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Hydrolysis of *N*-Sulfinylamines and Isocyanates: A Computational Comparison

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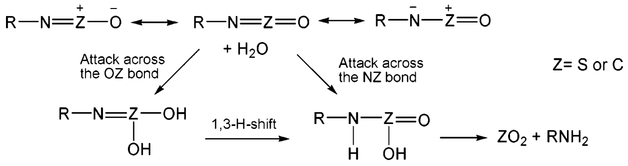
A comparative study of the concerted hydrolysis of H-, CF_3-, CH_3-, and Ph-substituted *N*-sulfinylamines (R−NSO) and isocyanates (R−NCO) was performed using B3LYP/6-31+G(2d,2p). The "two-water-molecule" model was found to be sufficient for a proper description of the hydrolysis reaction for both classes of compounds. Despite their overall similar reactivity, *N*-sulfinylamines react across both the N═S and the S═O bonds, whereas isocyanates hydrolyze predominantly through the N═C bond, in agreement with the proton affinities of the nitrogen and oxygen atoms. The charges on sulfur (N═S═O) and carbon (N═C═O) were found to correlate well with the activation enthalpy for hydrolysis. While the reactivity of an *N*-sulfinylamine toward water increases with increasing electron-withdrawing ability of the substituent, the substituent effect on isocyanates becomes notable only in the presence of the strongly electron-withdrawing CF_3 group.

1. Introduction

N-Sulfinylamines, R−N═S═O, were synthesized for the first time more than a century ago[1] and have since found wide application in synthetic organic chemistry. Various reactions resulting in the formation of N,S-heterocycles have been explored, including 1,2-cyclo-, 1,3-dipolar-, and 1,4-cycloaddition reactions, where *N*-sulfinylamines can act as dienes and dienophiles,[2,3] as well as reactions with "active" hydrogen atoms.[3] When handling a compound, one of the first properties of interest is often its reactivity with water. Curiously, therefore, while the synthetic value of *N*-sulfinylamines has been well explored, their hydrolysis, a seemingly straightforward reaction, is not well understood. In particular, the fact that the substituent R has a dramatic effect on the reactivity of compounds R−N═S═O with water[3,4] has not been investigated extensively. While the aliphatic *N*-sulfinylamines are reported to hydrolyze readily, the aromatic compounds and *N*-sulfinylhydrazides (R−CO−NH−N═S═O) are less moisture-sensitive, and *N*-sulfinylhydrazines (R−NH−N═S═O) do not react with water.[4] Many of these general observations are unfortunately not supported by quantitative data, and there are only a few kinetic studies on the hydrolysis of aromatic *N*-sulfinylamines.[5,6] Consequently, an understanding of the effect of the substituent on the reactivity of *N*-sulfinyl species with water is desirable.

While data from the related and more thoroughly studied alcoholysis reaction could be used for reference,[3,7−10] another interesting perspective for comparison is offered in the form of the much better known isocyanates, R−N═C═O. At first glance, both *N*-sulfinylamines and isocyanates possess terminal cumulated double bonds[11,12] and similar resonance structures[2,11] as shown in Scheme 1, where Z is either sulfur or carbon, and could therefore be expected to show similar reactivities. However, in contrast to *N*-sulfinylamines, for isocyanates the aromatic compounds were shown to be more reactive than the aliphatic compounds.[12,13]

SCHEME 1



With a few exceptions,[11,14,15] the known reactions of *N*-sulfinylamines and isocyanates proceed through interaction across the N═S or N═C bond, and if both π and σ bonds are broken, then this results in the evolution of SO_2 or CO_2, respectively.[2] This is the case in their hydrolyses, where primary amines are formed as products (Scheme 1). The neutral hydrolysis is a slow process for both *N*-sulfinylamines and isocyanates, but the reaction can be catalyzed by both acids and bases. In the base-catalyzed reaction, the complexation of a tertiary amine to water increases the nucleophilicity of the water molecule and thus facilitates the hydroxylation of the sulfur or carbon atom, with hydroxylation being the rate-determining step of the reaction.[5,16] In this respect, the importance of the formation of dimeric and trimeric agglomerates of water or alcohol molecules has been described,[9,17−19] and the participation of chains of water molecules in hydrolysis reactions is supported by the rate increase in non-coordinating solvents.[5,16] The similarity of the hydrolyses of *N*-sulfinylamines and isocyanates seems to be established from a rough comparison of available kinetic parameters, even though a thorough comparison is impossible due to the lack of identical experimental conditions. The enthalpies of activation of 5.7 and 5.9 kcal mol^{-1}, along with activation entropies of −51 and −58 eu, determined for the base-catalyzed hydrolysis[5] and methanolysis,[7] respectively, of *N*-sulfinylaniline (Ph−NSO) do not differ much from the values of 8.2 kcal mol^{-1} and −44.5 eu given for the noncatalyzed methanolysis of *p*-chlorophenyl isocyanate.[16] The nearly identical kinetic isotope effects k_H/k_D of 1.73[5] and 1.65[17] seem to further support the like reactivity of these two classes of compounds.

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TABLE 1: Selected Geometrical Parameters (Bond Lengths in pm, Angles in deg), Dipole Moments (μ, D), and Atomic Charges (q, au) of *N*-Sulfinylamines I−IV

	I	II	III	IV
S═O	146.9	146.1	147.5	148.1
	(145.1 ± 0.5)[a]		(146.6 ± 0.4)[b]	(145.84)[c]
N═S	152.4	153.0	152.6	153.4
	(151.2 ± 0.5)[a]		(152.5 ± 0.4)[b]	(151.60)[c]
H−N or C−N	102.4	142.5	145.5	139.3
	(102.9 ± 1.0)[a]		(142.1 ± 0.5)[b]	(140.12)[c]
NSO	120.0	120.3	119.6	120.4
	(120.4 ± 0.5)[a]		(117.0 ± 2)[b]	(120.61)[c]
HNS or CNS	115.7	126.3	124.5	132.3
	(115.8 ± 1)[a]		(126.0 ± 2)[b]	(131.23)[c]
μ	0.88	1.92	1.84	2.69
	(0.911 ± 0.003)[a]		(1.70 ± 0.02)[d]	(2.30 ± 0.06)[e]
q(O)	−1.115	−1.077	−1.127	−1.121
q(S)	1.942	1.983	1.878	1.828
q(N)	−1.240	−1.153	−1.191	−1.249
q(H or C)	0.414	2.014	0.399	0.374

[a] Experimental from ref 29 where distances are reported in angstroms. [b] Experimental from ref 30 where distances are reported in angstroms. [c] Experimental from ref 31 where distances are reported in angstroms. [d] Experimental from ref 32. [e] Experimental from ref 33.

