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Mechanism for the reactions of sulfides with hypochlorous acid and *N*-chlorosulfon-amides: Formation of solvated chlorosulfonium cation and λ^4-sulfane intermediates

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Abstract

DFT computations have been performed to study the mechanism of the reactions of sulfides with hypochlorous acid and *N*-chlorosulfonamides. Sulfides can attack HOCl both at chlorine and oxygen atoms. The attack at chlorine results in the formation of chlorosulfonium cation (R_2SCl^+) and OH^- intermediates, which transform to sulfoxide product. The high free energy of activation ($\Delta G^{\ddagger}$), which is needed for the formation of ionic intermediates, is decreased considerably by solvation in protic solvents. Since the attack of sulfides at the oxygen atom of HOCl has low $\Delta G^{\ddagger}$ value, the chlorination of sulfides can compete with the attack at the oxygen atom only in protic solvents. Kinetic studies showed that the reactivity of species, formed from *N*-chlorosulfonamides in protic solvents, increases in the course: $RSO_2NCl^- \ll RSO_2NHCl < RSO_2NCl_2$. The chlorination of sulfides with RSO_2NHCl or RSO_2NCl_2 results in the formation of R_2SCl^+ and RSO_2NH^- or RSO_2NCl^- intermediates, respectively, and the computed and experimentally derived $\Delta G^{\ddagger}$ data agree in these cases. Sulfilimine ($R_2S=NSO_2R$) and sulfoxide products are formed in the reaction of R_2SCl^+ with RSO_2NH^- and water, respectively. Acyloxy-chloro-λ^4-sulfane intermediates are produced in the reactions of *N*-chlorosulfonamides and sulfides, bearing 2-carboxy-phenyl group, without the intermediacy of chlorosulfonium cations. Explicit water molecules must also be included in computations for reactions proceeding with formation or destruction of ions, to get $\Delta G^{\ddagger}$ values, comparable with experimental data.

Supporting information may be found in the online version of this paper.

KEYWORDS
chlorination, DFT calculations, hypochlorous acid, *N*-chlorosulfonamides, sulfides
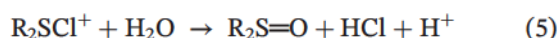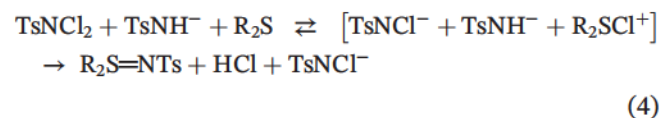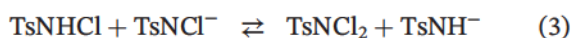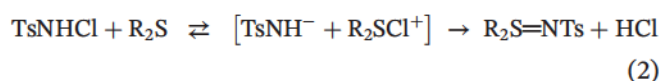
In memoriam Professor Árpád Kucsman

1 | INTRODUCTION

The mechanism of the reactions of sulfides with hypo-chlorites[1–8] and *N*-chloroamides[9–14] has been widely investigated by kinetic and nonkinetic methods. The reactions have been proposed to proceed by a polar mechanism, via the formation of chlorosulfonium cation[1–14] (R_2SCl^+) and oxychloro- or aminochloro-λ^4-sulfane[4,5,7,15] intermediates (earlier sulfuranes, R_2SClNu, Nu = R'O or $ArSO_2NH$, Equation (1)).

$$R_2S + NuCl \rightleftarrows [R_2SCl^+] + Nu^-$$
$$\rightarrow [R_2SClNu] \rightleftarrows R_2SNu^+ + Cl^- \quad (1)$$
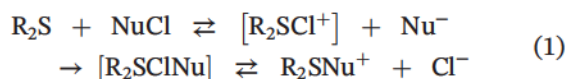
Trigonal bipyramidal λ^4-sulfane intermediates are produced via the addition of a nucleophile at the positively charged sulfur atom of chlorosulfonium cations. Chloride ion splits off easily from the sulfur atom of λ^4-sulfanes to form oxysulfonium or aminosulfonium cations (R_2SNu^+), which hydrolyze or deprotonate quickly to the sulfoxide ($R_2S=O$) or sulfilimine ($R_2S=NSO_2Ar$) products. It must be mentioned, however, that the supposed chlorosulfonium cation and λ^4-sulfane intermediates have never been isolated or detected in reaction mixtures containing nucleophiles and protic solvent. Chlorosulfonium salts[1,16] and λ^4-sulfanes[15,17–21] can be prepared only in nonnucleophilic and aprotic media.

On the basis of kinetic studies, an analogous mechanism has been proposed by us[10,22–24] for the reaction of sulfides with chloramine-T (TsNClNa, Ts = 4-Me-$C_6H_4SO_2$, (Equations 2–5). The chlorinating agents are the $TsNHCl$ and $TsNCl_2$ species. $TsNCl_2$ is formed when chloramine-T disproportionates in protic solvent (Equation (3)). Sulfilimine ($R_2S=NTs$) and sulfoxide products have been supposed to be formed in nucleophilic substitutions at the chlorosulfonium cation (R_2SCl^+) with sulfonamidate anion ($TsNH^-$) or water, respectively (Equations (2), (4) and (5)).

$$TsNHCl + R_2S \rightleftarrows [TsNH^- + R_2SCl^+] \rightarrow R_2S=NTs + HCl \quad (2)$$

$$TsNHCl + TsNCl^- \rightleftarrows TsNCl_2 + TsNH^- \quad (3)$$

$$TsNCl_2 + TsNH^- + R_2S \rightleftarrows [TsNCl^- + TsNH^- + R_2SCl^+]$$
$$\rightarrow R_2S=NTs + HCl + TsNCl^- \quad (4)$$

$$R_2SCl^+ + H_2O \rightarrow R_2S=O + HCl + H^+ \quad (5)$$

Recently, we have proposed[25] a different mechanism for the reaction of sulfides with hypochlorites (R'OCl, R' = H, Me, and *t*-Bu), involving the attack of the sulfur atom of sulfides at the oxygen atom of hypochlorites (Equation (6)). The formation of oxysulfonium cations ($R_2SOR'^+$) takes place with the leaving of Cl^-, in S_N2 type transition state (TS). The $R_2SOR'^+$ intermediate hydrolyses to sulfoxide with water or can be reverted to sulfide and R'OCl precursors by the attack of Cl^- at the positively polarized oxygen atom (Equation (6)). The attack of sulfide at chlorine of R'OCl, the formation of R_2SCl^+ was excluded, because DFT computations indicated that the reaction has very high energy of activation.[25]

$$R_2S + R'OCl \rightleftarrows [R_2S\cdots O(R')\cdots Cl]^{\ddagger} \rightleftarrows R_2SOR'^+ + Cl^- \quad (6)$$
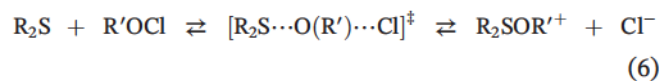
Ions are strongly solvated, however, in polar protic solvents, like water, and their energy decreases considerably by ion-dipole interactions, and by formation of hydrogen bonding. Therefore, we have performed DFT computations to study the formation of chlorosulfonium cations, surrounded by explicit water molecules, using also the polarizable continuum model of solvents. In this paper, we report on the results obtained for the reactions of sulfides with hypochlorous acid and *N*-chlorosulfonamide reactants. The aim of our work is to prove or disprove the participation of the supposed intermediates of the reactions. To validate the results, the computed free energy of activation values ($\Delta G^{\ddagger}$) have been compared with experimentally derived data, calculated from the rate constants of kinetic studies. The computed and experimentally derived $\Delta G^{\ddagger}$ values can be in reasonably good agreement, as it was observed previously by Jorgensen et al[26] and also by us in earlier studies.[27–32]

2 | RESULTS AND DISUCUSSIONS

2.1 | Attack of sulfur atom of sulfides at chlorine of HOCl

At first, DFT computations were performed without explicit water molecules, using only the polarizable continuum model of solvents. The attack of sulfur atom of dimethyl sulfide (**1a**) at the chlorine atom of HOCl (**2**) results in the formation of complex **3a** with decrease of total energy (Figure 1), and with small increase of free energy [Scheme 1, see $\Delta G^{\ddagger}$ and $\Delta E^{\ddagger}$ data in Table S1 in the Supporting Information (SI)]. In complex **3a**, the calculated distance of the S$\cdots$Cl nonbonded interaction is very long, but the Cl—O bond is only slightly longer than in HOCl (Table 1). At further decrease of the S$\cdots$Cl distance (**3a → 4a**), the total energy and the free energy of the interacting R_2S and HOCl molecules increase very

