**Responses to Reviewers' Comments on Manuscript egusphere-2025-1662**

(Acid-catalyzed hydrolysis kinetics of organic hydroperoxides: Computational strategy and structure-activity relationship)

## ***Reviewer 2***

**Reviewer:** **General comment**

*Organic hydroperoxides are formed during the photochemical oxidation of organic compounds and represent a non-negligible fraction of the atmospheric aerosol mass. This study introduces a computational strategy to evaluate the hydrolysis rate constants of organic hydroperoxides and uses this strategy to explore the dependence of hydrolysis rate on molecular structure of hydroperoxides and also on medium acidity. The study is well executed, the results are mostly sound, and the manuscript is well written. I believe that it can be published subject to several changes as described below.*

**Response:** Thanks for your insightful comments. We have made point-by-point responses in the following section.

**Reviewer:** **Special Suggestions and Comments**

**Reviewer:** 1). *The introduction section must be expanded a bit to make it easier to understand the chemistry of the processes under consideration. The two possible hydrolysis mechanisms, concerted single-step and two-step depicted in Figure 2b, must be introduced in the introduction section. Adding a variant of Figure S7 to the introduction section would also be beneficial. The meaning of the proton model needs to be defined on the first occurrence. Is it "proton model" or "proton donor model"?*

**Response:** Thanks for the comment. We have expanded the introduction to include a clearer explanation of the acid-catalyzed hydrolysis mechanisms. Please see lines 49 - 53 in the revised manuscript. Regarding the term used, based on literature (Agmon et al., 2016; Schran et al., 2020; Fournier et al., 2015), "protonated water clusters, $H^+(H_2O)_n$" is consistently used to describe molecular clusters formed between $H^+$ and water molecules via hydrogen bonding. Thus, we have replaced "proton model" with "protonated water cluster model" or "$H^+(H_2O)_n$ model" throughout the manuscript, adding the definition at its first occurrence. Please see lines 14 - 16, 66 - 71, 77, 101 - 109, 128, 136, 138, 318 in the revised manuscript.

**Reviewer:** 2). *A highly non-monotonic dependence of the hydrolysis rate constant on the size of the proton model (the number of water molecules clustered around hydronium ion) is observed. One and three water molecules produce a nearly similar effect while with two water molecules the rate is significantly slower. This effect needs to be discussed, and its origin must be established.*

**Response:** We thank the reviewer for pointing out this issue. We have double-checked the non-monotonic dependence of the hydrolysis rate constants on the size of the protonated water cluster models. We found that in the original version of the manuscript, the ROOH molecule first replaced one $H_2O$ molecule in the protonated water cluster model $H^+(H_2O)_4$ (i.e., $H_3O^+(H_2O)_3$), differing from the direct protonation of ROOH by the other three protonated water cluster models $H^+(H_2O)_{1-3}$ (i.e., $H_3O^+(H_2O)_{0-2}$) during the reaction. This discrepancy could be the reason for the non-monotonic dependence of the hydrolysis rate constants. After careful consideration, we recognized that we should not break the protonated water cluster model. Therefore, we recalculated the rate constants for the reaction involving direct protonation of ROOH by $H^+(H_2O)_4$ and found that the updated hydrolysis rate constants decrease monotonically with increasing cluster size ($n$ = 1 to 4) for the reactions of ROOHs with $H^+(H_2O)_n$. We have revised the corresponding part in the manuscript accordingly. Please see line 141, Fig. 1 in the revised manuscript, and Figs. S3-S6 in the SI.

**Reviewer:** 3). *The largest enhancement in the hydrolysis rate is reported for the nitrogen-containing hydroperoxides, and it is assumed that the amino groups remain unprotonated. This is grossly incorrect, as in the pH range considered in this study the fraction of the free, unprotonated form of $-NH_2$ and $-N(CH_3)_2$ will be exceedingly small. To calculate the correct* *lifetime of these N-containing hydroperoxides, the fraction of the unprotonated form must be evaluated based on $pK_b$. The latter can be estimated based on the data available for similar compounds in the literature or calculated explicitly from the Gibbs free energy of the amino group protonation evaluated by DFT.*

