Re-examination of the Solvolysis of Acyl Chlorides. Rethinking the Role of Both Carbonyl and Chloride

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This letter describes a computational investigation into the hydrolysis mechanism of carbonyl compounds. Hydrolysis has previously been thought to be a very well-understood process. The molecules formaldehyde (CH_2O), formyl chloride (HCOCl), and phosgene ($COCl_2$) were used to probe the initial steps of the hydrolysis mechanism. A combination of quantum mechanics calculations and application of Bader's AIM analysis was used to study the mechanism. The results show that the carbon−oxygen double bond is more akin to the polarized bond between phosphorus and oxygen rather than to a true double bond such as that found in ethylene. Further, the results show that the initial step of the reaction is formation of a strongly hydrogen-bonded complex as opposed to direct addition of a nucleophile to the carbonyl center. Finally, the results show that chlorine plays a substantial role in stabilizing the carbocationic center resulting from the initial hydrogen bond formation. These results strongly suggest the mechanism of carbonyl hydrolysis is more subtle and complex than previously thought.
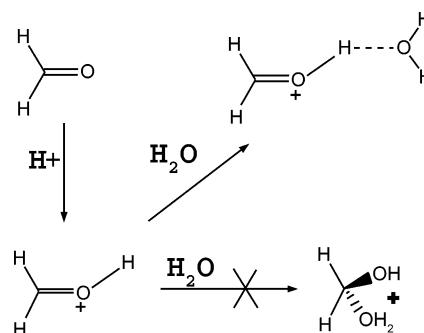
The solvolysis of activated carbonyl compounds is one of the mainstays of organic synthetic methodology.[1] Formation of esters and amides from acyl chlorides is taught in all introductory organic chemistry courses. This reaction is as ubiquitous as it is believed to be understood. The currently accepted wisdom for this reaction is that a nucleophile attacks the sp^2-hybridized carbonyl carbon, resulting in a tetrahedral intermediate. This tetrahedral intermediate is inherently unstable, reforming the carbon−oxygen double bond with the concomitant expulsion of the chloride leaving group.[2]

This reaction is believed to be dominated by the electronegativity of the leaving group. Acyl fluorides are less reactive than acyl chlorides, which in turn are less reactive than the bromides or iodides. The substitution of an electronegative substituent on the carbonyl is believed to enhance the electropositive character of the carbonyl carbon, making it more prone to nucleophilic attack. After formation of the tetrahedral intermediate, the carbonyl moiety is reformed. The stability of the carbon−oxygen double bond, as well as the leaving group, drives the reaction.[3]

Recent work in our laboratories has been focused on the hydrolysis mechanism for phosgene. Herein we would like to report on our computational investigation into the initial steps of its hydrolysis mechanism. Using quantum mechanics and atoms-in-molecules (AIM) theory,[4] we have explored the potential energy surface for the reaction of phosgene with water. We believe the results require a substantial rethinking of the role of chlorine in stabilizing intermediates in solvolysis reactions as well as the nature of the carbon−oxygen double bond.

The methodology for studying this was optimization of the ground-state carbonyl compound, followed by optimization of

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SCHEME 1: Protonation and Hydration Mechanism for Formaldehyde

the oxygen-protonated carbonyl complex, and by optimization of the cationic complex with water. Optimizations were performed at the B3LYP/6-311+g** level of theory.[5,6] Each optimization was done using Gaussian 03[7] with tight convergence criteria. The intermediates so obtained were subjected to a frequency analysis to validate that the complexes were true zero-order minima on the potential energy surface. Wave function files were generated in Cartesians (6D 10F) for each minimum energy structure.

As a baseline to our work, we explored the acid-catalyzed hydration of formaldehyde. Complexation of protonated formaldehyde with water was done so as to generate a tetrahedral intermediate. This is shown in Scheme 1. However, despite many attempts, we could not find a minimum corresponding to a tetrahedral intermediate. Instead, water hydrogen bonded to the proton on the carbonyl (Scheme 1). It is interesting to note that the carbonyl oxygen−hydrogen bond length is 1.10 Å. This is extremely long compared to typical O−H bond lengths, which are of the order of 0.96 Å.[8] Further, the distance between that hydrogen and the oxygen in water was 1.33 Å, indicative of a very strong hydrogen-bonded interaction.