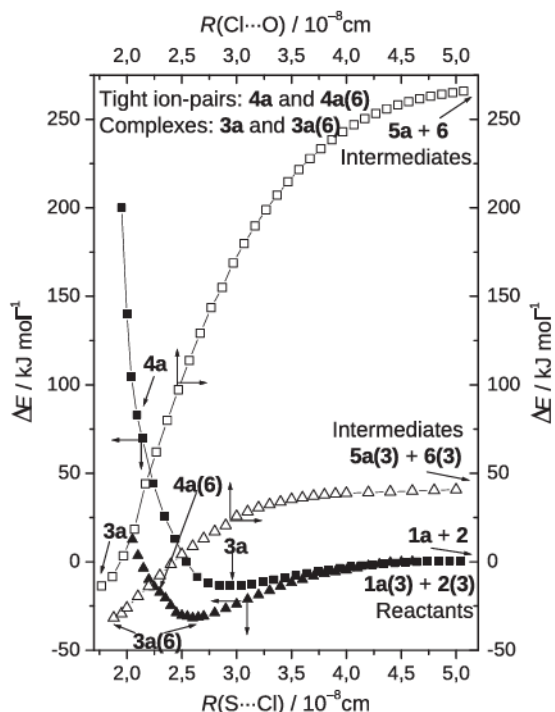**FIGURE 1** ΔE vs $R(S \cdots Cl)$ plots for the attack of Me$_2$S at the chlorine atom of HOCl (1a + 2 $\rightleftarrows$ 3a $\rightleftarrows$ 4a), and ΔE vs R (Cl$\cdots$O) plots for the dissociation of complex 3a to Me$_2$SCl$^+$ and OH$^-$ ions (3a $\rightarrow$ 5a + 6, Schemes 1 and 2). Calculations were performed without and with explicit water molecules, using also the polarizable continuum model of solvents, at DFT(B3LYP)/6-31G(d) level of theory in water at 25°C. $\Delta E = 0$ for the separated reactants. Number of explicit water molecules is given in parenthesis

steeply (Figure 1). At $R(S—Cl) = 2.045$ Å, which is the distance of the sulfur and chlorine atoms in the Me$_2$SCl$^+$ ion (5a), the ΔE vs $R(S \cdots Cl)$ plot does not show any extreme value, neither stable tight ion pair (4a) nor TS is formed. The structure of a hypothetical tight ion pair 4a was optimized taking the sulfur-chlorine distance to be constant. The relatively small charges of the sulfur and chlorine atoms, and the R (Cl$\cdots$O) distance,

calculated for the hypothetical tight ion pair 4a (Table 1), indicate that charge separation would be only partial, and the interaction between the Me$_2$SCl and OH moieties would be very strong at this stage. Therefore, chlorine cannot be transferred to sulfur by decreasing their distance. The dissociation of complex 3a to free Me$_2$SCl$^+$ (5a) and OH$^-$ (6) ions could proceed with the increase of the distance of the chlorine and oxygen atoms of complex 3a (3a $\rightarrow$ 5a + 6, Figure 1). Very high increase of total and free energy was obtained for this reaction if calculations were performed only with the polar continuum model of solvents (Figure 1, Scheme 1, and Table S1 in the SI). The results indicate that these ions cannot be formed from complex 3a without the support of solvent molecules.

On the other hand, the hydrolysis of chlorosulfonium cation 5a would be very fast. The attack of hydroxide ion at the sulfonium center of cation 5a proceeds with a great decrease of total and free energy and results in the formation λ^4-sulfane intermediate 7a (Scheme 1, Table S1 in the SI). The O, S, and Cl atoms of 7a are in linear arrangement; the hypervalent S—Cl bond is very long (Table 1). The lengths of hypervalent bonds of λ^4-sulfanes and the distances of nonbonded interactions in complexes are of the same extent.[18–21] The chlorine of λ^4-sulfane 7a dissociates, and the hydroxysulfonium cation 8a deprotonates to sulfoxide 10a (Scheme 1).

The interaction between charges and dipoles of ions and solvent molecules, and the formation of hydrogen bonding decrease the energy of reactants, intermediates, and TSs. DFT calculations have been performed, therefore, for species 1 to 11, surrounded by explicit water molecules (Scheme 2), using also the polarizable continuum model of solvents. The number of explicit water molecules is given in parenthesis. The positively charged sulfur atoms in species 4(6) and 5(3) are surrounded by the oxygen atoms of water molecules (Scheme 2). On the other hand, hydrogen bondings are formed with the
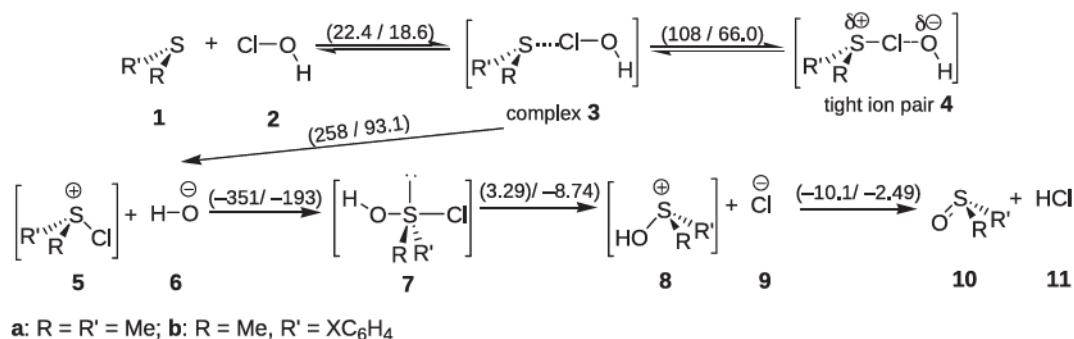
SCHEME 1 Mechanism for the formation of chlorosulfonium cation (5) and λ^4-sulfane (7) intermediates in the reaction of sulfides (1) and hypochlorous acid (2). Free energy changes (ΔG) for the reactions of Me$_2$S (1a) are given in kJ mol^{-1} unit, in the direction of the neighboring arrow. Calculations were performed at DFT(B3LYP)/6-31G(d) /DFT(B3LYP)/6-311 + G(d,p) levels of theory, in water, at 25°C without explicit water molecules.

TABLE 1 Selected net Mulliken atomic charges (Q, a.u.), atomic distances (R, Å), and bond angles (θ, degree) for species formed in the chlorination of Me$_2$S (**1a**) with HOCl (**2**, Schemes 1 and 2). Calculations were performed at DFT(B3LYP)/6-31G (d) level of theory in water, at 25°C

| Compound	Q(S)	Q (Cl)	Q(O)	R (SCl)	R (SO)	R (ClO)	θ (SClO or OSCl)
2	-	0.138	−0.609	-	-	1.727	-
2(3)	-	0.203	−0.616	-	-	1.726	-
3a	0.091	0.100	−0.663	2.877	-	1.779	178[a]
3a(6)	0.153	0.077	−0.697	2.539	-	1.892	179[a]
4a	0.317	0.009	−0.849	2.045	-	2.034	179[a]
4a(6)	0.347	−0.015	−0.771	2.189	-	2.122	180[a]
5a	0.588	0.022	-	2.045	-	-	-
5a(1)	0.587	−0.062	−0.707[b]	2.088	2.564[b]	-	175[c]
5a(3)	0.596	−0.216	−0.823[b]	2.189	2.220[b]	-	178[c]
7a	0.808	−0.822	−0.688	2.928	1.682	-	176[c]
7a(6)	0.847	−0.739	−0.689	3.014	1.679	-	166[c]
7a(6$^+$)	0.843	−0.726	−0.702	2.943	1.691	-	170[c]
8	0.857	-	−0.641	-	1.641	-	-
8a(3)	0.879	-	−0.650	-	1.645	-	-
8a(3$^+$)	0.879	-	−0.655	-	1.648	-	-
10a	0.741	-	−0.699	-	1.526	-	-
10a(3)	0.792	-	−0.710	-	1.553	-	-
10a(3$^+$)	0.810	-	−0.726	-	1.564	-	-

[a]θ (SClO).

[b]Data of the O atom of the explicit water molecule.

