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# Concerted SN2 mechanism for the hydrolysis of acid chlorides. Comparison of reactivities calculated by the density functional theory with experimental data

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**Concerted SN2 mechanism for the hydrolysis of acid chlorides. Comparison of reactivities calculated by the density functional theory with experimental data**

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3 **Concerted S<sub>N</sub>2 mechanism for the hydrolysis of acid chlorides.**  
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5 **Comparisons of reactivities calculated by the density functional theory**  
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7 **with experimental data**  
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9 **Ferenc Ruff\*<sup>[a]</sup> and Ödön Farkas<sup>[a]</sup>**  
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15 **Abstract** DFT computations have been performed in acetone and water solvents in order to  
16 investigate the mechanism of hydrolysis of acid chlorides. Acetyl chloride and chloroacetyl  
17 chloride hydrolyze via concerted, one-step S<sub>N</sub>2 mechanism, with the attack of water at the sp<sup>2</sup>  
18 hybridized carbon atom of the C=O group, and the transition state (TS) has distorted  
19 tetrahedral geometry. Solvent molecules act as general base and general acid catalysts. The  
20 TS of chloroacetyl chloride is tighter and less polar than the TS of acetyl chloride. The  
21 structure of the S<sub>N</sub>2 TS for the hydrolysis of benzoyl chlorides changes with the substituents  
22 and the solvent. Tight and loose TSs are formed for substrates bearing electron withdrawing  
23 (e-w) and electron donating (e-d) groups, respectively. In acetone, only the e-w effect of the  
24 substituents increase the reactivity of the substrates, and the change of the structure of the TSs  
25 with the substituents is small. In water, polar and very loose TSs are formed in the reactions  
26 of benzoyl chlorides bearing e-d substituents, and the rate enhancing effect of both e-d and e-  
27 w groups can be computed at higher level of theory. Calculated reactivities and the changes of  
28 the structure of the TSs with substituents and solvent are in accordance with the results of  
29 kinetic studies. In S<sub>N</sub>2 nucleophilic substitutions late/early TSs are formed if the attacking  
30 reagent is poorer/better nucleophile than the leaving group, and loose/tight TSs are formed for  
31 substrates bearing e-d/e-w substituents and in protic/aprotic solvents.  
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46 *Supporting information may be found in the online version of this article*  
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49 **Keywords:** nucleophilic substitution; acid chlorides; substituent effect; solvent effect; DFT  
50 calculations  
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## INTRODUCTION

Nucleophilic substitutions at the carbonyl group are considered to proceed via the tetrahedral mechanism.<sup>[1-4]</sup> The nucleophile (Nu) is supposed to attack the substrate (**1**) at the carbonyl group to give an intermediate (**2**), which bears both the nucleophile and the leaving group (L), and the leaving group may split off in the second step of the addition-elimination reaction (Ad-E, Scheme 1). The intermediacy of the tetrahedral species (**2**) was supported by the isotope exchange of the carbonyl oxygen atom (<sup>18</sup>O) in hydrolysis reactions,<sup>[5]</sup> by isolation of the intermediates<sup>[6,7]</sup> and by spectroscopic methods.<sup>[4,8]</sup> There is evidence, however, that bimolecular, one-step, S<sub>N</sub>2-type reactions can also take place, especially when L is a good leaving group.<sup>[9]</sup> In these cases the reaction pass through a transition state (TS **3**), the structure of which has not been investigated thoroughly yet. Unimolecular S<sub>N</sub>1-type mechanism, involving acylium ion intermediates (**5**) was also proposed for substrates bearing very good leaving groups, and strongly electron donating R substituents, in protic media.<sup>[2,3,10]</sup>

Kinetic studies have been performed on substituent and solvent effects<sup>[2,3,11]</sup> to investigate the mechanism of solvolyses of acid chlorides. S<sub>N</sub>2, S<sub>N</sub>1 and Ad-E mechanisms have been proposed for the reactions, depending on the structure of the substrates and on the media. S<sub>N</sub>2 like, approximately concerted bimolecular mechanism has been suggested for the solvolyses of acid chlorides, bearing weakly electron-donating (e-d) or electron-withdrawing (e-w) substituents, in media containing small amount of protic solvent.<sup>[2,3,11-16]</sup> S<sub>N</sub>1 like pathways, with the dominance of ionization of chloride ion, were considered to occur for compounds bearing very strong e-d groups in strongly polar protic solvents.<sup>[17-19]</sup> Competing S<sub>N</sub>2 and S<sub>N</sub>1 mechanisms were proposed for hydrolyses with increasing contribution of the S<sub>N</sub>1 pathway, when the water content of the solvent mixtures increased.<sup>[12,20-25]</sup> The mechanism of the hydrolyses of acid chlorides bearing strong e-w groups was considered to change for an Ad-E pathway with rate determining addition step.<sup>[12,16,25-28]</sup> Nevertheless, it was also suggested that not the mechanisms but only the structure of the TSs changes with the substituents and solvents.<sup>[29,30]</sup> The hydrolysis of acid chlorides was also supposed to occur at the hydrated form of the substrates.<sup>[31-33]</sup> Hydrates of acid chlorides could be the intermediates of the oxygen exchange reaction,<sup>[34]</sup> too.

Earlier we have performed DFT calculations on aliphatic S<sub>N</sub>2 and S<sub>N</sub>1 nucleophilic substitutions.<sup>[35-39]</sup> The medium effect on reactivity was computed using the polarizable continuum model (PCM) of solvents (see Section Computational methods). The free energy of activation ( $\Delta G^\ddagger$ ) values were found to be in reasonably good agreement with the experimentally derived data, calculated from rate constants of kinetic studies, using the

Eyring equation. Activation parameters, computed by quantum chemical methods refer only to the reaction, but experimental data contain also contributions from the rearrangement of the solvent molecules, which proceed during the reaction. The very fast rearrangement of solvent molecules influences, however, mainly the values of the experimentally derived enthalpy ( $\Delta H^\ddagger$ ) and entropy of activation ( $\Delta S^\ddagger$ ) data, and has only a relatively small effect on  $\Delta G^\ddagger$ . The experimentally derived  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  values increase/decrease namely, together with the decrease/increase of solvation of the TS, and approximately compensate each others changes according to the equation  $\delta\Delta G^\ddagger = \delta\Delta H^\ddagger - T\delta\Delta S^\ddagger$ . The rearrangement of the solvent molecules cannot be computed with the applied methods, therefore the computed and experimentally derived  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  parameters can be different, but the corresponding  $\Delta G^\ddagger$  data are similar to each other, and can be used to validate the mechanism of the reactions.

In this paper we report on DFT computations, performed on hydrolyses of acetyl chloride, chloroacetyl chloride and substituted benzoyl chlorides, at different levels of theory in water and acetone solvents. Explicit water and acetone molecules have also been included to study the participation of solvent molecules in the proton transfer steps. To validate the results, the computed  $\Delta G^\ddagger$  values have been compared with experimental data, derived from second order rate constants of hydrolyses of acid chlorides.

## RESULTS AND DISCUSSIONS

### Hydrolysis of acetyl chloride

The solvolysis of acetyl chloride (**6a**) has been the subject of kinetic studies for a long time, and bimolecular displacement mechanism has been proposed,<sup>[2,3,11,40,41]</sup> which involve loose, tetrahedral TS, with carbocation character and nucleophilic solvation.<sup>[14,15,42,43]</sup> Earlier, the rate-determining  $S_N1$  type ionization of the chloride ion of acetyl chloride has also been taken into consideration<sup>[23]</sup> because the slopes of the  $\log k$  vs.  $Y$  plots in acetone-water ( $m = 0.92$ )<sup>[41]</sup> and dioxane-water mixtures ( $m = 0.81$ )<sup>[23]</sup> are close to the value of  $S_N1$  nucleophilic substitutions<sup>[44-46]</sup> ( $m = 1$ ). Recent DFT computations,<sup>[47]</sup> performed on the methanolysis of protonated acetyl chloride, have led to the conclusion, that the results are consistent with the ionization of  $Cl^-$ . It is to be noted, however, that acetyl chloride is not protonated in solvolyses under normal reaction conditions.<sup>[48,49]</sup> It has also been suggested that dissociation of the chloride ion may follow the hydration of acetyl chloride,<sup>[23,32,33]</sup> though neither the fast<sup>[10,11]</sup> nor the slow<sup>[14]</sup> prior formation of the hydrate was supported by experimental data.<sup>[42]</sup>

In order to find the TS for the hydrolysis of acetyl chloride (**6a**) we have performed DFT calculations by decreasing stepwise the distance between the C(=O) and O(H<sub>2</sub>) atoms of the reactants, and by increasing the distance between the C(=O)⋯Cl atoms of acetyl chloride. The energy passes through a maximum at the decrease of the distances of the C<sup>1</sup>⋯O<sup>2</sup> atoms in the S<sub>N</sub>2 process (**6a** + **7** ⇌ TS **8a**, Fig. 1, Scheme 2). On the other hand, the total energy of the system increases steeply till the fission of the C<sup>1</sup>⋯Cl<sup>1</sup> bond at 3.2 Å in the S<sub>N</sub>1 process, (**6a** ⇌ TS **9a**). The formation of hydrogen bonding between the leaving chlorine and a water molecule in the **6a** + **7** ⇌ TS **10a** pathway of the S<sub>N</sub>1 reaction decreases the total energy but increases the free energy of activation of the dissociation, as compared to the **6a** ⇌ TS **9a** step (Fig. 1, Scheme 2). TSs **8a**, **9a** and **10a** were calculated with optimization; structural parameters are listed in Table 1 and Table S1 in the Supporting Information (SI). Since the total energies ( $\Delta E^\ddagger$ ) and the free energy of activation data ( $\Delta G^\ddagger$ ) for the acylium ion like TSs **9a** and **10a** [ $\theta(\text{O}^1\text{C}^1\text{C}^2) \sim 180^\circ$ ] are higher than those of TS **8a** (Fig. 1), one may conclude that acetyl chloride hydrolyzes via the more favorable S<sub>N</sub>2 mechanism. Intrinsic reaction coordinate computations (IRC, see Section Computational Methods) for the backward and forward directions show that TS **8a** is converted directly to complexes of reactants and products, respectively (Fig. 2), and no other intermediates should be taken into account.

TS **8a** has distorted tetrahedral geometry and C=O double bond [ $Q(\text{O}^1) = -0.322$  a.u.;  $R(\text{C}^1=\text{O}^1) = 1.168$  Å,  $\theta(\text{O}^1\text{C}^1\text{C}^2) = 137.3^\circ$ ,  $\theta(\text{O}^2\text{C}^1\text{C}^2) = 102.5^\circ$ ,  $\theta(\text{Cl}^1\text{C}^1\text{C}^2) = 97.5^\circ$ ,  $\theta(\text{Cl}^1\text{C}^1\text{O}^2) = 87.8^\circ$ , Table 1 and Table S1 in the SI], which is similar to the C=O bond of acetyl chloride [**6a**,  $Q(\text{O}^1) = -0.360$  a.u.;  $R(\text{C}^1=\text{O}^1) = 1.188$  Å,  $\theta(\text{O}^1\text{C}^1\text{C}^2) = 129.2^\circ$ ]. TS **8a** has one imaginary vibration, which results in the formation of the C<sup>1</sup>–O<sup>2</sup>, and the fission of the C<sup>1</sup>–Cl<sup>1</sup> bonds. Late TS is formed in the S<sub>N</sub>2 hydrolysis of acetyl chloride carried out with one water molecule, because water is poorer nucleophile than the leaving chloride ion. Approximate bond orders  $n \sim 0.65$  and  $0.35$  have been calculated for the C<sup>1</sup>⋯O<sup>2</sup> and C<sup>1</sup>⋯Cl<sup>1</sup> bonds, respectively, for TS **8a** in acetone and water solvents, using the Pauling equation<sup>[50]</sup> (Eqn 1, Items 1-4 in Table 2).

$$R - R_0 = a \ln(n) \quad (1)$$

The  $a$  coefficient of equation (1) was calculated from the C–Cl and C–O(H<sub>2</sub>) distances ( $R_0$ ) of CH<sub>3</sub>COCl (**6a**) and CH<sub>3</sub>COOH<sub>2</sub><sup>+</sup> (**13**, Scheme 3), and from the  $R_s(\text{C}^1\cdots\text{Cl}^1)$  and  $R_s(\text{C}^1\cdots\text{O}^2)$  distances of the symmetric TSs **14** and **15** ( $n = 0.5$ ) of the chlorine and water exchange reactions, respectively. Bond orders were obtained using the corresponding calculated  $R_r$  bond distances of TS **8a** (Table 2).

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3 The calculated  $R(\text{Cl}^1\cdots\text{H}^2)$  distance in TS **8a** (Table 1, Scheme 2) refer to a hydrogen  
4 bonding between one of the hydrogen atoms of the attacking water molecule and the leaving  
5 chlorine. This interaction may modify the structure and the energy of TS **8a**, but it is unlikely  
6 to occur in hydrolysis reactions in the presence of a great number of water molecules.  
7 Therefore TS **8a** cannot be considered to be the right model for the TS of the hydrolysis of  
8 acetyl chloride. It was supposed earlier<sup>[2,3,10,51]</sup> that more than one protic solvent molecule can  
9 take part in the solvolyses of acid chlorides, because the rate of reactions showed second-  
10 order dependence on protic solvents.<sup>[15,16,24,25]</sup> For this reason we used clusters of solvent  
11 molecules (**16** – **18**, Scheme 4) to study the effect of hydrogen bonding in the hydrolysis of  
12 acetyl chloride. TSs **19a** and **20a** with two and three explicit water molecules were calculated  
13 in water (**6a** + **16**  $\rightleftharpoons$  TS **19a**, **6a** + **17**  $\rightleftharpoons$  TS **20a**, Scheme 5, Table 1 and Table S1 in the SI).  
14 The explicit water molecules increase the nucleophilicity of the attacking water molecule, and  
15 help the leaving of the chloride ion with formation of hydrogen bonding. Namely, water  
16 molecules may act as nucleophile, as well as general base and general acid catalysts in the  
17 reaction. TSs **8a**, **19a** and **20a** are getting earlier, the  $\text{C}^1\cdots\text{Cl}^1$  bond orders (Items 4-6 in Table  
18 2), the  $Q(\text{O}^2)$  negative charges and the  $R(\text{C}^1\cdots\text{O}^2)$  distances increase, the  $Q(\text{Cl}^1)$  negative  
19 charges and the  $R(\text{C}^1\cdots\text{Cl}^1)$  distances decrease for these TSs in the given order (Table 1). The  
20  $\text{C}^1$  atom vibrates between  $\text{O}^2$  and  $\text{Cl}^1$ , and the  $\text{H}^2$  atom vibrates between  $\text{O}^2$  and  $\text{O}^3$  in the  
21 transition vectors of TSs **19a** and **20a**. The  $\text{H}^2$  atom is bonded more strongly to  $\text{O}^2$  than to  $\text{O}^3$   
22 [cf. the  $R(\text{O}^2\text{--}\text{H}^2)$  and  $R(\text{O}^3\cdots\text{H}^2)$  distances in Table 1]. The  $\text{H}^4$  and  $\text{H}^6$  hydrogen atoms are not  
23 transferred between the oxygen atoms in the TSs. In solvent mixtures of low water content,  
24 molecules of the dipolar aprotic solvent may also participate as hydrogen bond acceptor,  
25 instead of the water molecules. Acetone was proposed<sup>[25,52]</sup> to act as general base catalyst in  
26 hydrolysis reactions of acid chlorides. TS **21a** was computed for the hydrolysis of acetyl  
27 chloride in acetone containing only a small amount of water (**6a** + **18**  $\rightleftharpoons$  TS **21a**, Scheme 5).  
28 IRC computations for TSs **19a-21a** lead also to the complexes of reactants and products, other  
29 intermediates need not to be taken into account (Fig S1 and S2 in the SI).

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51 The values of  $\Delta G^\ddagger = 67$  and  $91 \text{ kJ mol}^{-1}$  have been calculated by extrapolation for the  
52 hydrolysis of acetyl chloride in water and acetone, at  $25^\circ\text{C}$ , respectively, from the  
53 dependence of the rate constants on solvent polarity parameters.<sup>[53-55]</sup> The  $\Delta G^\ddagger = 72.4$ ,  $74.0$   
54 and  $89.8 \text{ kJ mol}^{-1}$  values, computed at (B3LYP)/6-31G(d) level of theory for TSs **19a** and **20a**  
55 in water and for TS **21a** in acetone, respectively, approximate the experimentally derived data  
56 well (Scheme 5, Table 1 and Table S7 in the SI). It must be mentioned, however, that the  
57 values of the calculated  $\Delta G^\ddagger$  parameters increase with the increasing level of theory, and in  
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3 the case of MP2 calculations (Table S7 in the SI), as it was observed earlier<sup>[37,38]</sup> for other  
4 reactions, too (see also Section Computational Methods).

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6 The hydrolyses of acid chlorides were also supposed<sup>[23,32,33]</sup> to proceed through the hydrated  
7 substrates, though these intermediates have neither been synthesized nor detected in the  
8 reaction mixtures. Acetyl chloride hydrate could be formed if the nucleophilic attack of water  
9 on the carbonyl group would be accompanied by a proton transfer towards the oxygen atom of  
10 the C=O group. TS **22a** has been calculated for this process (Scheme 5), in which two water  
11 molecules form a bridge between the attacking water molecule and the carbonyl group.<sup>[56]</sup>  
12 IRC calculations proved, however, that TSs, like **22a** are transformed spontaneously only to  
13 the complexes of reactants and products of the hydrolysis (**6a** + **17** ⇌ TS **22a** → **11a** + **12** +  
14 **16**, Scheme 5, Fig. S2 in the SI), but do not collapse to the complexes of acid chloride  
15 hydrates and two water molecules (**23a**). The H<sup>6</sup> hydrogen atom does not move spontaneously  
16 towards the neighboring O<sup>1</sup> carbonyl oxygen atom, and the prior protonation of acetyl  
17 chloride can also be excluded because of the very low basicity of the C=O group.<sup>[1,48,49]</sup> If one  
18 moves the H<sup>6</sup> hydrogen atom arbitrarily, stepwise towards the O<sup>1</sup> carbonyl oxygen atom, the  
19 reacting system passes through a barrier, the energy of which is much higher than that of TS  
20 **22a** (Fig S3 in the SI). Computations also showed, however, that the hydrate complex **23a**  
21 could decompose through the acetyl chloride hydrate TS (**24a**) and the complex of protonated  
22 acetic acid and chloride ion (**25a**) to acetic acid and HCl products (**11a** + **12**, Scheme 5, Table  
23 S7 in the SI). Nevertheless, we cannot prove that these species participate in hydrolyses of  
24 acid chlorides, because complex **23a** or acetyl chloride hydrate (TS **24a**) are not formed at the  
25 nucleophilic attack of water on the C=O group of acetyl chloride.  
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#### 44 Hydrolysis of chloroacetyl chloride

45 Kinetic studies have led to the conclusion that chloroacetyl chloride (**5b**) hydrolyzes via Ad-E  
46 pathway, with rate-determining addition step.<sup>[16,25,43]</sup> The rate of the reaction showed low  
47 sensitivity to solvent ionizing power, and high sensitivity to solvent nucleophilicity,<sup>[43]</sup> and  
48 higher kinetic solvent isotope effect (KSIE = 2.18) was observed for the reaction of  
49 chloroacetyl chloride,<sup>[25,43]</sup> than in the case of acetyl chloride<sup>[14]</sup> (KSIE = 1.3). The reaction of  
50 substrate **5b** exhibits second order kinetics on protic solvents,<sup>[25]</sup>  
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56 Analogous S<sub>N</sub>2 type TSs (**8b**, **19b-22b**) have been calculated for hydrolyses of chloroacetyl  
57 chloride (**6b**) as for acetyl chloride (**6a**, Scheme 2 and 5, Table 3 and Tables S2 and S8 in the  
58 SI). In TSs **19b-22b**, bearing explicit solvent molecules, the H<sup>2</sup> atom is strongly bonded to  
59 two oxygen atoms (O<sup>2</sup>...H<sup>2</sup>...O<sup>3</sup>), therefore the solute cavity can only be build up using the  
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3 Radii=UAHF option (see Section Computational Methods). To be able to compare the results,  
4 obtained for hydrolyses of the substrates **6a** and **6b**, calculations were also performed for TSs  
5 **8a** and **19a-22a** of the hydrolysis of acetyl chloride (**6a**) with the Radii=UAHF option.  
6 Results, computed for TSs **8a** and **19a-22a** show that the structural parameters change  
7 slightly, and energies are about 10 kJ mol<sup>-1</sup> higher if the Radii=UAHF option is used for the  
8 calculation of the solvent cavity (Tables 1 and 3). IRC calculations on TSs **8b** and **19b-22b**  
9 proved that these TSs are converted directly to the complexes of reactants and products  
10 without the formation of tetrahedral intermediates (Fig. 2 and Fig S2 in the SI). The  
11 spontaneous transformation of TS **22b** to complex **23b** and TS **24b** (Scheme 5) of  
12 chloroacetyl chloride hydrate was also not observed, therefore the participation of complex  
13 **23b** and TS **24b** in the hydrolysis may be ruled out.

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Though the structures of the computed S<sub>N</sub>2 type TSs are similar, the  $Q(O^2)$  and  $Q(Cl^1)$   
negative charges, as well the  $R(C^1 \cdots O^2)$  and  $R(C^1 \cdots Cl^1)$  distances are smaller, but the  
 $R(O^2 \cdots H^2)$  distance is longer for TSs **19b – 22b** of the hydrolysis of chloroacetyl chloride, than  
for TSs **19a – 22a** of acetyl chloride (Table 3). Tighter and less polar S<sub>N</sub>2 TSs, with weaker  
ionization of chlorine and stronger nucleophilic attack of water are formed for reactant **6b**  
than for **6a**. According to the stronger nucleophilic attack of water, the fission of the O<sup>2</sup>⋯H<sup>2</sup>  
bond is also more advanced in TSs **19b – 22b**. These conclusions are in accordance with the  
observed higher KSIE and sensitivity on solvent nucleophilicity, as well on the lower  
sensitivity on solvent ionizing power of the reaction of chloroacetyl chloride.<sup>[25,43]</sup>

$\Delta G^\ddagger = 75.2$  kJ mol<sup>-1</sup> was derived for the hydrolysis of the reactant **6b** in water by the  
extrapolation of the rate constants, measured<sup>[57]</sup> in acetone water mixtures at -10<sup>o</sup> C. This is in  
accordance with the  $\Delta G^\ddagger = 79.5$ -83.5 kJ mol<sup>-1</sup> values, computed for TSs **19b**, **20b** and **22b** at  
(B3LYP)/6-31G(d) level of theory at the same circumstances (Scheme 5, Table 3 and Table  
S8 in the SI). Results of computations support that the hydrolysis of chloroacetyl chloride  
proceeds with the same concerted S<sub>N</sub>2 mechanism as acetyl chloride, but the structures of the  
TSs of the reactions are different.

