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Heteroatom Tuning of Bimolecular Criegee Reactions and Its Implications

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Abstract: High-level quantum chemical calculations have been performed to understand the key reactivity determinants of bimolecular Criegee + H-X (X = O, S, Se, and Te) reactions. Criegee intermediates are implicated as key intermediates in atmospheric, synthetic organic and enzymatic chemistry. Generally, it is believed that the nature and location of substituent at the Criegee carbon plays a key role in determining the reactivity. However, the present work suggests that it is not only the Criegee substitution, but the nature of heteratom in H-X that also plays a crucial role in determining the reactivity of the Criegee-H-X interaction. The barriers for the Criegee-H-X reactions satisfy an inverse correlation with the bond strength of X-H in H-X, and a direct correlation with the first pK_a of H-X. This heteroatom tuning causes a substantial barrier lowering of 8-11 kcal/mol in the Criegee reaction barrier in going from H-O to H-Se. The reactions of Criegee intermediate with water or acid catalysis, thioaldehydes could be detected in a hydrogen-bonded complexed state, which is significantly more stable than their uncomplexed form. As a result, simpler aliphatic thioaldehydes could be selectively synthesized in laboratory, which, otherwise, has been a significant synthetic challenge because of their ability to oligomerize.

Understanding Criegee chemistry has become a hot topic of research in the recent past. Criegee intermediates are carbonyl oxides that are principally produced in the atmospheric ozonolysis and hydroxyl radicals, organic acids, hydroperoxides, nitrates, sulfates, and zwitterionic carbonyl oxides that are principally produced in the ozone-elimination reaction cycles of flavin and Baeyer-Villiger monooxygenases that provide an environmentally benign route for forming enantiopure drugs.14 Because of its broad profile, factors influencing Criegee reactivity have been extensively investigated by means of experimental and theoretical means. The nature and location of the derivatives on the Criegee intermediate significantly tunes its reactivity.16 Criegee intermediates having a methyl substituent in the anti position react faster than Criegee intermediates having a methyl substituent in syn position. Criegee intermediates with electron withdrawing substituents and zwitterionic character react faster than those having electron releasing substituents. Substitution in the Criegee intermediate can cause up to ten orders of magnitude differences in its reactivity. The unimolecular and bimolecular reactions of the Criegee intermediate CH_3CHOO represent one of the well-studied conformer-dependent Criegee reactivity profile.

Criegee intermediates participate in various bimolecular reactions. Though the effect of Criegee substitution in bimolecular reactions has been well explored, the effect of substituent in the non-Criegee reacting partner is less so. For example, the most probable bimolecular Criegee reaction in troposphere is the reaction with water. However, it is not clear whether the nature of heteratom X in H-X (X = O, S, Se and Te) would alter the energetics of the Criegee-H-X reaction i.e., does there exist any correlation between the Criegee reaction barrier and the heteroatom nature? If yes, what are its implications? If not, what other factors influence the Criegee-H-X reaction? A detailed knowledge of these determinants may provide general guidelines for synthesizing useful organic compounds, which are otherwise difficult to synthesize, and in addition, may also reveal new source of atmospherically important thioaldehydes, thus improving molecular details of existing atmospheric models.

Here it is shown using high-level quantum chemical calculations that such a tuning of the barrier for the Criegee-H-X reaction is indeed possible and more importantly, this heteroatom tuning is also found to be a general trend among other atmospherically important reactions. Firstly, examining the gas-phase reaction between the simplest Criegee intermediate, CH_3OO and H-X; the reaction energetics are computed by performing single point calculations using the coupled cluster single and double substitution method with a perturbative treatment of triple excitations (CCSD(T)) and the augmented correlation-consistent triplet zeta basis set aug-cc-pVTZ at the M06-2X/aug-cc-pVTZ optimized geometries. (See Supporting Information for details). The CH_3OO-H_X reaction is a multi-step reaction that converts the Criegee moity, -COO into -C=O functional group. The reaction consists of two main steps namely chalcogen hydride (H_X) addition and hydrogen peroxide (H_2O) elimination with the latter step being the rate determining step. Overall, the reaction is at least 24.1 kcal/mol exoergic. For the CH_3OO-H_2O reaction, the addition step has a barrier of 9.2 kcal/mol relative to Int, whereas the elimination step has a barrier of 49.1 kcal/mol relative to Int, H_2C(OH)(OOH). These barriers are significantly reduced upon changing the heteroatom X in H-X. For the CH_3OO-H_2S reaction, the