[c]θ (OSCl).

oxygen atoms for all of the species, and with negatively charged or polarized chlorine atoms of λ^4-sulfane **7(6)**, furthermore with the Cl$^-$ ion [**9(3)**] and HCl molecule [**11(3)**]. The calculated total energy decreases at the solvation for all of species; however, free energy decreases also at the solvation of ions (cf. ΔE^o and ΔG^o values in the SI in Table S1 for entries 14-19).

The total energies of hydrated complex **3a(6)** and that of the hypothetical tight ion pair **4a(6)** are smaller, but the free energies of these species are higher than the sum of the energies of reactants **1a(3)** and **2(3)** (Figure 1, Scheme 2, and Table S1 in the SI). The increases of the total and free energy at the formation of hydrated ions **5a(3)** and **6(3)** from complex **3a(6)** are, however, much smaller than those obtained without explicit water molecules (**3a → 5a + 6**; Figure 1 and Scheme 1 and 2, Table S1 in the SI). In the hydrated chlorosulfonium cation **5a(3)**, the chlorine atom and the oxygen atom of one of the solvating water molecules are bonded to the sulfur atom with hypervalent bonds (Scheme 2, Table 1). The hydrated species **5a(3)** has λ^4-sulfane type trigonal bipyramidal structure, the O, S, and Cl atoms are in linear arrangement (Table 1). The

hydrated ions **5a(3)** and **6(3)** can be transformed easily to hydrated λ^4-sulfane **7a(6)**, which decompose to sulfoxide product with the dissociation of Cl$^-$ and deprotonation [**7a(6) → 8a(3) + 9(3) → 10a(3) + 11(3)**]. The hydrolysis of the chlorosulfonium cation **5a(3)** with water can also proceed via λ^4-sulfane intermediate **7a(6$^+$)**, which has a similar structure to that of λ^4-sulfane **7a(6)** (Scheme 3, Table 1).

Because the chlorosulfonium cation [**5a(3)**] and the hydroxide ion [**6(3)**] intermediates are species of highest energy, the total and free energy of activation for chlorination of sulfides with HOCl can be taken to be equal to the sum of the energy changes of formation and decomposition complex **3a(6)** [**1a(3) + 2(3) ⇌ 3a(6) ⇌ 5a(3) + 6(3)**]. The TS of the dissociation cannot be calculated because the total energy does not show any maximum during the process (Figure 1). The change of free energy may have a maximum, as we showed[29] discussing the dissociation of *t*-BuCl, but its value and the structure of the TS cannot be optimized with the Gaussian program. The calculated total and free energy of activation of water-assisted multistep chlorination of Me$_2$S with HOCl are $\Delta E^\ddagger = 40.1$ kJ mol^{-1} and $\Delta G^\ddagger =$
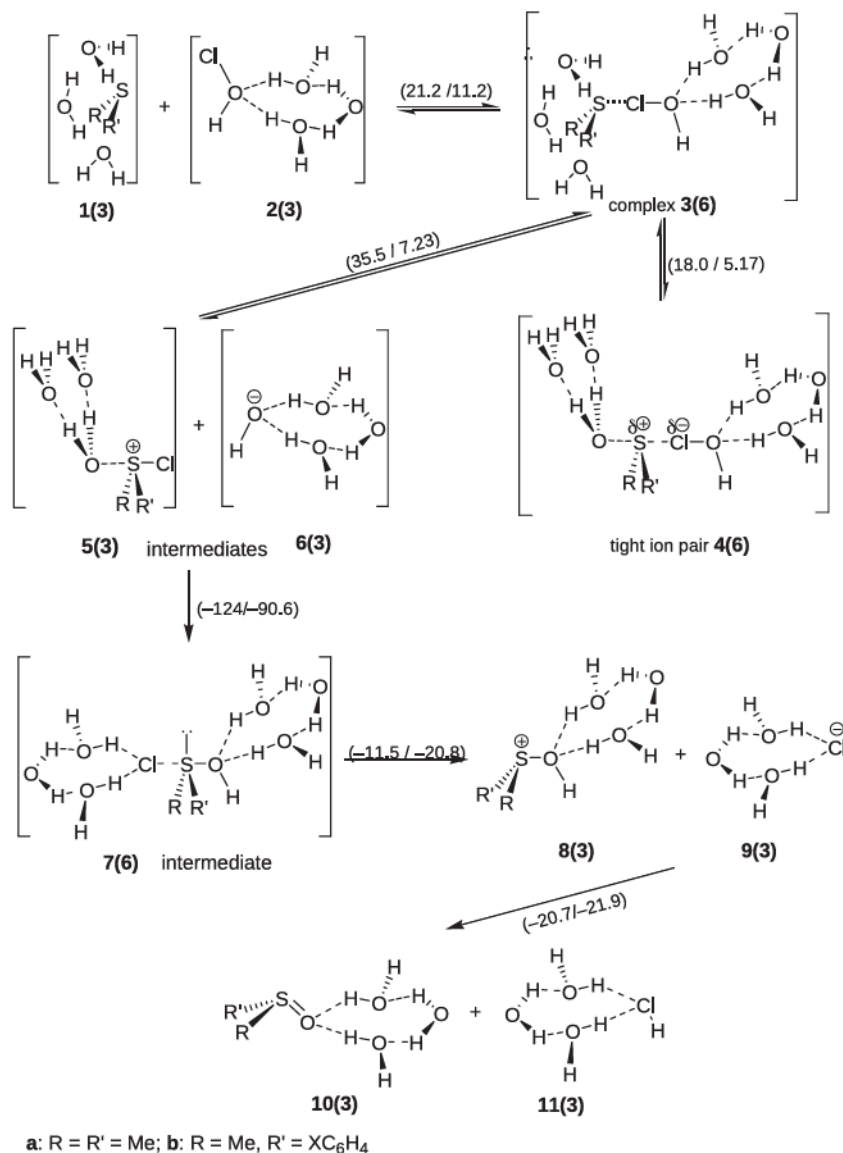
SCHEME 2 Mechanism for the formation of chlorosulfonium cation (5) and λ^4-sulfane (7) intermediates in the reaction of sulfides (1) and hypochlorous acid (2). Free energy changes (ΔG) for the reactions of Me_2S (1a) are given in kJ mol^{-1} unit, in the direction of the neighboring arrow. Calculations were performed at DFT(B3LYP)/6-31G(d) /DFT(B3LYP)/6-311 + G(d,p) levels of theory, in water, at 25°C. Number of explicit water molecules is given in parenthesis.

a: R = R' = Me; b: R = Me, R' = XC$_6$H$_4$

a: R = R' = Me; b: R = Me, R' = XC$_6$H$_4$
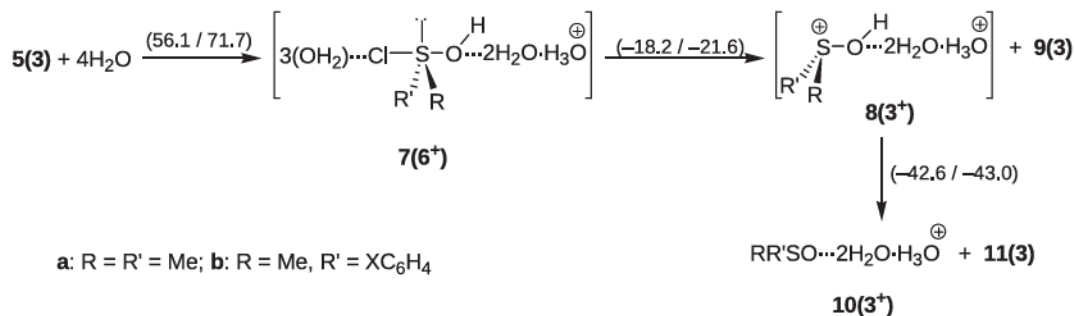
SCHEME 3 Mechanism for the hydrolysis of chlorosulfonium cation (5) with water. Free energy changes (ΔG) for the reactions of Me_2S (1a) are given in kJ mol^{-1} unit, in the direction of the neighboring arrow. Calculations were performed at DFT(B3LYP)/6-31G(d) / DFT(B3LYP)/6-311 + G(d,p) levels of theory, in water, at 25°C with explicit water molecules. Number and charge of explicit water molecules are given in parenthesis.