### Hydrolysis of benzoyl chlorides

The mechanism of the hydrolysis of benzoyl chlorides was widely investigated by kinetic  
methods.<sup>[2,3,11,26,51,58]</sup> Nevertheless, G3 calculations were also carried out on the stability of  
acylium ion intermediates in the gas phase,<sup>[42]</sup> and homodesmotic stabilization energies were  
estimated<sup>[59]</sup> for reactants and intermediates of the reactions. The pathways of hydrolyses  
were suggested to depend on the substituents of the aromatic ring and on the solvent.

$S_N1$  mechanism, with acylium ion, or solvent separated acylium-chloride ion-pair intermediates were proposed<sup>[17-19,26,60]</sup> for the hydrolysis of benzoyl chlorides bearing strong e-d substituents (e.g. 4-MeO). No acylium ion intermediate was found, however, to have sufficiently long lifetime that can be trapped by chloride ion, because no common ion effect was observed.<sup>[26]</sup> Competing  $S_N2$  and  $S_N1$  mechanisms were suggested for the reaction of benzoyl chloride and its derivatives, bearing weakly e-d or e-w groups.<sup>[17,20,21,60-62]</sup> In highly aqueous media benzoyl chloride was considered to hydrolyze by an  $S_N1$  mechanism, but an  $S_N2$  process was proposed in the 0-30 % water content range.<sup>[20]</sup> Benzoyl chlorides with strong e-w groups (e.g. 4-NO<sub>2</sub>) were suggested to react via Ad-E pathway,<sup>[13,26,62-65]</sup> with the general base catalyzed rate limiting attack of water and little or no bond breaking of the leaving group in the TS, even in highly aqueous media.<sup>[13]</sup> Doubtful was, however, if there were an addition intermediate with significant long lifetime on the reaction path.<sup>[26]</sup>

We have computed TSs **27** and **28**, bearing the clusters of one water and one acetone molecule (**18**), as well as two water molecules (**16**), respectively, for the  $S_N2$ -type hydrolysis of benzoyl chlorides (**26**) (Scheme 6, Table 4 and Tables S3 and S4 in the SI). IRC calculations, performed on the  $S_N2$  TSs of the 4-MeO (**28b**) and 4-NO<sub>2</sub> (**28m**) derivatives in water at (B3LYP)/6-31G(d) level of theory (Fig. 3) support that the reactions proceed in one-step. TSs are formed directly from the reactants, and transformed to products without the intermediacy of any other species. IRC computations at the higher (B3LYP)/6-311+G(d,p) level of theory were successful only for the 4-NO<sub>2</sub> derivative (**28m**), in the backward direction.

The  $\Delta G^\ddagger$  values, computed for the hydrolyses of benzoyl chlorides in acetone, are plotted against the Hammett  $\sigma$  constants together with the experimentally derived data,<sup>[22]</sup> determined in 95 % v/v acetone-water mixture, at 25° (Fig. 4, Table S11 in the SI). The  $\sigma$  substituent constants were used in the correlations, because no through conjugation takes place between the C<sup>7</sup> atom and the substituents of the benzene ring in the less polar TSs, formed in acetone. The  $\Delta G^\ddagger$  values, computed for TS **28** at (B3LYP)/6-31G(d) level of theory are smaller than the experimental data. However, there is little likelihood of the participation of two water molecules in the TS of the hydrolysis in a media, which contain only very small amount of water. Acetone can also participate as proton acceptor in the reaction,<sup>[25,52]</sup> nevertheless, computations can only be performed using the Radii=UAHF option, because the H<sup>2</sup> atom of the attacking water molecule, is strongly bonded to two oxygen atoms (O<sup>2</sup> and O<sup>3</sup>) in TS **27**. The  $\Delta G^\ddagger$  values, computed for TS **27** at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory, are higher than the experimentally derived data, and increase with the

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3 increasing level of theory of calculations (Fig. 4). It must also be taken into consideration,  
4 however, that calculations were performed in acetone, while kinetic studies were carried out  
5 in the slightly more polar 95 % v/v acetone-water mixture.  
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8 In acetone the slopes of the computed and experimentally derived  $\Delta G^\ddagger$  vs.  $\sigma$  plots are very  
9 similar (Fig. 4). In moderately polar media, which contain only a small amount of protic  
10 solvent, the increasing e-w effect of the substituents increase the reactivity of benzoyl  
11 chlorides,<sup>[22,66]</sup> and decrease the  $\Delta G^\ddagger$  values. Rate enhancing effect for e-d groups cannot be  
12 observed or computed in these solvents. The structures of the tetrahedral TSs **27** change with  
13 the substituent of the benzene ring. Tighter and less polar TSs are formed with the increase of  
14 the e-w effect of the substituents, as the  $Q(\text{Cl}^1)$  negative charge of the leaving chlorine, and  
15 the  $R(\text{C}^7 \cdots \text{Cl}^1)$  and  $R(\text{C}^7 \cdots \text{O}^2)$  distances decrease with the increase of the  $\sigma$  substituent  
16 constants (Fig. 5, Table 4 and Figs. S4 and S5, Table S4 in the SI). The  $\text{H}^2$  atom moves from  
17  $\text{O}^2$  to  $\text{O}^3$  atom [cf. the  $R(\text{O}^2 \cdots \text{H}^2)$  and  $R(\text{O}^3 \cdots \text{H}^2)$  distances in Fig. 5], the elongation of  $\text{H}^2$   
18 atom becomes greater in the imaginary mode of the TSs bearing e-w substituents. The  
19 character of the C=O double bond in the TSs is very similar to that of the benzoyl chlorides,  
20 the  $R(\text{C}^7=\text{O}^1)$  and  $\theta(\text{O}^1\text{C}^7\text{C}^1)$  values change slightly with the increasing e-d effect of the  
21 substituents of the TSs (cf. the data in Table 4 and Tables S3 and S4 in the SI). We can  
22 confirm therefore that the hydrolysis proceeds via concerted  $\text{S}_{\text{N}}2$  mechanism on the C=O  
23 group of benzoyl chlorides in dipolar media, which contain only a small amount of water.  
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37 TS **28** has been computed for the general base and general acid catalyzed  $\text{S}_{\text{N}}2$  type  
38 hydrolysis of benzoyl chlorides with cluster of two water molecules (**26** + **16**  $\rightleftharpoons$  TS **28**,  
39 Scheme 6), at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory, using the  
40 Radii=UAHF option, in water, at 25° C. The computed  $\Delta G^\ddagger$  values have been plotted against  
41 the  $\sigma^+$  substituent constants (Fig. 6) together with experimentally derived data.<sup>[67,68]</sup> The  $\sigma^+$   
42 substituent constants were used in the correlations because through conjugation takes place in  
43 the loose TSs between the positively polarized  $\text{C}^7$  atom and the e-d substituents of the  
44 benzene ring. The experimentally derived  $\Delta G^\ddagger$  vs.  $\sigma^+$  plot is broken at  $\sigma^+ \sim 0.35$  (Fig. 6), both  
45 e-d and e-w groups decrease the  $\Delta G^\ddagger$  values, and increase the rate of hydrolysis in water,  
46 similarly to the results obtained in solvent mixtures containing more than 50 % water.<sup>[21,26,69]</sup>  
47 Such broken Hammett plots has been explained usually by the change of the mechanism with  
48 the substituents.<sup>[70-73]</sup> However, the  $\Delta G^\ddagger$  vs.  $\sigma^+$  plots, computed for the concerted  $\text{S}_{\text{N}}2$   
49 mechanism are also broken (Fig. 6).  $\Delta G^\ddagger$  values obtained at (B3LYP)/6-31G(d) level of  
50 theory for compounds with e-w groups agree with the experimental data, but the rate  
51 enhancing effect of e-d groups can not be calculated at this medium level of theory. On the  
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other hand, the  $\Delta G^\ddagger$  vs.  $\sigma^+$  plot, computed at (B3LYP)/6-311+G(d,p) level of theory for the  $S_N2$  mechanism is very similar to the plot of the experimental data (Fig. 6), in this case e-d substituents also decrease the  $\Delta G^\ddagger$  values. Nevertheless, the  $\Delta G^\ddagger$  values, computed at this higher level of theory are greater than the experimental data, as it was observed for other reactions, too.<sup>[37,38]</sup>

The structures of the  $S_N2$  TSs **28** change continuously with the electronic effects of the substituents, the structural parameters vs.  $\sigma^+$  substituent constants plots (Fig. 7, and Figs. S6 and S7 in the SI) are broken at the same  $\sigma^+$  values, as in the case of the  $\Delta G^\ddagger$  vs.  $\sigma^+$  plots (Fig. 6). The computed structure of the TS of the 4-nitro derivative (**28m**) is tight, the  $R(C^7 \cdots Cl^1)$  and  $R(C^7 \cdots O^2)$  distances are both the shortest, the  $H^2$  is moved from  $O^2$  to  $O^3$  atom. The  $R(H^4 \cdots Cl^1)$  distance is long, because the charge of the  $Cl^1$  atom is small, and the  $H^4 \cdots Cl^1$  hydrogen bonding is weak (Table 4, Fig. 7 and Figs. S6 and S7 in the SI). The elongations of the  $C^7$  and the  $H^2$  atoms are great in the imaginary mode of TS **28m**. The TS of the 4-MeO derivative (**28b**) is very loose, the  $R(C^7 \cdots Cl^1)$  and  $R(C^7 \cdots O^2)$  distances are both the longest, the  $H^2$  atom is close to the  $O^2$  atom, the  $R(H^4 \cdots Cl^1)$  distances is the shortest, because the negative charge of the  $Cl^1$  atom is great, and the  $H^4 \cdots Cl^1$  hydrogen bonding is strong (Table 4, Figure 7 and Figures S6 and S7 in the SI). The elongation of the  $C^7$  atom is small and the  $H^2$  atom moves only slightly in the imaginary mode of TS **28b**. Considerable changes take place in the structure of the C=O group of the TSs with the substituents in water (Table 4 and Tables S3 and S4 in the SI). The Ar-C=O moiety of the 4- $NO_2$  derivative (TS **28m**,  $\theta(O^1C^7C^1) = 129.2^\circ$ ) is similar to that of 4- $NO_2$ -benzyl chloride (**26m**,  $\theta(O^1C^7C^1) = 126.0$ ), while that of the 4-MeO derivative (TS **28b**,  $\theta(O^1C^7C^1) = 166.2$ ) is more similar to an acylium ion ( $R(C^7O^1) \sim 1.12 \text{ \AA}$ ,  $\theta(O^1C^7C^1) \sim 180^\circ$ ). The changes of the structural parameters of the TSs are much greater in water than in acetone (Table 4), and they are compatible with the observed substituent, solvent and isotope effects, investigated by kinetic studies.

## CONCLUSIONS

DFT computations support that the hydrolysis of acid chlorides proceed in one step, without the formation of acylium ion or tetrahedral adduct intermediates. The structure of the TSs shows features, typical for concerted  $S_N2$  reactions on the  $sp^2$  hybridized carbon atom of the C=O group. Late TSs are formed in hydrolyses of acid chlorides, because water is poorer nucleophile than the leaving chloride ion, but the TSs become earlier in the general base catalyzed reactions. The structure of the TSs changes with the substituents and the solvent. Very loose and polar TSs can be formed only in protic solvent, like water, in the presence of

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3 e-d groups, which can also accelerate the substitution reactions under these circumstances. In  
4 such media, the weak attack of the water nucleophile is necessary and sufficient to push out  
5 the leaving chloride ion, therefore both the formed C $\cdots$ O, and the splitting C $\cdots$ Cl bonds are  
6 weak and long. A more advanced attack of the nucleophile is needed for substrates, bearing e-  
7 w groups, the C $\cdots$ O, and C $\cdots$ Cl bonds are both relatively short and strong in the TSs of these  
8 substrates. E-w substituents accelerate the hydrolysis of acid chlorides in every type of  
9 solvents. The formation of hydrogen bonding and the proton transfer are important steps of  
10 the reactions. Proton acceptor molecules promote the nucleophilic attack of water; protic  
11 solvents help the leaving of chloride ion. The reaction is general base and general acid  
12 catalyzed, but the base catalysis is more important than the acid catalysis. The proton splits  
13 off from the attacking water molecule in the TS; other proton transfer steps take place  
14 afterwards at the formation of the products.

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The conclusions, drawn for the mechanism of the hydrolysis of acid chlorides, have been supported by comparing the computed and experimentally derived  $\Delta G^\ddagger$  data and the substituent effect. As we have found earlier,<sup>[37,38]</sup> the best agreement between computed and experimentally derived  $\Delta G^\ddagger$  data can be obtained when computations are performed at the medium (B3LYP)/6-31G(d) level of theory. This may happen because errors rise from the applied approximations compensate each other at this medium level of calculation. The agreement between the computed and experimentally derived  $\Delta G^\ddagger$  values, presented in our papers, is similar to those, obtained by combined quantum and molecular mechanical methods.<sup>[74]</sup> The substituent effect was evaluated applying the Hammett equation to the  $\Delta G^\ddagger$  data. For compounds, bearing e-w groups, good agreement was obtained between computed and experimentally derived slopes of the Hammett plots both in acetone and in water, at different levels of computations. For the hydrolysis of benzoyl chlorides with e-d substituents, which pass over very loose TSs in water, the computed slope of the  $\Delta G^\ddagger$  vs.  $\sigma^+$  plot agree with the experimental data only if calculations have been performed at (B3LYP)/6-311+G(d,p) level of theory, using more diffuse functions. The reason for the break of the  $\Delta G^\ddagger$  vs.  $\sigma^+$  plots is that strong e-d through conjugation takes place for derivatives bearing e-d substituents in protic media, which can stabilize the polar TSs.

Summing up the results, obtained in this and in our earlier papers<sup>[35-39]</sup> concerning the structure of the TSs in  $S_N2$  nucleophilic substitutions, we can conclude that early TSs are formed if the attacking reagent is better, and late TSs are formed if the attacking reagent is poorer nucleophile than the leaving group. On the other hand, loose TSs are formed if e-d, and

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3 tight TSs are formed if e-w substituents are bonded to the substrates. TSs are looser and more  
4 polar in protic than in aprotic solvents.  
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## 7 8 9 COMPUTATIONAL METHODS

10 The geometries of reactants and TSs were fully optimized without symmetry constraints by  
11 use of the Gaussian 03 software package<sup>[75]</sup> at DFT(B3LYP)/6-31G(d) and DFT(B3LYP)/6-  
12 311+G(d,p) levels of theory in acetone and water, at 25° C for the hydrolysis reactants **6a** and  
13 **26**, and at -10° C for reactant **6b**. Temperatures are the same as used in the corresponding  
14 kinetic studies. The B3LYP functional was found<sup>[76,77]</sup> to perform well in investigation of  
15 trends in nucleophilic substitutions. The solvent effect was incorporated by applying the  
16 polarizable continuum model<sup>[78]</sup> in the integral equation formalism<sup>[79,80]</sup> (IEF-PCM) of the  
17 corresponding solvent. The Radii=UAHF option was used to build up the solute cavity<sup>[75,81]</sup> if  
18 protons were bonded strongly to two oxygen atoms in the TS. Intrinsic reaction coordinate  
19 (IRC) calculations<sup>[82]</sup> were performed on the TSs, to check the reaction pathways. Structures  
20 were characterized as energy minima or TSs by calculating the harmonic vibrational  
21 frequencies, with the use of analytical second derivatives. No or one imaginary frequency was  
22 obtained for reactants and TSs, respectively. Selected data for the optimized structures  
23 obtained by means of DFT calculations are listed in Tables S1-S4, in the SI.  
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26 The sums of the electronic and thermal free energies (*G*) and enthalpies (*H*) and also the  
27 entropies of formation (*S*) for reactants and TSs were obtained by the standard procedure in  
28 the framework of the harmonic approximation,<sup>[83,84]</sup> and are listed together with the calculated  
29 total energies (*E*) and value of imaginary frequencies in Tables S5, S6, S9 and S10 in the SI.  
30 The computed entropy values, obtained in solutions, agree with the data measured or  
31 calculated by application of Benson's rule<sup>[85,86]</sup> in the gas phase. As examples, the *S* values of  
32 195, 295 and 288 J mol<sup>-1</sup> K<sup>-1</sup> were obtained for H<sub>2</sub>O (**7**), CH<sub>3</sub>COCl (**6a**) and CH<sub>3</sub>COOH  
33 (**11a**), respectively, by DFT calculations in solution. In comparison, the values of *S* = 189,  
34 295 and 288 J mol<sup>-1</sup> K<sup>-1</sup> were measured<sup>[87]</sup> for compounds **7**, **6a** and **11a**, respectively, and *S*  
35 = 297 J mol<sup>-1</sup> K<sup>-1</sup> was calculated for **11a** on application of Benson's rule.  
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38 The  $\Delta E^\ddagger$ ,  $\Delta G^\ddagger$ ,  $\Delta H^\ddagger$ ,  $\Delta S^\ddagger$  activation parameters of the reactions were calculated from the  
39 differences in the *E*, *G*, *H* and *S* values of the TSs and reactants (Eqn 2,  $P = E, G, H$  or *S*).  
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$$42 \Delta P^\ddagger = P_{\text{TS}} - \sum P_{\text{R}} \quad (2)$$

43 The generated  $\Delta E^\ddagger$ ,  $\Delta G^\ddagger$  and  $\Delta H^\ddagger$  values were multiplied by 2625.5 in order to convert them  
44 from atomic into kJ mol<sup>-1</sup> units. Experimentally derived activation parameters were calculated  
45 from the second order rate constants ( $k_2 = k_1/[\text{Nuc}]$ ) using the Eyring equation.<sup>[48,49]</sup> Computed  
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3  $\Delta E^\ddagger$ ,  $\Delta G^\ddagger$  and  $\Delta H^\ddagger$  parameters increase with the increasing level of theory of calculations,  
4 while the values of  $\Delta S^\ddagger$  are almost independent of it (Table 1 and Tables S7, S8 and S11 in  
5 the SI). The  $\Delta G^\ddagger$  data, computed at (B3LYP)/6-31G(d) level of theory agree with the  
6 experimental data well.<sup>[37,38]</sup> The computed  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  parameters are close to the  
7 experimental data, determined in dipolar media, containing only a few % of protic solvent.  
8 E.g.  $\Delta H^\ddagger = 31.8 \text{ kJ mol}^{-1}$  and  $\Delta S^\ddagger = -198 \text{ J mol}^{-1} \text{ K}^{-1}$  were measured<sup>[53,54]</sup> for the hydrolysis  
9 acetyl chloride (**6a**) in 1.77 % water-acetone mixture, and  $\Delta H^\ddagger = 36.9 \text{ kJ mol}^{-1}$  and  $\Delta S^\ddagger = -$   
10  $177 \text{ J mol}^{-1} \text{ K}^{-1}$  were computed at (B3LYP)/6-31G(d) level of theory, in acetone. In more  
11 aqueous media the experimentally derived  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  parameters<sup>[35,53]</sup> increase because of  
12 the greater ordering of the solvent, and deviate from computed data to a greater extent.

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21 The computed and experimentally derived activation parameters were correlated with the  
22 Hammett substituent constants, as described previously<sup>[35-39]</sup> (Eqn 3,  $P = E, G, H$  or  $S$ ).

$$23 \quad \Delta P^\ddagger = \delta \Delta P^\ddagger \sigma + \Delta P_o^\ddagger \quad (3)$$

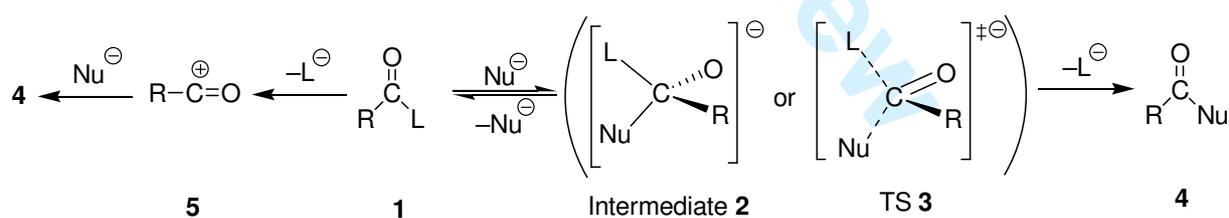
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26 The  $\delta \Delta P^\ddagger$  reaction constants characterize the effect of substituents on activation parameters,  
27  $\Delta P^\ddagger$  and  $\Delta P_o^\ddagger$  are the data of substituted and unsubstituted compounds, respectively. The best  
28 agreement can be expected for calculated and experimentally derived  $\delta \Delta G^\ddagger$  reaction  
29 constants. The values of computed  $\delta \Delta G^\ddagger$  and  $\delta \Delta H^\ddagger$  are very similar to each other, because the  
30 computed  $\Delta S^\ddagger$  data do not depend on the substituents, therefore  $\delta \Delta S^\ddagger \sim 0$ . On the other hand,  
31 the experimentally derived  $\delta \Delta H^\ddagger$  and  $\delta \Delta S^\ddagger$  reaction constants are influenced by solvation, and  
32  $\delta \Delta S^\ddagger$  exhibit positive/negative sign if solvation of the TS decrease/increase with the increasing  
33 e-w effect and  $\sigma$  constant of the substituent. E.g.  $\delta \Delta G^\ddagger = -13.2 \text{ kJ mol}^{-1} \sigma^{-1}$ ,  $\delta \Delta H^\ddagger = -14.2 \text{ kJ}$   
34  $\text{mol}^{-1} \sigma^{-1}$  and  $\delta \Delta S^\ddagger \sim 0 \text{ J mol}^{-1} \text{ K}^{-1} \sigma^{-1}$  were computed for the hydrolyses of benzoyl chlorides  
35 in acetone, at (B3LYP)/6-31G(d) level of theory, and  $\delta \Delta G^\ddagger = -12.0 \text{ kJ mol}^{-1} \sigma^{-1}$ ,  $\delta \Delta H^\ddagger = -$   
36  $23.0 \text{ kJ mol}^{-1} \sigma^{-1}$  and  $\delta \Delta S^\ddagger = -39.3 \text{ J mol}^{-1} \text{ K}^{-1} \sigma^{-1}$  were calculated from rate constants,<sup>[22]</sup>  
37 measured in 95 % v/v acetone-water mixture, at 25° C. The Hammett  $\sigma$  and  $\sigma^+$  constants were  
38 taken from the compilation Hans et al.<sup>[48,88]</sup> Structural parameter vs.  $\sigma$  or  $\sigma^+$  plots were used to  
39 demonstrate the changes for the structure of the TSs with the substituents.

