm}^{-1}$, with the most negative corresponding to the earliest, lowest barrier transition state (R = CF_3), and the most positive corresponding to the latest, highest barrier transition state (R = CH_3). The barrier heights are easily rationalized by considering that as the carbonyl carbon becomes more electron-deficient, the barrier to ring-closing is lowered.

Given the importance of the substitutent/anion interactions in the alkoxy dioxirane clear from the results in Table 1, the transition structures were re-optimized using the 6-31+G(d,p) basis set, to yield barriers of 12.8, 13.6, and 7.0 kcal/mol for R = H, CH_3, and CF_3, respectively. However, when the COSMO solvation model is included, the substituent/anion interactions are again attenuated, and the barriers to isomerization are lowered, e.g. 6.8 kcal/mol for performate.[12] Since the relative energies of the hydroxydioxirane isomers were much higher than the neutral

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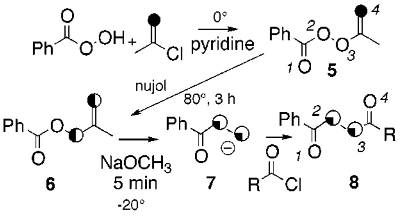
Scheme 1

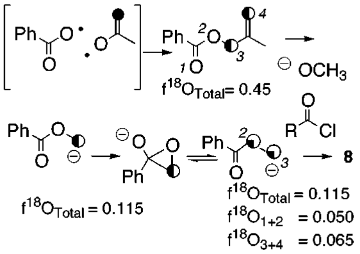


peroxy acids, we did not pursue extensive calculations of the transition state structures of their isomerization.

Labeled peroxybenzoic acid was prepared according to Scheme 1. Thus, acetyl chloride labeled with ^{18}O in the carbonyl carbon[13] was reacted with peroxybenzoic acid and the labeled unsymmetric diacyl peroxide **5** was heated in Nujol at 80 °C for 3 h ($\tau_{1/2} =$ 2.8 h) to partially scramble the oxygen label into the peroxide oxygen ($O_4 \rightarrow O_3$).[14] The position of the oxygen label in **5** was monitored by electron spray ionization tandem mass spectrometry (ESI-MS/MS). ESI-MS/MS of **5** labeled at O_4 gave an $[M + NH_4]^+$ adduct at *m/z* 198 for unlabeled and *m/z* 200 for the ^{18}O-labeled species.[15] In fact, comparison of these two adducts permitted determination of total label present in **5** labeled at any of the oxygens, $f(^{18}O_{Total}) = I_{200}/(I_{198} + I_{200})$. Collision-induced dissociation (CID) of the labeled adduct, *m/z* 200, gave characteristic fragments at *m/z* 141 and 139 for the labeled and unlabeled species, $[PhCOO/NH_4]^{+\bullet}$. Thus, CID on adduct *m/z* 200 from **5** labeled at either position O_3 or O_4 yielded only *m/z* 139, with no *m/z* 141 fragment, while **5** labeled at either O_1 or O_2 gave no *m/z* 139 adduct and only *m/z* 141. In this way, a decision about whether the label was on the benzoyl (O_1 and O_2) or acetyl side (O_3 and O_4) of **5** was determined by analysis of the CID spectrum, $f(^{18}O_{1+2}) = I_{141}/(I_{139} + I_{141}) \cdot f(^{18}O_{Total})$ defining this distribution.[15]

Heating **5** having $f(^{18}O_{Total}) = 0.45$ for 2 h at 80 °C resulted in substantial decomposition of the peroxide. Recovered **6** from this experiment (40% recovery) had the same $f(^{18}O_{Total})$ as starting **5**. None of the label on the acetyl side of **5** scrambles to the benzoyl side of the peroxide during thermolysis since $f(^{18}O_{1+2})$ is neglible for both **5** and **6**.[15] Treatment of this recovered peroxide with sodium methoxide[16] at −20 °C for 5 min led to complete consumption of **6** and formation of labeled sodium perbenzoate **7**. The −20 °C solution of **7** was treated with acetyl chloride or propionyl chloride and the diacyl peroxide **8** was recovered by chromatography. Analysis of **8** (R = Me) by ESI-MS/MS showed that $f(^{18}O_{Total}) = 0.115$, $f(^{18}O_{1+2}) = 0.050$, and $f(^{18}O_{3+4}) = 0.065$. We interpret these experiments to indicate that during the methanolysis of **6** the label scrambled from O_3 to O_2 in the peroxy anion such that the ratio $^{18}O_2$:$^{18}O_3$ = 1:1.3. If, rather than reaction with acid chloride the sodium perbenzoate **7** was converted to the peroxy acid and then to **8** by reaction with acid chloride and pyridine, the $f(^{18}O_{Total})$ and $f(^{18}O_{1+2})$ were identical to those determined for the direct conversion of the peroxy anion to **8**.

Scheme 2



The labeling data can be understood by the mechanism presented in Scheme 2. Thermolysis of the diacylperoxide gives a radical pair that partially scrambles the carbonyl label into the peroxide bond.[14] The total label in the molecule is not depleted but the distribution of label between O_4 and O_3 changes. Methanolysis[16] of the diacyl peroxide gives the peroxy anion which scrambles the label via the dioxirane anion, **4** with R = Ph. Reacylation of the peroxy anion gives a diacyl peroxide and MS analysis of that peroxide indicates that the label is now scrambled into the benzoyl side of the peroxide. Scrambling of peroxide label occurs readily in the anion, even at −20 °C.

We note that there are several examples of base-promoted reactions of peroxy acids reported in the literature. These include the decomposition of peroxy acids to oxygen and carboxylic acids,[17] the epoxidation of electron-deficient alkenes,[4] and the oxidation of sulfoxides to sulfones.[18] The computational and experimental studies reported here suggest that dioxiranes are accessible intermediates from peroxy acids, particularly in reactions involving peroxy acid conjugate bases, and it would seem advisable to keep this possibility in mind when considering mechanisms for peroxy acid reactions.

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Supporting Information Available: Experimental procedures, mass spectral data for labeled compounds, transition state structures, and Cartesian Coordinates for the rearrangement of **3** to **4** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) Attempts to find the transition structures for the isomerization of peracetate and trifluoroperacetate using the COSMO solvation model were unsuccessful. The result was usually a second-order saddle point, with relative energies of 8.4 and 8.9 kcal/mol for the peracetate and trifluoroperacetate, respectively. Thus, the barriers for the true transition structures must be less than these values. For these calculations, force constants were calculated numerically, as analytical second derivatives are not available with Gaussian 98 for this type of calculation.

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