TABLE 2: Activation Enthalpies[a] ($\Delta H^{\ddagger}_{298}$, kcal mol^{-1}) for the Reaction of *N*-Sulfinylamines I−IV with 1−3 Water Molecules across the S═O (a) and N═S (b) Bonds and for the Consecutive 1,3-Hydrogen Shift[b] in the Reaction across the S═O Bond

	I		II		III		IV	
n H_2O	a	b	a	b	a	b	a	b
1	29.8	30.3	28.6	28.9	30.5	32.5	31.8(32.4)	35.7
	(31.0)		(30.4)		(31.4)		(32.4)	
	[21.9]		[20.4]		[20.2]		[16.9]	
2	12.9	11.1	10.8	11.3	15.0	14.2	16.7	18.8
	(20.8)	(18.3)	(19.7)	(19.1)	(22.9)	(21.1)	(24.3)	(24.8)
3	4.1	0.9	−3.0	−1.3	6.8	2.6	8.4	7.3
	(19.2)	(15.7)	(13.0)	(14.8)	(21.9)	(16.3)	(22.4)	(19.9)

[a] Reaction barriers are based on the enthalpies of the reactants. Results based on the enthalpies of the complexes are shown in parentheses. [b] Given in square brackets.

The mechanism for hydrolysis was proposed to consist of hydroxylation of sulfur or carbon and protonation of the NSO or NCO group (Scheme 1).[5,18] This was confirmed in computational studies for the hydrolysis of *N*-sulfinylaniline with 1−5 water molecules[20] and for isocyanic acid in the presence of 1−3 water molecules.[21] In fact, two mechanisms are possible, a one-step reaction across the N═S or N═C bond and a two-step reaction across the S═O or C═O bond with the formation of sulfurimidic or carbonimidic acid and a subsequent 1,3-hydrogen shift to give the unstable sulfinamic or carbamic acids, respectively (Scheme 1). Interestingly, while both mechanisms are feasible for *N*-sulfinylaniline,[20] isocyanic acid predominantly reacts through the N═C bond.[21] After all of the similarities in reactivity listed above, such a dissimilarity is not entirely unexpected, though, because the two cumulated systems are electronically rather different. While the two π bonds in the NSO group are parallel and are best described as a conjugated system,[22,23] those in the NCO group are orthogonal,[16] but the effect of this difference in electronic structure on the reactivity toward water is not immediately obvious.

In this paper, we present the comparative study of the hydrolysis of substituted *N*-sulfinylamines and isocyanates with 1−3 water molecules to determine the relative reactivity within and between these classes of compounds, the preferred mechanism, as well as any substituent effect on the activation energy or mechanism that would account for the experimental findings.

2. Computational Details

All calculations were performed with the Becke3[24]−Lee, Yang, and Parr[25] hybrid density functional (B3LYP)[26] with the 6-31+G(2d,2p) basis set, using the Gaussian 98[27] and Gaussian 03[28] suites of programs. We have chosen this model chemistry based on its very good performance in the reproduction of experimentally observed geometries and dipole moments of *N*-sulfinylamines[29−33] and isocyanates.[34−38] The accuracy of the calculations was verified by the counterpoise correction (CP) method,[39] in that basis set superposition errors of less than 0.7 and 1.3 kcal mol^{-1} were determined with geometry optimization for the ternary (CP = 3) and quaternary (CP = 4) complexes of *N*-sulfinylaniline with two and three water molecules, respectively.[20] All geometries were fully optimized. In several cases, geometrical constraints were used in preliminary optimizations, followed by the release of all constraints and a tight optimization. The nature of the saddle points was verified by frequency calculations.

We chose to use gas-phase calculations throughout because although it is known that the rates of hydrolysis or alcoholysis reactions of *N*-sulfinylamines[5,9] and isocyanates[16] increase with increasing solvent polarity the specific interactions of the reactant with the solvent are believed to have a more significant effect on the reaction rate and on the number of participating water molecules.[5,9,16,18]

To be consistent with our previous paper on the hydrolysis of *N*-sulfinylaniline,[20] we will use the enthalpy term (ΔH_{298} and $\Delta H^{\ddagger}_{298}$, kcal mol^{-1}) throughout. The electronic and zero-point energy (unscaled) corrected energies, the enthalpies of the modeled molecules, complexes and transition states, as well as the free energies, where these were used in estimations of rate constants, are summarized in Table S1 of the Supporting Information. The entropy contribution $-T\Delta S$ for hydrolysis of the *N*-sulfinylamines, averaged for the different substituents and based on the prereaction complexes, consists of 5.9 kcal mol^{-1},

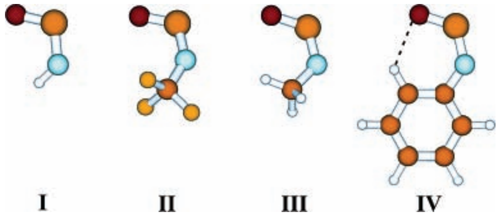

Figure 1. Optimized *N*-sulfinylamines **I**−**IV**. The C−H···O interaction in **IV** is shown by the dotted line.

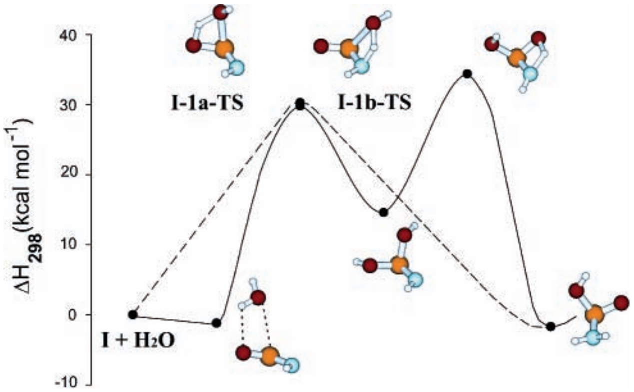

Figure 2. Enthalpy profile for the formation of sulfinamic acid in the reaction of *N*-sulfinylamine **I** with one water molecule. The solid line shows attack across the S═O bond, and the dashed line that across the N═S bond. Weak interactions in the complex are shown with dotted lines.

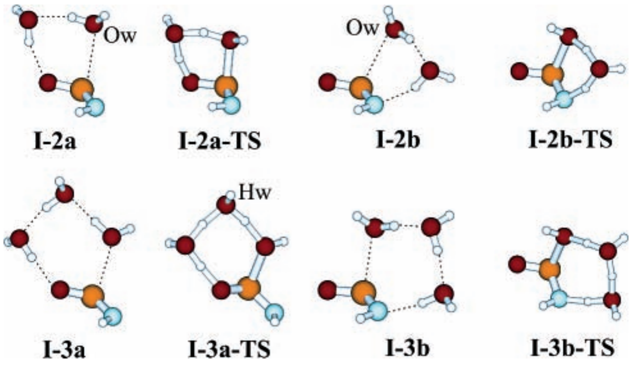

Figure 3. Optimized complexes and transition states for the reaction of *N*-sulfinylamine **I** with two and three water molecules (reaction across the S═O (**a**) and N═S bonds (**b**)). Weak interactions in the complexes are shown with dotted lines.

independent of the number of water molecules. However, when based on the energies of the reactants rather than the complexes, the entropy contribution to the reaction barrier, averaged for both *N*-sulfinylamines and isocyanates, was determined to be additive, with 11.5, 22.9, and 33.1 kcal mol^{-1} for one, two, and three water molecules, respectively.

Atomic charges and weak bonding interactions in the molecules, complexes, and transition states (TSs) were determined from the electron density within the quantum theory of Atoms in Molecules (QTAIM),[40] using the AIMPAC series of programs.[41] Only the relevant results are included in the present paper.