## 50 51 52 53 SUPPORTING INFORMATION

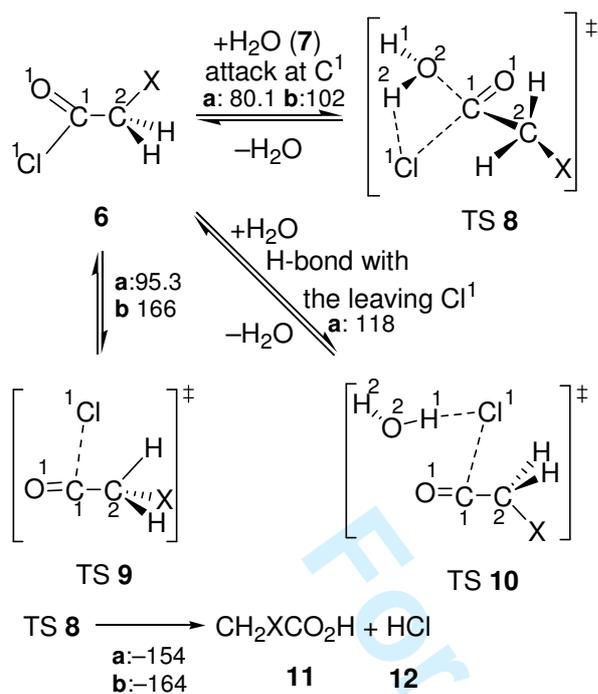
54 IRC plots, plots of calculated structural data against the substituent constants, selected atomic  
55 charges, bond distances and angles, as well as calculated total energies, sums electronic and  
56 thermal free energies and enthalpies, entropies of formation and value of imaginary  
57 frequencies are listed in the supporting information, which can be found in the online version  
58 of this article.  
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### Acknowledgement

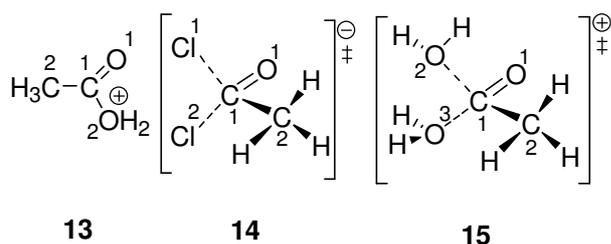
This work was supported by the Hungarian Scientific Research Foundation (OTKA No. K 60889).



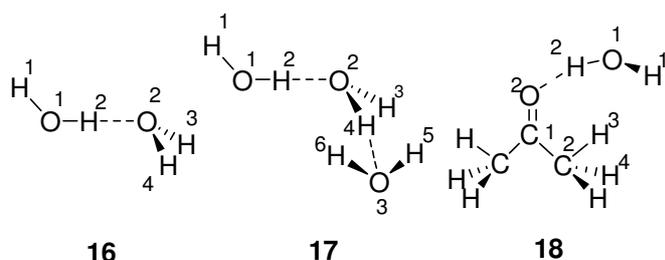
**Scheme 1.** Mechanisms of nucleophilic substitution at carbonyl compounds.



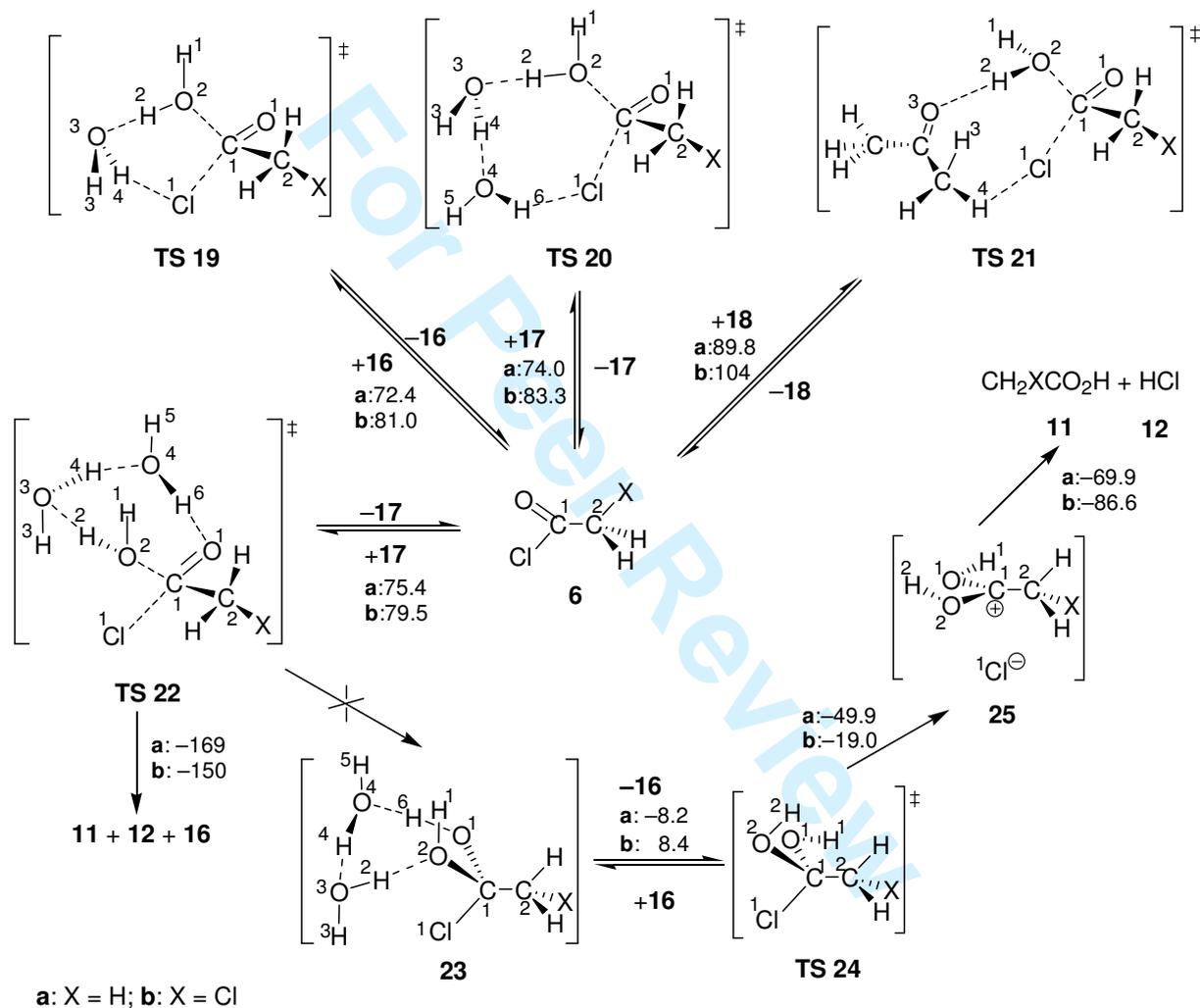
**Scheme 2.** Mechanisms for hydrolyses of acetyl chloride (**6a**) and chloroacetyl chloride (**6b**), involving one water molecule. Free energies of activation ( $\Delta G^\ddagger$ ) for the reaction steps of reactants **6a** and **6b**, in the direction of the neighboring arrow, are given in  $\text{kJ mol}^{-1}$  units, as calculated at (B3LYP)/6-31G(d) level of theory, in water at 25° C for compound **6a** and at – 10° C for **6b**.



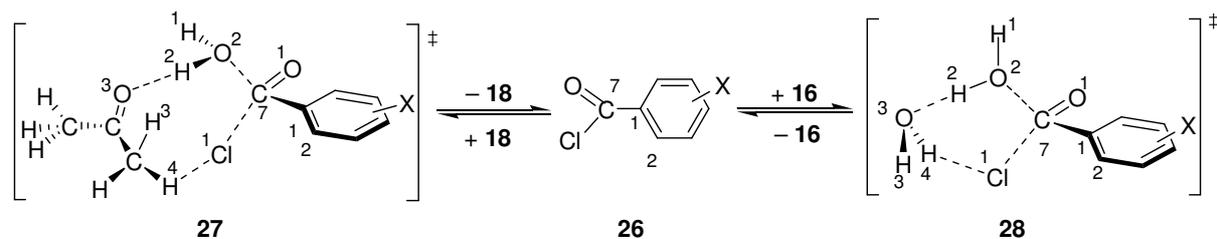
**Scheme 3.** Structures of protonated acetic acid and TSs of chlorine and water exchange reactions.



Scheme 4. Clusters of solvent molecules

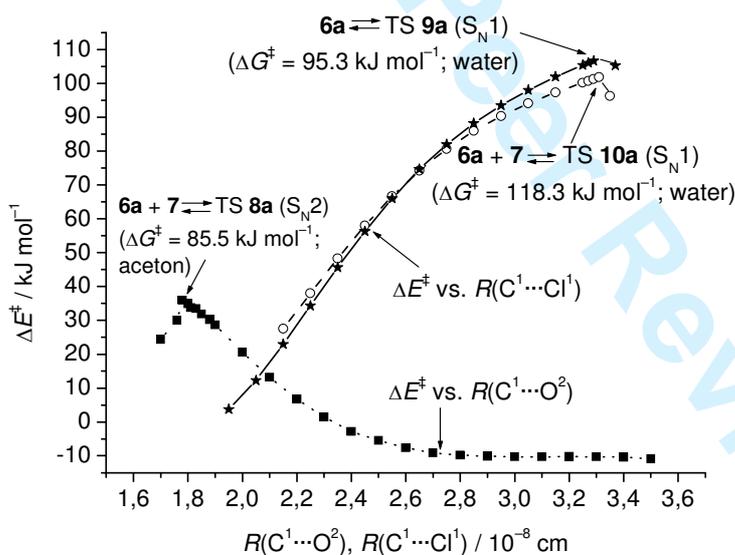


Scheme 5. Mechanisms for hydrolyses of acetyl chloride (**6a**) and chloroacetyl chloride (**6b**), involving explicit solvent molecules. TSs **19-21** are transferred to products (TS **19** → **11 + 12 + 7**; TS **20** → **11 + 12 + 16**; TS **21** → **11 + 12 + acetone**). Free energy of activations ( $\Delta G^\ddagger$ ) and changes of free energies ( $\Delta G^\circ$ ) for reaction steps of reactants **6a** and **6b** in directions of the neighboring arrow are given in  $\text{kJ mol}^{-1}$  units, as calculated at (B3LYP)/6-31G(d) level of theory, in water at 25° C for reactant **6a** and at -10° C for reactant **6b**.

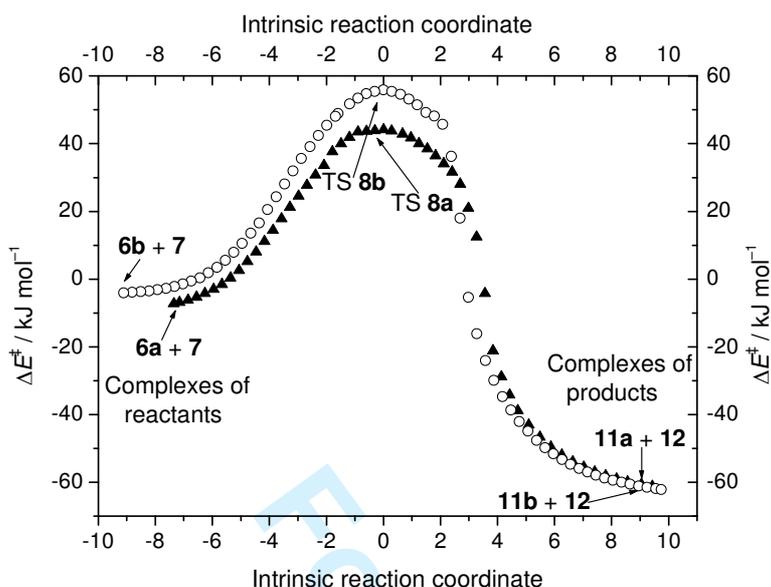


**a:** X = H; **b:** X = 4-MeO; **c:** X = 4-Me; **d:** X = 3-Me; **e:** X = 4-F; **f:** X = 3-MeO; **g:** X = 4-Cl; **h:** X = 3-Cl; **i:** X = 3-CF<sub>3</sub>; **j:** X = 4-CF<sub>3</sub>; **k:** X = 4-CN; **l:** X = 3-NO<sub>2</sub>; **m:** X = 4-NO<sub>2</sub>.

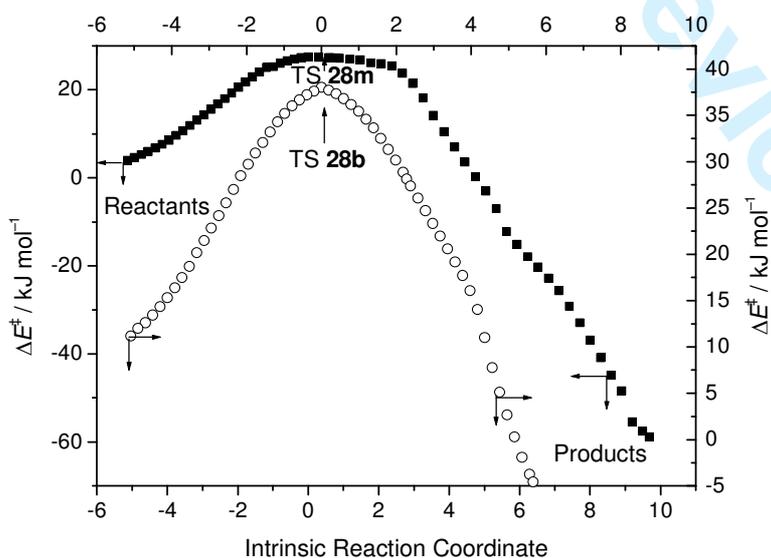
**Scheme 6.** Mechanisms for hydrolyses of benzoyl chlorides (**26**) with clusters of two water (**16**) as well with one acetone and one water molecules (**18**), as calculated at (B3LYP)/6-311+G(d,p) level of theory, using the Radii=UAHF option, in water and acetone, at 25° C. TSs **27** and **28** are converted to products (TS **27** → XC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>H + HCl + acetone; TS **28** → XC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>H + HCl + H<sub>2</sub>O).



**Figure 1.**  $\Delta E^\ddagger$  vs.  $R(\text{C}^1 \cdots \text{O}^2)$  and  $\Delta E^\ddagger$  vs.  $R(\text{C}^1 \cdots \text{Cl}^1)$  plots for the decrease of  $\text{C}^1 \cdots \text{O}^2$  and the increase of  $\text{C}^1 \cdots \text{Cl}^1$  distances in the  $\text{S}_{\text{N}2}$  and  $\text{S}_{\text{N}1}$  hydrolyses of acetyl chloride (**6a**, Scheme 2), respectively, as calculated at (B3LYP)/6-31G(d) level of theory, in acetone and water, at 25° C. Free energy of activation values ( $\Delta G^\ddagger$ ) are given in parentheses.

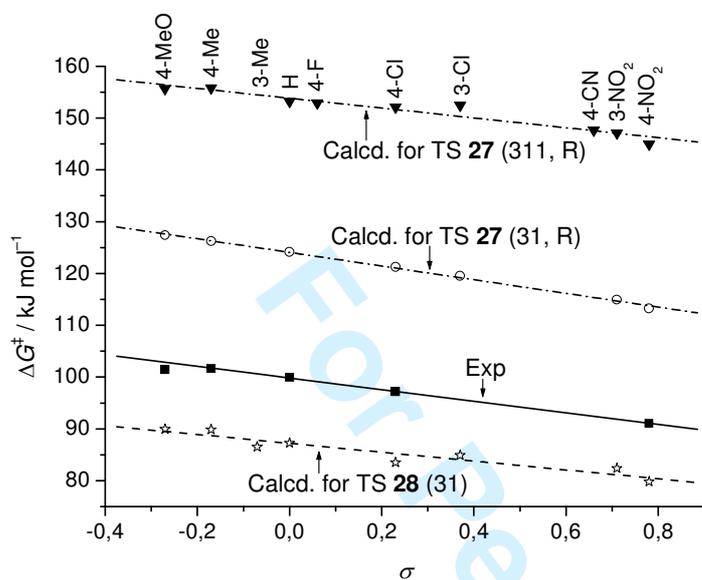


**Figure 2.**  $\Delta E^\ddagger$  vs. IRC plots for the hydrolysis of acetyl chloride ( $6\mathbf{a} + 7 \rightleftharpoons \text{TS } 8\mathbf{a} \rightarrow 11\mathbf{a} + 12$ ) and chloroacetyl chloride ( $6\mathbf{b} + 7 \rightleftharpoons \text{TS } 8\mathbf{b} \rightarrow 11\mathbf{b} + 12$ ) with one water molecule (Scheme 2). IRC calculations were performed at (B3LYP)/6-31G(d) level of theory, using the Radii=UAHF option, in water at 25 and  $-10^\circ\text{C}$  for TSs  $8\mathbf{a}$  and  $8\mathbf{b}$ , respectively.  $\Delta E$  values refer to separated reactants ( $\Delta E = 0$ ).

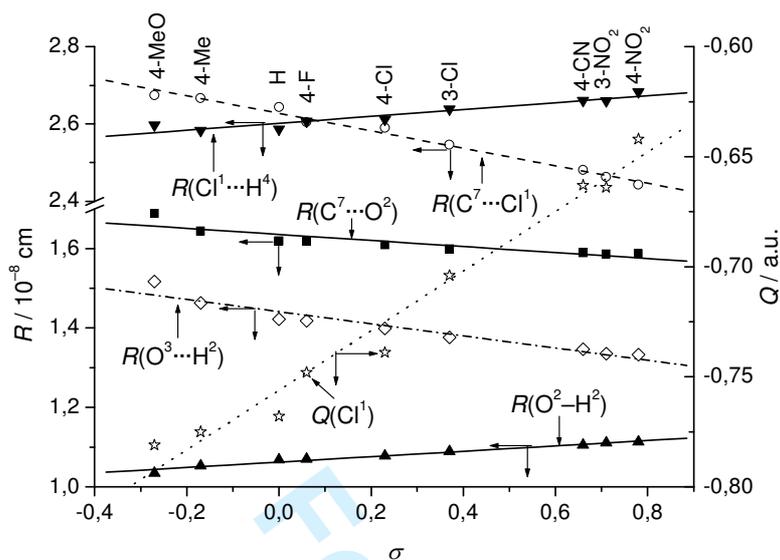


**Figure 3.**  $\Delta E^\ddagger$  vs. IRC plots for hydrolyses of 4-MeO-C<sub>6</sub>H<sub>4</sub>COCl ( $26\mathbf{b} + 16 \rightleftharpoons \text{TS } 28\mathbf{b}$ ) and 4-NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>COCl ( $26\mathbf{m} + 16 \rightleftharpoons \text{TS } 28\mathbf{m}$ ) with a cluster of two water molecules (Scheme 6).

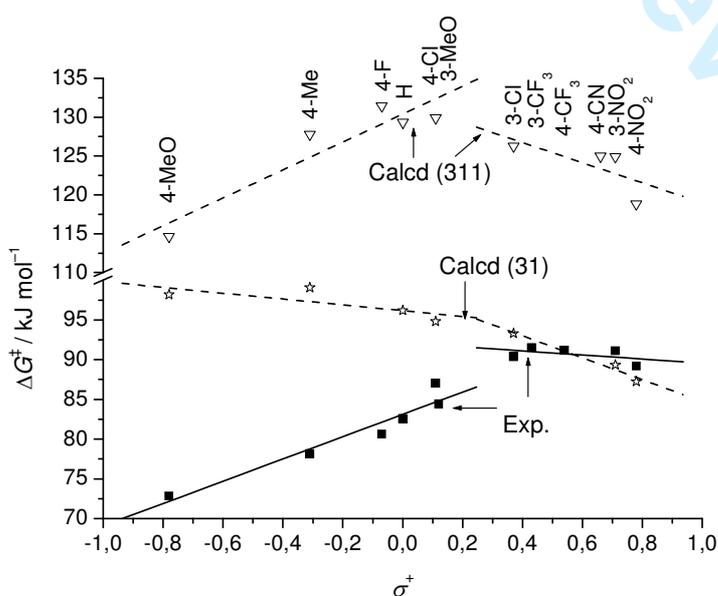
IRC calculations were performed at (B3LYP)/6-31G(d) level of theory, using the Radii=UAHF option, in water at 25° C.  $\Delta E$  values refer to separated reactants ( $\Delta E = 0$ ).



**Figure 4.**  $\Delta G^\ddagger$  vs.  $\sigma$  plots for hydrolyses of benzoyl chlorides (**26**, Scheme 6) with the cluster of one water and one acetone (**26** + **18**  $\rightleftharpoons$  TS **27**) and two water molecules (**26** + **16**  $\rightleftharpoons$  TS **28**). Calculations were performed for TS **27** at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory [marked with (31, R) and (311, R), respectively], using the Radii=UAHF option, and for TS **28** at (B3LYP)/6-31G(d) level of theory, in acetone, at 25° C. Experimental data were measured<sup>[22]</sup> in 95% v/v acetone-water mixture at 25° C. [Correlations: TS **27** (31, R),  $\Delta G^\ddagger = -13.2\sigma + 124.1$  ( $r = 0.998$ ); TS **27** (311, R),  $\Delta G^\ddagger = -9.51\sigma + 152.8$  ( $r = 0.965$ ); TS **28** (31),  $\Delta G^\ddagger = -8.55\sigma + 87.2$  ( $r = 0.998$ ); Exp.  $\Delta G^\ddagger = -12.0\sigma + 97.9$  ( $r = 0.997$ )].