![Figure 1: CClSD(T)/aug-cc-pVTZ/M06-2X/aug-cc-pVTZ calculated zero-point-corrected reaction profiles for the reaction between the simplest Criegee intermediate, CH_3OO and various chalcogen hydrides, H-X (X = O, S, Se and Te). The energies are given in kcal/mol units.](image)

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Supporting information for this article is given via a link at the end of the document.
addition barrier is just 2.5 kcal/mol and the H₂O elimination barrier is 44.1 kcal/mol. For the H₂Se and H₂Te reactions, the addition steps involve barriers < 1.0 kcal/mol whereas the barriers for the elimination step are lowered to 41.1 and 38.4 kcal/mol, respectively. It is important to mention here that the hydroperoxide (ln₂ or ln₃) in the addition step is formed with an excess energy of at least 42.2 kcal/mol that significantly compensates the high barrier for the elimination step. These results clearly suggest that there is a correlation between the Criegee reaction barrier and the nature of X in H₂X. This correlation can be explained in terms of the X-H bond length or atomic radius of X (Figure 2). Moving down the chalcogen group, the atomic radius increases and the H-X bond becomes weaker. Since the H₂X addition to Criegee intermediate involves breakage of one of the H-X bonds, a weaker H-X bond in H₂X would promote the H₂X addition across the Criegee moiety. Oxygen atom has the shortest atomic radius of 66 pm, and the O-H bond (96 pm) with an enthalpy of 483.3 kJ/mol is the strongest X-H bond whereas Te atom has the largest radius (158 pm), and the Te-H bond (169 pm) with an enthalpy of 267 kJ/mol is the weakest X-H bond. This explains why the H₂O reaction has the largest barriers whereas the H₂Te reaction has the lowest ones. The barriers for the H₂X reactions also directly correlate with first pKₐ of H₂X (Figure S1). H₂O has the largest first pKₐ of 15.7 where H₂Te has the lowest first pKₐ of 3.0, which is consistent with the barrier trends. This implies that chalcogen hydrides with heteroatoms lying in the lower end of periodic table would react faster with Criegee intermediate.

We then examined the reactions of the next larger Criegee intermediate, CH₃CHO with H₂X. There are two conformers possible for CH₃CHO: (i) anti-CH₃CHO, and (ii) syn-CH₃CHO. We studied reactions involving both of these conformers. The calculations suggest that the barriers for the anti-CH₃CHO reactions are relatively lower than those for the syn-CH₃CHO reactions (Figure 2), which is consistent with previous studies suggesting that anti-CH₃CHO is more reactive than syn-CH₃CHO towards bimolecular reactions. For the H₂O or H₂S reactions, the addition barrier for the anti-CH₃CHO case is ~5.0 kcal/mol lower than that for the syn-CH₃CHO case. More importantly, the calculated barriers for the addition and elimination steps of the anti- and syn-CH₃CHO-H₂X reactions correlate well with the bond length of H-X bond of H₂X (Figures S2 and S3) or their first pKₐ values. In going from H₂O → H₂Te, the addition barrier for the anti-CH₃CHO case is lowered by 7.8 kcal/mol and the H₂X addition occurs in a near-barrierless manner for X = Se or Te. For the syn-CH₃CHO case, the larger barrier lowering of 11.0 kcal/mol is observed in moving from H₂O → H₂Te. Since the H₂X addition to anti or syn-CH₃CHO should lead to the same hydroperoxide, (HX)(CH₃)HCOOH, we only examined H₂O elimination from the anti-CH₃CHO + H₂X reaction. The barrier for the H₂O elimination from the (HX)(CH₃)HCOOH is lowered from 45.3 kcal/mol to 37.3 kcal/mol in going from H₂O → H₂Te, which again inversely correlates with the X-H bond strength and directly correlates with first pKₐ of H₂X.