56.7 kJ mol^{-1}, while those of the simple one-step oxygen transfer reaction between the Me_2S and HOCl reactants[25] are $\Delta E^{\ddagger}$ = 14.0 kJ mol^{-1} and $\Delta G^{\ddagger}$ = 57.4 kJ mol^{-1} (Equation (6); R = Me, R' = H). One may conclude, therefore, that chlorination of sulfide with HOCl might compete with the attack of sulfides at the

oxygen atom of HOCl only in media, which solvate the chlorosulfonium and hydroxide ion intermediates very strongly, like water. Calculations performed at higher level of theory show the same order of reactivity (Scheme 1–3, Table S1 in the SI).

## 2.2 | Reactions of sulfides with *N*-chlorosulfonamides

One could suppose that the reactions of sulfides with *N*-chlorosulfonamides take place via the attack of the sulfur atom of sulfides at the nitrogen atom of reactants **12**, **15**, and **18**, which are formed in the equilibria of *N*-chlorosulfonamides, in protic solvents[33,34] (Scheme 4). This mechanism would be analogous to the attack of sulfides at the oxygen atom of HOCl (Equation (6)).[25] The same free energies of activation ($\Delta G^{\ddagger}$) values have been calculated for the reactions of Me$_2$S (**1a**) with MsNCl$^-$ (**12x**, Q = Me), MsNHCl (**15x**), and MsNCl$_2$ (**18x**), through TSs **13ax**, **16ax**, and **19ax**, respectively (Scheme 4). According to these computations, the species of *N*-chlorosulfonamides would react with sulfides at about the same rate. The calculated $\Delta G^{\ddagger} \sim 120$ kJ mol^{-1} values refer to very slow reactions. The results of the computations are not in accordance with results of kinetic studies. It has been observed[10] for the analogous *N*-chlorotosylamide derivatives that the TsNCl$^-$ anion (**12y**, Q = 4-Me-C$_6$H$_4$) does not react with sulfides at all, the reactions of TsNHCl (**15y**) proceed at medium rate, and the reactions of TsNCl$_2$ (**18y**) are extremely fast. Therefore, one can conclude that, in contrast with the

reactions of sulfides with HOCl,[25] the reactions of sulfides with *N*-chlorosulfonamides do not proceed with the S$_N$2 mechanism, presented on Scheme 4.

N-chloroamides are widely used chlorinating agents[11,35,36]; the chlorine transfer reactions to sulfides[1,9–14] and amines[37–40] have been thoroughly investigated. The chlorine potential of *N*-chlorosulfonamides increases with the increasing acidity of the protons of parent amides (MsNH$^-$ << MsNH$_2$ < < MsNHCl).[35,41–43] While the *N*-chlorosulfonamidate anions (**12**, Q = Me or 4-Me-C$_6$H$_4$) cannot transfer chlorine cation at all, the *N*-chlorosulfonamides (**15**) are good, and the *N,N*-dichlorosulfonamides (**18**) are extremely strong reactants. *N*-chlorosulfonamides (**15**) can also chlorinate the N-chlorosulfonamidate anions (**12**) to form *N,N*-dichlorosulfonamides (**18**) in disproportionation (Scheme 5). *N,N*-dichlorosulfonamides (**18**) chlorinate sulfonamidate anions (**21**) in the backward step of the equilibrium.[10,34] Calculations have been performed for the reactions of *N*-chloro-methanesulfonamide derivatives [**15x(n)** + **12x(n)** ⇄ **21x(n)** + **18x(n)**; Q = Me] without and with one and three explicit water molecules (Scheme 5, n = 0, 1, and 3, Table 2, entry 1), using also the polarizable continuum model of solvents. The calculated $\Delta G^{\ddagger}$ values depend only slightly on the number of explicit water molecules (Scheme 5), because the number of charges does not change in the reactions. Similarly, $\Delta G^{\ddagger} = 58.8$ and 45.0 kJ mol^{-1} were computed for the formation of TsNCl$_2$ [**15y(n)** + **12y(n)** ⇄ **21y(n)** + **18y(n)**; Q = 4-Me-C$_6$H$_4$] in water, without (n = 0) and with three explicit water molecules (n = 3), respectively. On the other hand, $\Delta G^{\ddagger} = 61.9$, just as 64.4 kJ mol^{-1} were

17 + Cl$^{\ominus}$ ⟶ 14 + HCl
20 + H$_2$O + Cl$^{\ominus}$ ⟶ 14 + HOCl + HCl
a: R = R' = Me; **x**: Q = Me
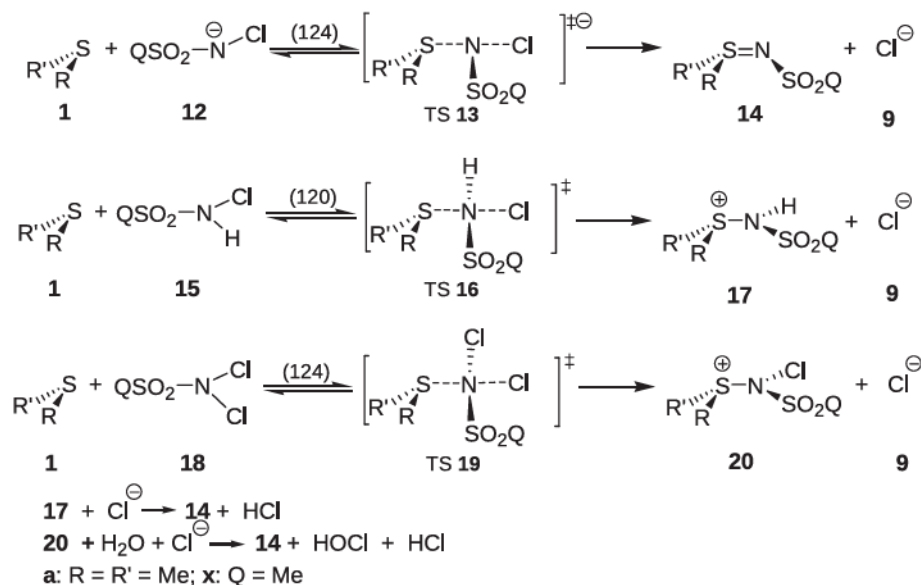
SCHEME 4 Hypothetical nucleophilic attack of sulfides (**1**) at the nitrogen atom of *N*-chlorosulfonamides (**12**, **15**, and **18**). Free energies of activation data ($\Delta G^{\ddagger}$) for the reactions of Me$_2$S (**1a**) with MsNCl$^-$ (**12x**), MsNHCl (**15x**), and MsNCl$_2$ (**18x**) are given in parentheses, in kJ mol^{-1} unit, in the direction of the neighboring arrow, calculated at DFT(B3LYP)/6-31G(d) level of theory in water, at 25°C.
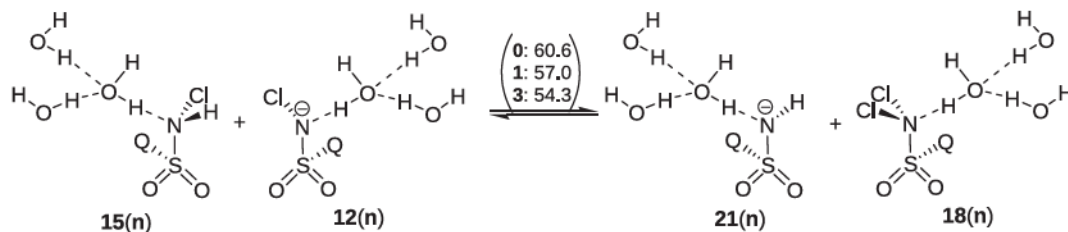
x: Q = Me, y: Q = 4-Me-C₆H₄, n = 0, 1, 3 : number of external H₂O molecules

SCHEME 5   Mechanisms for the formation of *N,N*-dichlorosulfonamide (**18**). Free energies changes (ΔG), calculated without, and with one, and three explicit water molecules (n = 0, 1, and 3), for the reaction of derivatives of methanesulfonamide [**12x**, **15x**, and **18x**, Q = Me], are given in parentheses, in the unit of kJ mol^{-1}, in the direction of the neighboring arrow. Calculations were performed at DFT(B3LYP)/6-31G(d) level of theory in water at 25°C.