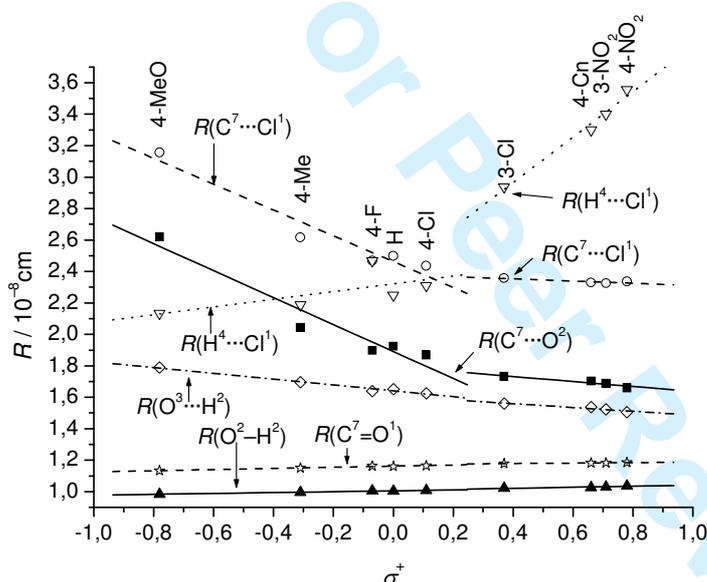


**Figure 5.** Plots of bond distances ( $R$ ) and charge of chlorine ( $Q$ ) against the Hammett  $\sigma$  constants for TS **27** in the hydrolysis of benzoyl chlorides (Scheme 6), as calculated at (B3LYP)/6-311+G(d,p) level of theory, using the Radii=UAHF option, in acetone, at 25° C. [Correlations:  $R(C^7 \cdots O^2) = -0.0760\sigma + 1.636$  ( $r = 0.894$ );  $R(C^7 \cdots Cl^1) = -0.226\sigma + 2.628$  ( $r = 0.993$ );  $R(O^2 \cdots H^2) = 0.0679\sigma + 1.062$  ( $r = 0.987$ );  $R(H^4 \cdots Cl^1) = 0.0892\sigma + 2.601$  ( $r = 0.956$ );  $R(O^3 \cdots H^2) = -0.153\sigma + 1.441$  ( $r = 0.965$ );  $Q(Cl) = 0.135\sigma - 0.756$  ( $r = 0.987$ )].



**Figure 6.**  $\Delta G^\ddagger$  vs.  $\sigma^+$  plots for hydrolyses of benzoyl chlorides (**26**, Scheme 6). Calculations were performed for TS **28** at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory

[marked with (31) and (311), respectively], using the Radii=UAHF option, in water, at 25° C. Experimental data were determined<sup>[67]</sup> in water at 25° C. [Correlations: for compounds with substituents 4-MeO - 4-Cl,  $\Delta G^\ddagger(31) = -3.66\sigma^+ + 96.2$  ( $r = 0.759$ );  $\Delta G^\ddagger(311) = 18.0\sigma^+ + 130.4$  ( $r = 0.932$ );  $\Delta G^\ddagger(\text{Exp}) = 14.0\sigma^+ + 83.1$  ( $r = 0.963$ ); for compounds with substituents 3-Cl - 4-NO<sub>2</sub>,  $\Delta G^\ddagger(31) = -13.8\sigma^+ + 98.5$  ( $r = 0.983$ );  $\Delta G^\ddagger(311) = -13.0\sigma^+ + 131.9$  ( $r = 0.700$ );  $\Delta G^\ddagger(\text{Exp}) = -2.59\sigma^+ + 92.1$  ( $r = 0.492$ )].



**Figure 7.** Plots of bond distances ( $R$ ) against the  $\sigma^+$  constants for TSs **28** in the hydrolyses of benzoyl chlorides (**26**, Scheme 6), as calculated at (B3LYP)/6-311+G(d,p) level of theory, using the Radii=UAHF option, in water, at 25° C. [Correlations for compounds with substituents 4-MeO - 4-Cl;  $R(\text{C}^7 \cdots \text{O}^2) = -0.858 \sigma^+ + 1.891$  ( $r = 0.967$ );  $R(\text{C}^7 \cdots \text{Cl}^1) = -0.821 \sigma^+ + 2.463$  ( $r = 0.970$ );  $R(\text{O}^2 \cdots \text{H}^2) = 0.0273 \sigma^+ + 1.0045$  ( $r = 0.989$ );  $R(\text{H}^4 \cdots \text{Cl}^1) = 0.245 \sigma^+ + 2.321$  ( $r = 0.669$ );  $R(\text{O}^3 \cdots \text{H}^2) = -0.186 \sigma^+ + 1.641$  ( $r = 0.990$ );  $R(\text{C}^7 \cdots \text{O}^1) = 0.0366 \sigma^+ + 1.162$  ( $r = 0.987$ ). Correlations for compounds with substituents 3-Cl - 4-NO<sub>2</sub>;  $R(\text{C}^7 \cdots \text{O}^2) = -0.157 \sigma^+ + 1.795$  ( $r = 0.933$ );  $R(\text{C}^7 \cdots \text{Cl}^1) = -0.0699 \sigma^+ + 2.381$  ( $r = 0.856$ );  $R(\text{O}^2 \cdots \text{H}^2) = 0.0323 \sigma^+ + 1.008$  ( $r = 0.933$ );  $R(\text{H}^4 \cdots \text{Cl}^1) = 1.45 \sigma^+ + 2.387$  ( $r = 0.991$ );  $R(\text{O}^3 \cdots \text{H}^2) = -0.121 \sigma^+ + 1.608$  ( $r = 0.947$ );  $R(\text{C}^7 \cdots \text{O}^1) = 0.0161 \sigma^+ + 1.172$  ( $r = 0.987$ ).]

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5 acetone,<sup>[54]</sup> at 24.8 °C,  $\Delta G^\ddagger = 90.8 \text{ kJ mol}^{-1}$ ,  $\Delta H^\ddagger = 31.8 \text{ kJ mol}^{-1}$ ,  $\Delta S^\ddagger = -198 \text{ J mol}^{-1} \text{ K}^{-1}$ ;  
6 in 10 % v/v water in acetone,<sup>[41]</sup> at 25 °C,  $\Delta G^\ddagger = 84.7 \text{ kJ mol}^{-1}$ ; in 25 % v/v water in  
7 acetone,<sup>[55]</sup> at 25 °C,  $\Delta G^\ddagger = 79.9 \text{ kJ mol}^{-1}$ ,  $\Delta H^\ddagger = 55.7 \text{ kJ mol}^{-1}$ ,  $\Delta S^\ddagger = -81.3 \text{ J mol}^{-1} \text{ K}^{-1}$ .  
8 The values  $\Delta G^\ddagger = 66.8, 65.6$  and  $64.7 \text{ kJ mol}^{-1}$  were calculated for water solvent ( $Y =$   
9  $3.493$ ),<sup>[47]</sup> extrapolating the data of kinetic measurements, obtained in 10-25 % v/v water  
10 in acetone at 25 °C [ $\Delta G^\ddagger = -3,343Y + 78.5$  ( $r = 1.000$ )],<sup>[41]</sup> in 19.6 – 75.6 % v/v water in  
11 dioxane at 27 °C [ $\log k = 0.821Y + 0.529$  ( $r = 0.999$ )]<sup>[23]</sup> and in 50-90 % v/v water-acetone  
12 mixtures, at 0 °C [ $\log k = 0.19Y - 0,740$  ( $r = 0.999$ )]<sup>[14]</sup> respectively.  $\Delta G^\ddagger = 67.9$  and  $69.1$   
13  $\text{kJ mol}^{-1}$  were calculated for TSs **21a** and **22a**, respectively, at (B3LYP)/6-31G(d) level of  
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19 because the negative charge of the carbonyl oxygen becomes very small, and no hydrogen  
20 bond is formed between C=O group and the water molecule when calculations are carried  
21 out at the higher (B3LYP)/6-311+G(d,p) level of theory.  
22 [57] Extrapolation of the rate constants of kinetic studies<sup>[25]</sup> gave  $k = 0.35 \text{ s}^{-1}$ ,  $k_2 = 0.00633$   
23  $\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$  and  $\Delta G^\ddagger = 75.2 \text{ kJ mol}^{-1}$  in water, at  $-10 \text{ °C}$ .  
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3 [68]  $\Delta G^\ddagger = 72.9, 77.7, 81.0, 87.5$  and  $89.8 \text{ kJ mol}^{-1}$  were obtained by polynomial curve fits,  
4 for the hydrolyses of 4-MeO,<sup>[13,17]</sup> 4-Me,<sup>[13]</sup> H,<sup>[20]</sup> 4-Cl<sup>[13]</sup> and 4-NO<sub>2</sub><sup>[13,62,65]</sup> substituted  
5 benzoyl chlorides, in water, at 25° C respectively, using the dependence of the  $\Delta G^\ddagger$  data  
6 on  $Y$  solvent polarity parameter<sup>[47]</sup> in acetone-water mixtures.  
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13 for change of the mechanism with the substituents. The analogous  $\Delta G^\ddagger$  vs.  $\sigma$  plots are  
14 concave downward, like plots in Fig. 6, as their slopes are the opposite of that of the  $\log k$   
15 vs.  $\sigma$  plots, because the greater the rate of the reaction the smaller the value of  $\Delta G^\ddagger$ .  
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**Table 1.** Selected charges ( $Q$ , a.u.), atomic distances ( $R$ , Å), bond angles ( $\theta$ , degree) and free energy of activation ( $\Delta G^\ddagger$ , kJ mol<sup>-1</sup>) for TSs of the hydrolyses of acetyl chloride (**6a**, Schemes 2 and 5), as calculated at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory [marked as 6-31 and 6-311, respectively], in water and acetone, at 25°C.

	TS 8a	TS 8a	TS 21a	TS 8a	TS 8a	TS 19a	TS 19a	TS 20a	TS 20a	TS 22a
Level	6-31	6-311	6-31	6-31	6-311	6-31	6-311	6-31	6-311	6-31
Solvent	acetone					water				
$Q(O^1)$	-0.312	-0.088	-0.357	-0.322	-0.103	-0.365	-0.125	-0.362	-0.077	-0.430
$Q(O^2)$	-0.699	-0.349	-0.712	-0.701	-0.324	-0.737	-0.410	-0.755	-0.450	-0.716
$Q(Cl)$	-0.720	-0.737	-0.690	-0.728	-0.763	-0.601	-0.644	-0.507	-0.607	-0.480
$R(C^1=O^1)$	1.166	1.150	1.179	1.168	1.153	1.180	1.164	1.181	1.158	1.202
$R(C^1\cdots O^2)$	1.813	1.869	1.718	1.798	1.815	1.816	1.817	1.892	1.906	1.740
$R(C^1\cdots Cl^1)$	2.526	2.651	2.455	2.505	2.633	2.290	2.434	2.210	2.424	2.156
$R(O^2-H^2)$	0.991	0.983	1.026	0.992	0.989	1.022	1.011	1.024	1.010	1.049
$R(O^3\cdots H^2)$	-	-	1.593	-	-	1.594	1.602	1.588 <sup>a</sup>	1.614 <sup>b</sup>	1.501 <sup>c</sup>
$R(Cl^1\cdots H^d)$	2.359	2.367	2.845	2.513	2.797	3.137	3.115	2.358	2.265	3.309
$\theta(O^1C^1C^2)$	138.0	141.9	132.8	137.3	140.4	133.2	136.6	133.1	138.8	128.0
$\Delta G^\ddagger$	84.5	110.7	89.8	80.1	105.7	72.4	105.9	74.0	115.3	75.4

<sup>a</sup>  $R(O^3-H^4) = 0.996$  Å,  $R(O^4\cdots H^4) = 1.728$  Å,  $R(O^4-H^6) = 0.978$  Å.

<sup>b</sup>  $R(O^3-H^4) = 0.986$  Å,  $R(O^4\cdots H^4) = 1.750$  Å,  $R(O^4-H^6) = 0.976$  Å.

<sup>c</sup>  $R(O^3-H^4) = 1.000$  Å,  $R(O^4\cdots H^4) = 1.701$  Å,  $R(O^4-H^6) = 0.979$  Å,  $R(O^1\cdots H^6) = 1.917$  Å.

<sup>d</sup> Distance of chlorine and the next neighboring H atom of the explicit solvent molecule.

**Table 2.** Calculated bond orders ( $n$ ) for the TSs, generated in the hydrolysis acetyl chloride (Scheme 2 and 5).<sup>a</sup>

Item	TS	Solvent	Bond	$R_s^{b,c}$	$R_o^{c,d}$	$a^e$	$R_r^{c,f}$	$n$
1	<b>8a</b>	acetone	CO	2.064 ( <b>15a</b> )	1.568 ( <b>13a</b> )	-0.7156	1.813 ( <b>8a</b> )	0.643
2	<b>8a</b>	acetone	CCl	2.285 ( <b>14a</b> )	1.849 ( <b>6a</b> )	-0.6290	2.526 ( <b>8a</b> )	0.341
3	<b>8a</b>	water	CO	2.040 ( <b>15a</b> )	1.556 ( <b>13a</b> )	-0.6983	1.798 ( <b>8a</b> )	0.707
4	<b>8a</b>	water	CCl	2.301 ( <b>14a</b> )	1.850 ( <b>6a</b> )	-0.6507	2.505 ( <b>8a</b> )	0.365
5	<b>19a</b>	water	CCl	2.301 ( <b>14a</b> )	1.850 ( <b>6a</b> )	-0.6507	2.290 ( <b>19a</b> )	0.509
6	<b>20a</b>	water	CCl	2.301 ( <b>14a</b> )	1.850 ( <b>6a</b> )	-0.6507	2.210 ( <b>20a</b> )	0.575

<sup>a</sup> Bond orders were calculated according to Pauling<sup>[50]</sup> [Equation (1)]. Atomic distances were calculated at (B3LYP)/6-31G(d) level of theory.

<sup>b</sup> Atomic distances (Å) calculated for symmetric TSs ( $n = 0.5$ ).

<sup>c</sup> The numbering of the relating species is given in parentheses.

<sup>d</sup> Bond lengths (Å) calculated for reactants.

<sup>e</sup> Constants calculated for Equation (1).

<sup>f</sup> Atomic distances (Å) calculated for TSs.

**Table 3.** Selected charges ( $Q$ , a.u.), atomic distances ( $R$ , Å), bond angles ( $\theta$ , degree) and free energy of activation ( $\Delta G^\ddagger$ , kJ mol<sup>-1</sup>) for TSs of the hydrolyses of acetyl chloride (**6a**) and chloroacetyl chloride (**6b**, Schemes 2 and 5), as calculated at (B3LYP)/6-31G level of theory, using the Radii=UAHF option, in water (for TSs **8**, **19**, **20** and **22**) and in acetone (for TS **21**), at 25° (for reactant **6a**) and -10 °C (for reactant **6b**).

	TS 8a	TS 19a	TS 20a	TS 21a	TS 22a	TS 8b	TS 19b	TS 20b	TS 21b	TS 22b
$Q(O^1)$	-0.306	-0.336	-0.374	-0.396	-0.443	-0.365	-0.368	-0.393	-0.409	-0.476
$Q(O^2)$	-0.700	-0.737	-0.731	-0.662	-0.690	-0.667	-0.708	-0.714	-0.690	-0.689
$Q(Cl)$	-0.692	-0.616	-0.528	-0.764	-0.530	-0.656	-0.570	-0.474	-0.642	-0.409
$R(C^1=O^1)$	1.165	1.174	1.183	1.187	1.206	1.171	1.183	1.189	1.193	1.217
$R(C^1\cdots O^2)$	1.839	1.832	1.814	1.536	1.654	1.722	1.706	1.727	1.550	1.617
$R(C^1\cdots Cl)$	2.549	2.389	2.264	2.661	2.235	2.509	2.324	2.201	2.429	2.107
$R(O^2\cdots H^2)$	0.995	1.024	1.034	1.084	1.077	1.002	1.056	1.059	1.143	1.133
$R(O^3\cdots H^2)$	-	1.589	1.550	1.420	1.427	-	1.496	1.471	1.310	1.318
$R(O^3\cdots H^4)$	-	0.984	0.998 <sup>a</sup>	-	1.005 <sup>b</sup>	-	0.982	1.002 <sup>c</sup>	-	1.015 <sup>d</sup>
$R(Cl\cdots H)^e$	2.187	2.271	2.263	2.541	2.874	2.147	2.343	2.332	2.644	3.048
$\theta(O^1C^1C^2)$	138.9	135.6	132.7	131.4	127.5	135.5	131.6	129.1	129.8	124.7
$\Delta G^\ddagger$	94.2	84.1	83.4	115.9	89.7	101.0	81.0	83.3	104.3	79.5

<sup>a</sup>  $R(O^4\cdots H^4) = 1.715$  Å,  $R(O^4-H^6) = 0.982$  Å.

<sup>b</sup>  $R(O^4\cdots H^4) = 1.674$  Å,  $R(O^4-H^6) = 0.981$  Å,  $R(O^1\cdots H^6) = 1.892$  Å.

<sup>c</sup>  $R(O^4\cdots H^4) = 1.686$  Å,  $R(O^4-H^6) = 0.980$  Å.

<sup>d</sup>  $R(O^4\cdots H^4) = 1.622$  Å,  $R(O^4-H^6) = 0.985$  Å,  $R(O^1\cdots H^6) = 1.850$  Å.

<sup>e</sup> Distance of chlorine and the next neighboring H atom of the solvent cluster.

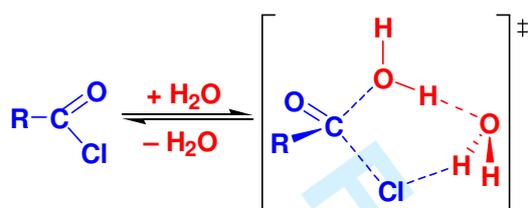
**Table 4.** Selected charges ( $Q$ , a.u.) atomic distances ( $R$ , Å) and bond angles (degere) for TSs **27** and **28** of the hydrolyses of benzoyl chlorides ( $X-C_6H_4COCl$ , **26**, Scheme 6), as calculated at (B3LYP)/6-311+G(d,p) level of theory, using the Radii=UAHF option, in acetone and in water, at 25 °C.

TS	TS <b>27</b>			TS <b>28</b>		
	acetone			water		
solvent						
X	4-MeO	H	4-NO <sub>2</sub>	4-MeO	H	4-NO <sub>2</sub>
$Q(O^1)$	-0.148	-0.167	-0.223	0,033	-0.136	-0.241
$Q(O^2)$	-0.332	-0.344	-0.347	-0.670	-0.445	-0.308
$Q(Cl^1)$	-0.775	-0.768	-0.642	-0.898	-0.723	-0.649
$R(C^1=O^1)$	1.173	1.178	1.187	1.133	1,166	1.185
$R(C^1\cdots O^2)$	1.688	1.619	1.587	2.620	1.924	1.659
$R(C^1\cdots Cl^1)$	2.674	2.644	2.443	3.157	2.498	2.336
$R(O^2\cdots H^2)$	1.035	1.068	1.113	0.983	1.003	1.036
$R(O^3\cdots H^2)$	1.517	1.422	1.333	1.789	1.651	1.505
$R(Cl^1\cdots H^4)$	2.597	2.586	2.683	2.133	2.256	3.556
$\theta(O^1C^7C^1)$	134.8	132.2	128.6	166.2	138.3	129.3

## Graphical Table of Contents

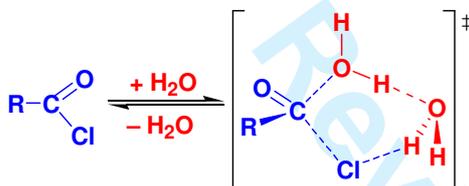
**Concerted S<sub>N</sub>2 mechanism for the hydrolysis of acid chlorides. Comparisons of reactivities calculated by the density functional theory with experimental data**

Ferenc Ruff\* and Ödön Farkas

**R = CH<sub>3</sub>, CH<sub>2</sub>Cl, X-C<sub>6</sub>H<sub>4</sub>; X = 4-MeO - 4-NO<sub>2</sub>****Solvent: water, acetone**

Acid chlorides hydrolyze via concerted, general base and general acid catalyzed S<sub>N</sub>2 mechanism. The structure of the tetrahedral TS changes with substituents and solvent. Late/early TSs are formed if the attacking reagent is poorer/better nucleophile than the leaving group, and loose/tight TSs are formed for substrates bearing electron-donating /electron-withdrawing substituents.