3. Results and Discussion

3.1. General Considerations. With a similar computational approach to that used in the study of the hydrolysis of *N*-sulfinylaniline (**IV**),[20] here we present the results for the reaction of *N*-sulfinylamines **I**−**III** and isocyanates **V**−**VIII** with one, two, and three water molecules; results for **IV** are included for comparison. We chose substituents H (**I** and **V**), CF_3 (**II** and **VI**), CH_3 (**III** and **VII**), and Ph (**IV** and **VIII**) for their distinctively varying electron-donating, electron-withdrawing, and conjugating abilities, aiming to gain insight into the effect of substituents on the hydrolysis reaction of these two classes of compounds.

Despite the fact that the formation of sulfinamic (for *N*-sulfinylamines) and carbamic (for isocyanates) acids is not the final stage of the hydrolysis, for the determination of the reactivity we only present calculations for the rate-determining step of the reactions. Given the possibility of two reaction mechanisms, we use "**a**" for the reaction across the S═O or C═O bond and "**b**" for the reaction across the N═S or N═C bond throughout this paper. The number of participating water molecules precedes the letter "**a**" or "**b**" in the identification of the species. The subscript "w" is used for the description of atoms belonging to water molecules involved in the interaction with the NSO and NCO groups.

3.2. Hydrolysis of *N*-Sulfinylamines. *3.2.1. N-Sulfinylamines.* Selected geometrical parameters, dipole moments, and atomic charges of *N*-sulfinylamines **I**−**IV** are summarized in Table 1, and the structures are shown in Figure 1. Unlike the almost linear isocyano group, the *N*-sulfinyl moiety is bent with an NSO angle of about 120°, and while both syn and anti configurations are possible, this paper deals with the more stable syn configuration.[30,31] Our report on the substituent effect on the preference of syn over anti configurations will be presented elsewhere. *N*-Sulfinylamines **I**−**IV** have a planar H−N−S−O or C−N−S−O skeleton. For *N*-sulfinylaniline (**IV**) this leads to conjugation of the N═S═O group with the aromatic ring,[42−44] and the oxygen atom is found to interact with an ortho hydrogen atom on the ring.[45] Figure 1 shows that **II** and **III** exhibit different conformations, a C−H bond in **III** being aligned with the S═O bond in a favorable interaction of bond dipoles, whereas such an alignment is avoided for a C−F bond in **II**. The conformation given for **III** in Figure 1 was confirmed experimentally, although the barrier for rotation of the CH_3 group was reported to be only 335 ± 15 cal mol^{-1}.[32] Table 1 shows that calculated dipole moments agree qualitatively with measured values.

A comparison of computational and available experimental geometrical parameters from Table 1 shows good agreement. With increasing electron-donating ability of the substituent, with **I** taken as the standard, a distinct elongation of the S═O bond is observed. In contrast, the variation in the N═S bond length is less pronounced, because nitrogen as the transmitter of the substituent effect shows a higher sensitivity to the combination of electronic and steric characteristics of the substituent. This also can be seen from the dramatic widening of the CNS bond angle in **II**−**IV** compared to that in HNS of **I**, with a maximum increase of 16.6° found for **IV**. The large bond angle on nitrogen in **IV** might, in part, be due to steric congestion, though. In that respect, it is interesting to note that **IV** prefers a widening of the nitrogen bond angle (by about 8° calculated from that in **III**) to a twist about the C−N bond, which would lead to a reduction in strength of both π-conjugation and C−H···O interaction.

The difference in electron demand of the substituents is also seen from the variation of the atomic charges within the NSO moiety. With increasing electron-donating ability of the substituent, going from **II** to **IV**, the positive charge on sulfur decreases. We will show below that this is important for the susceptibility of the sulfur atom to attack by water. The charges

TABLE 3: Selected Geometrical Parameters (Bond Lengths in pm, Angles in deg) of Complexes and Transition States in the Reaction of *N*-Sulfinylamines I−IV with Two Water Molecules across the S═O (a) and N═S (b) Bonds[a]

	I-2				**II-2**				**III-2**				**IV-2**			
	a	**a-TS**	**b**	**b-TS**	**a**	**a-TS**	**b**	**b-TS**	**a**	**a-TS**	**b**	**b-TS**	**a**	**a-TS**	**b**	**b-TS**
S═O	147.9	155.9	146.6	146.8	147.0	154.0	145.9	145.7	148.6	156.9	147.2	146.7	149.2	157.1	147.7	146.1
	(1.0)	(9.0)	(−0.3)	(−0.1)	(0.9)	(7.9)	(−0.2)	(−0.4)	(1.1)	(9.4)	(−0.3)	(−0.8)	(1.1)	(9.0)	(−0.4)	(−2.0)
N═S	152.2	152.3	153.3	159.7	152.7	152.9	154.2	161.7	152.1	151.7	153.4	159.3	152.8	151.9	154.4	160.0
	(−0.2)	(−0.1)	(0.9)	(7.3)	(−0.3)	(−0.1)	(1.2)	(8.7)	(−0.5)	(−0.9)	(0.8)	(6.7)	(−0.6)	(−1.5)	(1.0)	(6.6)
H−N or C−N	102.4	102.2	102.4	102.2	142.1	140.5	141.9	141.3	145.4	145.6	145.8	146.7	139.3	140.0	139.7	142.2
	(0.0)	(−0.2)	(0.0)	(−0.2)	(−0.4)	(−2.0)	(−0.6)	(−1.2)	(−0.1)	(0.1)	(0.3)	(1.2)	(0.0)	(0.7)	(0.4)	(2.9)
NSO	118.4	113.8	118.2	112.0	118.9	114.4	118.5	113.9	118.4	114.0	118.0	112.4	119.2	115.9	119.3	114.3
	(−1.6)	(−6.2)	(−1.8)	(−8.0)	(−1.4)	(−5.9)	(−1.8)	(−6.4)	(−1.2)	(−5.6)	(−1.6)	(−7.2)	(−1.2)	(−4.5)	(−1.1)	(−6.1)
HNS or CNS	115.5	115.3	114.8	110.9	126.5	126.0	125.2	122.1	124.9	125.7	123.8	121.0	133.2	134.6	131.8	127.0
	(−0.2)	(−0.4)	(−0.9)	(−4.8)	(0.2)	(−0.3)	(−1.1)	(−4.2)	(0.4)	(1.2)	(−0.7)	(−3.5)	(0.9)	(2.3)	(−0.5)	(−5.3)
$S\cdots O_w$	290.1	205.0	298.0	210.1	273.6	198.6	269.8	203.1	305.2	210.9	335.5	217.9	314.6	212.0	377.9	219.7
$NSOO_w$	109.3	110.5	106.4	104.3	104.3	108.7	105.6	101.2	105.8	111.3	115.5	104.8	109.8	110.7	131.2	101.1

[a] The deviations of geometrical parameters in the complexes and transition states from the geometries of the non-interacting *N*-sulfinylamines are shown in parentheses.

on nitrogen and oxygen are less affected and become more negative with the increasing electron-donating ability of the substituent. The slightly smaller charge on oxygen in **IV** as compared to **III** could be attributed to the intramolecular C−H···O interaction that this oxygen is involved in.[45]

3.2.2. Reaction with One Water Molecule. In line with our previous results on *N*-sulfinylaniline (**IV**),[20] for **I**−**III** we were able to locate prereaction complexes for reaction across the S═O bond. Similar to **IV**,[20] the attack by water occurs in a close to perpendicular orientation to the plane of the NSO group, and the $NSOO_w$ improper dihedral angle varies from 102° to 114°, depending on the substrate. Any attempts to find the minima for one water molecule complexed toward the N═S bond (path **b**) were unsuccessful due to the fact that perpendicular attack of the oxygen atom of water (O_w) toward the sulfur atom and simultaneous in-plane $O_w-H_w\cdots N$ hydrogen bonding to the nitrogen lone pair are hardly possible. Because of this lack of comparison (we were also unable to locate any prereaction complexes for the isocyanates), complexes of *N*-sulfinylamines with one water molecule are not discussed further, and their geometries are presented in Table S2 of the Supporting Information.