TABLE 2   Calculated and experimentally derived free energy of activation values (kJ mol^{-1}) for the equilibrium formation of *N,N*-dichlorosulfonamides (**18**) and for the reactions of *N*-chlorosulfonamides (**15**) and *N,N*-dichlorosulfonamides (**18**) with sulfides (**1**, Schemes 6 and 7). Calculations were performed with without and with three explicit water molecules (n = 0 and 3), at DFT(B3LYP)/6-31G (d) level of theory, using the polarizable continuum model of solvents, in water, at 25°C

		$\Delta G^{\ddagger}_{Calc.}$		
Entry	Reaction[a]	n = 0	n = 3	$\Delta G^{\ddagger}_{Exp}$
1	MsNHCl + MsNCl⁻ ⇌ MsNH⁻ + MsNCl₂	60.6	54.3	-
2	TsNHCl + TsNCl⁻ ⇌ TsNH⁻ + TsNCl₂	58.8	45.0	61.9[b]
3	Me₂S + MsNHCl ⇌ Me₂SCl⁺ + MsNH⁻	136	63.3	-
4	PhMeS + MsNHCl ⇌ PhMeSCl⁺ + MsNH⁻	145	77.6	-
5	2-CO₂⁻-C₆H₄SMe + MsNHCl ⇌ TS **26x**	60.5	-	-
6	Me₂S + MsNCl₂ ⇌ Me₂SCl⁺ + MsNCl⁻	75.5	27.7[c]	-
7	Me₂S + TsNHCl ⇌ Me₂SCl⁺ + TsNH⁻	132	56.5	46.9[d]
8	PhMeS + TsNHCl ⇌ PhMeSCl⁺ + TsNH⁻	141	75.7	64.3[d]
9	2-CO₂⁻-C₆H₄SMe + TsNHCl ⇌ TS **26y**	61.1	-	56.7[d]
10	PhMeS + TsNCl₂ ⇌ PhMeSCl⁺ + TsNCl⁻	82.0	30.7	27.6[d]

[a]Ms = MeSO₂; Ts = 4-MeC₆H₄SO₂.

[b]Measured[34] in water, at 25°C. In 1:1 (v/v) ethanol-water, at 20°C $\Delta G^{\ddagger}$ = 64.3 kJ mol^{-1} was obtained.[10]
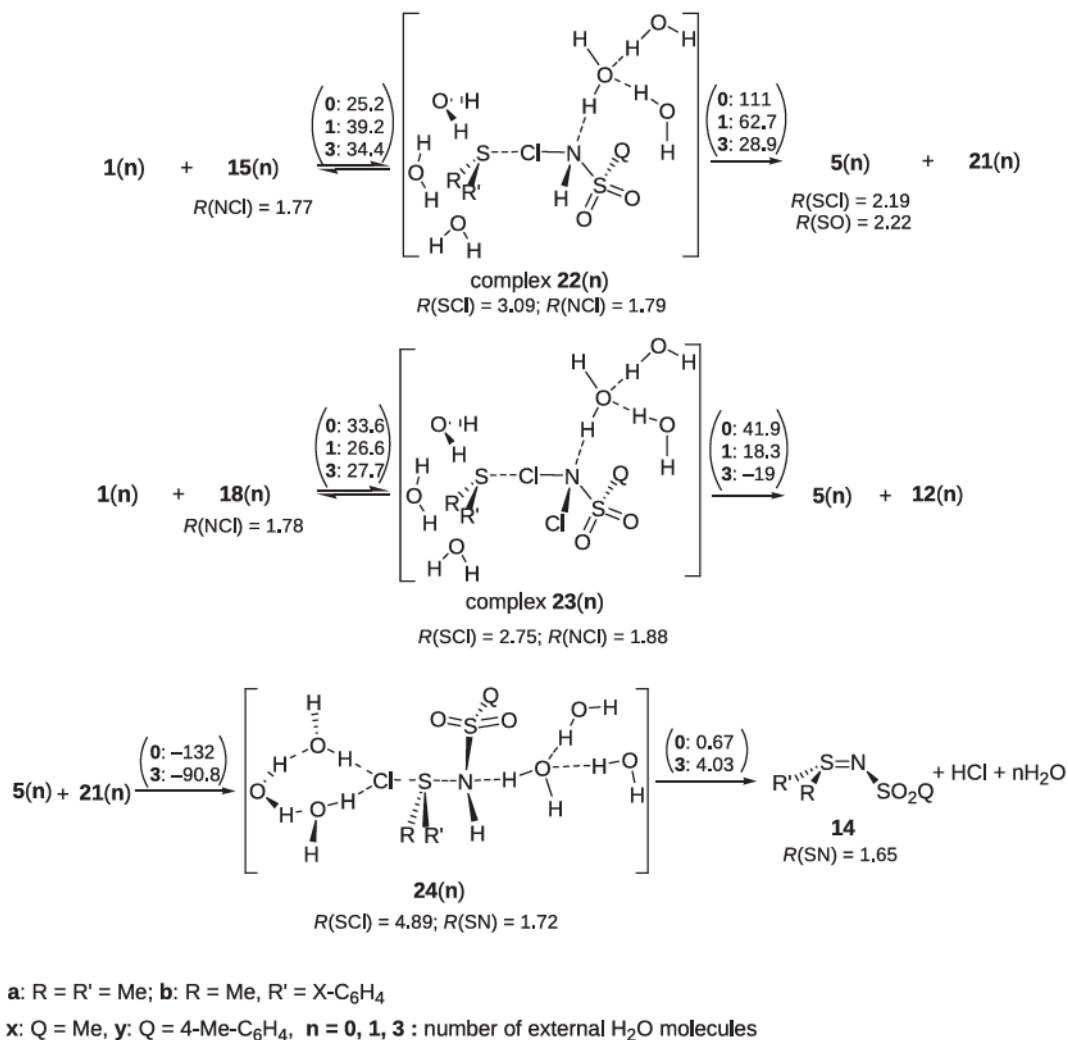
[c]$\Delta G^{\ddagger}$ value of the formation of complex **23ax**. Dissociation of complex **23ax** proceeds with decrease of free energy (Scheme 6).

[d]Measured[10] in 1:1 (v/v) ethanol-water, at 20°C.

derived for this reaction from rate constants, measured in water[34] and in 1:1 (v/v) ethanol-water mixture,[10] respectively (Table 2, entry 2).

Complexes **22ax** and **23ax** are formed in the first step of chlorination of Me₂S (**1a**) with MsNHCl (**15x**) and MsNCl₂ (**18x**), respectively, decreasing the distance between the sulfur and chlorine atoms of the reactants [Scheme 6; Figure 2, ΔE vs $R(S\cdots Cl)$ plots]. The calculated $R(S\cdots Cl)$ distances in complexes **22ax** and **23ax** are long, the charges of the sulfur and chlorine atoms are small, and the $R(N—Cl)$ bond lengths are only slightly longer than in reactants **15x** and **18x** (Scheme 6, Q = Me, Table S4 in the SI). Tight ion pairs [TIP, (R₂SCl)⁺(NHQ)⁻] are not formed in the chlorination of sulfides with

N-chlorosulfonamides, because the total energy of the reacting species increases continuously with decrease of the distance between the sulfur and chlorine atoms [Figure 2, ΔE vs $R(S\cdots Cl)$ plots]. Extreme value cannot be found on the ΔE vs $R(S\cdots Cl)$ plots at $R(S—Cl)$ = 2.045 Å bond length of Me₂SCl⁺ (**5a**). The chlorine atom of complexes **22ax** and **23ax** can be transferred to sulfur with the increase of the distance between nitrogen and chlorine atoms [Figure 2, ΔE vs $R(N—Cl)$ plots], to form Me₂SCl⁺ cation (**5a**) and MsNH⁻ (**21x**) or MsNCl⁻ (**12x**) anion intermediates. Calculations performed without explicit water molecules (n = 0) showed that the formation of ions from complex **23ax** needs twice smaller energy than the analogous reaction of complex **22ax**

a: R = R' = Me; **b**: R = Me, R' = X-C$_6$H$_4$

x: Q = Me, **y**: Q = 4-Me-C$_6$H$_4$, **n = 0, 1, 3** : number of external H$_2$O molecules

SCHEME 6 Mechanisms for the chlorination of sulfides (**1**) with *N*-chlorosulfonamide (**15**) and *N,N*-dichlorosulfonamide (**18**) and the formation of sulfilimine (**14**). Free energies changes (ΔG), calculated without and with one and three explicit water molecules (**n = 0, 1,** and 3), for the reactions of Me$_2$S (**1a**), and derivatives of *N*-chloromethanesulfonamide [**12x, 15x,** and **18x**, Q = Me] are given in parentheses, in the unit of kJ mol^{-1}, in the direction of the neighboring arrow. Bond lengths (R, in Å unit) are given for species R = R' = Me and Q = Me, with three explicit water molecules (**n = 3**). Calculations were performed at DFT(B3LYP)/6-31G(d) level of theory in water at 25°C.