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## Supporting Information

Concerted S<sub>N</sub>2 mechanism for the hydrolysis of acid chlorides. Comparisons of reactivities calculated by the density functional theory with experimental data

Ferenc Ruff\* and Ödön Farkas

## Contents

 $\Delta E^\ddagger$  vs. IRC and  $\Delta E$  vs.  $R(O^1 \cdots H^6)$  plots

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Selected structural parameters for species **6 - 28**

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 $\Delta E^\ddagger$ ,  $\Delta G^\ddagger$ ,  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$  parameters for hydrolyses

Tables S7, S8 and S11

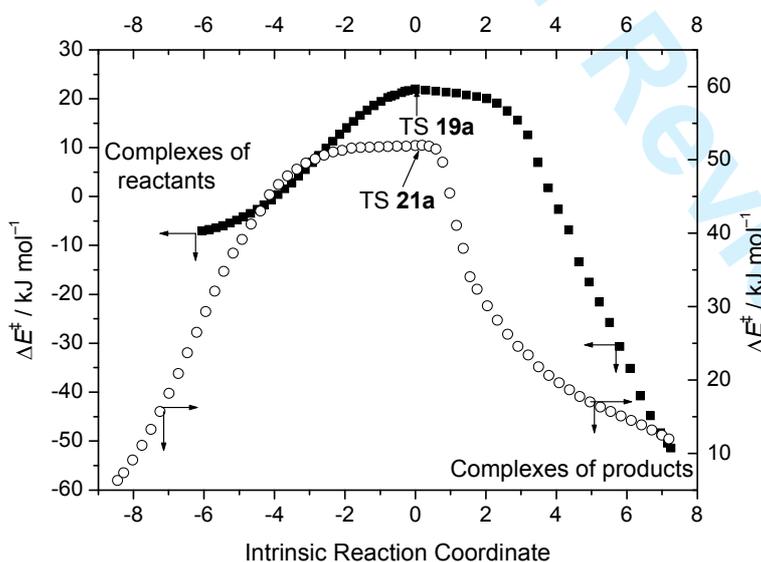


Figure S1.  $\Delta E^\ddagger$  vs. IRC plots for the hydrolysis of acetyl chloride with clusters of two water molecules (**6a** + **16**  $\rightleftharpoons$  TS **19a**  $\rightarrow$  **11a** + **12** + **7**) in water, and with a cluster of one water and one acetone molecule, in acetone (**6a** + **18**  $\rightleftharpoons$  TS **21a**  $\rightarrow$  **11a** + **12** + acetone, Scheme 5). IRC calculations were performed at (B3LYP)/6-31G(d) level of theory, using the Radii=UAHF option.  $\Delta E$  values refer to the separated reactants ( $\Delta E = 0$ ).

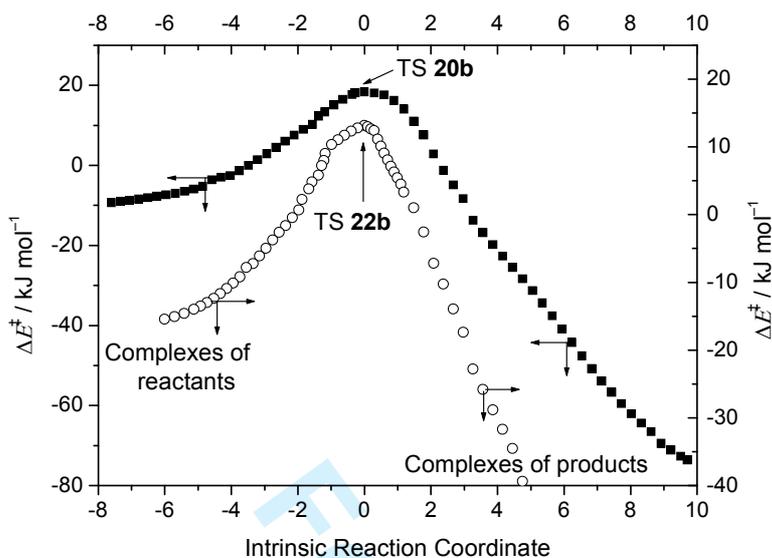


Figure S2.  $\Delta E^\ddagger$  vs. IRC plots for the hydrolysis of chloroacetyl chloride with clusters of three water molecules [**6b** + **17**  $\rightleftharpoons$  (TS **20b** or TS **22b**)  $\rightarrow$  **11b** + **12** + **16**; Scheme 5] in water. IRC calculations were performed at (B3LYP)/6-31G(d) level of theory, using the Radii=UAHF option.  $\Delta E$  values refer to the separated reactants ( $\Delta E = 0$ ).

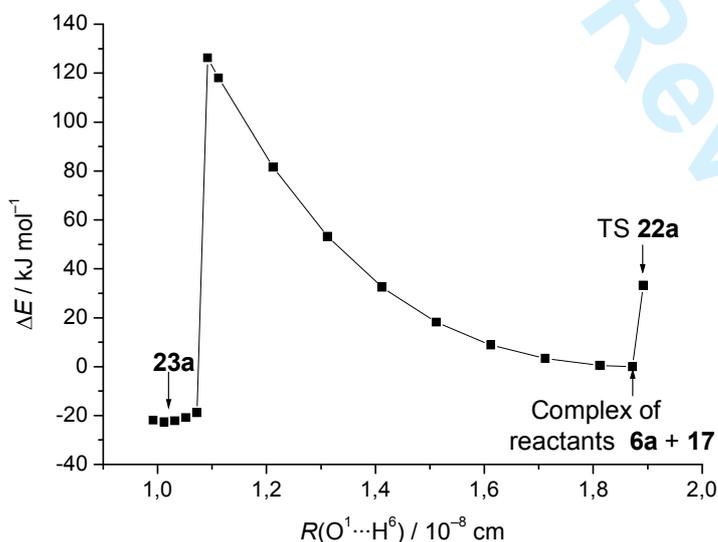


Figure S3.  $\Delta E$  vs.  $R(\text{O}^1 \cdots \text{H}^6)$  plot for the transfer of  $\text{H}^6$  hydrogen to  $\text{O}^1$  oxygen atom for the formation of the complex of acetyl chloride hydrate and two water molecules (**23a**) from TS **22a** (Scheme 5). Calculations were performed at (B3LYP)/6-31G(d) level of theory with optimization, using the Radii=UAHF option, decreasing stepwise the  $R(\text{O}^1 \cdots \text{H}^6)$  distance.  $\Delta E$  values refer to the complex of acetyl chloride (**6a**) and cluster of three water molecules (**17**).

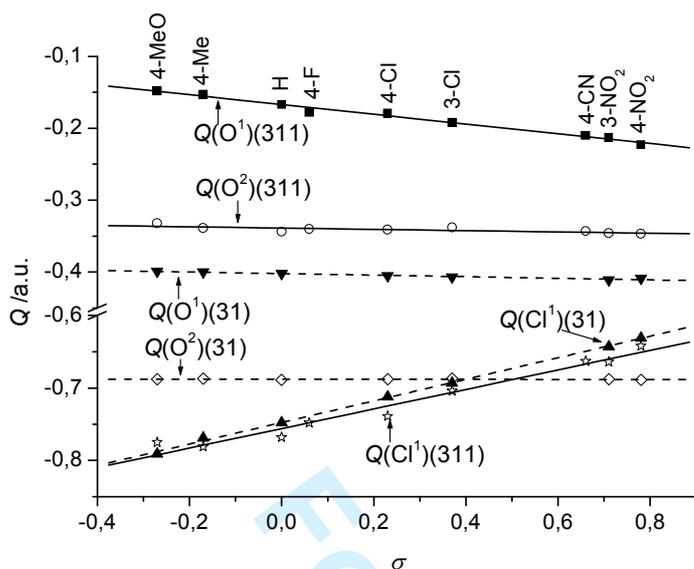


Figure S4. Plots of charges ( $Q$ ) for TS **27** (Scheme 6) against the Hammett  $\sigma$  constants, as calculated at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory [marked as (31) and (311), respectively], using the Radii=UAHF option, in acetone, at 25° C. [Correlations:  $Q(O^1)(311) = -0.0679\sigma - 0.167$  ( $r = 0.993$ );  $Q(O^2)(311) = -0.00893\sigma - 0.339$  ( $r = 0.759$ );  $Q(Cl^1)(311) = 0.135\sigma - 0.755$  ( $r = 0.983$ );  $Q(O^1)(31) = -0.0109\sigma - 0.402$  ( $r = 0.980$ );  $Q(O^2)(31) = -5.7 \times 10^{-4}\sigma - 0.688$  ( $r = 0.288$ );  $Q(Cl^1)(31) = 0.149\sigma - 0.747$  ( $r = 0.999$ )].

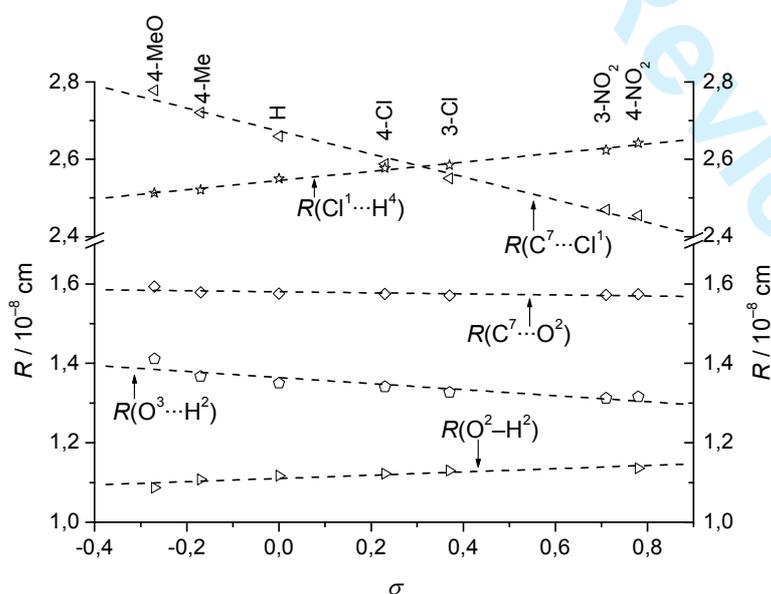


Figure S5. Plots of bond distances for TS **27** (Scheme 6) against the Hammett  $\sigma$  constants, as calculated at (B3LYP)/6-31G(d) level of theory, using the Radii=UAHF option, in acetone, at 25° C. [Correlations:  $R(C^7 \cdots O^2) = -0.0133\sigma + 1.580$  ( $r = 0.730$ );  $R(C^7 \cdots Cl^1) = -0.296\sigma +$

2.673 ( $r = 0.992$ );  $R(O^2 \cdots H^2) = 0.0408\sigma + 1.110$  ( $r = 0.904$ );  $R(H^4 \cdots Cl^1) = 0.118\sigma + 2.545$  ( $r = 0.996$ );  $R(O^3 \cdots H^2) = -0.0762\sigma + 1.364$  ( $r = 0.909$ ).]

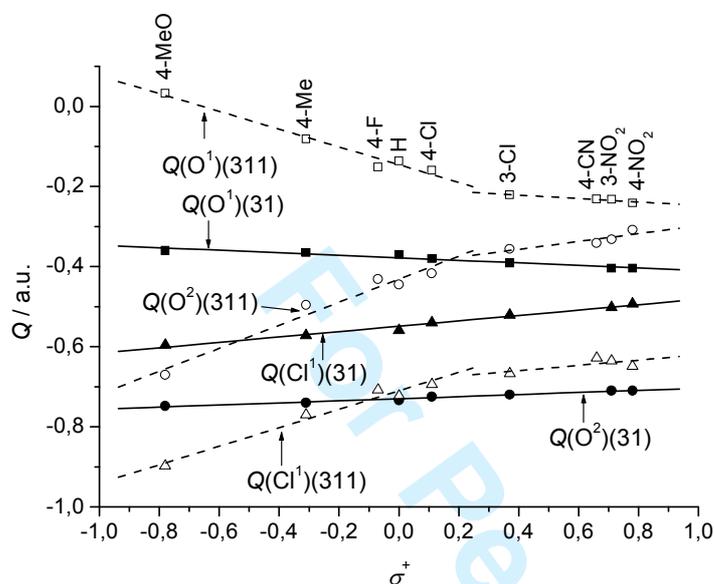


Figure S6. Plots of charges ( $Q$ ) for TS **28** (Scheme 6) against the  $\sigma^+$  constants, as calculated at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory [marked as (31) and (311), respectively], using the Radii=UAHF option, in water, at 25° C. [Correlations for compounds with substituents 4-MeO - 4-Cl;  $Q(O^1)(311) = -0.222\sigma^+ - 0.145$  ( $r = 0.986$ );  $Q(O^2)(311) = 0.288\sigma^+ - 0.431$  ( $r = 0.980$ );  $Q(Cl^1)(311) = 0.231\sigma^+ - 0.710$  ( $r = 0.986$ ), and for compounds with substituents 3-Cl - 4-NO<sub>2</sub>;  $Q(O^1)(311) = -0.0429\sigma^+ - 0.204$  ( $r = 0.945$ );  $Q(O^2)(311) = 0.0982\sigma^+ - 0.396$  ( $r = 0.881$ );  $Q(Cl^1)(311) = 0.0660\sigma^+ - 0.686$  ( $r = 0.691$ ). Correlations for compounds with substituents 4-MeO - 4-NO<sub>2</sub>,  $Q(O^1)(31) = -0.0314\sigma^+ - 0.378$  ( $r = 0.965$ );  $Q(O^2)(31) = 0.0260\sigma^+ - 0.730$  ( $r = 0.987$ );  $Q(Cl^1)(31) = 0.0672\sigma^+ - 0.549$  ( $r = 0.991$ ).]

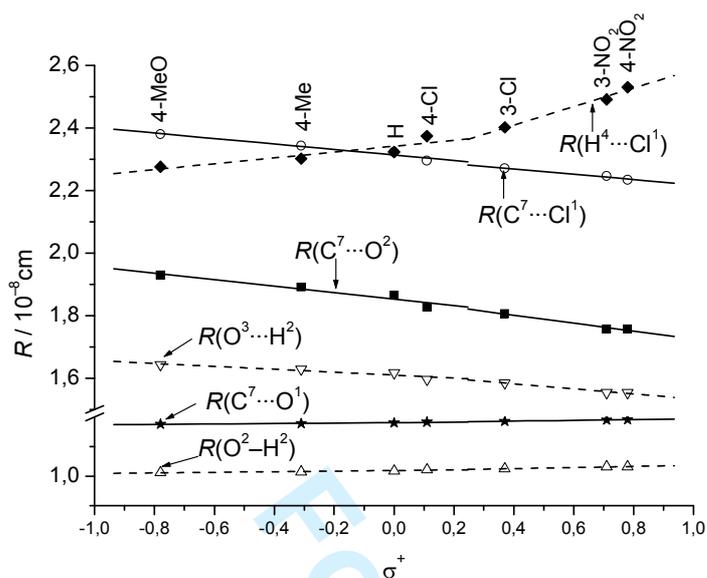


Figure S7. Plots of bond distances for TSs **28** (Scheme 6) against the  $\sigma^+$  constants, as calculated at (B3LYP)/6-31G(d) level of theory, using the Radii=UAHF option, in water, at 25° C. [Correlations for compounds with substituents 4-MeO - 4-Cl;  $R(C^7 \cdots O^2) = -0.104 \sigma^+ + 1.853$  ( $r = 0.962$ );  $R(C^7 \cdots Cl^1) = -0.0876 \sigma^+ + 2.314$  ( $r = 0.977$ );  $R(O^2 \cdots H^2) = 0.0101 \sigma^+ + 1.019$  ( $r = 0.945$ );  $R(H^4 \cdots Cl^1) = 0.0936 \sigma^+ + 2.342$  ( $r = 0.898$ );  $R(O^3 \cdots H^2) = -0.0465 \sigma^+ + 1.610$  ( $r = 0.930$ );  $R(C^7 \cdots O^1) = 0,00700 \sigma^+ + 1.181$  ( $r = 0.934$ ). Correlations for compounds with substituents 3-Cl - 4-NO<sub>2</sub>;  $R(C^7 \cdots O^2) = -0.127 \sigma^+ + 1.852$  ( $r = 0.987$ );  $R(C^7 \cdots Cl^1) = -0.0849 \sigma^+ + 2.303$  ( $r = 0.987$ );  $R(O^2 \cdots H^2) = 0.0182 \sigma^+ + 1.018$  ( $r = 0.987$ );  $R(H^4 \cdots Cl^1) = 0,296 \sigma^+ + 2.291$  ( $r = 0.990$ );  $R(O^3 \cdots H^2) = -0.0806 \sigma^+ + 1.614$  ( $r = 0.987$ );  $R(C^7 \cdots O^1) = 0,0121 \sigma^+ + 1.181$  ( $r = 1,000$ ).]

Table S1. Selected net Mulliken atomic charges ( $Q$ , a.u.), atomic distances ( $R$ , Å), bond and dihedral angles ( $\theta$  and  $\varphi$ , degree), as calculated at (B3LYP)/6-31G(d) level of theory for the optimized structures in the hydrolysis of acetyl chloride, in water, at 25 °C (Scheme 2 and 5).

<b>6a</b>		<b>10a</b>		<b>15</b>		<b>18</b>	
$Q(O^1)$	-0.360	$Q(O^1)$	-0.159	$Q(O^1)$	-0.296	$\theta(H^1O^1H^2)$	103.0
$Q(Cl)$	-0.125	$Q(O^2)$	-0.881	$Q(O^2)$	-0.743	$\theta(O^1H^2O^2)$	170.7
$Q(C^1)$	0.343	$Q(Cl^1)$	-0.870	$Q(O^3)$	-0.768	$\theta(O^1O^2C^1)$	112.7
$R(C^1O^1)$	1.188	$R(C^1O^1)$	1.125	$R(C^1O^1)$	1.159	$\theta(O^2C^1C^2)$	121.8
$R(C^1Cl^1)$	1.850	$R(C^1Cl^1)$	3.270	$R(C^1O^2)$	1.945	$\varphi(O^1O^2C^1C^2)$	-0.75
$\theta(O^1C^1C^2)$	129.2	$R(Cl^1H^1)$	2.290	$R(C^1O^3)$	2.040	$\varphi(H^1O^1O^2C^1)$	-89.5
$\theta(Cl^1C^1C^2)$	111.7	$R(O^2H^1)$	0.980	$\theta(O^1C^1C^2)$	141.6	$\varphi(O^2C^1C^2H^4)$	-121.4
$\theta(O^1C^1Cl^1)$	119.1	$\theta(O^1C^1C^2)$	175.2	$\theta(O^2C^1C^2)$	99.8		
$\varphi(O^1C^1C^2Cl^1)$	180	$\theta(O^1C^1Cl^1)$	102.3	$\theta(O^3C^1C^2)$	96.88	<b>19a</b>	
<b>7</b>		$\theta(Cl^1H^1O^2)$	171.4	$\theta(O^2C^1O^3)$	87.11	$Q(O^1)$	-0.365
$Q(O)$	-0.851	$\varphi(O^1C^1C^2Cl^1)$	179.6	$\varphi(O^1C^1C^2O^2)$	142.8	$Q(O^2)$	-0.737
$Q(H)$	-0.426	$\varphi(O^1C^1Cl^1H^1)$	12.4	$\varphi(O^1C^1C^2O^3)$	-129.1	$Q(Cl)$	-0.601
$R(OH)$	0.977	$\varphi(O^1C^1Cl^1O^2)$	12.1	<b>16</b>		$R(C^1O^1)$	1.180
$\theta(HOH)$	102.6	<b>11a</b>		$Q(O^1)$	-0.895	$R(C^1O^2)$	1.816
<b>8a</b>		$Q(O^1)$	-0.516	$Q(O^2)$	-0.815	$R(C^1Cl^1)$	2.290
$Q(O^1)$	-0.322	$Q(O^2)$	-0.580	$R(O^1H^2)$	0.983	$R(O^2H^2)$	1.022
$Q(O^2)$	-0.701	$R(C^1O^1)$	1.218	$R(O^2H^2)$	1.847	$R(O^3H^2)$	1.594
$Q(Cl)$	-0.728	$R(C^1O^2)$	1.345	$\theta(H^1O^1H^2)$	103.0	$R(Cl^1H^4)$	3.137
$Q(C^1)$	0.543	$R(O^2H)$	0.996	$\theta(O^1H^2O^2)$	179.6	$\theta(O^1C^1C^2)$	133.2
$R(C^1O^1)$	1.168	$\theta(O^1C^1C^2)$	125.3	$\theta(H^2O^2H^4)$	103.7	$\theta(O^2C^1C^2)$	101.1
$R(C^1O^2)$	1.798	$\theta(O^2C^1C^2)$	111.7	$\varphi(H^1O^1O^2H^4)$	123.1	$\theta(Cl^1C^1C^2)$	110.6
$R(C^1Cl^1)$	2.505	$\theta(C^1O^2H)$	107.7	$\varphi(H^1O^1O^2H^3)$	-129.5	$\theta(C^1O^2H^2)$	107.3
$R(O^2H^2)$	0.996	<b>12</b>				$\theta(O^2H^2O^3)$	175.2
$R(Cl^1H^2)$	2.513	$Q(Cl)$	-0.330	<b>17</b>		$\varphi(O^1C^1C^2O^2)$	134.3
$\theta(O^1C^1C^2)$	137.3	$R(ClH)$	1.320	$Q(O^1)$	-0.901	$\varphi(O^1C^1C^2Cl)$	-132.1
$\theta(O^2C^1C^2)$	102.5	<b>13</b>		$Q(O^2)$	-0.856	<b>20a</b>	
$\theta(C^1C^1C^2)$	97.5	$Q(O^1)$	-0.324	$Q(O^3)$	-0.815	$Q(O^1)$	-0.362
$\theta(O^2C^1Cl^1)$	87.6	$Q(O^2)$	-0.649	$R(O^1H^2)$	0.986	$Q(O^2)$	-0.755
$\theta(O^1C^1Cl^1)$	108.2	$R(C^1O^1)$	1.172	$R(O^2H^2)$	1.813	$Q(Cl)$	-0.507
$\varphi(O^1C^1C^2O^2)$	143.2	$R(C^1O^2)$	1.556	$R(O^2H^4)$	0.989	$R(C^1O^1)$	1.181
$\varphi(O^1C^1C^2Cl)$	-127.5	$\theta(O^1C^1C^2)$	135.8	$R(O^3H^4)$	1.780	$R(C^1O^2)$	1.892
$\varphi(O^1C^1Cl^1O^2)$	-112.2	$\theta(O^2C^1C^2)$	109.4	$\theta(O^1H^2O^2)$	179.2	$R(C^1Cl^1)$	2.210
<b>9a</b>		$\varphi(O^1C^1C^2O^2)$	-175.4	$\theta(O^2H^4O^3)$	179.4	$R(O^2H^2)$	1.024
$Q(O^1)$	-0.163	<b>14</b>		$\theta(H^2O^2H^4)$	104.0	$R(O^3H^2)$	1.588
$Q(Cl)$	-0.903	$Q(O^1)$	-0.331	$\theta(H^4O^3H^6)$	106.2	$R(Cl^1H^4)$	2.358
$R(C^1O^1)$	1.126	$Q(Cl)$	-0.620	$\varphi(H^1O^1O^2H^4)$	129.1	$\theta(O^1C^1C^2)$	133.1
$R(C^1Cl^1)$	3.307	$R(C^1O^1)$	1.176	$\varphi(H^2O^2O^3H^6)$	-21.7	$\theta(O^2C^1C^2)$	99.3
$\theta(O^1C^1C^2)$	179.9	$R(C^1Cl^1)$	$Q(O^2)$	$\varphi(H^2O^2O^3H^5)$	-130.8	$\theta(Cl^1C^1C^2)$	102.6
$\theta(O^1C^1Cl^1)$	104.4	$\theta(O^1C^1C^2)$	133.5	<b>18</b>		$\theta(C^1O^2H^2)$	105.7
$\varphi(O^1C^1C^2Cl^1)$	-33.1	$\theta(Cl^1C^1C^2)$	100.5	$Q(O^1)$	-0.865	$\theta(O^2H^2O^3)$	175.8
		$\varphi(O^1C^1C^2Cl)$	130.1	$Q(O^2)$	-0.480	$\varphi(O^1C^1C^2O^2)$	129.4
				$R(O^1H^2)$	0.979	$\varphi(O^1C^1C^2Cl)$	-136.4
				$R(O^2H^2)$	1.917		
				$R(O^2C^1)$	1.227		