In the following, the reaction with one water molecule is discussed in detail for **I** as the prototype. An account for **IV** has been given,[20] yet the results are included in Table 2 for comparison with those for **I**−**III**. As mentioned above, we will focus on the initial steps of the hydrolysis reaction, the formation of sulfinamic acid directly (reaction across N═S, path **b**) or via sulfurimidic acid (reaction across S═O, path **a**) with subsequent 1,3-hydrogen shift (Figure 2). The highly strained four-membered-ring transition state structures, **I-1a-TS** and **I-1b-TS** in Figure 2, result in the unrealistically high activation enthalpies of 29.8 and 30.3 kcal mol^{-1} (Table 2) for the reaction across the S═O and the N═S bond, respectively. The 1,3-hydrogen shift in sulfurimidic acid in path **a** leading to sulfinamic acid requires 21.9 kcal mol^{-1}, but this barrier can be dramatically reduced by the inclusion of a second water molecule. Thus, a decrease in the activation enthalpy from 15.9 to 5.5 kcal mol^{-1} upon participation of a second water molecule was shown for the 1,3-hydrogen shift in the hydrolysis of **IV**.[20] As a final note, in Figure 2, two enantiomeric *N*-sulfinamic acids are formed from the two mechanisms, but as this is not important in the present context, only one structure is shown.

For *N*-sulfinylamines **I**−**IV**, the hydroxylation of sulfur and concurrent protonation of nitrogen or oxygen is the rate-determining step of the hydrolysis reaction. The subsequent 1,3-hydrogen shift in sulfurimidic acid is much less energetically demanding. Table 2 shows that in the reaction with one water molecule attack across the S═O bond (path **a**) is always favored; however, the preference for this path becomes smaller with the increasing electron-withdrawing ability of the substituent. The large reaction barriers in all cases agree well with the high strain in the four-membered-ring transition states and suggest the necessity for increasing the number of water molecules that participate in the reaction for a more accurate description of the hydrolysis reaction, as was done earlier for *N*-sulfinylaniline.[20]

3.2.3. Reaction with Two and Three Water Molecules. The prereaction complexes with two and three water molecules forming a chain were located for *N*-sulfinylamines **I**−**IV**. A staggered orientation of water molecules with respect to each other in the ternary complexes is favored over an eclipsed arrangement by approximately 0.2 kcal mol^{-1}. The representative structures of the complexes and transition states for the simplest *N*-sulfinylamine **I** are shown in Figure 3. Those for **II** and **III** are similar, as are those for **IV**, which have been reported.[20]

Table 3 summarizes selected geometrical parameters for prereaction complexes and transition states of the rate-determining step of the reaction of *N*-sulfinylamines **I**−**IV** with two water molecules, based on our previous result of the "two-water-molecule" model being sufficiently descriptive and less computationally expensive than the model with three water molecules.[20] The geometrical parameters for reaction with three water molecules are summarized in Table S3 of the Supporting Information because of the similarity between the two models. As can be seen from the $NSOO_w$ improper dihedral angles, the interaction in all cases occurs in a close to perpendicular orientation of the water molecule and the NSO group. In accord with attack on sulfur and concomitant rehybridization, the bond angle on sulfur (NSO) in the complexes decreases by 1.1−1.8° and in the transition states by up to 8.0°. Geometry changes in the complexes and transition states from those of the non-interacting species are given in Table 3 in parentheses.

One of the main geometrical features for both paths consists of a pronounced elongation of the bond across which the complexation and following reaction occurs, along with a small contraction of the other cumulated bond. These changes exhibit only a small substituent effect: While in general elongation of the S═O bond is more pronounced, for **II** with its electron-withdrawing CF_3 substituent elongation is more pronounced for the N═S bond.

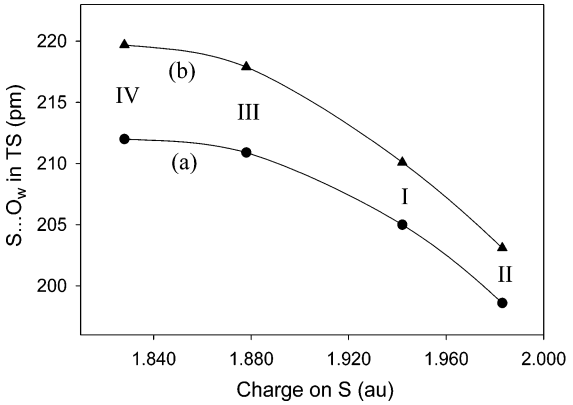

Figure 4. Dependence of the S···O$_w$ intermolecular distance in the transition state of the reaction of **I**−**IV** with two water molecules on the charge on sulfur. Reaction across (**a**) the S═O (●) and (**b**) the N═S (▲) bonds. Data points have been traced.

In contrast, the S···O$_w$ distance in the complexes and transition states appreciably correlates with the electron-donating/electron-withdrawing ability of the substituent. Thus, the strong electron-withdrawing substituent in **II** enhances the electrophilicity of sulfur, which consequently forms the tightest complexes with water for both mechanisms. The conjugating phenyl group in **IV** leads to the weakest complexes and loosest transition states. From the different possible descriptors for the electrophilicity of an atom,[46] we have chosen the charge on sulfur (Table 1) as the most straightforward to be a measure of the susceptibility of the *N*-sulfinylamines toward nucleophilic attack by water. Figure 4 presents the relationship between the charge on sulfur of the non-interacting *N*-sulfinylamines and the S···O$_w$ distance in the transition state of the reactions with two water molecules, which is the obvious choice for comparison between mechanisms "**a**" and "**b**" and for later comparison with the reactivity of the isocyanates, due to the absence of prereaction complexes for the latter. Although the type of correlation (linear or exponential; the data points have simply been traced) is unclear for this small series, the trend is obvious: An increase in the electrophilicity of sulfur leads to a shorter S···O$_w$ distance and therefore a stronger interaction in the transition state.