(Figure 2). The reason may be that delocalization of the negative charge in MsNCl⁻ (**12x**) is more effective than in MsNH⁻ (**21x**), and MsNCl⁻ is a better leaving group than MsNH⁻. The formation of ions from complexes **22ax** and **23ax** needs much smaller energy than the dissociation of complex **3a** in the reaction of Me$_2$S and HOCl (Figure 1). The MsNH⁻ and MsNCl⁻ anions are better leaving groups than OH⁻.

Chlorination of sulfides (**1**) with *N*-chlorosulfonamides (**15, 18**) has also been calculated with explicit water molecules (Scheme 6, **n = 1** and **3**). The positively charged or polarized sulfur atoms of species **5, 22,** and **23** are surrounded by the oxygen atoms of the explicit water molecules. Hydrogen bonding is formed with the nitrogen atoms of all species. The calculated $\Delta G^{\ddagger}$ data depend only slightly on the number of explicit water molecules

for those reaction steps which proceed without the change of the number of charges. On the other hand, the $\Delta G^{\ddagger}$ values, calculated for the formation of ions, decrease considerably with the increase of the number of explicit water molecules. [Cf. steps **1(n) + 15(n)** ⇄ **22(n)** and **1(n) + 18(n)** ⇄ **23(n)** with **22(n)** → **5(n) + 12(n)**, and **23(n)** → **5(n) + 12(n)** in Scheme 6, **n = 0, 1,** and 3, and $\Delta G^{\ddagger}$ values in Table 2, entries 3, 4, 6-8, 10]. The chlorosulfonium cations (**5**) and the sulfonamidate anions (**12, 21**) are the intermediates of highest energy; their formation can be regarded as the rate-determining step of the reactions of sulfides and *N*-chlorosulfonamides. The $\Delta G^{\ddagger}$ values are the sum of the free energy changes of the formation of complexes **22** and **23**, and their dissociation to ions **5, 21,** and **12** (Scheme 6, Table 2). $\Delta G^{\ddagger}$(calc) values, calculated for the
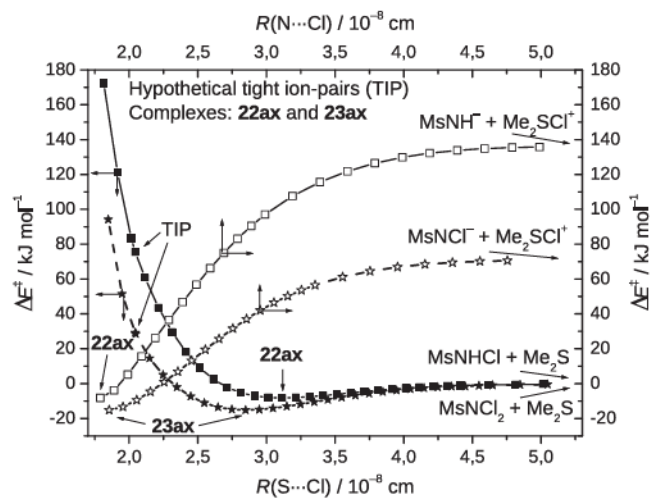
FIGURE 2 ΔE vs $R(S\cdots Cl)$ plots for the attack of Me$_2$S at the chlorine atoms of MsNHCl (**1a** + **15x** $\rightleftarrows$ **22ax**) and MsNCl$_2$ (**1a** + **18x** $\rightleftarrows$ **23ax**), and ΔE vs $R(N\cdots Cl)$ plots for the dissociation of complexes **22ax** and **23ax** to ions Me$_2$SCl$^+$, MsNH$^-$' and MsNCl$^-$ (**22ax** → **5a** + **21x** and **23ax** → **5a** + **12x**, Scheme 6). Calculations were performed without explicit water molecules, using the polarizable continuum model of solvents, at DFT(B3LYP)/6-31G(d) level of theory in water at 25°C. $\Delta E = 0$ for the separated reactants

reactions of TsNHCl (**15y**) and TsNCl$_2$ (**18y**) with Me$_2$S (**1a**) and PhSMe (**1b**) with three explicit water molecules (**n** = 3) and with the polarizable continuum model of solvent, is close to the $\Delta G^{\ddagger}$(exp) data, derived from the rate constants of kinetic measurements[10] (Table 2, entries 7, 8, and 10).

Electron-donating substituents on the phenyl ring of aryl methyl sulfides (**1b**) decrease the $\Delta G^{\ddagger}$ values and increase the rate of the reactions with TsNHCl (**15y**) and TsNCl$_2$ (**18y**, Figure 3). This is in accordance with the increase of the positive charge of the sulfur atom at the formation chlorosulfonium cation intermediate.[10] Both the calculated and the experimentally derived $\Delta G^{\ddagger}$ values give good correlations with the Hammett σ substituent constants. The calculated ρ reaction constants of the Hammett equation[44–46] are similar to the experimental data[10] (Figure 3).

Sulfilimines (**14**) are produced in the reaction of chlorosulfonium cation (**5**) and sulfonamidate anion (**21**) intermediates, through sulfonamido-chloro-λ^4-sulfanes (**24**, Scheme 6). Water molecules promote the dissociation of the chlorine of λ^4-sulfane **24(6)**; the distance between the sulfur and chlorine atoms is very long in this species. Sulfoxides are produced via the hydrolysis of chlorosulfonium cations (Scheme 2 and 3). The formation of products from intermediates is a fast reaction; it proceeds with the decrease of free energy.

Earlier, we have found that the *ortho*-carboxy group has a neighboring group effect in the reactions of aryl
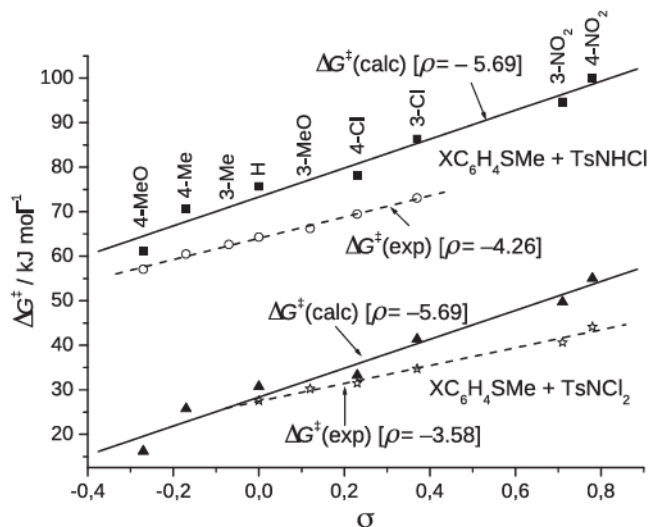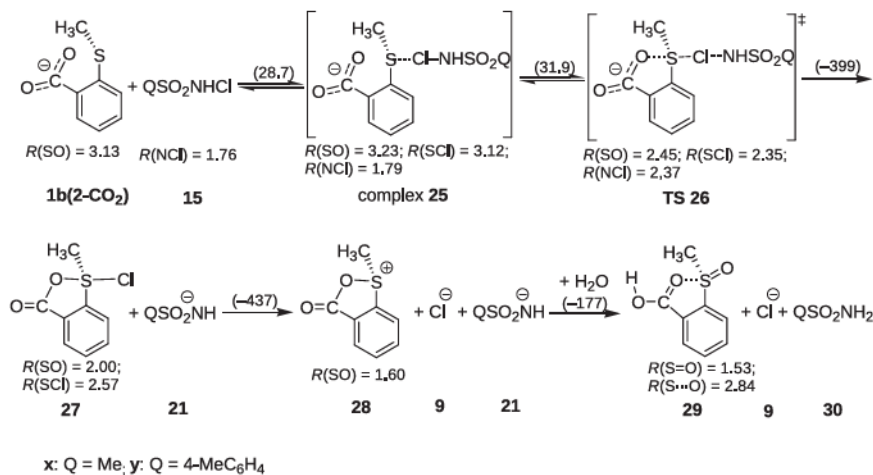