The calculated addition and elimination barriers for the reactions of (CH₃)₂COO with H₂X also satisfy a correlation with the X-H bond length (Figures 2, S2 and S3) or first pKₐ of H₂X, which is indicative of the fact that the correlation between the Criegee reaction barrier and the nature of X in H₂X is a common reactivity trend, and is independent of the structure of the Criegee intermediate involved in the reaction. The comparative analysis suggests that the calculated elimination barriers for the (CH₃)₂COO reactions are not only lower than those for the syn-CH₃CHO, but are the lowest ones. For example, the elimination barriers for H₂O and H₂Te reactions are lowered from 49.1 and 38.4 kcal/mol to 43.9 and 36.2 kcal/mol, respectively, in going from CH₃OO to (CH₃)₂COO. This is due to the fact that the substitution at the hydroperoxyl carbon of (HX)(CH₃)HCOOH promotes the H₂O elimination, i.e., greater the extent of substitution, lower would be the elimination barrier.

Figure 2. CCSD(T)/aug-cc-pVTZ/M06-2X/aug-cc-pVTZ calculated zero-point-corrected barriers (top panels: addition reactions and bottom panels: elimination reactions) for the reactions between various Criegee intermediates and chalcogen hydrides. The barriers are given in kcal/mol units. The correlation between the calculated barriers for the reactions of the simplest Criegee intermediate, CH₃OO with chalcogen hydrides and X-H (X = O, S, Se, and Te) bond distances are given in right side panels.

Figure 3. CCSD(T)/aug-cc-pVTZ/M06-2X/aug-cc-pVTZ calculated zero-point-corrected reaction profiles for the reactions between various Criegee intermediates and hydrogen sulfide with (bottom panel) and without water catalyst (top panel). The energetics are given in kcal/mol units.

The correlation between the Criegee reaction barrier and the nature of heteroatom in H₂X may have important implications for atmospheric and synthetic organic chemistry. For example, thioformaldehyde (HCHS) has been detected in dark clouds, the interstellar clouds and circumstellar envelope around an asymptotic giant branch star. Few lines of HCHS have also been identified in the Orion KL nebula.
and in the atmosphere of the comet Hale-Bopp. The present calculations suggest that HCHS in the atmosphere could be formed in a near-barrierless manner from the reaction between CH$_2$OO and H$_2$S. This reaction could be feasible in the atmosphere because the estimated H$_2$S concentration in the lower troposphere lies in the 1–1000 ppt range. Another important implication of our results is for the laboratory synthesis of thioaldehydes. In synthetic organic chemistry, thioaldehydes are used as key building blocks. The Diels–Alder additions of thioaldehydes and thiketones offer useful routes for the incorporation of sulfur heteroatoms into the synthesis of heterocycles such as substituted pyridines, furans, and dihydrothiopyrans or natural products.

However, experimental detection of simpler aliphatic thioaldehydes such as HCHS has been a significant challenge because it is unstable at room temperature and readily trimersizes to t-trithiane. From this work suggest that if the Criegee-H$_2$S reaction could be performed under water or acid catalysis (Figure 3 and Table S2), thioaldehydes would be barrierlessly formed in an extensively hydrogen-bonded complexed state, which is significantly more stable than their uncomplexed one. Thus, the catalyzed Criegee-H$_2$S reaction could selectively produce thioaldehyde, avoiding any oligomerization. This could prove useful synthetic guidelines for the laboratory synthesis of simpler thioaldehydes that does not require harsh experimental conditions.

In short, high level quantum chemical calculations reveal an inverse correlation between the Criegee-H$_2$X reaction barrier and the bond length of the X-H bond in H$_2$X or a direct correlation with the first pK$_a$ of H$_2$X. This heteroatom-induced tuning causes a 8-12 kca/mol lowering in the reaction barrier, thus significantly impacting the overall energetics of the Criegee-H$_2$X reaction. Considering that bimolecular chemistries are abundant in atmosphere, the heterolysis tuning of the reaction barrier could be a common reactivity determinant of atmospheric addition reactions.

**Keywords:** Criegee Intermediate • organocatalysis • water catalysis • CCSD(T) theory • atmospheric chemistry • chalcogen hydride • Thioaldehydes

The calculated barriers for the bimolecular Criegee-H₂X reactions inversely correlate with the bond strength of X-H bond of H₂X or directly correlate with first pKₐ of H₂X. Thus, it is not only the Criegee substitution, but the nature of heteroatom in H₂X that also plays a crucial role in determining the reactivity of the Criegee-H₂X interaction.