3.2.4. Summary and Conclusions on N-Sulfinylamine Hydrolysis. Figure 5 shows the dependence of the reaction barrier of the hydrolysis of *N*-sulfinylamines **I**−**IV** on the number of water molecules for reaction across the S═O bond only. The graphical representation of the results for reaction across the N═S bond is very similar, with the exact values summarized in Table 2. For the solid lines in Figure 5, on the basis of the enthalpies of the reactants, it is immediately obvious that the activation enthalpy drops significantly as the number of water molecules is increased. In general, the addition of the second water molecule has a larger effect than that of the third. This is only different for **II** with its CF$_3$ substituent, which causes the overall largest changes. The comparatively larger decrease in the reaction barrier for **II-3a-TS** might be explained by the presence of one additional hydrogen-bonding interaction between the dangling hydrogen of the central water molecule (equivalent to H$_w$ in Figure 3) and a fluorine atom of the CF$_3$ group, with a concurrent conformational change about the C−N bond on going from **II** to **II-3a-TS**. This additional O$_w$H$_w$···F interaction is not present in the complex **II-3a**, and so the smaller activation enthalpy for **II-3a-TS** is found irrespective of the chosen reference (cf. the dashed line in Figure 5).

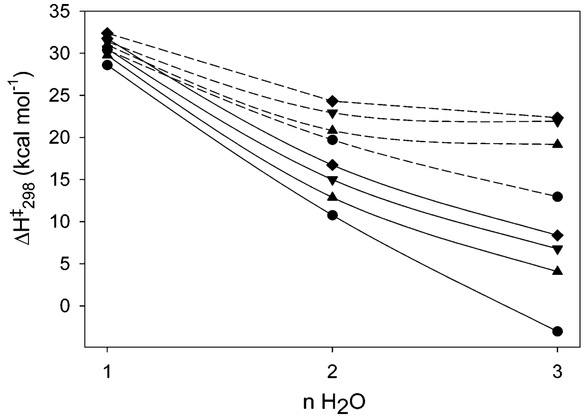

Figure 5. Dependence of the reaction barrier for hydrolysis of *N*-sulfinylamines **I**−**IV** for attack across the S═O bond (path **a**) on the number of water molecules. Activation enthalpies based on the enthalpies of the reactants are shown by solid lines, and those based on the enthalpies of the complexes are shown by dashed lines. Data points have been traced for easier comparison of the trends (H, ▲; CF$_3$, ●; CH$_3$, ▼; Ph, ◆).

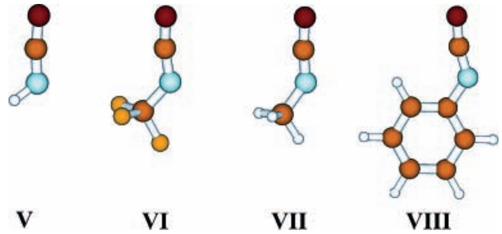

Figure 6. Optimized isocyanates **V**−**VIII**.

The progression of the dashed lines in Figure 5, because the data are based on the enthalpies of the complexes, is in fact more relevant to our discussion. The overall changes are smaller than those discussed above, and there already seems to be a leveling off for addition of the third water molecule, as the reaction barrier decreases by only 1−7 kcal mol^{-1}, with the largest change for **II** for the reason already discussed. These findings confirm the necessity and sufficiency of the "two-water-molecule" model for the proper description of *N*-sulfinylamine hydrolysis.

Two additional conclusions can be drawn. First, a higher activation enthalpy for the hydrolysis of *N*-sulfinylaniline (**IV**) than that for *N*-sulfinylmethylamine (**III**) agrees well with the qualitative experimental observation of a higher reactivity of aliphatic *N*-sulfinylamines toward water.[3] In fact, our free energies allow one to estimate a rate constant increase of about 1−3 orders of magnitude on going from **IV** to **III** (free energies are provided in Table S1 of the Supporting Information). Second, with an average difference of about 2.1 kcal mol^{-1}, the preference for either mechanism is not pronounced, and which mechanism is preferred computationally can depend on whether energies of reactants or of prereaction complexes are used for the determination of the barriers, at least for reaction with one water molecule. We will present the factors that determine the reactivity of the *N*-sulfinylamines after a detailed analysis of the hydrolysis of isocyanates.

3.3. Hydrolysis of Isocyanates. *3.3.1. Isocyanates.* Figure 6 shows that, in contrast to the angular NSO group in *N*-sulfinylamines, isocyanates **V**−**VIII** possess a more or less linear NCO group, as has been reported from numerous experimental and computational studies.[21,34] Selected geometrical data for **V**−**VIII** are presented in Table 4. The NCO bond angle in **V**−**VIII** varies insignificantly in the range of 172.8−173.8°, whereas the bond angle on nitrogen varies widely with the substituent, in line with the findings for **I**−**IV** above.

TABLE 4: Selected Geometrical Parameters (Bond Lengths in pm, Angles in deg), Dipole Moments (μ, D), and Atomic Charges (q, au) of Isocyanates V−VIII

	V	VI	VII	VIII
C═O	116.8	116.1	117.7	117.3
	(119 ± 3)[a]		(118 ± 3)[a]	(117.1)[b]
N═C	121.6	121.8	120.2	120.6
	(119 ± 3)[a]		(119 ± 3)[a]	(120.7)[b]
H−N or C−N	100.8	140.4	144.4	140.0
	(101)[a]		(147)[a]	(137.0)[b]
NCO	172.8	173.4	173.7	173.8
HNC or CNC	124.5	129.8	138.4	139.1
	(125)[a]		(125 ± 5)[a]	(140.6)[b]
			(140.0)[c]	
μ	2.16	0.49	3.03	2.56
	(1.59)[d]		(2.81)[c]	(2.3)[e]
q(O)	−1.146	−1.112	−1.151	−1.137
q(C)	1.958	1.999	1.976	1.974
q(N)	−1.286	−1.184	−1.317	−1.345
q(H or C)	0.473	2.065	0.479	0.409

[a] Experimental from ref 34 where distances are reported in angstroms. [b] Experimental from ref 35 where distances are reported in angstroms. [c] Experimental from ref 36. [d] Experimental from ref 37. [e] Experimental from ref 38.

The substituent effect on the variation of the N═C and C═O bond lengths is not pronounced, and unlike in the *N*-sulfinylamines, where an increase in electron-donating ability of the substituent results in the elongation of both cumulated bonds of the N═S═O group, an elongation of the C═O combined with a contraction of the N═C bond is found for the isocyanates. Geometrical parameters in Table 4 suggest that methyl and phenyl substituents in **VII** and **VIII**, respectively, exert a similar effect on the N═C═O group, in line with the negligible conjugation energy between the N═C bond and the substituent on nitrogen found earlier for methyl, ethyl, and phenyl isocyanates.[16] The available experimental data agree quite well with our calculated results, with the exception of the underestimated dipole moment of HNCO (**V**). The difficulties with interpreting the large difference between the dipole moments of methyl isocyanate (**VII**) and isocyanic acid (**V**) were addressed earlier, and the significant variation in the nitrogen bond angle was given as a possible reason for the difference.[36]

As was found for **II**, with the largest positive charge on sulfur, the trifluoromethyl-substituted **VI** possesses the largest positive charge on the NCO carbon. The charges on sulfur in **I**−**IV**, though, vary more widely in the range of 0.155 au compared to the 0.041 au range for carbon in **V**−**VIII**. In addition, the loss of positive charge (0.050 au) on sulfur in **IV** from that in **III** is larger than that (0.002 au) on carbon in **VIII** from that in **VII**, further corroborating the idea of a similar effect of methyl and phenyl substitution on the NCO group. The charges on nitrogen and oxygen in the two classes of compounds are generally comparable and more negative for the isocyanates, as expected.