FIGURE 3 Calculated and experimentally derived $\Delta G^{\ddagger}$ vs σ plots for the reactions of X-C$_6$H$_4$SMe sulfides [**1b(3)**] with TsNHCl [**15y(3)**] and TsNCl$_2$ [**18y(3)**, Scheme 6]. Calculations were performed with three explicit water molecules (**n** = 3), using also the polarizable continuum model of solvents, at DFT(B3LYP)/6-31G(d) level of theory in water at 25°C. Kinetic measurements[10] were carried out 1:1 (v/v) ethanol-water mixtures at 20°C. The ρ constants of the Hammett equation were calculated from the slopes of the $\Delta G^{\ddagger}$ vs σ plots[44–46] [Correlations: **1b(3)** + **15y(3)**: $\Delta G^{\ddagger}$(calc) = 32.5σ + 73.3 (r = 0.983), $\Delta G^{\ddagger}$(exp) = 23.9σ + 64.0 (r = 0.997); **1b(3)** + **18y(3)**: $\Delta G^{\ddagger}$(calc) = 32.5σ + 28.3 (r = 0.983), $\Delta G^{\ddagger}$(exp) = 20.1σ + 27.4 (r = 0.993)]

methyl sulfides (**1b**) and *N*-chlorosulfonamides.[23,47] The reactions are anchimerically assisted, and λ^4-sulfanes can be prepared from 2,2′-dicaboxy-diphenyl sulfides in anhydrous media.[17,19,21,48] The reactions were supposed[23] to proceed through chlorosulfonium cation intermediate. DFT calculations showed, however, that complex **25x** is formed in the first step from 2-CO$_2$$^-$-C$_6H_4$SMe [**1b(2-CO$_2$)**] and MsNHCl (**15x**, Scheme 7). Complex **25x** is converted via TS **26x** to acyloxy-chloro-λ^4-sulfane **27** and MsNH$^-$ (**21x**) without the intermediacy of a chlorosulfonium cation. The hypervalent S—Cl bond of λ^4-sulfane **27** is long; chloride ion dissociates easily to produce acyloxy-sulfonium cation **28**, which hydrolyzes to the sulfoxide product (**29**, Scheme 7). In accordance with the experimentally observed anchimeric assistance, the calculated $\Delta G^{\ddagger}$ values for the reaction of 2-CO$_2$$^-$-C$_6H_4$SMe [**1b(2CO$_2$)**] with MsNHCl (**15x**) or TsNHCl (**15y**) are smaller than those of the reactions of PhSMe (**1b**, Table 2, entries 4, 5, 8, and 9). The experimentally derived $\Delta G^{\ddagger}$ value of the reaction 2-CO$_2$$^-$-C$_6H_4$SMe [**1b(2-CO$_2$)**] with TsNHCl (**15y**) agrees with data calculated without explicit water molecule (**n** = 0), because the reaction proceeds without the change of the number of charges (Table 2, entry 9).

SCHEME 7 Mechanism for the reaction of 2-CO^--C_6H_4SMe [**1b(2-CO_2)**] with *N*-chlorosulfonamides (**15**). Free energy changes (ΔG), calculated without explicit water molecules for the reactions with $MeSO_2NHCl$ (**15x**, Q = Me), are given in parentheses, in the unit of kJ mol^{-1}, in the direction of the neighboring arrow. Bond lengths (R, in Å unit) are given for derivatives bearing the Q = Me group. Calculations were performed at DFT(B3LYP)/6-31G(d) level of theory in water at 25°C.

3 | CONCLUSIONS

The reaction of sulfides with hypochlorous acid can proceed with the attack of sulfur atom at the oxygen atom of HOCl (Equation (6)), or with the formation of chlorosulfonium cation and hydroxide ion intermediates via the attack at the chlorine atom of HOCl (Scheme 1). The second reaction path has comparable free energy of activation value to the former one only in polar protic solvents, when the ion intermediates [**5(3)** and **6(3)**] are strongly solvated. Solvation decreases the high free energy of activation, which is needed for the formation of ions, and promotes the departure of the very poor OH$^-$ leaving group. The attack of sulfides at the oxygen atom of HOCl (Equation (6)) can proceed in less polar solvents, because the polarity of the TS is relatively small,[25] and the Cl$^-$ is a much better leaving group than OH$^-$. The conclusions are in accordance with the results obtained for the reaction of HOCl with amines, that *N*-chlorination is kinetically more favored than hydroxylation in more polar media.[49]

In the reaction of sulfides with *N*-chlorosulfonamides, the formation of chlorosulfonium cation (**5**, Scheme 6) is preferred, because the leaving of the sulfonamidate anions (**12** and **21**), having delocalized negative charge, needs small free energy of activation. The results of kinetic studies are in accordance with this mechanism. On the other hand, DFT calculations indicated that the attacks of sulfides at the nitrogen atom of *N*-chlorosulfonamides are very slow reactions; the calculated and experimental $\Delta G^{\ddagger}$ data do not agree with each other (Scheme 4).

The application of the polarizable continuum model of solvents seems to be satisfactory for the calculation of $\Delta G^{\ddagger}$ values of reactions if ions are not formed, or if the number of charges does not change in the reaction of ions and neutral molecules. Explicit water molecules must be included, however, when the reaction proceeds with the formation or destruction of ions. Ions must be solvated with at least three explicit water molecules to get free energy of activation values, comparable with the experimental data.

4 | COMPUTATIONAL METHODS

Geometries of reactants, intermediates, TSs, and products were fully optimized without symmetry constraints using the Gaussian 09 software package[50] at DFT(B3LYP)/6-31G(d) and DFT(B3LYP)/6-311 + G(d,p) levels of theory in water, at 25°C. The solvent effect was incorporated by applying the polarizable continuum model[51] in the integral equation formalism[52,53] (IEF-PCM) of the corresponding solvent. Explicit water molecules have also been included for modeling the participation of water molecules in the formation and destruction of ions. The B3LYP functional was found to perform well in investigation of trends in the reactions of nucleophiles.[54,55] Internal reaction coordinate (IRC) calculations[56] were performed to identify the minima connected through the TS. Structures were characterized as energy minima or TSs by calculating the harmonic vibrational frequencies. No imaginary frequency was obtained for reactants, complexes, and products. TSs had only one imaginary frequency. Selected data for the optimized structures, obtained by means of DFT calculations, are listed in Table S4 in the SI.

The sums of the electronic and thermal free energies (G), and enthalpies (H), as well as the entropies of formation (S) for the reactants, complexes, products, and TSs were obtained by the standard procedure in the framework of the harmonic approximation,[57,58] and are listed together with the calculated total energies (E) and value of imaginary frequencies in Table S3 in the SI.

The $\Delta E^{\ddagger}$, $\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$ activation parameters of the reactions were calculated from the differences in the

E, G, H, and S values of TSs and reactants[27–32] (Equation (7), $P = E$, G, H, or S), and are listed in Tables S1 and S2 in the SI.

$$\Delta P^{\ddagger} = P_{TS} - \sum P_R \qquad (7)$$

The generated $\Delta E^{\ddagger}$, $\Delta G^{\ddagger}$, and $\Delta H^{\ddagger}$ values were multiplied by 2625.5 in order to convert them from atomic units into kJ mol^{-1}. The experimentally derived activation parameters were calculated from the second-order rate constants using the Eyring equation.[59,60] The $\Delta G^{\ddagger}$ values are influenced somewhat by the level of theory of computations[29,30] (Table S1 in the SI), but they are in agreement with the conclusions.

The free energy of activation data were correlated with the Hammett σ substituent constants (Figure 3), as described previously[27–32] (Equation (8)).

$$\Delta G^{\ddagger} = \delta \Delta G^{\ddagger} \sigma + \Delta G_o^{\ddagger} \qquad (8)$$

$\Delta G^{\ddagger}$ and $\Delta G_o^{\ddagger}$ are the data of substituted and unsubstituted compounds, respectively. The ρ constant of the Hammett equation can be calculated from the $\delta \Delta G^{\ddagger}$ slope of the $\Delta G^{\ddagger}$ vs σ plots.[44–46] The Hammett σ constants were taken from the compilation by Hansch et al.[59,61]

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REFERENCES

[1] S. Oae, _Organic Sulfur Chemistry; Structure and Mechanism_, CRC Press, Boca Roton **1991** 261 and references therein.

[2] L. Skattebol, B. Boulette, S. Solomon, _J. Org. Chem._ **1967**, _32_, 3111.