Table S1. Continued

<b>21a</b>		<b>22a</b>		<b>23a</b>		<b>25a</b>	
$Q(O^1)$	-0.357	$\varphi(O^1C^1C^2O^2)$	131.7	$\theta(O^2H^2O^3)$	159.8	$Q(O^1)$	-0.504
$Q(O^2)$	-0.712	$\varphi(O^1C^1C^2Cl)$	-132.6	$\theta(H^2O^3H^4)$	94.3	$Q(O^2)$	-0.539
$Q(Cl)$	-0.690	$\theta(O^1C^1C^2)$	128.0	$\theta(O^3H^4O^4)$	165.4	$Q(Cl)$	-0.937
$R(C^1O^1)$	1.179	$\theta(O^2C^1C^2)$	102.4	$\theta(H^4O^4H^6)$	102.9	$R(C^1O^1)$	$Q(O^2)$
$R(C^1O^2)$	1.715	$\theta(ClC^1C^2)$	103.3	$\theta(O^4H^6O^1)$	178.0	$R(C^1O^2)$	1.283
$R(C^1Cl^1)$	2.455	$\theta(C^1O^2H^2)$	108.1	<b>24a</b>		$R(C^1Cl^1)$	3.036
$R(O^2H^2)$	1.026	$\theta(O^2H^2O^3)$	176.0	$Q(O^1)$	-0.575	$R(O^1H^1)$	1.007
$R(O^3H^2)$	1.593	<b>23a</b>		$Q(O^2)$	-0.600	$R(O^2H^2)$	1.014
$R(Cl^1H^4)$	2.845	$Q(O^1)$	-0.596	$Q(Cl)$	-0.267	$\theta(O^1C^1C^2)$	125.1
$\theta(O^1C^1C^2)$	133.9	$Q(O^2)$	-0.621	$R(C^1O^1)$	1.362	$\theta(O^2C^1C^2)$	117.0
$\theta(O^2C^1C^2)$	103.9	$Q(O^3)$	-0.841	$R(C^1O^2)$	1.368	$\theta(ClC^1C^2)$	88.67
$\theta(ClC^1C^2)$	97.2	$Q(O^4)$	-0.851	$R(C^1Cl^1)$	1.970	$\theta(H^1O^1C^1)$	115.0
$\theta(C^1O^2H^2)$	109.7	$Q(Cl)$	-0.269	$R(O^1H^1)$	0.991	$\theta(H^2O^2C^1)$	112.6
$\theta(O^2H^2O^3)$	168.8	$R(C^1O^2)$	1.402	$R(O^2H^2)$	0.990	$\varphi(C^2C^1O^1H^1)$	12.75
$\varphi(O^1C^1C^2O^2)$	144.2	$R(O^2H^2)$	1.910	$\theta(O^1C^1C^2)$	115.5	$\varphi(C^2C^1O^2H^2)$	176.2
$\varphi(O^1C^1C^2Cl)$	-124.1	$R(O^3H^2)$	0.981	$\theta(O^2C^1C^2)$	115.1		
<b>22a</b>		$R(O^3H^4)$	1.734	$\theta(ClC^1C^2)$	115.2		
$Q(O^1)$		$R(O^4H^4)$	0.995	$\theta(H^1O^1C^1)$	111.0		
$Q(O^2)$	-0.849	$R(O^4H^6)$	1.613	$\theta(H^2O^2C^1)$	110.3		
$Q(Cl)$	-0.480	$R(O^1H^6)$	1.018	$\varphi(C^2C^1O^1H^1)$	48.3		
$R(C^1O^1)$	1.202	$R(C^1O^1)$	1.336	$\varphi(C^2C^1O^2H^2)$	37.7		
$R(C^1O^2)$	1.740	$R(C^1Cl^1)$	2.661				
$R(C^1Cl^1)$	2.156	$\theta(O^1C^1C^2)$	111.8				
$R(O^2H^2)$	1.049	$\theta(O^2C^1C^2)$	113.4				
$R(O^3H^2)$	1.501	$\theta(ClC^1C^2)$	105.8				
$R(O^1H^6)$	1.917	$\theta(C^1O^2H^2)$	117.6				

Table S2. Selected net Mulliken atomic charges ( $Q$ , a.u.), atomic distances ( $R$ , Å), bond and dihedral angles ( $\theta$  and  $\varphi$ , degree), as calculated at (B3LYP)/6-31G(d) level of theory using the Radii=UAHF option, for the optimized structures in the hydrolysis of chloroacetyl chloride, in water, at  $-10$  °C (Scheme 2 and 5).

<b>6b</b>		<b>16</b>		<b>19b</b>		<b>21b</b>	
$Q(O^1)$	-0.341	$\theta(O^1H^2O^2)$	179.9	$\theta(O^2C^1C^2)$	99.8	$\theta(O^2H^2O^3)$	163.2
$Q(Cl)$	-0.069	$\theta(H^2O^2H^4)$	104.5	$\theta(Cl^1C^1C^2)$	93.3	$\varphi(O^1C^1C^2O^2)$	141.1
$R(C^1O^1)$	1.186	$\varphi(H^1O^1O^2H^4)$	127.1	$\theta(C^1O^2H^2)$	109.4	$\varphi(O^1C^1C^2Cl^1)$	-122.6
$R(C^1Cl^1)$	1.827	$\varphi(H^1O^1O^2H^3)$	-124.8	$\theta(O^2H^2O^3)$	174.1	$\varphi(O^1C^1C^2Cl^2)$	-39.9
$\theta(O^1C^1C^2)$	129.8			$\varphi(O^1C^1C^2O^2)$	135.6	$\varphi(Cl^1C^1C^2Cl^2)$	82.7
$\theta(Cl^1C^1C^2)$	109.4	<b>17</b>		$\varphi(O^1C^1C^2Cl^1)$	-129.2	<b>22b</b>	
$\varphi(Cl^1C^1C^2Cl^2)$	179.8	$Q(O^1)$	-0.892	$\varphi(O^1C^1C^2Cl^2)$	-51.5	$Q(O^1)$	-0.476
<b>7</b>		$Q(O^2)$	-0.850	$\varphi(O^2C^1C^2Cl^2)$	177.0	$Q(O^2)$	-0.689
$Q(O)$	-0.841	$Q(O^3)$	-0.807	$\varphi(Cl^1C^1C^2Cl^2)$	81.9	$Q(Cl^1)$	-0.409
$Q(H)$	0.420	$R(O^1H^2)$	0.986	<b>20b</b>		$R(C^1O^1)$	1.217
$R(OH)$	0.975	$R(O^2H^2)$	1.817	$Q(O^1)$	-0.393	$R(C^1O^2)$	1.617
$\theta(HOH)$	102.7	$R(O^2H^4)$	0.989	$Q(O^2)$	-0.840	$R(C^1Cl^1)$	2.107
<b>8b</b>		$R(O^3H^4)$	1.781	$Q(Cl^1)$	-0.479	$R(O^2H^2)$	1.133
$Q(O^1)$	-0.322	$\theta(O^1H^2O^2)$	179.7	$R(C^1O^1)$	1.189	$R(O^3H^2)$	1.318
$Q(O^2)$	-0.667	$\theta(O^2H^4O^3)$	178.2	$R(C^1O^2)$	1.727	$R(O^1H^6)$	1.850
$Q(Cl)$	-0.656	$\theta(H^2O^2H^4)$	102.6	$R(C^1Cl^1)$	2.201	$\theta(O^1C^1C^2)$	124.7
$R(C^1O^1)$	1.171	$\theta(H^4O^3H^6)$	106.5	$R(O^2H^2)$	1.059	$\theta(O^2C^1C^2)$	101.4
$R(C^1O^2)$	1.722	$\varphi(H^1O^1O^2H^4)$	134.2	$R(O^3H^2)$	1.471	$\theta(Cl^1C^1C^2)$	103.8
$R(C^1Cl^1)$	2.509	$\varphi(H^2O^2O^3H^6)$	-23.7	$R(Cl^1H^4)$	2.332	$\theta(C^1O^2H^2)$	109.3
$R(O^2H^2)$	1.002	$\varphi(H^2O^2O^3H^5)$	-133.6	$\theta(O^1C^1C^2)$	129.8	$\theta(O^2H^2O^3)$	176.1
$R(Cl^1H^2)$	2.147	<b>18</b>		$\theta(O^2C^1C^2)$	113.8	$\varphi(O^1C^1C^2O^2)$	131.0
$\theta(O^1C^1C^2)$	135.5	$Q(O^1)$	-0.840	$\theta(Cl^1C^1C^2)$	112.4	$\varphi(O^1C^1C^2Cl^1)$	-131.5
$\theta(O^2C^1C^2)$	101.5	$Q(O^2)$	-0.465	$\theta(C^1O^2H^2)$	109.4	$\varphi(O^1C^1C^2Cl^2)$	-51.9
$\theta(Cl^1C^1C^2)$	98.7	$R(O^1H^2)$	0.979	$\theta(O^2H^2O^3)$	174.1	$\varphi(Cl^1C^1C^2Cl^2)$	79.6
$\varphi(O^1C^1C^2O^2)$	145.6	$R(O^2H^2)$	1.912	$\varphi(O^1C^1C^2O^2)$	131.5	<b>23b</b>	
$\varphi(O^1C^1C^2Cl^1)$	-130.4	$R(O^2C^1)$	1.226	$\varphi(O^1C^1C^2Cl^1)$	-133.3	$Q(O^1)$	-0.597
$\varphi(O^1C^1C^2Cl^2)$	-42.6	$\theta(H^1O^1H^2)$	103.1	$\varphi(O^1C^1C^2Cl^2)$	-51.4	$Q(O^2)$	-0.618
$\varphi(Cl^1C^1C^2Cl^2)$	87.8	$\theta(O^1H^2O^2)$	168.8	$\varphi(O^2C^1C^2Cl^2)$	177.0	$Q(O^3)$	-0.834
<b>9b</b>		$\theta(O^1O^2C^1)$	112.2	$\varphi(Cl^1C^1C^2Cl^2)$	81.9	$Q(O^4)$	-0.846
$Q(O^1)$	-0.166	$\theta(O^2C^1C^2)$	121.9	<b>21b</b>		$Q(Cl^1)$	-0.175
$Q(Cl)$	-0.773	$\varphi(O^1O^2C^1C^2)$	-0.079	$Q(O^1)$	-0.409	$R(C^1O^2)$	1.337
$R(C^1O^1)$	1.130	$\varphi(H^1O^1O^2C^1)$	-90.6	$Q(O^2)$	-0.690	$R(O^2H^2)$	1.928
$R(C^1Cl^1)$	3.266	$\varphi(O^2C^1C^2H^4)$	-121.3	$Q(Cl^1)$	-0.642	$R(O^3H^2)$	0.980
$\theta(O^1C^1C^2)$	176.2	<b>19b</b>		$R(C^1O^1)$	1.193	$R(O^3H^4)$	1.735
$\theta(C^1C^2Cl^1)$	110.0	$Q(O^1)$	-0.368	$R(C^1O^2)$	1.550	$R(O^4H^4)$	0.995
$\theta(C^1C^2Cl^2)$	85.5	$Q(O^2)$	-0.708	$R(C^1Cl^1)$	2.429	$R(O^4H^5)$	1.610
$\theta(Cl^1C^2Cl^2)$	130.9	$Q(Cl)$	-0.570	$R(O^2H^2)$	1.143	$R(O^1H^5)$	1.018
<b>16</b>		$R(C^1O^1)$	1.183	$R(O^3H^2)$	1.310	$R(C^1O^1)$	1.408
$Q(O^1)$	-0.888	$R(C^1O^2)$	1.706	$R(Cl^1H^4)$	2.644	$R(C^1Cl^1)$	1.905
$Q(O^2)$	-0.807	$R(C^1Cl^1)$	2.324	$\theta(O^1C^1C^2)$	129.1	$\theta(O^1C^1C^2)$	111.9
$R(O^1H^2)$	0.982	$R(O^2H^2)$	1.050	$\theta(O^2C^1C^2)$	105.0	$\theta(O^2C^1C^2)$	108.4
$R(O^2H^2)$	1.852	$R(O^3H^2)$	1.496	$\theta(Cl^1C^1C^2)$	97.2	$\theta(Cl^1C^1C^2)$	108.2
$\theta(H^1O^1H^2)$	103.0	$R(Cl^1H^4)$	2.343	$\theta(C^1O^2H^2)$	122.2	$\theta(C^1O^2H^2)$	116.3
		$\theta(O^1C^1C^2)$	131.6				

Table S2. Continued

<b>23</b>		<b>24b</b>		<b>25b</b>	
$\theta(\text{O}^2\text{H}^2\text{O}^3)$	158.4	$\theta(\text{H}^1\text{O}^1\text{C}^1)$	111.2	$\theta(\text{Cl}^1\text{C}^1\text{C}^2)$	106.9
$\theta(\text{O}^3\text{H}^4\text{O}^4)$	160.0	$\theta(\text{H}^2\text{O}^2\text{C}^1)$	111.2	$\theta(\text{H}^1\text{O}^1\text{C}^1)$	111.5
$\theta(\text{O}^4\text{H}^5\text{O}^1)$	179.6	$\varphi(\text{H}^1\text{O}^1\text{C}^1\text{C}^2)$	60.6	$\theta(\text{H}^2\text{O}^2\text{C}^1)$	108.8
$\varphi(\text{O}^1\text{C}^1\text{C}^2\text{Cl}^2)$	-51.8	$\varphi(\text{H}^2\text{O}^2\text{C}^1\text{C}^2)$	23.9	$\varphi(\text{H}^1\text{O}^1\text{C}^1\text{C}^2)$	65.2
$\varphi(\text{Cl}^1\text{C}^1\text{C}^2\text{Cl}^2)$	65.2	$\varphi(\text{O}^2\text{C}^1\text{C}^2\text{Cl}^2)$	-177.6	$\varphi(\text{H}^2\text{O}^2\text{C}^1\text{C}^2)$	166.9
<b>24b</b>		$\varphi(\text{H}^1\text{O}^1\text{C}^1\text{C}^2)$	60.6	$\varphi(\text{O}^1\text{C}^1\text{C}^2\text{Cl}^2)$	-119.9
$Q(\text{O}^1)$	-0.575	<b>25b</b>		$\varphi(\text{O}^2\text{C}^1\text{C}^2\text{Cl}^2)$	116.0
$Q(\text{O}^2)$	-0.596	$Q(\text{O}^1)$	-0.583	$\varphi(\text{Cl}^1\text{C}^1\text{C}^2\text{Cl}^2)$	66.6
$Q(\text{Cl}^1)$	-0.178	$Q(\text{O}^2)$	-0.573		
$R(\text{C}^1\text{O}^1)$	1.366	$Q(\text{Cl}^1)$	-0.248		
$R(\text{C}^1\text{O}^2)$	1.368	$R(\text{C}^1\text{O}^1)$	1.361		
$R(\text{C}^1\text{Cl}^1)$	1.913	$R(\text{C}^1\text{O}^2)$	1.350		
$R(\text{O}^1\text{H}^1)$	0.982	$R(\text{C}^1\text{Cl}^1)$	1.964		
$R(\text{O}^2\text{H}^2)$	0.987	$R(\text{O}^1\text{H}^1)$	0.983		
$\theta(\text{O}^1\text{C}^1\text{C}^2)$	115.3	$R(\text{O}^2\text{H}^2)$	0.991		
$\theta(\text{O}^2\text{C}^1\text{C}^2)$	111.4	$\theta(\text{O}^1\text{C}^1\text{C}^2)$	116.5		
$\theta(\text{Cl}^1\text{C}^1\text{C}^2)$	107.3	$\theta(\text{O}^2\text{C}^1\text{C}^2)$	106.7		

Table S3. Selected net Mulliken atomic charges ( $Q$ , a.u.), atomic distances ( $R$ , Å), bond and dihedral angles ( $\theta$  and  $\varphi$ , degree), as calculated at (B3LYP)/6-311+G(d,p) level of theory using the Radii=UAHF option, for the optimized structures of benzoyl chlorides ( $\text{XC}_6\text{H}_4\text{COCl}$ , **26**), in water and acetone, at 25° C, respectively (Scheme 6).

<b>26 (water)<sup>[a]</sup></b>	H	4-MeO	4-Me	4-Cl	3-Cl	3-NO <sub>2</sub>	4-NO <sub>2</sub>
$Q(\text{O}^1)$	-0.168	-0.181	-0.171	-0.162	-0.163	-0.151	-0.144
$R(\text{C}^7\text{O}^1)$	1.190	1.192	1.191	1.190	1.190	1.189	1.189
$R(\text{C}^7\text{Cl}^1)$	1.843	1.854	1.848	1.837	1.832	1.822	1.822
$\theta(\text{O}^1\text{C}^7\text{C}^1)$	127.3	128.1	127.6	127.0	126.8	126.2	126.0
$\theta(\text{Cl}^1\text{C}^7\text{C}^1)$	115.5	115.2	115.3	115.4	115.4	115.5	115.6
<b>26 (acetone)<sup>[a]</sup></b>	H	4-MeO	4-Me	4-Cl	3-Cl	3-NO <sub>2</sub>	4-NO <sub>2</sub>
$Q(\text{O}^1)$	-0.147	-0.157	-0.148	-0.140	-0.141	-0.129	-0.124
$R(\text{C}^7\text{O}^1)$	1.189	1.191	1.190	1.189	1.189	1.188	1.188
$R(\text{C}^7\text{Cl}^1)$	1.840	1.851	1.845	1.834	1.830	1.820	1.820
$\theta(\text{O}^1\text{C}^7\text{C}^1)$	126.8	127.5	127.1	126.5	126.3	125.8	125.7
$\theta(\text{Cl}^1\text{C}^7\text{C}^1)$	115.3	115.0	115.2	115.3	115.3	115.4	115.5

[a]  $\varphi(\text{O}^1\text{C}^7\text{C}^1\text{C}^2) \sim 180^\circ$ ,  $\varphi(\text{Cl}^1\text{C}^7\text{C}^1\text{C}^2) \sim 0^\circ$

Table S4. Selected net Mulliken atomic charges ( $Q$ , a.u.), atomic distances ( $R$ , Å), bond and dihedral angles ( $\theta$  and  $\varphi$ , degree), as calculated at (B3LYP)/6-311+G(d,p) level of theory using the Radii=UAHF option, for the optimized structures of TSs **27** and **28** for hydrolyses of benzoyl chlorides (**26**), in acetone and water, at 25° C (Scheme 6).

<b>27</b> (in acetone)	H	4-MeO	4-Me	4-Cl	3-Cl	3-NO <sub>2</sub>	4-NO <sub>2</sub>
$Q(O^1)$	-0.167	-0.148	-0.153	-0.174	-0.192	-0.213	-0.223
$Q(O^2)$	-0.344	-0.332	-0.339	-0.341	-0.338	-0.346	-0.347
$Q(Cl^1)$	-0.768	-0.775	-0.771	-0.739	-0.704	-0.664	-0.642
$Q(H^2)$	0.510	0.475	0.495	0.514	0.513	0.534	0.530
$R(C^7O^1)$	1.178	1.173	1.176	1.180	1.182	1.186	1.187
$R(C^7O^2)$	1.619	1.688	1.644	1.609	1.599	1.586	1.587
$R(O^2H^2)$	1.068	1.035	1.053	1.078	1.089	1.111	1.113
$R(O^3H^2)$	1.422	1.517	1.463	1.399	1.376	1.335	1.333
$R(C^7Cl^1)$	2.644	2.674	2.667	2.590	2.546	2.463	2.443
$R(Cl^1H^4)$	2.586	2.597	2.583	2.612	2.638	2.660	2.683
$\theta(O^1C^7C^1)$	132.2	134.8	133.3	131.3	130.5	128.8	128.6
$\theta(O^2C^7C^1)$	108.8	107.2	108.3	108.9	109.0	109.0	109.2
$\theta(Cl^1C^7C^1)$	95.6	97.1	96.1	95.3	95.1	94.9	94.4
$\theta(O^2H^2O^3)$	170.7	168.4	169.7	170.7	170.8	171.4	171.4
$\varphi(O^1C^7C^1O^2)$	154.6	154.7	154.8	153.9	152.3	149.4	149.1
$\varphi(O^1C^7C^1Cl^1)$	-115.8	-117.9	-116.2	-116.6	-117.1	-118.7	-118.6
$\varphi(O^1C^7C^1C^2)$	170.3	177.8	174.9	172.0	168.2	167.9	163.6
<b>28</b> (in water)	H	4-MeO	4-Me	4-Cl	3-Cl	3-NO <sub>2</sub>	4-NO <sub>2</sub>
$Q(O^1)$	-0.136	0.033	-0.081	-0.159	-0.221	-0.232	-0.241
$Q(O^2)$	-0.445	-0.670	-0.496	-0.417	-0.356	-0.332	-0.308
$Q(Cl^1)$	-0.723	-0.898	-0.770	-0.694	-0.667	-0.635	-0.639
$Q(H^2)$	0.420	0.385	0.405	0.428	0.475	0.486	0.472
$R(C^7O^1)$	1.160	1.133	1.151	1.165	1.178	1.183	1.185
$R(C^7O^2)$	1.924	2.620	2.043	1.869	1.732	1.688	1.659
$R(O^2H^2)$	1.003	0.983	0.996	1.007	1.021	1.030	1.036
$R(O^3H^2)$	1.651	1.789	1.695	1.625	1.560	1.524	1.505
$R(C^7Cl^1)$	2.498	3.157	2.616	2.436	2.358	2.325	2.336
$R(Cl^1H^4)$	2.250	2.133	2.187	2.310	2.937	2.961	3.556
$\theta(O^1C^7C^1)$	138.3	166.3	143.6	135.8	131.3	129.6	129.3
$\theta(O^2C^7C^1)$	102.9	98.0	101.4	103.4	105.5	105.9	106.7
$\theta(Cl^1C^7C^1)$	100.2	95.3	99.4	100.4	100.3	99.6	98.7
$\theta(O^2H^2O^3)$	169.4	166.3	168.0	170.6	174.7	174.4	172.0
$\varphi(O^1C^7C^1O^2)$	140.8	147.8	142.0	139.9	141.0	140.9	142.6
$\varphi(O^1C^7C^1Cl^1)$	-127.5	-124.2	-127.6	-127.7	-126.3	-125.7	-124.0
$\varphi(O^1C^7C^1C^2)$	171.0	173.5	172.9	170.1	167.6	168.2	166.9

Table S5. Total energy ( $E$ , a.u.), sum of electronic and thermal free energy ( $G$ , a.u.) and enthalpy ( $H$ , a.u.), entropy of formation ( $S$ , J mol<sup>-1</sup> K<sup>-1</sup>) and value of imaginary frequency ( $\nu$ , cm<sup>-1</sup>) for species of the hydrolysis of acetyl chloride (Scheme 2 and 5), as calculated at (B3LYP)/6-31G(d), (B3LYP)/6-311+G(d,p) and MP2/6-31G(d) levels of theory, in water and acetone, at 25 °C.