3.3.2. *Reaction with One Water Molecule.* Similar to the results of the computational work of Raspoet et al. on the hydrolysis of isocyanic acid (**V**),[21] we did not find any prereaction complexes for the reaction of isocyanates **V**−**VIII** with either one, two, or three water molecules. Consequently, all reaction barriers for this part of our study are based on the enthalpies of the reactants. Unlike *N*-sulfinylamines, whose attack by water occur perpendicular to the plane of the NSO group, isocyanates react with water in the plane of the NCO group, where the nucleophilic attack of oxygen O_W on the carbon atom is concerted with the protonation of either nitrogen or oxygen.

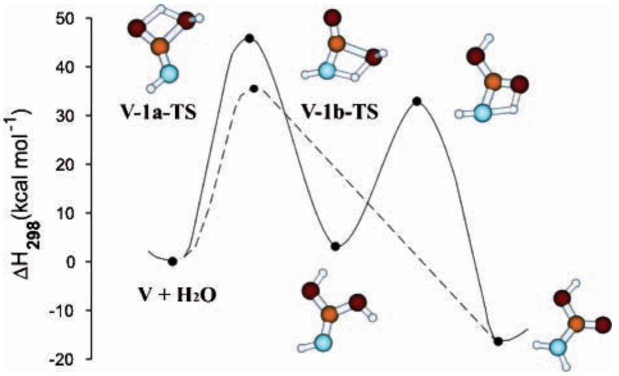

Figure 7. Enthalpy profile for the formation of carbamic acid in the reaction of isocyanic acid (**V**) with one water molecule. The solid line shows attack across the C═O bond, and the dashed line that across the N═C bond.

TABLE 5: Activation Enthalpies[a] ($\Delta H^{\ddagger}_{298}$, kcal mol^{-1}) for the Reaction of Isocyanates V−VIII with 1−3 Water Molecules across the C═O (a) and N═C (b) Bonds and for the Consecutive 1,3-Hydrogen Shift[b] in the Reaction across the C═O Bond

	V		VI		VII		VIII	
n H$_2$O	a	b	a	b	a	b	a	b
1	45.8	35.5	42.1	32.8	45.5	33.8	45.6	33.9
	[29.7]		[30.2]		[27.6]		[24.7]	
2	19.4	12.9	12.2	8.0	19.3	12.9	18.9	13.2
3	7.4	3.0	−1.7	−3.3	7.2	3.4	6.4	3.9

[a] Reaction barriers are based on the enthalpies of the reactants. [b] Given in square brackets.

Again, we only deal with the first stage of the hydrolysis, and the discussion of the mechanism in the presence of one water molecule is based on the simplest isocyanate model compound, isocyanic acid (**V**). Even though the computational analysis of the hydrolysis of **V** (optimized with the HF/6-31G(d,p) model chemistry, single-point energies with MP2/6-311++G(d,p) and QCISD(T)/6-31G(d,p), and with use of Onsager and polarized continuum models) has been reported,[21] we include **V** here for comparison. Irrespective of the model chemistry used, the outcome for the hydrolysis of **V** in the presence of one water molecule is essentially the same: As for the *N*-sulfinylamines, the high strain of the four-membered-ring transition state results in an unrealistically large value for the activation enthalpy (energy).[21,48] The enthalpy profile for both mechanisms is presented in Figure 7.

The activation enthalpy for the one-step reaction across the N═C bond (path **b**), which yields carbamic acid directly, is found to be 35.5 kcal mol^{-1} and compares favorably to the reaction barrier of 36.8 kcal mol^{-1} calculated with QCISD(T)/6-31G(d,p).[21,48] The reaction across the C═O bond (path **a**) requires a significantly higher activation enthalpy of 45.8 kcal mol^{-1} and yields an intermediate carbonimidic acid, which further undergoes a 1,3-hydrogen shift with an activation enthalpy of 29.7 kcal mol^{-1}. These barriers were earlier found to be 46.1 and 31.5 kcal mol^{-1}, respectively.[21,48] In analogy to the hydrolysis of *N*-sulfinylamines, the hydroxylation of carbon is the rate-determining step of isocyanate hydrolysis. Table 5 presents the reaction barriers for the hydrolyses of **V**−**VIII** and reveals an interesting substituent effect. Unlike for *N*-sulfinylamines, the replacement of hydrogen in **V** by a methyl or phenyl group does not change the activation enthalpy for the reaction across the C═O bond and decreases it by only 1.6−1.7 kcal mol^{-1} for the reaction across the N═C bond. Only the strong electron-withdrawing CF$_3$ group in **VI** leads to a more substan-

TABLE 6: Selected Geometrical Parameters (Bond Lengths in pm, Angles in deg) of Transition States in the Reaction of Isocyanates V−VIII with Two Water Molecules across the C═O (a) and N═C (b) Bonds[a]

	V-2		**VI-2**		**VII-2**		**VIII-2**	
	a-TS	**b-TS**	**a-TS**	**b-TS**	**a-TS**	**b-TS**	**a-TS**	**b-TS**
C═O	125.4	119.6	123.5	119.2	125.8	119.6	125.3	119.7
	(8.6)	(2.8)	(7.4)	(3.1)	(8.1)	(1.9)	(8.0)	(2.4)
N═C	126.7	129.7	128.0	131.2	126.1	129.0	126.8	129.8
	(5.1)	(8.1)	(6.2)	(9.4)	(5.9)	(8.8)	(6.2)	(9.2)
H−N or C−N	101.7	101.3	139.5	139.8	145.8	146.3	140.7	141.3
	(0.9)	(0.5)	(−0.9)	(−0.6)	(1.4)	(1.9)	(0.7)	(1.3)
NCO	140.6	143.2	139.7	141.0	140.0	142.9	140.6	143.1
	(−32.2)	(−29.6)	(−33.7)	(−32.4)	(−33.7)	(−30.8)	(−33.2)	(−30.7)
HNC or CNC	110.2	111.7	118.6	118.1	117.5	116.3	123.2	121.8
	(−14.3)	(−12.8)	(−11.2)	(−11.7)	(−20.9)	(−22.1)	(−15.9)	(−17.3)
C···O_w	154.0	163.2	151.3	156.9	154.2	165.3	153.2	162.7
$NCOO_w$	179.6	179.8	179.6	179.6	179.3	179.7	179.4	179.9

[a] The deviations of geometrical parameters in the transition states from those of the non-interacting isocyanates are shown in parentheses.

tial decrease in the activation enthalpies of both mechanisms. This will be rationalized in a following section. For isocyanates **V−VIII**, reaction across the N═C bond is always favored by about 10 kcal mol^{-1}. We also note that while the reaction barriers for the 1,3-hydrogen shift in the sulfurimidic acids increase in the series CF_3, H, CH_3, and Ph the corresponding barriers for the carbonimidic acids become smaller.