**Response:** We appreciate the comment and agree that $-NH_2$ and $-N(CH_3)_2$ groups are predominantly protonated (i.e., $-NH_3^+$ and $-NH(CH_3)_2^+$) under the pH conditions considered in this study. However, the rapid reaction of ROOHs with the unprotonated $-NH_2$ and $-N(CH_3)_2$ species may shift the equilibrium $-NH_3^+$ ($-NH(CH_3)_2^+$) + $H_2O \leftrightarrow -NH_2$ ($-N(CH_3)_2$) + $H_3O^+$ toward the unprotonated form. Recent studies (Ji et al., 2020; Shi et al., 2024) have reported fast reactions between small α-dicarbonyls and amines or ammonia in acidic aqueous solutions, with corresponding products detected experimentally. This indicates the ROOHs with unprotonated $-NH_2$ and $-N(CH_3)_2$ can still participate in the reaction. In addition, Enami et al. (2010) found that trimethylamine remains largely unprotonated at the air-water interface even at pH 4.0. These findings suggest that both aqueous-phase and interfacial transformations of α-$NH_2$/$N(CH_3)_2$-substituted ROOHs in unprotonated form are plausible, highlighting their significance in atmospheric aqueous-phase chemistry. We have incorporated this discussion in the revised manuscript. Please see lines 209 - 216 in the revised manuscript.

**Reviewer:** 4). A free carbocation is shown in Figure S7. Is using an implicit solvent model sufficient to stabilize this carbocation? How much would the reaction energetics change if this carbocation is stabilized explicitly, e.g., by hydration?

**Response:** Thanks for the comment. To evaluate hydration effects on the reaction energetics, we conducted additional calculations using $C(CH_3)_2(OCH_3)OOH$ as a model compound. We identified the most stable monohydrated configurations for both the reactant (R, $C(CH_3)_2(OCH_3)OOH$) and its corresponding carbocation intermediate (IM), and compared the reaction energetics with those obtained using only the implicit solvation model. As shown in Fig. R1, adding one explicit $H_2O$ molecule to R and IM increases the reaction energetics by only 1.46 or 1.74 kcal $mol^{-1}$, respectively, indicating that hydration has a minimal effect on the overall reaction energetics. This discussion has been added to the revised manuscript. Please see lines 227 - 229 in the revised manuscript and Fig. S14 in the SI.

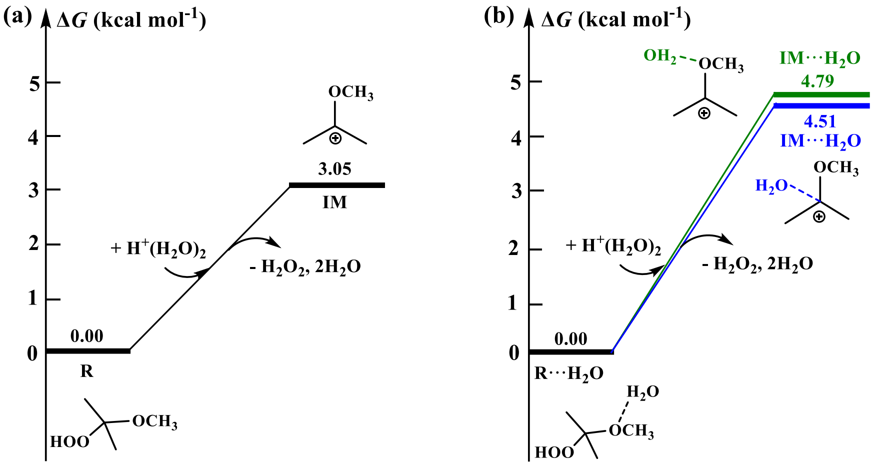

**Figure R1. Changes in reaction energetics for carbocation intermediate formation during acid-catalyzed hydrolysis of $C(CH_3)_2(OCH_3)OOH$ under (a) implicit solvation only vs. (b) explicit monohydration. Free energies (*G*) computed at SMD/M06-2X/6-311++G(3df,2pd)//M06-2X/6-31+G(d,p) level. R and IM denote the reactant and carbocation, while R ··H2O and IM ··H2O are their monohydrated forms.**

**Reviewer:** 5). *Having read the title, I assumed that the paper will eventually present some kinds of quantitative structure-reactivity relationship. It did not and it is a pity, as a pretty large dataset has been produced. Is it possible to relate the rate constant with some parameters of the substituents, e.g., similar as in the Hammett equation? This would be very beneficial for the modeling studies.*

**Response:** Thanks for the suggestion. We agree a quantitative structure-reactivity relationship would be highly valuable. Similar to Hammett constants the reviewer mentioned, Taft ($\sigma^*$) constants are widely used to quantify substituent effects in aliphatic systems (Perrin et al., 1981). We have now established correlation equations linking $\sigma^*$ to the logarithms of the acid-catalyzed hydrolysis second-order rate constants (log $k_A$) for the selected ROOH model compounds. For more detailed information, please see lines 118 - 124, 268 - 278 in the revised manuscript and Figs. S15-S16 in the SI.

**Reviewer:** 6). L35: more hydrophilic HYDROperoxide groups

**Response:** Thanks for the comment. We have revised it. Please see line 38.

**Reviewer:** 7). L45: remove “extremely”

**Response:** Thanks for the comment. We have revised it. Please see line 47.

## References

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