Compound	Solvent	Level of theory	$E$	$G$	$H$	$S$	$\nu$
<b>6a</b>	water	6-31	-613.451193	-613.431853	-613.398351	295.0	-
<b>6a</b>	water	6-311	-613.531076	-613.512294	-613.478769	295.2	-
<b>6a</b>	water	MP2	-612.400991	-612.380497	-612.347208	293.1	-
<b>6a</b>	acetone	6-31	-613.450857	-613.431485	-613.397989	295.0	-
<b>6a</b>	acetone	6-311	-613.530701	-613.511884	-613.478365	295.2	-
<b>6a</b>	acetone	MP2	-612.400688	-612.380176	-612.346887	293.1	-
<b>7</b>	water	6-31	-76.421330	-76.419444	-76.397315	194.9	-
<b>7</b>	water	6-311	-76.472426	-76.470625	-76.448514	194.7	-
<b>7</b>	water	MP2	-76.210391	-76.208335	-76.186204	194.9	-
<b>7</b>	acetone	6-31	-76.420572	-76.418601	-76.396474	194.8	-
<b>7</b>	acetone	6-311	-76.471536	-76.469638	-76.447529	194.7	-
<b>7</b>	acetone	MP2	-76.209563	-76.207425	-76.185296	194.9	-
<b>8a</b>	water	6-31	-689.860334	-689.820796	-689.781892	342.6	-176.8
<b>8a</b>	water	6-311	-689.980941	-689.942670	-689.903195	347.6	-166.0
<b>8a</b>	water	MP2	-688.594145	-688.555538	-688.514909	357.8	-254.1
<b>8a</b>	acetone	6-31	-689.857646	-689.817530	-689.779030	339.0	-194.3
<b>8a</b>	acetone	6-311	-689.977903	-689.939371	-689.900028	346.5	-187.8
<b>8a</b>	acetone	MP2	-688.591343	-688.550934	-688.511906	343.7	-237.9
<b>9a</b>	water	6-31	-613.411011	-613.395543	-613.360703	306.8	-102.9
<b>10a</b>	water	6-31	-689.836155	-689.804020	-689.758497	400.9	-67.1
<b>11a</b>	water	6-31	-229.095670	-229.062205	-229.029479	288.2	-
<b>11a</b>	acetone	6-31	-229.094745	-229.061142	-229.028416	288.2	-
<b>12</b>	water	6-31	-460.804893	-460.817235	-460.795994	187.0	-
<b>12</b>	acetone	6-31	-460.804241	-460.816462	-460.795225	187.0	-
<b>13</b>	water	6-31	-229.477333	-229.435289	-229.401485	297.7	-
<b>13</b>	acetone	6-31	-229.471758	-229.429572	-229.395696	298.3	-
<b>14</b>	water	6-31	-1073.810885	-1073.794499	-1073.756439	335.2	-226.8
<b>14</b>	acetone	6-31	-1073.806260	-1073.789732	-1073.751775	334.2	-217.1
<b>15</b>	water	6-31	-305.904874	-305.842319	-305.802845	347.6	-151.4
<b>15</b>	acetone	6-31	-305.899434	-305.836848	-305.797196	349.2	-143.9
<b>16</b>	water	6-31	-152.851205	-152.832663	-152.800111	286.6	-
<b>16</b>	water	6-311	-152.949117	-152.930772	-152.898194	286.9	-
<b>17</b>	water	6-31	-229.282646	-229.244666	-229.205302	346.6	-
<b>17</b>	water	6-311	-229.426581	-229.391100	-229.348624	374.0	-
<b>18</b>	acetone	6-31	-269.589928	-269.514770	-269.472268	374.3	-
<b>19a</b>	water	6-31	-766.296759	-766.236943	-766.191248	402.4	-190.7
<b>19a</b>	water	6-311	-766.460568	-766.402740	-766.356092	410.8	-204.4
<b>20a</b>	water	6-31	-842.730841	-842.648334	-842.597680	446.1	-204.2
<b>20a</b>	water	6-311	-842.938731	-842.859487	-842.806779	464.2	-225.7
<b>21a</b>	acetone	6-31	-883.027560	-882.912056	-882.856205	491.8	-129.7

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<b>22a</b>	water	6-31	-842.731528	-842.647794	-842.598659	432.7	-197.6
<b>23a</b>	water	6-31	-842.750152	-842.663627	-842.615326	425.3	-
<b>24a</b>	water	6-31	-689.877404	-689.834085	-689.798526	313.1	-310.2
<b>25a</b>	water	6-31	-689.893104	-689.853079	-689.813372	349.7	-
<b>acetone</b>	acetone	6-31	-193.161640	-193.105914	-193.071338	304.3	-

Table S6. Total energy ( $E$ , a.u.), sum of electronic and thermal free energy ( $G$ , a.u.) and enthalpy ( $H$ , a.u.), entropy of formation ( $S$ , J mol<sup>-1</sup> K<sup>-1</sup>) and value of imaginary frequency ( $\nu$ , cm<sup>-1</sup>) for species of the hydrolysis of acetyl chloride (**6a**) and chloroacetyl chloride (**6b**, Scheme 2 and 5), as calculated at (B3LYP)/6-31G(d) level of theory, using the Radii=UAHF option, in water and acetone solvents, at 25 and -10 °C for the reaction of **6a** and **6b**.

Com- pound	Solvent	T / °C	$E$	$G$	$H$	$S$	$\nu$
<b>6a</b>	water	25	-613.451449	-613.432186	-613.398690	295.0	-
<b>6a</b>	acetone	25	-613.448897	-613.425455	-613.396776	286.3	-
<b>7</b>	water	25	-76.419457	-76.417310	-76.395188	194.8	-
<b>8a</b>	water	25	-689.854101	-689.813592	-689.775472	335.7	-213.7
<b>16</b>	water	25	-152.848149	-152.829240	-152.766643	287.1	-
<b>17</b>	water	25	-229.278519	-229.241940	-229.199635	372.5	-
<b>18</b>	acetone	25	-269.584544	-269.508784	-269.466416	373.1	-
<b>19a</b>	water	25	-766.291236	-766.229412	-766.185195	389.4	-187.3
<b>20a</b>	water	25	-842.726189	-842.642366	-842.592638	437.9	-191.8
<b>21a</b>	acetone	25	-883.013628	-882.896833	-882.842903	474.9	-108.2
<b>22a</b>	water	25	-842.724747	-842.639952	-842.591665	425.2	-180.3
<b>23a</b>	water	25	-842.746045	-842.658647	-842.610503	423.9	-
<b>6b</b>	water	-10	-1073.039450	-1073.027233	-1072.995790	313.9	-
<b>6b</b>	acetone	-10	-1073.034744	-1073.022050	-1072.990619	313.8	-
<b>7</b>	water	-10	-76.419457	-76.414730	-76.395563	190.6	-
<b>8b</b>	water	-10	-1149.437631	-1149.403222	-1149.368535	346.3	-228.0
<b>9b</b>	water	-10	-1072.971525	-1072.963887	-1072.931395	324.4	-153.0
<b>11b</b>	water	-10	-688.683884	-688.657354	-688.626643	306.6	-
<b>12</b>	water	-10	-460.799455	-460.808402	-460.790061	183.1	-
<b>16</b>	water	-10	-152.848149	-152.825457	-152.797613	278.0	-
<b>17</b>	water	-10	-229.278519	-229.237044	-229.201106	358.8	-
<b>18</b>	acetone	-10	-269.584544	-269.503885	-269.467967	358.6	-
<b>19b</b>	water	-10	-1225.877747	-1225.821833	-1225.782141	396.2	-179.0
<b>20b</b>	water	-10	-1302.310990	-1302.232546	-1302.188121	443.5	-180.1
<b>21b</b>	acetone	-10	-1342.597196	-1342.486213	-1342.438356	477.8	-421.1
<b>22b</b>	water	-10	-1302.312961	-1302.234002	-1302.191388	425.4	-299.7
<b>23b</b>	water	-10	-1302.336228	-1302.254126	-1302.211093	429.6	-
<b>24b</b>	water	-10	-1149.462667	-1149.425465	-1149.392475	329.3	-331.5
<b>25b</b>	water	-10	-1149.470243	-1149.432690	-1149.399088	335.3	-
<b>acetone</b>	acetone	-10	-193.162188	-193.102611	-193.073095	294.7	-

Table S7. Changes of the thermodynamic parameters for the reaction steps of the hydrolysis of acetyl chloride (Scheme 2 and 5), as calculated at (B3LYP)/6-31G(d) (6-31), (B3LYP)/6-311+G(d,p) (6-311) and MP2/6-31G(d) (MP2) levels of theory, in water and acetone, at 25 °C.

Reaction	Level of theory	Solvent	$\Delta E$ kJ mol <sup>-1</sup>	$\Delta G$ kJ mol <sup>-1</sup>	$\Delta H$ kJ mol <sup>-1</sup>	$\Delta S$ J mol <sup>-1</sup> K <sup>-1</sup>
<b>6a</b> ⇌ <b>TS 9a</b>	6-31	water	105.5	95.3	98.8	11.8
<b>6a</b> + <b>7</b> ⇌ <b>10a</b>	6-31	water	90.5	118.3	91.4	-90.4
<b>6a</b> + <b>7</b> ⇌ <b>TS 8a</b>	6-31	water	32.0	80.1	36.2	-147.3
	6-311	water	59.2	105.7	63.2	-142.3
	MP2	water	45.3	87.4	48.6	-130.3
	6-31	acetone	36.2	85.5	40.6	-150.8
	6-311	acetone	63.9	110.7	67.9	-143.4
	MP2	acetone	49.6	96.3	53.2	-144.3
<b>TS 8a</b> → <b>11a</b> + <b>12</b>	6-31	water	-105.6	-154.0	-114.4	132.7
	6-31	acetone	-108.5	-157.7	-117.1	132.6
<b>6a</b> + <b>16</b> ⇌ <b>TS 19a</b>	6-31	water	14.8	72.4	18.9	-179.3
	6-311	water	51.5	105.9	54.8	-171.3
<b>TS 19a</b> → <b>11a</b> + <b>12</b> + <b>7</b>	6-31	water	-66.0	-162.6	-82.8	267.7
<b>6a</b> + <b>17</b> ⇌ <b>TS 20a</b>	6-31	water	7.87	74.0	15.7	-195.6
	6-311	water	49.7	115.3	54.1	-205.1
<b>TS 20a</b> → <b>11a</b> + <b>12</b> + <b>16</b>	6-31	water	-54.9	-167.4	-73.3	315.7
<b>6a</b> + <b>18</b> ⇌ <b>TS 21a</b>	6-31	acetone	34.7	89.8	36.9	-177.4
<b>TS 21a</b> → <b>11a</b> + <b>12</b> + <b>acetone</b>	6-31	acetone	-86.8	-187.6	-101.8	287.7
<b>6a</b> + <b>17</b> ⇌ <b>TS 22a</b>	6-31	water	6.07	75.4	13.1	-209.0
<b>TS 22a</b> → <b>11a</b> + <b>12</b> + <b>16</b>	6-31	water	-50.7	-168.8	-70.7	329.1
<b>23a</b> ⇌ <b>TS 24a</b> + <b>16</b>	6-31	water	56.5	-8.19	43.8	174.7
<b>TS 24a</b> → <b>25a</b>	6-31	water	-41.2	-49.9	-39.0	36.5
<b>25a</b> → <b>11a</b> + <b>12</b>	6-31	water	-19.6	-69.2	-31.8	125.6

Table S8. Changes of the thermodynamic parameters for the reaction steps of the hydrolyses of acetyl chloride (**6a**) and chloroacetyl chloride (**6b**, Scheme 2 and 5), as calculated at (B3LYP)/6-31G(d) level of theory, using the Radii=UAHF option, in water and acetone, at 25 (for **a**) and  $-10$  °C (for **b**).

Reaction	T / °C	Solvent	$\Delta E$ kJ mol <sup>-1</sup>	$\Delta G$ kJ mol <sup>-1</sup>	$\Delta H$ kJ mol <sup>-1</sup>	$\Delta S$ J mol <sup>-1</sup> K <sup>-1</sup>
<b>6a</b> + <b>7</b> ⇌ TS <b>8a</b>	25	water	44.1	94.3	48.3	-154
<b>6a</b> + <b>16</b> ⇌ TS <b>19a</b>	25	water	22.0	84.1	26.6	-193
<b>6a</b> + <b>17</b> ⇌ TS <b>20a</b>	25	water	9.92	83.4	14.9	-230
<b>6a</b> + <b>18</b> ⇌ TS <b>21a</b>	25	acetone	58.7	115.9	58.3	-193
<b>6a</b> + <b>17</b> ⇌ TS <b>22a</b>	25	water	13.7	89.7	17.5	-242
<b>6b</b> ⇌ TS <b>9b</b>	-10	water	178.3	166.3	169.3	10.5
<b>6b</b> + <b>7</b> ⇌ TS <b>8b</b>	-10	water	55.9	101.7	60.1	-158
TS <b>8b</b> → <b>11b</b> + <b>12</b>	-10	water	-120.0	-164.2	-126.5	143
<b>6b</b> + <b>16</b> ⇌ TS <b>19b</b>	-10	water	25.9	81.0	20.6	-196
TS <b>19b</b> → <b>11b</b> + <b>12</b> + <b>7</b>	-10	water	-65.8	-154.0	-79.3	284
<b>6b</b> + <b>17</b> ⇌ TS <b>20b</b>	-10	water	18.3	83.3	23.0	-229
TS <b>20b</b> → <b>11b</b> + <b>12</b> + <b>16</b>	-10	water	-53.8	-154.0	-68.8	324
<b>6b</b> + <b>18</b> ⇌ TS <b>21b</b>	-10	acetone	58.0	104.3	53.1	-194
TS <b>21b</b> → <b>11b</b> + <b>12</b> + acetone	-10	acetone	-126.9	-215.7	-135.1	307
<b>6b</b> + <b>17</b> ⇌ TS <b>22b</b>	-10	water	13.2	79.5	14.5	-247
TS <b>22b</b> → <b>11b</b> + <b>12</b> + <b>16</b>	-10	water	-48.6	-150.2	-60.2	342
<b>23b</b> ⇌ TS <b>24b</b> + <b>16</b>	-10	water	66.7	8.41	55.1	177.7
TS <b>24b</b> → <b>25b</b>	-10	water	-20.0	-19.0	-17.4	6.12
<b>25b</b> → <b>11b</b> + <b>12</b>	-10	water	-34.4	-86.8	-46.3	154

Table S9. Total energy ( $E$ , a.u.), sum of electronic and thermal free energy ( $G$ , a.u.) and enthalpy ( $H$ , a.u.), entropy of formation ( $S$ , J mol<sup>-1</sup> K<sup>-1</sup>) and value of imaginary frequency ( $\nu$ , cm<sup>-1</sup>) for species of the hydrolysis of benzoyl chlorides (**26**, Scheme 6) as calculated at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory, using the Radii=UAHF option, in acetone, at 25 °C.

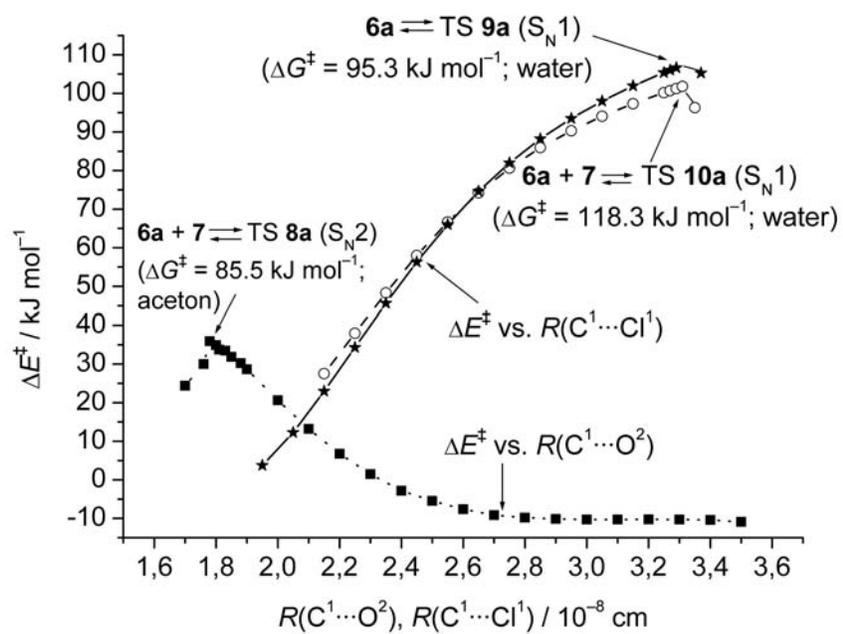
Compound	X	level of theory	$E$	$G$	$H$	$S$	$\nu$
<b>18</b>	-	6-31	-269.584544	-269.508784	-269.466416	373.1	-
<b>26a</b>	H	6-31	-805.188293	-805.120220	-805.078781	364.9	-
<b>26b</b>	4-MeO	6-31	-919.715918	-919.618422	-919.571044	417.2	-
<b>26c</b>	4-Me	6-31	-844.507875	-844.415850	-844.369010	412.5	-
<b>26g</b>	4-Cl	6-31	-1264.782949	-1264.726817	-1264.681993	394.7	-
<b>26h</b>	3-Cl	6-31	-1264.781645	-1264.725542	-1264.680692	394.9	-
<b>26l</b>	3-NO <sub>2</sub>	6-31	-1009.686706	-1009.620453	-1009.572250	424.5	-
<b>26m</b>	4-NO <sub>2</sub>	6-31	-1009.685735	-1009.619726	-1009.571326	426.2	-
<b>27a</b>	H	6-31	-1074.746132	-1074.581724	-1074.520090	542.7	-180.8
<b>27b</b>	4-MeO	6-31	-1189.273030	-1189.078688	-1189.010822	597.6	-80.6
<b>27c</b>	4-Me	6-31	-1114.065411	-1113.876558	-1113.809754	588.3	-138.5
<b>27g</b>	4-Cl	6-31	-1534.341860	-1534.189424	-1534.124440	572.2	-206.2
<b>27h</b>	3-Cl	6-31	-1534.340947	-1534.188795	-1534.123709	573.1	-243.9
<b>27l</b>	3-NO <sub>2</sub>	6-31	-1279.247870	-1279.085457	-1279.017279	600.4	-301.5
<b>27m</b>	4-NO <sub>2</sub>	6-31	-1279.247862	-1279.085383	-1279.017242	600.0	-290.2
<b>18</b>	-	6-311	-269.693554	-269.622505	-269.576510	403.3	-
<b>26a</b>	H	6-311	-805.311427	-805.244238	-805.202619	366.5	-
<b>26b</b>	4-MeO	6-311	-919.873018	-919.776999	-919.729374	419.4	-
<b>26c</b>	4-Me	6-311	-844.640897	-844.549694	-844.503082	410.5	-
<b>26e</b>	4-F	6-311	-904.580135	-904.522558	-904.478882	384.6	-
<b>26g</b>	4-Cl	6-311	-1264.933168	-1264.877808	-1264.832811	396.2	-
<b>26h</b>	3-Cl	6-311	-1264.931687	-1264.876395	-1264.831367	396.5	-
<b>26k</b>	4-CN	6-311	-897.576113	-897.513214	-897.467016	406.8	-
<b>26l</b>	3-NO <sub>2</sub>	6-311	-1009.871987	-1009.807294	-1009.758548	429.2	-
<b>26m</b>	4-NO <sub>2</sub>	6-311	-1009.871196	-1009.806740	-1009.757741	431.5	-
<b>27a</b>	H	6-311	-1074.970681	-1074.808384	-1074.745127	557.0	-102.2
<b>27b</b>	4-MeO	6-311	-1189.531723	-1189.340206	-1189.270523	613.6	-102.1
<b>27c</b>	4-Me	6-311	-1114.299623	-1114.112861	-1114.044673	600.5	-93.3
<b>27e</b>	4-F	6-311	-1174.239768	-1174.086830	-1174.021802	572.6	-109.9
<b>27g</b>	4-Cl	6-311	-1534.593057	-1534.442378	-1534.376175	583.0	-115.1
<b>27h</b>	3-Cl	6-311	-1534.591837	-1534.440826	-1534.375265	577.3	-137.2
<b>27k</b>	4-CN	6-311	-1167.238052	-1167.079470	-1167.013049	584.9	-180.6
<b>27l</b>	3-NO <sub>2</sub>	6-311	-1279.534026	-1279.373769	-1279.304794	607.4	-203.1
<b>27m</b>	4-NO <sub>2</sub>	6-311	-1279.534059	-1279.374030	-1279.304864	609.1	-209.3

Table S10. Total energy ( $E$ , a.u.), sum of electronic and thermal free energy ( $G$ , a.u.) and enthalpy ( $H$ , a.u.), entropy of formation ( $S$ , J mol<sup>-1</sup> K<sup>-1</sup>) and value of imaginary frequency ( $\nu$ , cm<sup>-1</sup>) for species of the hydrolysis of benzoyl chlorides (**26**, Scheme 6) as calculated at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory, using the Radii=UAHF option, in water, at 25 °C.