Letters

J. Phys. Chem. A, Vol. 108, No. 43, 2004 **9329**

TABLE 1: Donor−Acceptor Distances and Electron Density Topology for the O···H Interactions in Hydronium Ion/Activated Carbonyl Compound Complexes[a]

structure	$H_2O\cdots H$	$H\cdots O=C$	O−O distance	theta
formaldehyde	1.32949	1.10790	2.43732	179.1
$\rho(r)$	0.11643	0.22570		
$\nabla^2\rho(r)$	+0.07068	−1.06381		
formyl chloride	1.30654	1.11967	2.42618	179.5
$\rho(r)$	0.12406	0.21456		
$\nabla^2\rho(r)$	+0.03253	−0.91003		
carbonyl dichloride (phosgene)	1.16113	1.24661	2.40655	176.4
$\rho(r)$	0.18956	0.14367		
$\nabla^2\rho(r)$	−0.58352	−0.10450		

[a] Both the electron density, $\rho(r)$, and its Laplacian, $\nabla^2\rho(r)$, at the bond critical point are shown in atomic units (a.u.). Distances are shown in angstroms (Å), and angles are shown in degrees (°). The first line for each entry gives geometric data, and the second and third lines are the values for the electron density and its Laplacian, respectively.

The next step in the process was examination of the initial hydration of formyl chloride. Optimization of the supposed tetrahedral intermediate arising from the addition of water to the protonated formyl chloride again resulted in water hydrogen bonded to the hydrogen attached to the carbonyl oxygen, instead of a tetrahedral intermediate. The carbonyl oxygen−hydrogen bond length is 1.12 Å, slightly longer than that seen in formaldehyde. Further, the distance between water and that hydrogen is 1.31 Å, slightly shorter than the corresponding distance for the formaldehyde complex. This implies a rather strong hydrogen-bonded complex between the protonated formyl chloride and water.

Finally, we examined the initial hydration of phosgene (carbonyl dichloride). As before, no tetrahedral intermediate could be found when adding water to protonated phosgene. The hydrogen bonded complex, which is the minimum on the potential energy surface, is slightly different than those obtained previously. The carbonyl oxygen−hydrogen distance is 1.25 Å, whereas the water to proton distance is 1.16 Å. In this instance, however, the structure represents a hydronium ion (H_3O^+) interacting with the carbonyl of phosgene. The rather short distance of 1.25 Å between the hydronium ion proton and the carbonyl oxygen again implies a strong hydrogen-bonded interaction for this complex.

Since all three complexes with water showed unique structural features, we explored these minima using AIM theory, which calculates the electron density using the molecular wave function. The analysis of these wave function files was done using Popelier's MORPHY98.[9] This analysis provided many details including the electron density about each atom, its atomic volume, the location of bond critical points (BCPs), and the
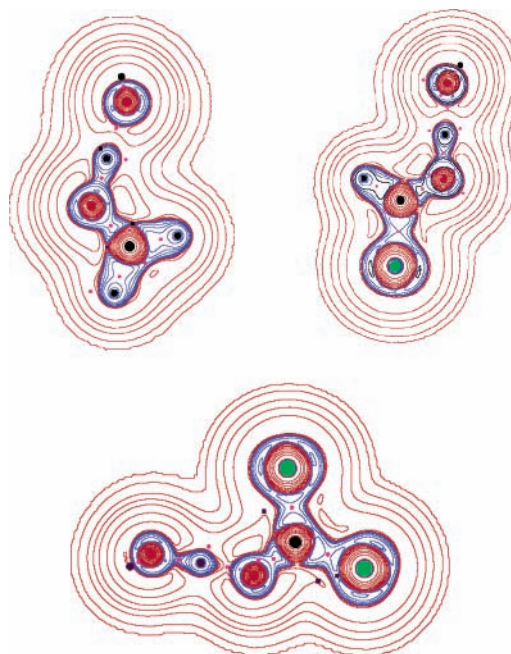
Figure 1. Laplacian contour plots for the formaldehyde, formyl chloride, and carbonyl dichloride (phosgene) complexes with H_3O^+.

ellipticity of the bonds (a measure of the degree of π character). Salient results of the AIM analysis are shown in Tables 1 and 2. Plots of the Laplacian of $\rho(r)$, $\nabla^2\rho(r)$, are shown for the formaldehyde, formyl chloride and phosgene complexes with the hydronium ion in Figure 1. Contours are shown for both negative (blue = relative electron excess) and positive (red = relative electron deficient) values of the Laplacian on a logarithmic scale 0.001, 0.002, 0.005, ..., 500.00 au.

There are several interesting aspects to the data in Tables 1 and 2. The first is to note the nature of the bond between the carbonyl oxygen and the hydrogen. As was noted before, the bond lengths for this O−H hydrogen bond are, by any standards, short for complexes involving formaldehyde and formyl chloride. AIM analysis shows that the electron density at the BCP for the O−H bond in these two structures is identical at 0.2 au with a strongly negative Laplacian (< −1.0 au), typical of a shared-shell covalent interaction. Furthermore, the location of the BCP is nearly equidistant from the two atoms. Thus, contrary to expectation, these O−H bonds are intermediate between a classical hydrogen bond and the O−H bonds in normal water. In phosgene, AIM analysis confirms that the complex contains H_3O^+ strongly hydrogen-bonded to the carbonyl of phosgene.