[3] C. R. Johnson, M. P. Jones, _J. Org. Chem._ **1967**, _32_, 2014.

[4] C. R. Johnson, J. J. Rigau, _J. Am. Chem. Soc._ **1969**, _91_, 5398.

[5] D. Swern, I. Ikeda, G. F. Whitfield, _Tetrahedron Lett._ **1972**, _13_, 2635.

[6] I. Jalsovszky, F. Ruff, M. Kajtár-Peredy, Á. Kucsman, _Synthesis_ **1990**, _1990_, 1037.

[7] I. Jalsovszky, F. Ruff, Á. Kucsman, _Tetrahedron_ **1993**, _49_, 8407.

[8] P. Kovalski, K. Mitka, K. Ossowska, Z. Kolarska, _Tetrahedron_ **2005**, _61_, 1933.

[9] S. Oae, N. Furukawa, _Sulfilimines and Related Derivatives_, ACS. Monograph 179, American Chemical Society, Washington D.C **1983** 7 and references therein.

[10] F. Ruff, Á. Kucsman, _J. Chem. Soc., Perkin_ **1975**, _2_, 509.

[11] M. M. Campbell, G. Johnson, _Chem. Rev._ **1978**, _78_, 65. and references therein

[12] I. V. Koval, _Sulfur Reports_ **1993**, _14_, 149.

[13] P. C. Taylor, _Sulfur Reports_ **1999**, _21_, 241.

[14] D. Thenraja, P. Subramanian, C. Srinivasan, _J. Chem. Soc., Perkin_ **2002**, _2_, 2125. and references therein

[15] R. J. Arhart, J. C. Martin, _J. Am. Chem. Soc._ **1972**, _94_, 4997. 5003-5010

[16] G. E. Wilson Jr., _Tetrahedron_ **1982**, _38_, 2597. and references therein

[17] I. Kapovits, A. Kálmán, _J. Chem. Soc. Chem. Commun._ **1971**, _0_, 649.

[18] Á. Kucsman, I. Kapovits, in _Organic Sulfur Chemistry: Theoretical and Experimental Advances_, (Eds: F. Bernardi, I. G. Csizmadia, A. Mangini), Elsevier, Amsterdam **1985**, Ch. 4 191 and references therein.

[19] R. A. Hayes, J. C. Martin, in _Organic Sulfur Chemistry: Theoretical and Experimental Advances_, (Eds: F. Bernardi, I. G. Csizmadia, A. Mangini), Elsevier, Amsterdam **1985**, Ch. 8 408 and references therein.

[20] J. Drabowicz, in _Chemistry of Hypervalent Compounds_, (Ed: K.-y. Akiba), Wiley-VCH, Chicherster **1999**, Ch. 7 211.

[21] D. Szabó, F. Ruff, Á. Kucsman, _Targets Heterocycl. Syst._ **2001**, _5_, 199.

[22] F. Ruff, K. Komoto, N. Furukawa, S. Oae, _Tetrahedron_ **1976**, _32_, 2763.

[23] F. Ruff, I. Kapovits, J. Rábai, Á. Kucsman, _Tetrahedron_ **1978**, _34_, 2767.

[24] F. Ruff, G. Szabó, J. Vajda, I. Kövesdi, Á. Kucsman, _Tetrahedron_ **1980**, _36_, 1631.

[25] F. Ruff, I. Jalsovszky, D. Szabó, J. Rábai, Ö. Farkas, Á. Kucsman, _J. Phys. Org. Chem._ **2012**, _25_, 1086.

[26] O. Acevedo, W. L. Jorgensen, _Acc. Chem. Res._ **2010**, _43_, 142. and references therein

[27] F. Ruff, Ö. Farkas, _J. Org. Chem._ **2006**, _71_, 3409.

[28] F. Ruff, Ö. Farkas, Á. Kucsman, _Eur. J. Org. Chem_ **2006**, _2006_, 5570.

[29] F. Ruff, Ö. Farkas, _J. Phys. Org. Chem._ **2008**, _21_, 53.

[30] A. Fábián, F. Ruff, Ö. Farkas, _J. Phys. Org. Chem._ **2008**, _21_, 988.

[31] F. Ruff, A. Fábián, Ö. Farkas, Á. Kucsman, _Eur. J. Org. Chem._ **2009**, _2009_, 2102.

[32] F. Ruff, Ö. Farkas, _J. Phys. Org. Chem._ **2011**, _24_, 480.

[33] J. C. Morris, J. A. Salazar, M. A. Wineman, _J. Am. Chem. Soc._ **1948**, _70_, 2036.

[34] T. Higuchi, K. Ikeda, A. Hussain, _J. Chem. Soc. (B)_ **1967**, _n/a_, 546.

[35] T. Higuchi, A. Hussain, I. H. Pitman, _J. Chem. Soc. (B)._ **1969**, _n/a_, 626.

[36] J. M. Antelo, F. Arce, J. Crugeiras, M. Parajo, _J. Phys. Org. Chem._ **1997**, _10_, 631.

[37] M. P. Snyder, D. W. Margerum, _Inorg. Chem._ **1982**, _21_, 2545.

[38] P. Calvo, J. Crugeiras, A. Rios, _J. Org. Chem._ **2009**, _74_, 5381.

[39] C. Pastoriza, J. M. Antelo, J. Crugeiras, _J. Phys. Org. Chem._ **2013**, _26_, 551.

[40] T. Tarade, V. Vrcek, *Int J. Quantum Chem.* **2013**, *113*, 881.

[41] I. H. Pitman, H. Dawn, T. Higuchi, A. Hussain, *J. Chem. Soc. (B)* **1969**, *n/a*, 1230.

[42] H. Dawn, I. H. Pitman, T. Higuchi, S. Young, *J. Pharm. Sci.* **1970**, *59*, 955.

[43] pK_a values of TsNH$_2$ and TsNHCl are 10.3[34] and 4.55,[33,34] respectively, in water, at 25°C.

[44] The ρ constants of the Hammett equation (log $k/k_o = \rho\sigma$) were calculated[45,46] using the equation: $\delta\Delta G^{\ddagger} = -2.303RT\rho$. $\delta\Delta G^{\ddagger}$ is the slope of the $\Delta G^{\ddagger}$ vs. σ plot.

[45] O. Exner, *Prog. Phys. Org. Chem.* **1973**, *10*, 411.

[46] F. Ruff, *Internet Electron. J. Mol. Des.* **2004**, *3*, 474. http://www.biochempress.com

[47] F. Ruff, Á. Kucsman, *J. Chem. Soc., Perkin* **1988**, *2*, 1123.

[48] I. Kapovits, J. Rábai, F. Ruff, Á. Kucsman, *Tetrahedron* **1979**, *35*, 1869.

[49] D. Sakic, M. Hanzeracki, D. M. Smith, V. Vrcek, *Org. Biomol. Chem.* **2015**, *13*, 11740.

[50] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. G. Scalmami, V. Barone, B. Mennucci, G. A. Peterson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Oglario, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, N. J. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Baken, C. Adamo, C. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Daprich, A. D. Daniels, M. Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, *Gaussian 09, Revision A.01*, Gaussian, Inc, Wallingford, CT **2009**.

[51] J. Tomasi, M. Persico, *Chem. Rev.* **1994**, *94*, 2027.

[52] E. Cancès, B. Mennucci, *J. Chem. Phys.* **2000**, *114*, 4744.

[53] D. M. Chipman, *J. Chem. Phys.* **2000**, *112*, 5558.

[54] A. P. Bento, M. Sola, F. M. Bickelhaupt, *J. Comput. Chem.* **2005**, *26*, 1497.

[55] M. Swart, M. Sola, F. M. Bickelhaupt, *J. Comput. Chem.* **2007**, *28*, 1551.

[56] C. Gonzales, H. B. Schlegel, *J. Chem. Phys.* **1989**, *90*, 2154.

[57] D. A. McQuarrie, J. D. Simon, *Molecular Thermodynamics*, University Science Books, Sausalito, CA **1999**.

[58] http://www.gaussian.com/g_whitepap/thermo/thermo.pdf

[59] F. Ruff, I. G. Csizmadia, *Organic Reactions: Equilibria, Kinetics and Mechanism*, Elsevier, Amsterdam **1994** 290.

[60] E. V. Anslyn, D. A. Dougherty, *Modern Physical Organic Chemistry*, University Science Books, Sausalito **2006** 461.

[61] C. Hansch, H. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165.

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