3.3.3. Reaction with Two and Three Water Molecules. As in the case of the *N*-sulfinylamines, we chose the isocyanate/water-dimer system as the necessary and sufficient model for a comparison of the geometrical features of the transition states and for a proper description of the hydrolysis reaction, a conclusion that was drawn before for **V**.[21] Table 6 summarizes the selected geometrical parameters of the transition structures for the reaction of isocyanates **V−VIII** with two water molecules; those for the reaction with three water molecules can be found in Table S4 of the Supporting Information. In all cases, the reaction again occurs in the plane of the NCO group, as can be seen from the improper torsional angles $NCOO_w$ (Table 6).

The most interesting feature in Table 6 is the significant decrease in the NCO and CNC or HNC bond angles, by 32° and 16° on average, respectively, upon formation of the transition states, leading to a shortening of the distance between the oxygen of the NCO group and atoms of the substituent R. In the case of **VIII,** this results in the appearance of a weak intramolecular C−H···O interaction between an ortho-hydrogen of the phenyl ring and the oxygen of the NCO moiety, confirmed through topological analyses of the electron densities and given as dotted lines in Figure 8. The C−H···O interactions in *N*-sulfinylaniline (**IV**)[45] and in the transition states for phenyl isocyanate (**VIII**) hydrolysis are best described as blue-shifting (or anti-) hydrogen bonds, characterized by the contraction of the interacting C−H bond from 108.3 to 108.0−108.1 pm in all cases, including the reaction of **VIII** with one water molecule, which was not specified above. The distances between the ortho-hydrogen and the oxygen atom of the NCO group and the CH···O angles resulting from these weak interactions also resemble those in **IV** and are very similar for complexes and transition states for the reactions of **IV** and **VIII** with two and three water molecules (presented in Tables S3 and S4 of the Supporting Information).

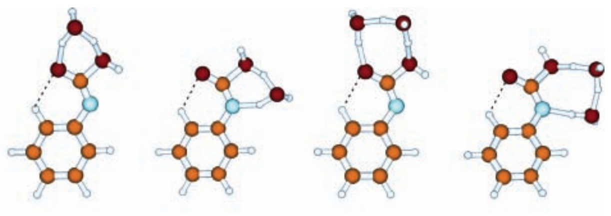
VIII-2a-TS **VIII-2b-TS** **VIII-3a-TS** **VIII-3b-TS**

Figure 8. Optimized transition states for the reaction of phenyl isocyanate (**VIII**) with two and three water molecules for reaction across the S═O (**a**) and the N═S bonds (**b**). Weak interactions determined from electron densities are shown as dotted lines.

The attack of the water dimer across the C═O or N═C bond causes elongation of that bond. No obvious effect of the substituent is found in the series of isocyanates **V−VIII**; however, unlike for *N*-sulfinylamines with their simultaneous contraction of the second cumulated bond, a lengthening for that bond is observed for all isocyanates. The extent of this elongation varies, depending on the mechanism of hydrolysis and therefore on which bond lengthens: For attack across the C═O bond (path **a**), it consists of 5.1−6.2 pm, while for attack across the N═C bond (path **b**) it is half that and varies in the range of 1.9−3.1 pm.

The spread of the charge on carbon is much smaller than that of sulfur in the *N*-sulfinylamines, as mentioned above, and even though a certain trend between the intermolecular distance and the charge on carbon is observed, it is less affected by the electron-donating/electron-withdrawing ability of the substituent. The dependence of the C···O_w distance in the transition state on the charge on carbon in the non-interacting isocyanates is presented in Figure S1 of the Supporting Information.

3.3.4. Summary and Conclusions on Isocyanate Hydrolysis. The increase in the number of water molecules again releases the strain of the four-membered-ring transition states in the reaction with one water, consequently decreasing the activation enthalpies for isocyanate hydrolysis dramatically, which is given in numerical form in Table 5 and in graphical representation in Figure S2 of the Supporting Information for the reaction across the C═O bond. The dependence on the number of water molecules for the reaction across the N═C bond is essentially the same and presented in Figure 9 for the comparison of the hydrolyses of *N*-sulfinylamines and isocyanates. For both mechanisms considered, the reaction barrier shows almost no sensitivity to the substituent in **V, VII**, and **VIII**, and the attack across the N═C bond is favored. A significant decrease in activation enthalpy, by approximately 5−9 kcal mol^{-1}, is found for **VI** with its strongly electron-withdrawing CF_3 group. Because the activation energies are only based on the enthalpies of the reactants and not on the (lower-energy) prereaction complexes, they even drop to negative values in the reaction with three water molecules, as was the case for **II** (cf. Table 2). Finally, from the free energies a rate constant increase for **VI** of about 3−5 orders of magnitude over those for the other

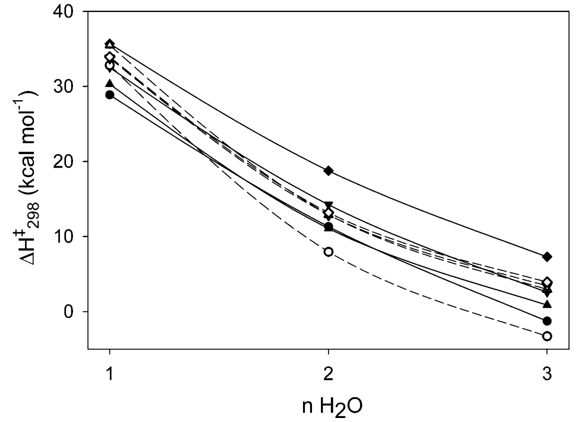

Figure 9. Dependence of the activation enthalpy for hydrolysis of *N*-sulfinylamines **I**−**IV** (solid lines; H, ▲; CF_3, ●; CH_3, ▼; Ph, ◆) and isocyanates **V**−**VIII** (dashed lines; H, △; CF_3, ○; CH_3, ▽; Ph, ◇) on the number of water molecules in the reaction across the N=S or the N=C bond (path **b**). Data points have been traced for easier comparison of the trends.

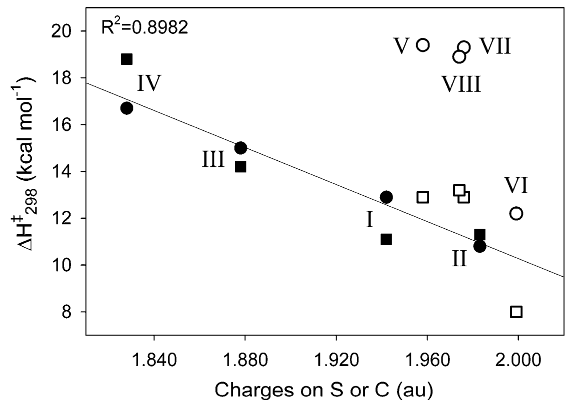

Figure 10. Dependence of the activation enthalpy for the reaction with two water molecules on the charge on sulfur (**I**−**IV**) and carbon (**V**−**VIII**): reaction across the S=O (path **a**, ●) and the N=S bond (path **b**, ■) for **I**−**IV**; reaction across the C=O (path **a**, ○) and the N=S bond (path **b**, □) for **V**−**VIII**. Activation enthalpies are based on the enthalpies of the reactants.

isocyanates can be estimated (free energies provided in Table S1 of the Supporting Information).

A detailed comparison of the reactivity of *N*-sulfinylamines and isocyanates toward water is presented in the final section.