The second interesting feature deals with the nature of the carbon−oxygen double bond. The Laplacian at the BCP is

TABLE 2: Electron Density Topological Analysis for the Carbon−Chlorine and Carbon−Oxygen Bonds in Formaldehyde, Formyl Chloride, and Phosgene Complexed with the H_3O^+ Ion, Showing the Electron Density, $\rho(r)$, at the BCP in A.U. the Laplacian of $\rho(r)$, $\nabla^2\rho(r)$, in A.U., and the Bond Ellipticity, ϵ

bond	$H_2C=O$	$H_2C=O/H_3O^+$	$HClC=O$	$HClC=O/H_3O^+$	$Cl_2C=O$	$Cl_2C=O/H_3O^+$
C=O						
$\rho(r)$	0.41612	0.38125	0.44082	0.38419	0.44738	0.39616
$\nabla^2\rho(r)$	+0.02348	+0.01428	+0.09114	−0.17363	+0.09309	−0.22010
ϵ	0.04197	0.07628	0.07497	0.02136	0.10278	0.07823
C−Cl (1)						
$\rho(r)$			0.18067	0.23834	0.19472	0.21908
$\nabla^2\rho(r)$			−0.19179	−0.41919	−0.23540	−0.32206
ϵ			0.04923	0.09149	0.05955	0.07730
C−Cl (2)						
$\rho(r)$					0.19472	0.22741
$\nabla^2\rho(r)$					−0.23540	−0.35671
ϵ					0.05955	0.08918

positive for formaldehyde, formyl chloride, and phosgene. Thus, the interaction between the carbon and the oxygen is a closed shell interaction (dative covalent), similar to that seen for P=O bonds in phosphates,[10] rather than a shared-shell C=C covalent interaction as seen in ethylene. Upon protonation and complexation with water, the sign of the C=O Laplacian becomes negative for both formyl chloride and phosgene, indicating a shared-shell or covalent interaction between carbon and oxygen. The ellipticity for the carbonyl in the protonated chlorine-containing species is quite low, implying the interaction between carbon and oxygen can be described as a single bond. Thus, these results appear to indicate that the carbonyl in these three systems is more ionic than covalent.

The third interesting feature is the strong interaction between the chlorine and the carbonyl carbon. The ellipticity for the carbon–chlorine bond in formyl chloride and phosgene is relatively high (0.0492 and 0.0596, respectively). When both compounds are protonated and complexed with water, the values for the carbon–chlorine bond ellipticity in complexed formyl chloride and phosgene are 0.0915 and 0.0773, respectively. Concomitantly, the ellipticity for the carbon–oxygen double bond in formyl chloride and phosgene *decreases* upon protonation complexation. Together, these results strongly suggest that the chlorine atom actually forms a halonium ion to stabilize the positive charge on the carbonyl carbon. Multireference natural resonance theory (NRT) analysis, as developed by Weinhold and co-workers,[11] supports the suggestion that chlorine acts to stabilize cationic centers.

This stabilization by chlorine is responsible for the extremely short, strong hydrogen bonds seen in these structures. Thus, the presence of chlorine enhances the stability of the electrophilic carbocation. This effect is not necessarily additive. NRT analysis shows that, for H_3O^+ interacting with formyl chloride, a formal halonium contributes 27% to the overall stability. For protonated formyl chloride interacting with water, this contributes 39%. This rationalizes why the predominant form of the complex is protonated formyl chloride hydrogen bonded to water. On the other hand, the halonium stabilizes 44% of the complex between H_3O^+ and phosgene (the predominant form) and 36% for protonated phosgene and water. NRT analysis also demonstrates that, as the two hydrogens of formaldehyde are substituted first by one and then by two chlorine atoms, the ratio of the percentage resonance structures containing a protonated carbonyl to the percentage containing H_3O^+ hydrogen bonded to the carbonyl oxygen drops dramatically. For formaldehyde, this ratio is 2.12, for formyl chloride 1.71, and for phosgene 0.60, reflecting the results obtained by AIM analysis. We believe the difference in the structure of the predominant complex is due to electronic effects between the carbonyl and its electronegative substituents.

In summary, we have identified that the carbon–oxygen double bond has considerable ionic character as opposed to being solely covalent. Furthermore, chlorine stabilizes cationic centers, and a carbon–chlorine double bond can be invoked to explain the unusual stability. Finally, the unusual nature of the carbon–oxygen double bond and the stabilizing influence of chlorine on electropositive centers creates unusually short, strong hydrogen bonds. These results have many implications in the mechanism of solvolysis not only for acyl chlorides but also for esters and amides. The study of all of these systems, including the other halogens, are underway and will be reported shortly.

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