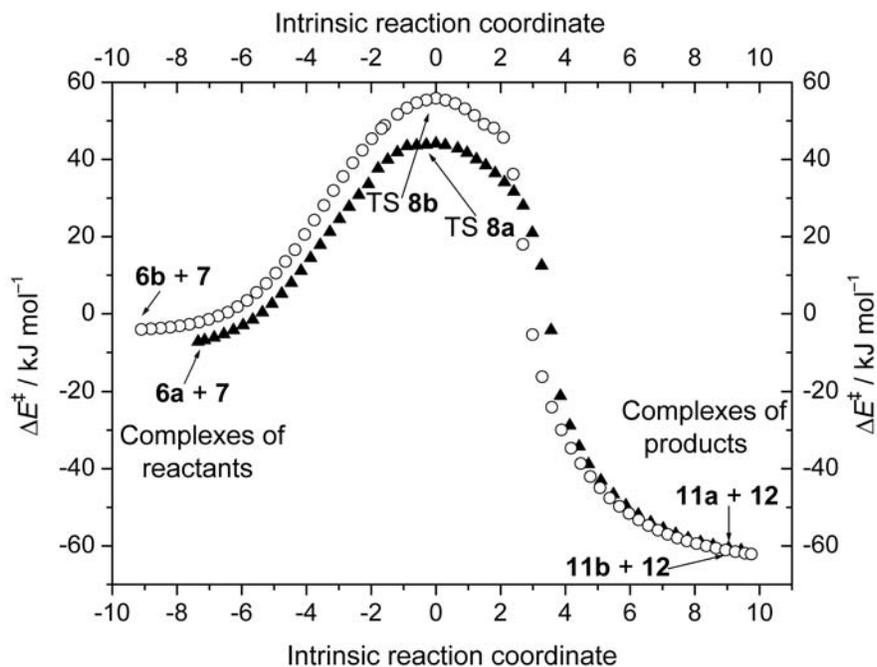
Com- pound	X	level of theory	$E$	$G$	$H$	$S$	$\nu$
<b>16</b>	-	6-31	-152.848149	-152.829240	-152.796643	287.1	-
<b>26a</b>	H	6-31	-805.191255	-805.123558	-805.082050	365.5	-
<b>26b</b>	4-MeO	6-31	-919.720354	-919.623408	-919.575953	417.9	-
<b>26c</b>	4-Me	6-31	-844.510952	-844.419312	-844.372468	412.5	-
<b>26g</b>	4-Cl	6-31	-1264.786460	-1264.730802	-1264.685892	395.5	-
<b>26h</b>	3-Cl	6-31	-1264.785136	-1264.729455	-1264.684559	395.3	-
<b>26l</b>	3-NO <sub>2</sub>	6-31	-1009.691332	-1009.625444	-1264.577184	425.0	-
<b>26m</b>	4-NO <sub>2</sub>	6-31	-1009.690276	-1009.624620	-1009.576173	426.6	-
<b>28a</b>	H	6-31	-958.026127	-957.916158	-957.863912	460.1	-203.5
<b>28b</b>	4-MeO	6-31	-1072.554029	-1072.415249	-1072.356536	517.0	-203.7
<b>28c</b>	4-Me	6-31	-997.345342	-997.210821	-997.153783	502.3	-203.0
<b>28g</b>	4-Cl	6-31	-1417.621693	-1417.523929	-1417.467512	490.9	-203.6
<b>28h</b>	3-Cl	6-31	-1417.620962	-1417.523156	-1417.467512	490.0	-201.7
<b>28l</b>	3-NO <sub>2</sub>	6-31	-1162.528359	-1162.420658	-1162.361542	520.6	-193.1
<b>28m</b>	4-NO <sub>2</sub>	6-31	-1162.527963	-1162.420632	-1162.361208	523.3	-189.3
<b>16</b>	-	6-311	-152.945795	-152.927081	-152.894403	287.8	-
<b>26a</b>	H	6-311	-805.314832	-805.248092	-805.206413	367.0	-
<b>26b</b>	4-MeO	6-311	-919.878188	-919.782803	-919.735120	419.9	-
<b>26c</b>	4-Me	6-311	-844.644476	-844.553802	-844.507135	410.9	-
<b>26e</b>	4-F	6-311	-904.584389	-904.527398	-904.483643	385.3	-
<b>26g</b>	4-Cl	6-311	-1264.937172	-1264.882347	-1264.837276	396.9	-
<b>26h</b>	3-Cl	6-311	-1264.935663	-1264.880872	-1264.835791	397.0	-
<b>26k</b>	4-CN	6-311	-897.581412	-897.518917	-897.472660	407.3	-
<b>26l</b>	3-NO <sub>2</sub>	6-311	-1009.877499	-1009.813175	-1009.764427	429.3	-
<b>26m</b>	4-NO <sub>2</sub>	6-311	-1009.876619	-1009.812476	-1009.763527	419.9	-
<b>28a</b>	H	6-311	-958.233556	-958.125915	-958.072378	471.4	-209.6
<b>28b</b>	4-MeO	6-311	-1072.798664	-1072.666223	-1072.602519	561.0	-17.1
<b>28c</b>	4-Me	6-311	-997.563274	-997.432207	-997.373164	519.9	-181.8
<b>28e</b>	4-F	6-311	-1057.502860	-1057.404411	-1057.349340	485.0	-216.4
<b>28g</b>	4-Cl	6-311	-1417.855794	-1417.759950	-1417.703181	499.9	-219.9
<b>28h</b>	3-Cl	6-311	-1417.854418	-1417.759859	-1417.702165	508.1	-196.6
<b>28k</b>	4-CN	6-311	-1050.501523	-1050.398399	-1050.340471	510.1	-184.0
<b>28l</b>	3-NO <sub>2</sub>	6-311	-1162.797589	-1162.692677	-1162.632275	531.9	-182.9
<b>28m</b>	4-NO <sub>2</sub>	6-311	-1162.797133	-1162.694292	-1162.631930	549.2	-162.5

Table S11. Activation parameters and their Hammett correlations for the hydrolysis of benzoyl chlorides (**26**, Scheme 6) as calculated at (B3LYP)/6-31G(d) and (B3LYP)/6-311+G(d,p) levels of theory, using the Radii=UAHF option, in acetone and water, at 25 °C.

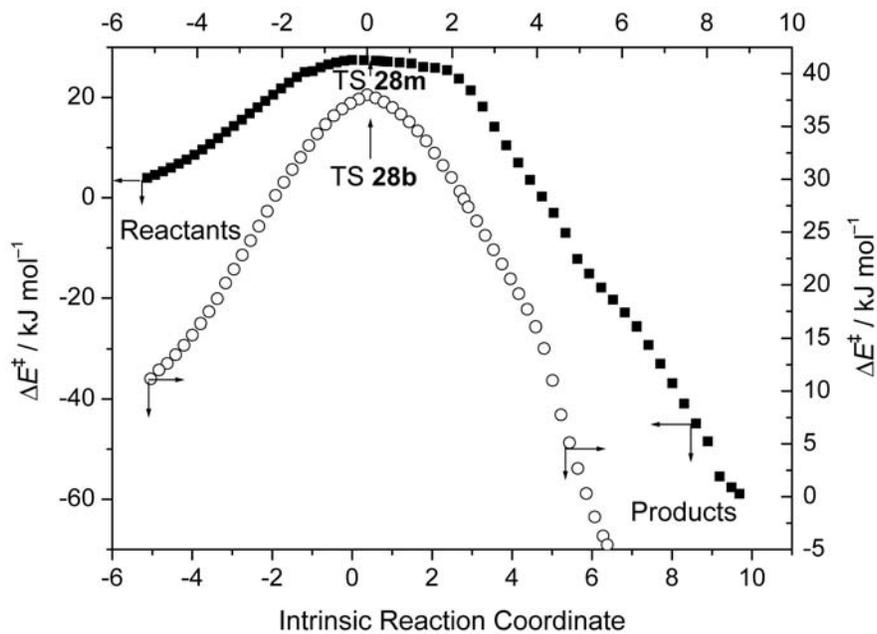
TS	X	Level of calc.	Solvent	$\Delta E^\ddagger$ kJ mol <sup>-1</sup>	$\Delta G^\ddagger$ kJ mol <sup>-1</sup>	$\Delta H^\ddagger$ kJ mol <sup>-1</sup>	$\Delta S^\ddagger$ J mol <sup>-1</sup> K <sup>-1</sup>
<b>27a</b>	H	6-31	acetone	70.1	124.1	65.9	-195.2
<b>27b</b>	4-MeO	6-31	acetone	72.0	127.4	70.0	-192.7
<b>27c</b>	4-Me	6-31	acetone	70.9	126.2	67.4	-197.3
<b>27g</b>	4-Cl	6-31	acetone	67.3	121.2	62.9	-195.6
<b>27h</b>	3-Cl	6-31	acetone	66.3	119.5	61.4	-194.9
<b>27l</b>	3-NO <sub>2</sub>	6-31	acetone	61.4	114.9	56.1	-197.2
<b>27m</b>	4-NO <sub>2</sub>	6-31	acetone	58.9	113.2	53.8	-199.3
$\Delta E^\ddagger = -11.9\sigma + 69.5$ ( $r = 0.983$ ); $\Delta G^\ddagger = -13.2\sigma + 124.1$ ( $r = 0.998$ ); $\Delta H^\ddagger = -14.2\sigma + 65.8$ ( $r = 0.993$ ); $\Delta S^\ddagger = -195.5 \pm 1.5$ J mol <sup>-1</sup> K <sup>-1</sup>							
<b>27a</b>	H	6-311	acetone	90.2	153.2	89.8	-212.7
<b>27b</b>	4-MeO	6-311	acetone	91.5	155.7	93.4	-209.0
<b>27c</b>	4-Me	6-311	acetone	91.4	155.8	92.2	-213.3
<b>27e</b>	4-F	6-311	acetone	89.0	152.9	88.7	-215.2
<b>27g</b>	4-Cl	6-311	acetone	88.3	152.1	87.6	-216.6
<b>27h</b>	3-Cl	6-311	acetone	87.7	152.5	86.1	-222.5
<b>27k</b>	4-CN	6-311	acetone	83.0	147.7	80.5	-225.2
<b>27l</b>	3-NO <sub>2</sub>	6-311	acetone	82.7	147.1	80.0	-225.1
<b>27m</b>	4-NO <sub>2</sub>	6-311	acetone	80.5	145.0	77.7	-225.7
$\Delta E^\ddagger = -10.1\sigma + 89.8$ ( $r = 0.975$ ); $\Delta G^\ddagger = -9.51\sigma + 153.8$ ( $r = 0.965$ ); $\Delta H^\ddagger = -14.2\sigma + 90.0$ ( $r = 0.991$ ), $\Delta S^\ddagger = -218.4 \pm 6.3$ J mol <sup>-1</sup> K <sup>-1</sup>							
<b>28a</b>	H	6-31	water	34.9	96.2	38.8	-192.5
<b>28b</b>	4-MeO	6-31	water	38.0	98.2	42.2	-187.9
<b>28c</b>	4-Me	6-31	water	36.1	99.1	40.2	-197.3
<b>28g</b>	4-Cl	6-31	water	33.9	94.8	37.7	-191.7
<b>28h</b>	3-Cl	6-31	water	32.4	93.3	35.9	-192.4
<b>28l</b>	3-NO <sub>2</sub>	6-31	water	29.2	89.3	32.3	-191.5
<b>28m</b>	4-NO <sub>2</sub>	6-31	water	27.5	87.2	30.5	-190.4
<u>4-MeO - 4Cl</u> : $\Delta E^\ddagger = -4.41\sigma^+ + 34.6$ ( $r = 0.993$ ); $\Delta G^\ddagger = -3.65\sigma^+ + 96.2$ ( $r = 0.759$ ); $\Delta H^\ddagger = -4.82\sigma^+ + 38.5$ ( $r = 0.989$ ); $\Delta S^\ddagger = -192.0 \pm 2.8$ J mol <sup>-1</sup> K <sup>-1</sup> ; <u>3-Cl - 4NO<sub>2</sub></u> : $\Delta E^\ddagger = -11.7\sigma^+ + 36.5$ ( $r = 0.981$ ); $\Delta G^\ddagger = -13.8\sigma^+ + 98.5$ ( $r = 0.983$ ); $\Delta H^\ddagger = -12.5\sigma^+ + 40.7$ ( $r = 0.987$ ); $\Delta S^\ddagger = -192.0 \pm 2.8$ J mol <sup>-1</sup> K <sup>-1</sup> ;							
<b>28a</b>	H	6-311	water	71.1	129.3	74.7	-183.3
<b>28b</b>	4-MeO	6-311	water	66.5	114.6	70.9	-146.6
<b>28c</b>	4-Me	6-311	water	70.9	127.8	74.5	-178.8
<b>28e</b>	4-F	6-311	water	71.7	131.5	75.4	-188.1
<b>28g</b>	4-Cl	6-311	water	71.3	129.9	74.8	-184.8
<b>28h</b>	3-Cl	6-311	water	71.0	126.3	73.6	-176.7
<b>28k</b>	4-CN	6-311	water	67.4	125.0	69.8	-185.0
<b>28l</b>	3-NO <sub>2</sub>	6-311	water	67.5	124.9	69.7	-185.2
<b>28m</b>	4-NO <sub>2</sub>	6-311	water	66.4	118.8	68.3	-169.7
<u>4-MeO - 4Cl</u> : $\Delta E^\ddagger = 5.63\sigma^+ + 71.5$ ( $r = 0.921$ ); $\Delta G^\ddagger = -18.0\sigma^+ + 130.4$ ( $r = 0.732$ ); $\Delta H^\ddagger = -4.61\sigma^+ + 75.0$ ( $r = 0.912$ ); $\Delta S^\ddagger = -177.6 \pm 12.9$ J mol <sup>-1</sup> K <sup>-1</sup> ; <u>3-Cl - 4NO<sub>2</sub></u> : $\Delta E^\ddagger = -11.1\sigma^+ + 75.1$ ( $r = 0.992$ ); $\Delta G^\ddagger = -13.0\sigma^+ + 131.9$ ( $r = 0.700$ ); $\Delta H^\ddagger = -13.4\sigma^+ + 78.5$ ( $r = 0.996$ ); $\Delta S^\ddagger = -177.6 \pm 12.9$ J mol <sup>-1</sup> K <sup>-1</sup> .							



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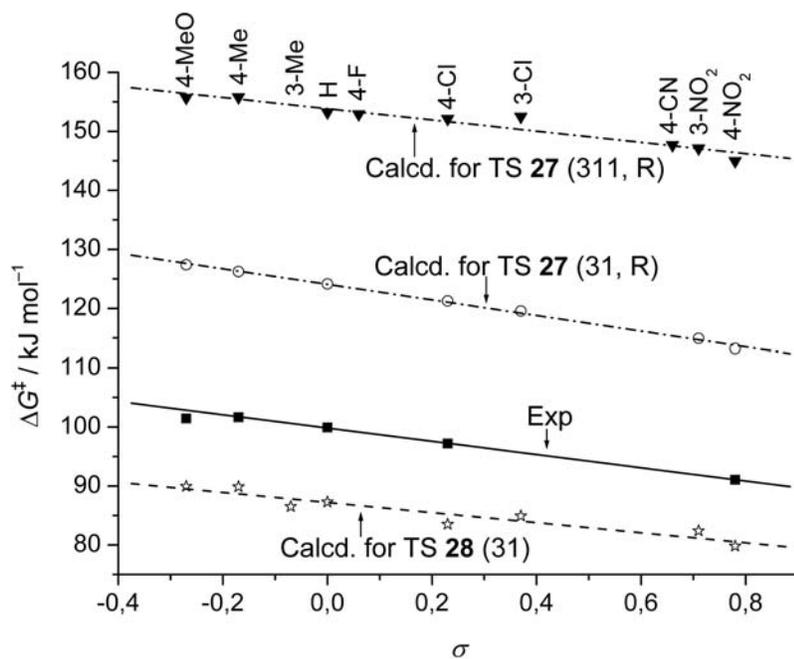


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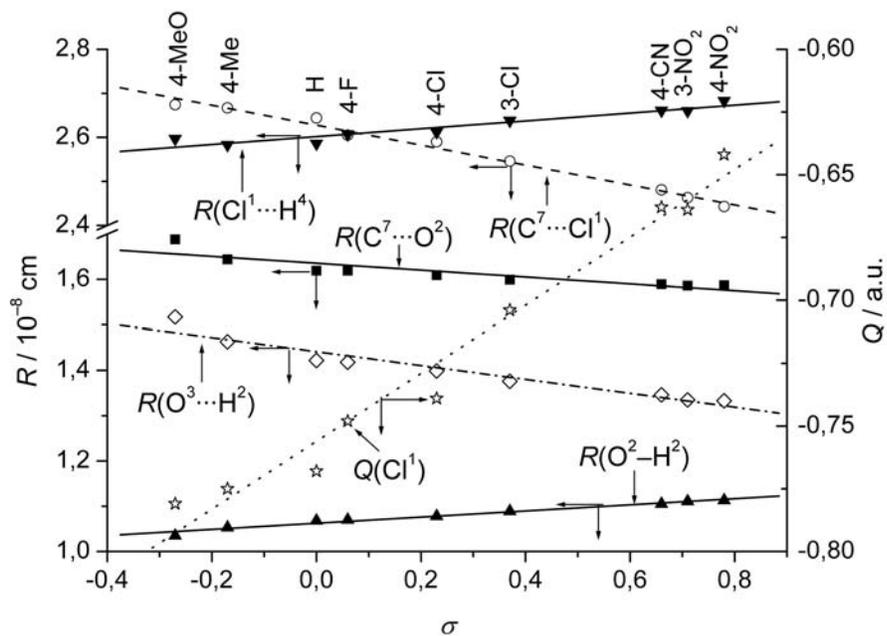


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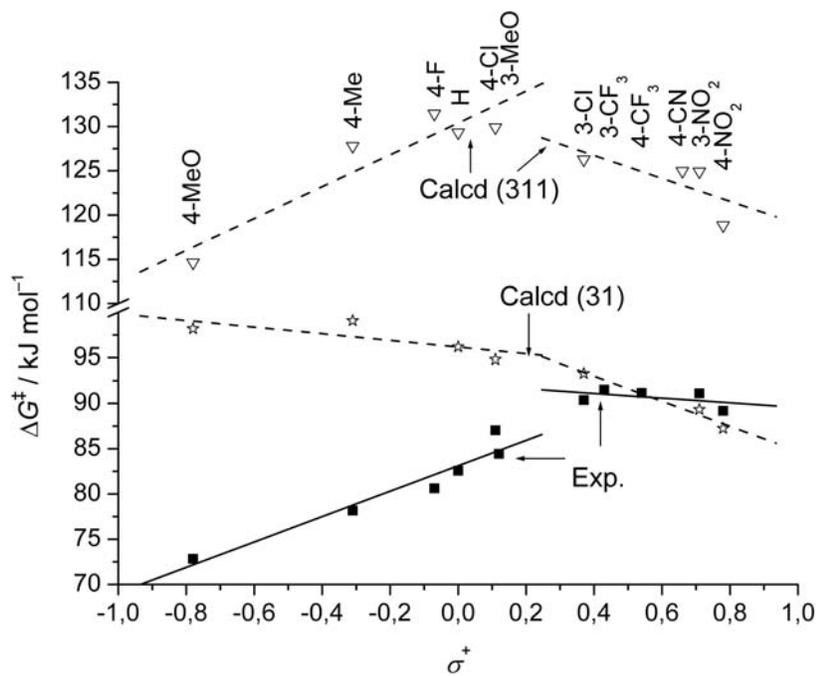


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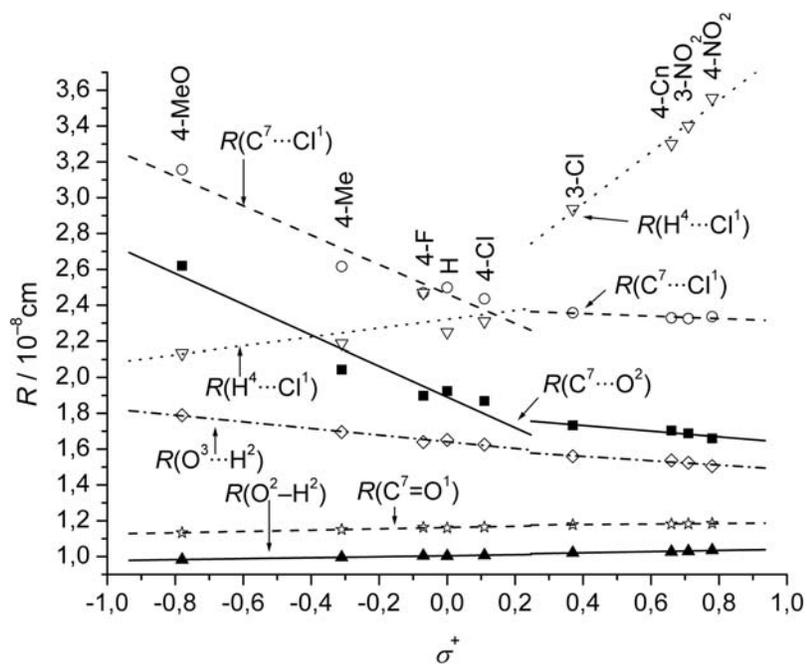


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