3.4. Comparison of the Hydrolyses of *N*-Sulfinylamines and Isocyanates. The results of this study confirm a certain similarity of the reactivities of *N*-sulfinylamines and isocyanates toward water, based on a comparison of the activation enthalpies for their hydrolyses, summarized in Tables 2 and 5 and presented in graphical form in Figure 9. It can be seen that the reaction barriers, based on the enthalpies of the reactants for the reaction with 1−3 water molecules across the N=S or N=C bond (Figure 9), essentially lie within the same range, with individual data points providing some spread. Unfortunately, as stated above, the more appropriate prereaction-complex-based activation enthalpies cannot be employed in this comparison. As expected, an increasing number of water molecules decreases the activation enthalpy, on average by 17.4 and 23.9 kcal mol^{-1} for addition of the second water and by 10.7 and 11.3 kcal mol^{-1} for addition of the third water molecule for *N*-sulfinylamines and isocyanates, respectively. While a gradual decrease of the reaction barrier with the increasing electron-withdrawing ability of the substituent was found for *N*-sulfinylamines **I**−**IV**, only the strongly electron-withdrawing trifluoromethyl group in **VI** has a major influence on isocyanate reactivity.

To gain further insight into this differing reactivity, we correlate the activation enthalpy for the reaction with two water molecules with the charge on the electrophilic center of **I**−**VIII** in Figure 10. As nucleophilic attack of water on sulfur or carbon is the rate-determining step of hydrolysis, the reactivity could be governed by the charge of this reactive center. Figure 10 shows that this is indeed the case. The sulfur atom of the *N*-sulfinylamines **I**−**IV** possesses a high sensitivity to the nature of the substituent, which results in a large variation in its charge. A reasonably linear correlation that includes reactions across both the N=S and the S=O bonds is found. Even though Figure 10 displays relative linearity only for path **a** (●) and a distinct curvature for path **b** (■), the correlation with both mechanisms simultaneously seems justified because the preference for either mechanism is not pronounced and is affected by the substituent, the number of water molecules, and the reference employed for the determination of the activation energies, as described above. Overall, an increase in the electron-withdrawing ability of the substituent causes an increase in the electrophilicity of the sulfur atom and its susceptibility to hydroxylation, consequently decreasing the reaction barrier for hydrolysis of the *N*-sulfinylamines.

The charge on carbon of the isocyanates **V**−**VIII** also correlates with the activation enthalpy for their hydrolysis. The insignificant variation of the charge in **V**, **VII**, and **VIII** results in negligible changes in their reactivity toward water, whereas trifluoromethyl isocyanate (**VI**), possessing the largest positive charge on carbon in the series, demonstrates an enhanced electrophilicity and hydrolyzes more readily. A linear regression has not been performed due to the poor spread in the data.

A comparison of data from Tables 2 and 5 indicates that while both mechanisms **a** and **b** are feasible for *N*-sulfinylamines the attack across the N=C bond is clearly favored by isocyanates. This preference, noted earlier for isocyanic acid (**V**), was explained as being “due to the more extended concentration of electron density”, a result obtained from Fukui functions, although a Mulliken population analysis predicted oxygen to be twice as negative as nitrogen, which bore the small charge of −0.17 au.[21] In other work[16] and in contrast, a comparison of molecular and bond dipoles in a series of isocyanates was used to propose that nitrogen is more negative than oxygen in **V**. The calculated charges presented in Tables 1 and 4 show that the nitrogen atom indeed possesses a more negative charge than oxygen in both *N*-sulfinylamines **I**−**IV** and isocyanates **V**−**VIII**, with a more substantial difference in isocyanates **VII** and **VIII**. This agrees well with the distinct preference for reaction across the N=C bond found for isocyanates but requires some comments for seeming outliers in *N*-sulfinylamine reactivity. Thus, first, for the R−NSO species, the transition state for reaction with one water molecule across the N=S bond, because of the requirements of perpendicular interaction toward sulfur and in-plane orientation to the nitrogen lone pair, is so highly strained that the reaction across the S=O bond becomes preferred. And, second, reaction of **II** with three water molecules across the S=O bond is facilitated by an additional hydrogen bond stabilizing this transition state.

The rate-limiting step in the concerted hydrolysis reaction involves the hydroxylation of sulfur in **I**−**IV** or carbon in **V**−**VIII** along with the protonation of either nitrogen or oxygen atoms. It may, therefore, not seem surprising that the actual pathway (**a** or **b**) taken also follows the proton affinities of these atoms. The proton affinities calculated from the 0 K enthalpies[49] are given in Table S5 of the Supporting Information. In general for **I**−**VIII**, the proton affinity for nitrogen is larger than that for oxygen, and the difference in proton affinities for these atoms (ΔPA) for an isocyanate **V**−**VIII** is twice that for an *N*-sulfinylamine **I**−**III**. This again explains the observed reactivity. Finally, while ΔPA for the phenyl-substituted **VIII** is in line with those for the other isocyanates, for *N*-sulfinylaniline (**IV**) the nitrogen and oxygen atoms exhibit an approximately equal affinity for protonation, in accord with the observed lack of preference for either mechanism and the fact that conjugation with the phenyl ring in **IV** extends over all atoms of the NSO group.

4. Conclusions

The "two-water-molecule" model is found to be adequate for the proper description of the hydrolysis of *N*-sulfinylamines **I**−**IV** and isocyanates **V**−**VIII**. Despite the overall similar reactivity of these two classes of compounds, reactions across both the N═S and the S═O bonds are feasible for *N*-sulfinylamines, while the reaction across the N═C bond is strongly favored for isocyanates. This dissimilarity is rooted in the different proton affinities of the nitrogen and oxygen atoms in the NSO and NCO groups. *N*-Sulfinylamines exhibit a pronounced sensitivity to substitution, and the smaller reaction barrier encountered with a more electron-withdrawing substituent agrees well with the experimentally determined higher reactivity of the aliphatic species as compared to aromatic *N*-sulfinylamines. The similar reactivity of aromatic and aliphatic isocyanates agrees with the previously reported close to zero conjugation energy between the substituent and the NCO group in aliphatic and phenyl isocyanates, although an increase in reactivity can be achieved through a strongly electron-withdrawing (CF_3) substituent. The correlations found between the charges on sulfur and carbon with the $S\cdots O_w$ and $C\cdots O_w$ intramolecular distances in the transition state and, consequently, with the activation enthalpy for hydrolysis of *N*-sulfinylamines and isocyanates suggests that these atomic charges could be used as a measure of electrophilicity of the reactive center in future studies. With estimated ranges of gas-phase rate constants of $10^{-18}-10^{-12}$ s^{-1} for *N*-sulfinylamines and $10^{-19}-10^{-11}$ s^{-1} for isocyanates within even the small series covered here, this could prove a welcome aid for experimentalists.

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Supporting Information Available: Tables for energies and enthalpies of all species, geometrical parameters for complexes of **I**−**IV** with one water molecule, geometrical parameters for complexes and transition states of **I**−**IV** with three water molecules, geometrical parameters for transition states of **V**−**VIII** with three water molecules, and proton affinities of **I**−**VIII** and figures for hydrolysis of **V**−**VIII**: $C\cdots O_w$ distance versus charge on C and activation enthalpy versus number of water molecules. This material is available free of charge via the Internet at http://pubs.acs.org

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